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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.

INFLUENCE OF TRANSIENT LUNG INFLATION ON THE SUBSEQUENT BREATH IN THE CONSCIOUS DOG.

A. Aberman*, J. G. Jones* and J. A. Nadel. Cardiovascular Research Institute, University of California Medical Center, San Francisco, California.

We tested the effect of transient lung inflation on the first postinflation breath in conscious dogs. The dogs had tracheostomies, breathed pure O_2 and their cervical vagi were exteriorized in skin loops. While the dogs were breathing spontaneously we used a pressure-triggered ventilator to deliver a single inflation of varying volumes during the time of one normal inspiration. The dogs were then allowed to exhale passively and we studied the time of onset and the tidal volume of the first spontaneous postinflation breath. The end-tidal CO_2 tension of the inflated breath was kept to within 1-2 mm Hg of control values by inflating with the appropriate CO_2 in O_2 mixture. We found no change in the time of onset of the first postinflation breath compared to the preinflation cycle length when the inflation volumes varied up to 300% of the spontaneous tidal volume. However with increasing inflation volumes, there was a progressive decrease in the tidal volume of the first postinflation breath. After unilateral cervical vagal block, this decrease was still present but was significantly less than when both vagi were intact. Bilateral cervical vagal block abolished this postinflation depression. Thus in contrast to the maintained inflation necessary to demonstrate the classical Hering-Breuer reflex, we have shown that even a transient lung inflation elicits vagally mediated inhibition of subsequent inspiratory activity. (Supported in part by Grant HL-06285 from NHLI.)

THE EFFECTS OF ANESTHETICS ON BLOOD-BRAIN BARRIER (BBB) PERMEABILITY IN THE RAT. E. Aboul-Eish, K. Skena and E. Nemoto, (intr. by P. Safar), Dept. of Anes., Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.15213

To determine the effect of general anesthetics on metabolite permeability across the BBB, we tested BBB permeability for L-lactate (LA),D-Glucose (G), D-Mannitol (M) Cyclic-AMP (CAMP) and sodium (Na) in awake, sodium pentobarbital and ketamine anesthetized rats. One μCi each of the labeled test sub. and $^{3}H_2O$ was injected intracarotid and the rats decapitated at 16 secs. post-injection. The brain was assayed for ^{14}C and ^{3}H activity by liquid and ^{22}Na by well scintillation counting. Percent extraction of the test substance was calc. from the ratio of ^{14}C or ^{22}Na in the brain sample, divided by a similar ratio for the injectate. The results show that the permeability of the BBB to LA was sig. incr. with NaPentobarb and ketamine anes. ketamine (50 mg/kg) produced a greater incr. in BBB permeability to LA than Na-pentobarb. While at 100 mg/kg there was a decr. back towards the control (awake) level. Glucose and Mannitol permeability appear ed to be elevated, Na unaffected and CAMP reduced during Na-pentobarb. anes. These results suggest that the effect of anesthetics on BBB permeability may be biphasic. The differential effect of anesthetics on permeability across the BBB may be related to the primary mode of BBB penetration by the metabolite(i.e. simple diffusion, facilitated or active transport).

		% EXTRACTION				
		LA	G	M	Na	CAMP
AWAKE	$\bar{x}$	12.06	32.07	8.23	10.57	37.99
	n	8	9	8	8	5
	Sem	1.07	3.76	1.08	2.39	5.34
Na-Pentobarb	$\bar{x}$	20.53*	39.59	11.02	10.49	29.22
	n	6	11	7	8	4
(60 mg/kg)	Sem	3.00	2.84	1.37	2.92	6.82
Ketamine	$\bar{x}$	32.39**				
	n	8				
(50 mg/kg)	Sem	4.153				
Ketamine	$\bar{x}$	18.68				
	n	6				
(100 mg/kg)	Sem	3.40				

*P<.05**P<.001

VAGINAL THERMAL CONDUCTANCE: A MEANS FOR PREDICTING ESTRUS IN DAIRY HEIFERS. R. M. Abrams, W. W. Thatcher*, F. W. Bazer* and J. R. Chenault*, Depts. of OB/GYN, Dairy Science and Animal Science, Univ. of Florida, Gainesville, Fla.

Previous studies have indicated a marked hyperemia of the reproductive tract in conjunction with the maturation of ovarian follicles or after injection of estrogens in diestrous or ovariectomized ewes. A significant rise in vaginal thermal conductance (K_{vag}) accompanied this estrogen-induced rise in blood flow rate. Utilizing a gradient layer heat flow device bonded to a 2"x6" cylinder of fine silver we found similar increases in K_{vag} associated with rising plasma estrogen concentrations in heifers. Water at 20°C circulating through the cylinder at 300 ml/min provided the sink for heat delivered through the vaginal wall. The device was easily inserted and self-retaining for the 5 min. period needed to make the measurement. Palpation of the ovaries and uterus per rectum confirmed the presence of large follicles and good uterine tone when high K_{vag} values were recorded. An elevated K_{vag} was first observed in some heifers three days prior to behavioral estrus. A fall in K_{vag} often occurred prior to or during estrus. The precise time relationships between the estrogen peak, the rise and fall of K_{vag}, the LH surge, and the time of ovulation remain to be determined. (Supported in part by USPHS Grant HD-04819).

COMPARATIVE CARDIOVASCULAR PHYSIOLOGY OF BEAGLE AND MONGREL DOGS. S. Sultan Ahmed*, Christos B. Moschos, Virender Sethi*, Philip O. Ettinger* and Timothy J. Regan, New Jersey Medical School, Department of Medicine, Newark, New Jersey.

Both mongrel and beagle dogs are utilized widely as experimental animals in cardiovascular research. Differences have been reported in rhythmogenicity and incidence of spontaneous and experimental coronary artery disease. We undertook this study to determine whether significant differences exist in the physiology of cardiovascular systems of these two groups. Nine male mongrels (M) weighing 23-29 kg and seven male beagle (B) dogs weighing 9-14 kg were catheterized under similar anesthesia for assessment of left ventricular (LV) function and volumes (indicator dilution). Whereas the heart rate, LV end-diastolic pressure and maximum rate of LV pressure rise (dp/dt) were similar, the M had higher aortic systolic (149±4 vs 122±7 mm Hg, $P<0.01$), and diastolic pressures (111±3 vs 76±4, $P<0.001$) but lower volumes ($P<0.02$). The stroke output in M was 0.41±0.05 ml/kg (B=1.42±0.25 ml/kg), and LV end-diastolic volume measured 1.45±0.2 ml/kg in M (B=3.16±0.42). The cardiac contractility of M was low compared to B as manifested by LV ejection fraction of 22±2% (B=44±3, $P<.001$) and Frank-Levinson Index (which measures end-isometric force-velocity-length relationship) of 1.4±0.14 (B=2.4±0.27, $P<0.01$). Electrophysiological studies, however, revealed similar His-Q and QRS conduction times in the two groups. The observed hemodynamic differences may be due to an altered response to anesthesia in M. Whereas lower pressures have been reported in conscious M, the arterial pressures in B are almost the same both in the anesthetized and conscious state. It thus appears that B may be a better model for study of cardiovascular diseases and pharmacology compared to M in whom the hemodynamics are altered appreciably by anesthesia alone.

EFFECTS OF TRICHLOROTRIFLUOROETHANE ON PRESSURE-VOLUME CURVES IN RAT LUNGS. Y. Alarie and J. Quealy (intr. by D. Minard). Graduate School of Public Health, Pittsburgh, Pa.

Air saturated with trichlorotrifluoroethane (TCTF) at 30°C was administered to rat lungs artificially ventilated in vitro. The TCTF vapor was given for 3 to 5 consecutive inflations of 8 to 10 ml each. Upon spontaneous deflation progressive atelectasis occurred following the first inflation with TCTF and complete atelectasis was observed after 3 to 5 inflations. The treated lungs retained no residual air volume and sank in water. Pressure-volume measurements (PVM) were made with air or isotonic saline solution as the inflating media following atelectasis with TCTF treatment and in control rats in which pulmonary atelectasis was obtained by oxygen absorption following nitrogen washout of the lungs. For both groups, PVM were identical when isotonic saline was used for inflation and deflation. The difference in PVM between the two groups was striking during inflation and deflation with air. Instability of the airspaces was indicated and little hysteresis was observed in the TCTF treated lungs. Also TCTF treated lungs returned to atelectasis upon deflation while control lungs retained 1 to 3 ml of air. The effects produced by TCTF treatment were reversible on second or third inflation with air if TCTF was allowed to evaporate from the lungs. We conclude that the mechanical behavior of the lung observed was due to the constant surface tension (18 dynes/cm) of a layer of TCTF at the alveolar surface.

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TOTAL BODY POTASSIUM DEPLETION IN SPACEFLIGHT, Alexander, W.C., Leach, C.S., and Johnson, P.C.*, NASA, Manned Spacecraft Center and *Baylor College of Medicine, Houston, Texas.

Adaptation to the weightless environment predictably includes a redistribution of body fluid and electrolyte in the adjustment of circulating blood volume. The overall adaptive process, while being considered a naturally occurring sequence of events is not without attendant physiological cost. Should external stressors (fatigue, high workloads, etc) magnify this cost to levels exceeding functional reserves of the organism, decompensation with demonstrable sequellae result. Such a situation was evidenced in the crew of Apollo 15 and was unlike responses to weightlessness recorded in previous missions. A significant ($p<0.05$) decrease in Total Body Exchangeable Potassium (K^{42}) commensurate with a significant increase ($p<0.05$) in urinary aldosterone was measured postflight. Urinary ADH was elevated postflight, but not significantly when compared with the range of preflight values. Likewise, urine volume was increased and osmolality decreased for a seventy-two hour period postflight. These findings possibly describe a renal tubular insensitivity to ADH in part mediated by the potassium deficit. The etiology of the potassium loss is presently unclear; however, insignificant changes in Total Body Water (H^3) indicate a stable lean body mass tending to negate muscle loss as a factor. Our present interpretation, although unconfirmed is a selective renal potassium loss early in the weightless exposure further driven by the compensatory aldosteronism. Whether or not the episodes of cardiac irregularity registered inflight in this mission are also a consequence of the potassium deficit is unclear; however, the overall functional state of the crewmen during the mission and immediately postmission must consider the integration of these and other factors portending decompensation.

MECHANICAL PROPERTIES OF IN SITU MAMMALIAN SKELETAL MUSCLE. P. D. Allen* and W. N. Stainsby (intr. by A. B. Otis), Dept. of Physiol., Univ. of Fla., Gainesville, Fla. 32601.

The purpose of these studies was to examine the mechanical properties of in situ dog skeletal muscle. Two muscles were studied with very different fiber arrangements; a) semitendinosis (ST) which is parallel-fibered and b) gastrocnemius-plantaris (GP) which is pennate. Force-velocity relationship for twitch and brief tetanic as well as the stress-strain of the series-elastic component (SE) were examined. The muscle, with circulation intact,was attached to a pneumatic myograph. Tension (P), Δ length (L), dP/dt, and dL/dt were recorded on a high frequency oscillograph. Contractions were produced by direct nerve stimulation at supra- and sub-maximal stimulation voltage. At the completion of the experiment rest length (L_r), weight, and cross-sectional area were measured directly. As expected from internal fiber arrangement the pennate GP developed up to 1.0 kg/g at optimal length (L_o) while the parallel-fibered ST developed 0.5 kg/g. The maximum velocity (Vmax) for GP, however, was slower; 3.0 muscle length/sec., compared to 5.7 for ST. Force-velocity ($dL/dt/L_r$ vs. P/P_o) curves for both muscles were qualitatively similar. With initial length (L_i) near L_o the curves were nearly straight. At shorter L_i they shifted to the left and became more vertical. As a result, Vmax changed little with change in L_i. The stress-strain SE measured by quick release (L/L_r vs. $\Delta P/P_o$) was quantitatively similar for both muscles and both curves were nearly linear over the entire range. Both muscles were found to have higher peak velocities than has been demonstrated on isolated frog or papillary muscles. Their curves representing force-velocity relationships and series-elastic component were more nearly linear than previously reported. (Supported by NIH Grant GM 06264-13)

ON THE RECEPTOR FUNCTION OF ANTIBODIES IN MUSCLE FIBERS. Francisco Alonso-deFlorida, Jesús G.Ninomiya* and Carlos Paz*. Depto.Fisiol., Fac.Med., U.N.A.M., México, D.F., México.

We have previously communicated (J.Gen.Physiol. 51: 677, 1968) certain experimental results supporting the idea that antibodies and chemo-receptors bear a similar function in muscle fibers; namely, that they both induce a ionic valving mechanism, which is reflected as membrane depolarization. Thereby an effect should be obtained in a muscle surface free of mast cells; and the normal functioning of the muscle fibers should not be affected subsequently to the antigen-antibody interaction. We presently report a depolarizing effect, recorded intracellularly upon antigen administration, in the allergized cremaster muscle of the guinea-pig. A preparation consisting in a single layer of muscle fibers, devoid of mast cells, was used as a experimental object. Indeed, the mast cells could be sucked off by means of micropipettes under phase-contrast microscopic observation. The muscle became desensitized after several doses of antigen, yet it showed constant responsiveness to acetylcholine and external potassium, regardless of previous exposition to antigen. On the other hand, the effect was obtained in either innervated or denervated preparations. Therefore, the experimental findings support the aforementioned postulations.

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PROSTAGLANDINS AND THE PULMONARY CIRCULATION. Joseph S. Alpert*, Florence W. Haynes, Paul A. Knutson*, James E. Dalen*, and Lewis Dexter. Department of Medicine, Peter Bent Brigham Hospital, Boston, Mass.

Prostaglandins (PG) E_1, E_2, $F_2\alpha$, and A_1 were infused into 15 normal mongrel dogs at doses varying from .04-6.0 µg/kg/min. PGE_1 was also infused following pulmonary embolism produced by autologous blood clot and lycopodium spores. Pressures were recorded from the pulmonary artery, left atrium and femoral artery; pulmonary blood volume and cardiac output were determined using sequential indicator dilution curves from injections into the pulmonary artery and left atrium. PGE_1 caused mild, active pulmonary vasodilatation, while $PGF_2\alpha$ resulted in mild, active vasoconstriction in the lung. PGE_2 and PGA_1 caused passive shrinkage of the pulmonary vascular bed secondary to a shift of blood to the peripheral circulation. Both clot and spore embolism resulted in marked decreases in pulmonary blood volume and vascular compliance which were not reversed by PGE_1 infusion. Differences in hemodynamic responses of the pulmonary circulation to PGE_1 infusion following clot and spore embolism can be explained by the largely mechanical effects of the macroemboli (clots) and the diffuse vasoconstricting effects of the microemboli (spores).

DIFFERENTIAL EFFECTS OF ANOXIA AND SUBSTRATE DEPLETION ON DRUG-INDUCED CONTRACTIONS OF VASCULAR SMOOTH MUSCLE (VSM). Bella T. Altura* and Burton M. Altura. Albert Einstein Col. of Med., Bronx, N.Y.

Previously, we reported data using rabbit aortic strips (RA), under aerobiosis (with complete dose-response curves [DRC]), which suggested that different vasoactive stimulants may utilize different metabolic pathways for generation of the energy required for activation of contraction of VSM (Am. J. Physiol. 219: 1698, 1970). In view of the latter preliminary findings, we decided to expand our studies with RA and use anoxia (with and without 10mM glucose) to determine whether certain vasoactive drugs are selectively affected by inhibition of oxidative metabolism in the presence and absence of exogenous substrate. The data indicate that the maximum contractile responses of RA to a variety of VSM stimulants are differentially depressed, and in many cases completely abolished under anoxic conditions (6-10 hr. in duration) in the presence of substrate. Most vasoactive substances such as epinephrine (E), angiotensin, acetylcholine (Ach), serotonin (5-HT), histamine (H) and barium (Ba^{++}) appear to require a continuous supply of exogenous substrate (glucose?) in order to maintain their potential contractile effects under anoxia, unlike potassium (K^+). The use of complete DRC, and repetitive drug stimulation, reveals that the affinities of certain vasoactive drugs (e.g., Ach, 5-HT, H) for their respective receptor sites, in RA, are markedly altered (i.e., DRC progressively shifted to the right) under anoxic conditions in the presence of glucose. Similar experimental conditions, however, fail to result in a shift of the E, K^+ or Ba^{++} DRC. Surprisingly, anoxia (with substrate) causes repetitive K^+ and Ba^{++}-induced maximal contractile responses to become progressively greater in magnitude with duration of anoxia. Overall, these data are consistent with the notion that different vasoactive stimulants may utilize different metabolic pathways for activation of contraction of VSM and/or be dependent on a continuous supply of exogenous substrate for maintenance of receptor conformation. (Supported by N.I.H. grants HL-12462, HL-11391 and 5-K3-GM-38, 603, U.S.P.H.S.)

COMPARATIVE EFFECTS OF BRADYKININ (BK), KALLIDIN (LYS-BK), METHIONYL-LYSYL-BRADYKININ (MET-LYS-BK) AND ELEDOISIN ON HUMAN UMBILICAL ARTERIES AND VEINS (HUAV). Burton M. Altura. Albert Einstein Col. of Med., Bronx, N.Y.

BK may play an important role in neonatal circulatory changes in both man and sheep. In-vitro experiments, using both helically and longitudinally cut HUAV, were designed to determine: 1) whether all three naturally occurring kinins, viz. BK, LYS-BK and MET-LYS-BK, can induce contraction of HUAV in low (physiologic?) concentrations; 2) the relative potency of these substances and eledoisin on HUAV; and 3) the existence of specific drug receptors for these peptides in HUAV. The data demonstrate that all three naturally occurring kinin polypeptides induce potent contractile responses on isolated longitudinally and helically cut HUAV. An extrapolation of these in-vitro contractile concentrations to the in-vivo situation suggests that threshold concentrations for BK and LYS-BK (10^{-10} - 10^{-9}M) would be in the range of maternal plasma levels, while umbilical cord plasma concentrations found at birth could be within a range whereby all three kinins could induce potent (25-60% maximal responses) contractions. These findings support previous suggestions that kinins may play a physiologic role in control of umbilical cord blood flow and effecting closure of the umbilical vessels at birth. The addition of a lysine moiety (in e.g., LYS-BK) or methionine and lysine moieties (in e.g., MET-LYS-BK) to BK not only can decrease the affinity of the resultant peptides for the kinin receptor in HUAV but the intrinsic activity (maximal response) as well. Although specific kinin receptors appear to exist in HUAV (i.e., antihistamines, antiserotonins, anticholinergic and anti-adrenergic drugs failed to block the actions of the peptides), the data suggest that heterogeneity of the kinin receptors, which subserve contraction in HUAV, exist within the circularly and longitudinally arranged vascular smooth muscle cells. (Supported by N.I.H. grants HL-12462, HL-11391 and 5-K3-GM, 38, 603, U.S.P.H.S.)

MEASUREMENT OF GAS PERMEABILITIES OF THE HEN'S EGG SHELL. A. Ar* and C. V. Paganelli. Department of Physiology, State University of New York at Buffalo, Buffalo, New York 14214.

We have developed a method which exploits density differences to measure the diffusive permeability($K_{1;2}$) of the hen's egg shell to gases. An empty egg shell is filled with gas 1 and suspended from a strain gauge in gas 2. Change in buoyancy of the egg with time is a function of $K_{1;2}$ on the assumption that bulk flow of gas through the shell is negligible. In our system buoyancy change follows a single exponential time course. From its half-time and the surface area and contained volume of the egg shell, $K_{1;2}$ (25°C, 1 ATA) is calculated. Values of $K_{1;2}$ (cm^3 STP . cm^{-2} . sec^{-1} . mm Hg^{-1}) . 10^6 so obtained in six gas pairs are: He/N_2: 4.64; He/O_2: 4.11; He/CO_2: 4.45; He/N_2O: 4.00; N_2/CO_2: 1.61; and N_2/N_2O: 1.38. When K values are compared with reported binary diffusion coefficients for these gas pairs, it seems that gas exchange rate across the dry egg shell and its membranes is not simply proportional to the binary diffusion coefficient of the gas pair involved, although a 10% coefficient of variation in $K_{1;2}$ makes this conclusion tentative. For example, CO_2 exchanges with all gases tested faster than expected on the basis of its binary diffusion coefficient. (Supported in part by ONR contract N00014-68-A-0216.)

DYNAMICS OF UTERO-OVIDUCTAL MOTILITY IN THE RABBIT*

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Balloon ended, fluid-filled polyethylene catheters were inserted in the lumen of the ampulla and the uterus of 14 adult rabbits. Pressure fluctuations were transmitted and recorded using pressure transducers, carrier preamplifier and a polygraph. Motility patterns were recorded during estrus and the first five days post-coitum. Oviductal contractions during estrus were characterized by high frequency and low amplitude with mild changes of tonus. One hr p.c. an active pattern developed with high amplitude of contractions and outbursts of increased tonus. At 24 hr p.c. this activity was reduced. An alternating rhythm dominated 48 hr p.c. with sets of rapid and slow contractions. Rapid sets were absent 72 hr p.c. Further daily progressive slowing down was noted. During estrus, there were three uterine patterns; rhythmic, arrhythmic and a combined. Uterine recordings showed increased activity 3-6 hr. p.c., followed by a gradual daily decrease, until the activity was blocked 72 hr. p.c. Simultaneous monitoring of both oviducts and one uterine horn, throughout the reproductive cycle, showed that the ipsilateral oviduct was relatively slower than the contralateral one.

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CARDIAC AFFERENTS IN THE LEFT THORACIC AUTONOMIC NERVES. J.A. Armour, Department of Physiology, Loyola University, Stritch School of Medicine Maywood, Illinois 60153.

Recording of single unit afferent impulses from the left cardiac autonomic nerves of twelve mongrel dogs demonstrated cardiovascular receptors located in the left atrium, right and left ventricles, pulmonary artery, and arch of the aorta. The innominate and VMCN nerves contain afferents from chemoreceptors as well as ventricular and aortic receptors. The dorsal cardiac nerve had only aortic receptor afferents and the left stellate cardiac nerve afferents from atrial and left ventricular receptors. In only one instance was the VLCN found to have afferent traffic and its receptor was in the left atrium. A great percentage (65%) of the receptors were located on the ascending and arch regions of the aorta. All of these receptors have impulse traffic rhythms which mimic the regional dynamic changes of the tissues where they are located. Aortic receptors demonstrate traffic which respond the dicrotic pressure notch and are greatly effected by the parasympathetic and sympathetic systems. Ventricular receptors in control states generally fire only in systole, although a few fire in diastole as well; ventricular receptor firing was augmented during inotropism. The left ventricular receptors were situated primarily in the outflow tract of the left ventricle. Sixteen chemosensitive receptors were located in the craniad portion of the ventricular septum or in the root of the aorta; these receptors responded to anoxia and cyanide infusion. The septal chemoreceptors were frequently found to increase impulse traffic following short periods of anterior descending coronary artery occlusion. The atria, ventricles, and aorta have numerous length sensitive receptors which continuously monitor regional cardiovascular dynamic changes. (Supported by Grant HE 08682 from the NHLI).

MOLTING IN MANDUCA SEXTA: NEUTRAL METAL CHELATOR-SENSITIVE PROTEASE ACTIVITY IN MOLTING FLUID. Maria L. Bade and Jonathan Shoukimas*. Department of Biology, Boston College, Chestnut Hill, Massachusetts 02167.

Electrophoretic separation of molting fluid enzymes from the tobacco hornworm Manduca sexta on cellulose acetate plate in basic buffer has revealed that the ability to digest casein migrates in a cathodic component which is characteristic of late (i.e. active) molting fluid. The proteolytic activity has now been characterized as belonging to the class of metal chelator-sensitive neutral proteases, a class of proteases hitherto described only in bacteria and molds. Enzymes from these sources are zinc metallo-enzymes containing calcium and are narrowly specific for peptide bonds. The insect enzyme(s) exhibit a specific requirement for calcium although zinc replaces calcium to some extent. The insect may derive a functional advantage from having enzymes with these particular requirements: molting enzymes must rapidly break down an insoluble substrate, the old cuticle, without attacking each other or the new cuticle. Chitinous cuticles invariably appear to contain some calcium. It is suggested that old-cuticle calcium activates molting enzymes by an induced-fit mechanism. (Supported by a grant from NSF).

EFFECT OF EXERCISE ON THE VENTILATORY RESPONSE TO INFUSED LACTIC ACID AND HCO_3^- IN THREE DOGS. Cedric R. Bainton, Depts. of Anesthesia and Physiology, U.C. Medical Center, San Francisco, California 94122.

The effect of exercise on the chemical stimuli to breathing has not been fully evaluated. In recent work (Fed. Proc. 30:270, 1971) we indicated that the increase in ventilation ($\dot{V}_E$) in response to inhaled CO_2 was greater during exercise than at rest, i.e., that the ventilatory stimulus of inhaled CO_2 and the stimulus of exercise interact. This study evaluates the effect of exercise on the ventilatory stimulus which occurs with acute acid-base disturbance. Studies were done in three dogs prepared with chronic tracheostomies and carotid loops. Ventilation was examined at rest (1/2 hr) and 3 mph exercise (1/2 hr). Then on separate days 250 cc normal saline alone (control) or saline with lactic acid (70 meq) or HCO_3^- (45 meq) was infused IV in 15 minutes. $\dot{V}_E$ was again measured at rest (1/2 hr) and 3 mph exercise (1/2 hr). $P_{A}O_2$ was maintained constant at 100 mmHg. Arterial P_{CO_2} ($PaCO_2$) was held constant for each dog at the mean resting $PaCO_2$ for that dog plus 2 mmHg CO_2. Inhaled CO_2 was altered as necessary to maintain constant $PaCO_2$. Saline infusion alone had no significant effect on arterial pH or on $\dot{V}_E$. Ventilation increased after lactic acid infusion (6 studies). The increase was greater during exercise than at rest. Ventilation decreased after HCO_3^- infusion (8 studies). The effect was again greater during exercise. All dogs gave similar results. Over a range of pH disturbance of 7.300 to 7.390 and constant $PaCO_2$, the increase in $\dot{V}_E$ at rest was 1 liter/min/-.1 pH and during exercise was 10-12 liters/min/-.1 pH. As far as is known this is the first evidence that alterations in fixed acid or base interact with exercise to effect ventilation. (Supported in part by USPHS, GM15571, GM00063, K04-GM42350).

EFFECT OF INSPIRATORY FLOW RATE ON VERTICAL VENTILATION DISTRIBUTION. B. Bake†, L.D.H. Wood†, B.G.J. Murphy*, P.T. Macklem and J. Milic-Emili. Respiratory Division, Royal Victoria Hospital, Montreal, Canada.

During quasistatic inspiration from FRC ventilation distribution is preferential to the dependent lung zones, but at inspiratory flows higher than 2.4 lps ventilation becomes more uniform (Robertson et al. JAP 26:438, 1969). In 7 seated subjects we have studied regional distribution patterns of ^{133}Xe boli inhaled from FRC at various constant inspiratory flows ($\dot{V}_I$) from 0.1 to 4.5 lps. The ratio of the upper to lower lung zone ventilation per alveolus ($\dot{V}_U/\dot{V}_I$) was found to increase with $\dot{V}_I$ in a curvilinear manner, rapidly at first and then progressively slower. The average results of 7 subjects were -

$\dot{V}_I$ (lps)	0.2	0.5	1.0	1.5	3.0	4.5
$\dot{V}_U/\dot{V}_L$	0.65	0.76	0.81	0.88	0.90	0.93

We conclude that during inhalation from FRC, the regional distribution of the initial portion of inspired gas is markedly flow dependent even at low $\dot{V}_I$'s . Apical ventilation per alveolus did not generally exceed basal ventilation even at the highest flows. If these results are due solely to gravity dependent mechanical time constant inequalities they are compatible with an apex to base compliance ratio of 0.65 and approximately equal apical and basal resistances. If regional resistances are inverseley related to regional lung expansion, the absence of greater apical than basal ventilation may be explained by greater dynamic pressure applied to the basal regions.Supp: by MRC Canada.

GLUCOSE REABSORPTION BY THE NEWBORN DOG KIDNEY. J.T. Baker* and L.I. Kleinman, Dept. of Physiol., Univ. of Cincinnati Col. of Med., Cincinnati, Ohio 45219.

Glucose titration and splay curve analyses were performed on 16 puppies, aged 1-36 days, and on 3 adult controls, using a perchloric acid precipitation, glucose-oxidase method. Classical titration curves of transport vs. load could not be obtained, since glucose transport (T_g) varied with spontaneous changes in glomerular filtration rate (GFR). In reverse titrations, comparison of fractional glucose reabsorption at similar filtered loads during control and final clearances, show glucose reabsorption to be essentially complete under both circumstances. Therefore, deterioration of glucose transport mechanisms does not account for the observations reported. When T_g and load (plasma glucose x GFR) were corrected for GFR, typical titration curves were obtained. Constant values of T_g/GFR, observed at saturating loads of glucose, were equated with T_m/GFR. Normalization of T_g/GFR and load/GFR to T_m/GFR resulted in classical splay curves. Puppies less than 2 weeks of age had greater splay than older puppies and adults, suggesting greater nephron heterogeneity in younger puppies. At filtered glucose loads at least 1.5 times $>$ T_g, a highly linear relationship ($r = .97$) between T_g and GFR was obtained from 2 randomly selected puppies of the same age. This linear relationship also existed for a mass plot of all animals ($r = .75$), indicating a constant relationship between ΔT_g and ΔGFR. On such a T_g-GFR plot, adults were shifted to the right of puppies, i.e., T_g was lower at any GFR compared to puppies. Since GFR per gram kidney was lower in puppies than adults ($p < .01$), maturation of tubular function occurs at a more rapid rate than maturation of GFR, resulting in relatively large T_m/GFR in younger puppies.

LOCOMOTOR ENERGETICS OF LIZARDS AND MAMMALS COMPARED. Robert T. Bakker (intr. by C. R. Taylor). Concord Field Station, Mus. Comp. Zool., Harvard Univ., Old Causeway Road, Bedford, Mass., 01730

Traditionally, the sprawling, widetrack reptilian locomotion has been considered energetically more expensive than the upright, narrow-track locomotion of mammals. Five species of lizards were run in enclosed treadmills. Steady state O_2 consumption increased linearly with speed in all lizards. Net cost of locomotion is defined here as the slope (ΔO_2 consumption/Δspeed) times speed plus the difference between the y-intercept (extrapolated zero running speed) and the resting O_2 consumption. In the lizards the slope was equal to or less than in mammals of the same weight, and the difference between the y-intercept and resting O_2 consumption was from 0.03 to 0.5 that of mammals of the same weight, calculated from the equations of Taylor et al (Amer. J. Physiol. 219:1104). Contrary to the widely held assumption, the energetic cost of locomotion in sprawling lizards seems to be less than in mammals. Supported by NSF Grant GB 27539 to C. R. Taylor.

LIZARD	WEIGHT (g)	SLOPE (ml O_2 g^{-1} km^{-1})		Y INTERCEPT - REST (ml O_2 g^{-1} hr^{-1})	
		Lizard Observed	Mammal Calculated	Lizard Observed	Mammal Calculated
Gerrhonotus	14	1.91	2.95	0.11	1.27
Tupinambis	16	1.66	2.79	0.46	1.23
Varanus sp.1	26	1.86	2.30	0.17	1.09
Ctenosaura	126	1.09	1.23	0.19	0.73
Varanus sp.2	145	1.28	1.17	0.20	0.71
Varanus sp.1	230	1.24	0.96	0.02	0.63
Varanus sp.2	630	0.56	0.64	0.19	0.49
Tupinambis	1200	0.35	0.50	0.22	0.42

Effect of electrical stimulation of diencephalic and mesencephalic structures on the generalized NaCl aversion after LiCl poisoning. S.Balagura, T.Ralph*, and R.Gold*. Univ. of Massachusetts, Amherst 01002, and S.U.N.Y., Cortland 13045

Once a rat has tasted LiCl and experienced its toxic post-ingestional effects it avoids lithium as well as equimolar NaCl solutions. We proposed to determine if electrical stimulation of the lateral hypothalamic area (LH) or of the mesencephalic reticular formation (RF), which we have shown to induce analgesia, would reduce the intensity of this generalized taste aversion. Ten male albino rats were implanted unilaterally with bipolar electrodes in either the LH or the RF. Five control animals were not implanted. Following adaptation to an 18hr water deprivation schedule,they were offered 10ml of 0.12M LiCl to drink and were stomach loaded with an additional 5ml of 0.24M LiCl to potentiate the toxic effect. This was followed by 6hr of brain stimulation (2-30 μA, 60Hz, adjusted individually), with water available. The next 3 days the rats were maintained on their schedule with water available for 6hr. On the next drinking session they were offered 0.12M NaCl instead of water. Both the LH and RF groups drank more NaCl than did the controls. LH and RF stimulation may diminish the generalized taste aversion by reducing the aversiveness of the poisonous lithium post-ingestional effects or by disrupting the association of taste and post-ingestional cues.

METABOLISM OF PULMONARY LECITHINS AND THE EFFECT OF TOBACCO SMOKE. J. A. Balint and E. C. Kyriakides*. Department of Medicine, Albany Medical College, Albany, N. Y.

The origin of pulmonary surfactant lecithin is still not established and data on its metabolic rate are conflicting. To examine these questions rats were killed 2, 4, 12, 24, 48, and 57 HRS after injection of 2-^{3}H-glycerol and 1-2-^{14}C-choline via the tail vein. For each time period 4 control and 4 tobacco smoke exposed rats were used. Rats were exposed to room air or standard tobacco smoke for 2.5 days prior to isotope injection and until sacrifice. Surfactant was obtained by endobronchial lavage and it, as well as lung, were extracted in chloroform:methanol (2:1) and their lecithins purified by column, thin layer and argentation chromatography and radioactivity measured, and half lives (T 1/2) determined by the method of least squares. The T 1/2 of glycerol in surfactant lecithin (> 75% palmitic acid) was 10.0 HRS in controls and 8.5 HRS in smoked rats ($p < .05$). The T 1/2 for choline in surfactant lecithin was 20.8 and 19.5 HRS, respectively. The corresponding value of T 1/2 for dipalmitoyl lecithin from whole lung were 21.1 and 19.8 HRS and 35.0 and 33.9 HRS, respectively. Peak specific activity of surfactant lecithin for both 2-^{3}H-glycerol and 1-2-^{14}C-choline was observed at 12 HRS; whereas in lung dipalmitoyl lecithin highest specific activities were seen at the earliest time examined. We conclude that (1) surfactant lecithin is a separate pool of dipalmitoyl lecithin in the lung, (2) that there is a significant delay in appearance of newly synthesized dipalmitoyl lecithin in surfactant and (3) that T 1/2 of 1-2-^{14}C-choline in lecithin gives an apparently longer T 1/2 for lecithin than that obtained with 2-^{3}H-glycerol. Supported by a grant from American Medical Association, Education and Research Foundation.

EFFECTS OF CHRONIC EXPOSURE TO 150 PPM CARBON MONOXIDE ON THE CARDIOVASCULAR SYSTEM OF DOGS. C.M. Banerjee, D.A. DeBias, N.C. Birkhead, L.A. Kazal, W.V. Harrer* and M.H.F. Friedman. Department of Physiology Thomas Jefferson University, Philadelphia, Pa. 19107

The hematologic and cardiovascular effects of continuous exposure to 150 ppm of CO for 24 weeks were investigated in dogs with or without myocardial infarction. Study consisted of four groups of animals: (1) normal, breathing room air, (2) normal, breathing 150 ppm CO, (3) infarcted breathing room air and (4) infarcted breathing 150 ppm CO. The mean carboxyhemoglobin level of the animals breathing CO was 15.44%. Gross and histopathological examination of hearts taken at sacrifice did not reveal any changes that could be attributed to carbon monoxide. The effects of 150 ppm exposure for 24 weeks include increased hematocrit, increased number of red blood cells, increased hemoglobin concentration and persistent T-wave changes in the EKG. The T-wave changes were more marked in infarcted dogs than in non-infarcted dogs breathing CO. Our findings suggest that myocardial ischemia was more intense in infarcted animals exposed to CO than in infarcted animals breathing room air.

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EFFECT OF AN ACUTE EXPOSURE TO 15% CO_2 IN AIR ON RAT LUNGS. Mukul R. Banerjee. Department of Anatomy-Physiology, Indiana University, Bloomington, Indiana 47401.

Following a 24-hour exposure to 15% CO_2 in air, lung characteristics of healthy adult male rats were studied. The animals were weighed before and after the exposure period. Following the CO_2-exposure, blood samples were obtained from abdominal aorta under nembutal anesthesia and their P_{O_2}, P_{CO_2} and pH were immediately determined. The lungs of the rats were then removed and their weights were taken. The volume of gas trapped in the lungs upon opening of the thorax was determined by buoyancy measurements in 0.9% saline. Compliance curves were recorded from the excised lungs both during inflation and deflation first with air and then with 0.9% saline. The average gain in body weight of the control rats was 8.5 gm during the 24 hour period while the CO_2-exposed rats lost 24.1 gm during that period. The mean values for wet and dry lung weights and trapped gas volume in the lung were essentially the same in the two groups of rats. As compared to control rats, the CO_2-exposed rats had a significantly higher Pa_{CO_2} and Pa_{O_2} and a significantly lower pHa. The lung tissue compliance as determined by saline infusion and withdrawal was not significantly different between the two groups of animals. One characteristic feature of the total lung compliance of the CO_2-exposed rats was a progressive decrease in the area of hysteresis loops. These would suggest instability of lung alveoli in these rats with a probable alteration in their surfactant activity. (Supported by U.S. Air Force F 44620-68-C-0014).

THE MAXIMUM RATE OF CHANGE OF LEFT VENTRICULAR PRESSURE AND LEFT VENTRICULAR INTERNAL DIAMETER AS INDICES OF INOTROPIC CHANGES IN THE CONSCIOUS DOG. George E. Barnes*, Robert L. Kaspar*, Lawrence D. Horwitz and Vernon S. Bishop. The University of Texas Medical School at San Antonio, San Antonio, Texas 78229.

The reliability of the maximum rate of change of left ventricular pressure (dP/dt) max and diameter (dD/dt) max as indices of the inotropic state of the left ventricle was studied in eight conscious dogs. The animals were previously instrumented with miniature solid state transducers for measuring left ventricular pressure and piezoelectric transducers for measurement of transverse left ventricular diameter. Neither dP/dt max nor dD/dt max were significantly affected by increased preload brought about by rapid intravenous infusion of Tyrode's solution or by increases in afterload elicited by phenylephrine. Increases in heart rate from a resting value of 110 ± 3.1 by atrial pacing at 120, 150, and 180 beats/minute resulted in 0%, 4%, and 7.8% increases in dP/dt max and 0%, 3.8%, and 8.5% increases in dD/dt max. Using isoproterenol infusion, a recognized positive inotropic intervention, large increases in dP/dt max (27%, 53%, and 78%) and dD/dt max (33%, 51%, and 83%) were seen when heart rate stabilized at levels comparable to atrial pacing. Thus, dP/dt max and dD/dt max are reliable indices of the inotropic state of the left ventricle in conscious dogs and are relatively insensitive to changes in preload, afterload, and heart rate. (Supported by NIH #2, RO1-HL12415-04, San Antonio Heart Association and AFOSR-71-2074).

The role of the larynx in the regulation of respiratory frequency. D. Bartlett, Jr., J. E. Remmers and H. Gautier*. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire 03755.

During quiet breathing the duration of expiration exceeds the time required for the relaxed respiratory system to return to FRC. As ventilation and respiratory frequency increase in response to chemical stimulation, the duration of expiration decreases markedly. One factor that regulates expiratory airflow is the variable resistance provided by the vocal cords. To assess the importance of this factor we have studied trans-laryngeal resistance in anesthetized cats and upper airway resistance in unanesthetized, unrestrained cats during air breathing and during progressive hypercapnia.

In anesthetized cats breathing air the vocal cords are abducted somewhat during inspiration and move toward the midline during expiration, increasing trans-laryngeal resistance. Hypercapnia enhances the inspiratory abduction of the cords and brings about a phasic abduction during expiration as well. These changes with hypercapnia lead to a slight decrease in inspiratory resistance and a striking decrease in expiratory resistance across the larynx. We have found a similar pattern of response to hypercapnia in upper airway resistance in unanesthetized, unrestrained cats, though quantitation of the changes is less precise than in the anesthetized animals.

The findings suggest that during quiet breathing the high resistance to expiratory airflow provided by the vocal cords prolongs expiration, thus delaying the onset of the following inspiration. This braking action of the larynx is diminished or abolished during hypercapnia -- a change which may facilitate the attendant increase in respiratory frequency. (This investigation was supported by General Research Support Grant 5 SO1 RR 05392-11.)

MYOCARDIAL AND WHOLE BODY UPTAKE OF RADIORUBIDIUM. C. A. Bashour*, C. S. Rutherford*, H. F. Downey, F. A. Bashour and S. J. Kechejian*. Cardiopulmonary Institute, Methodist Hospital and Univ. of Texas Southwestern Med. Sch., Dallas, Texas.

Following intra-arterial administration of ^{86}Rb, Sapirstein observed a constant ratio of heart to whole body radioactivity from 30 to 120 seconds and deduced that myocardial (E_M) and whole body (E_B) extraction ratios were equal (Am. J. Physiol. 193: 161, 1958). Because our computer simulation indicated that the myocardial fraction of the whole body radioactivity would be essentially constant over this period despite 35% differences in E_M and E_B, we measured these extraction ratios. In 18 anesthetized dogs, ^{86}Rb was constantly infused into the left atrium for 90 sec. Blood samples were collected simultaneously from the femoral and pulmonary arteries and coronary sinus during the last 30 sec. of the infusion. Mean extraction ratios in normal dogs were similar (E_M = .72±.06 (S.D.), E_B = .73±.05). They did not change in 5 dogs during nitroglycerine infusions (.6 mg/min), but following partial left coronary occlusion in 4 dogs E_M was significantly increased (E_M = .79±.08, $P<.05$). In conclusion, myocardial and whole body ^{86}Rb extraction ratios were similar under normal condition and with nitroglycerine, but differed when coronary flow was reduced.

FLUORESCENT SYMPATHETIC FIBRES AND NERVE CELL BODIES IN THE LUNGS OF QUIET AND STRESSED RATS. J. W. Bean and T. Nakamoto*. Department of Physiology, University of Michigan, Ann Arbor.

Hilar lung sections from adult rats, resting and stressed, including killing by post. occipital captive bolt were examined fluorometrically (Ross, J. Histochem. Cytochem. 17:814,1969) for noradrenalin as an approx. measure of adrenergic nerve activity (vEuler, Science, 173:202,1971). Experimental conditions and fluorescent intensity and its occurence arbitrarily expressed from + to +++++ are shown below:

Series	No.	Exp. Condition	Pulmonectomy under:	Reaction
1	6	quiet (control)	anesthesia	+
2	6	excited to belligerence	anesthesia	++++
3	8	excited to belligerence and	post. occip.cap.bolt	+++++
4	5	violent reflex on decap.	guillotine decapit.	++++
5	1	spontaneous belligerence	anesthesia	+++++
6	6	Gd.mal O_2(OHP)convulsion	terminal unconscious	+
7	4	Gd.mal Metrazol convul.	terminal unconscious	none

The results indicate a positive correlation between pulmonary adrenergic nerve activity and stress severity, particularly that of severe spontaneous and aggravated belligerence and lethal head injury by captive bolt. Adrenergic beaded fluorescence, related and unrelated to blood vessels, suggests functions other than vascular and bronchial control. Also, the presence of fluorescent sympathetic nerve cell bodies in the lung was demonstrated, a new finding not heretofore reported in the literature, suggestive of some significant sympathetic function. The data support earlier reports of possible direct sympathetic effects on the lung in the causation of centrogenic pulmonary pathology (Bean & Beckman, J. Appl. Physiol. 227:807,1969) including changes in compliance, insevere head injury. Low values in lethal Gd. mal OHP and Metrazol seizures suggest a depletion of noradrenalin. Supported in part by NIH Res. Grant HE01646.

BARBITURATE BLOCKADE OF TONIC LH SECRETION IN THE MALE AND FEMALE RAT. C.W. Beattie*, C.S. Campbell*, L.G. Nequin* and N.B. Schwartz. Depts. of Pharmacology and Psychiatry, Univ. of Ill. Coll. of Med., Chicago, Ill. 60680.

The site and mechanism of action of the barbiturate blockade of ovulation and the proestrous surge of LH are unknown. The present study investigated the effects of pentobarbital (PB) on LH release in gonadectomized rats. Serial blood samples (30 min) were withdrawn via chronic cannulae 21 days post-gonadectomy from 0800-1130 or 1300-1630 hrs. PB (30mg/kg ip) injection at 0830 hrs significantly reduced serum LH of ovariectomized rats from pre-drug control levels (0800) and from saline injected controls between 0900 and 1030 hrs. No significant variation in LH appeared in saline treated animals over the same time period. However, a significant rise in serum LH of saline treated (1330 hrs) rats was observed beginning at 1400 hrs and lasting through 1530 hrs. PB injected at 1330 hrs blocked this rise. Castrated male rats injected with saline (1330 hrs) did not show a significant rise in LH between 1300 and 1630 hrs. PB (30 mg/kg at 1330 hrs) lowered LH in castrated male rats from 1400 to 1430 hrs.

These observations suggest 1) the block of tonic LH release in either sex is directly related to the depth and duration of anesthesia; 2) barbiturates reduce LH secretion independently of gonadal steroid action on the hypothalamo-hypophyseal axis; and 3) a cyclic neural timing center may exist for LH release in the ovariectomized female. (Supported by PHS HD 00440, GM 81, MH 8396.)

RENAL HEMODYNAMICS, FUNCTION, AND RENIN SECRETION DURING HEMORRHAGIC HYPOTENSION, NORMOVOLEMIC NORMOTENSION AND HYPOTENSION. O. Beaty*, C.H. Sloop*, and H.E. Schmid. Bowman Gray Sch. Med., Winston-Salem, N.C. 27103.

Renal hemodynamics, function, and renin secretion were studied during hemorrhagic shock in acute dog experiments using a modified Wiggers protocol. The left kidney was exposed via a flank incision. Renal blood flow was measured via an electromagnetic flow probe and renal artery pressure via a 20 gauge needle inserted retrograde into the renal artery and connected to a pressure transducer. The animals were allowed to hemorrhage from a femoral artery cannula into an overhead reservoir. Previous investigators have shown that during hemorrhagic hypotension, renin secretion is increased and effective renal plasma flow is decreased. Renal hemodynamics, function, and renin secretion were measured during graded hemorrhagic pressure reductions from control to 100, 75 and 50 mm Hg. When 20% of the shed blood had been taken up spontaneously, the remaining volume was reinfused. The animals were then followed through the periods of normovolemic normo- and hypotension. Findings confirm an increased renin secretion and renal vascular resistance (RVR) during hemorrhagic hypotension. RVR, however, decreased in a manner similar to skeletal muscle during uptake of shed blood. As the pressure progressively fell during normovolemia, RVR again began to rise. It appears that the renal bed, un like skeletal muscle, is capable of increasing its resistance during the final stages of irreversible shock. Supported by N. C. Heart Assn. and NIH grants HE-5948 and HL-5392.

EFFECT OF VARIATIONS IN ANTRAL pH ON GASTRIN RELEASE. H. D. Becker,* D. D. Reeder,* C. S. Clark, Jr.* and J. C. Thompson. Univ. of Texas Med. Branch, Galveston, Texas.

Acidification of the antrum is known to diminish acid secretion by the gastric fundus. The development of a specific radioimmunoassay for gastrin has allowed us to study quantitatively changes in antral gastrin release in response to variations in antral mucosal pH. Method: In five anesthetized dogs, the blood supply of the antrum was dissected to allow intermittent sampling of the entire antral venous outflow, and a catheter for irrigation of the mucosa was placed into the isolated antrum. The pylorus was ligated around the catheter and a clamp was placed across the antro-fundic junction to isolate the antrum from acid. Blood samples from the antral vein for serum gastrin measurement by radioimmunoassay were obtained at 15 min. intervals for 4 hrs. After a 30 min. basal period the antral pH was changed every 30 min. by irrigating with solutions of varying acidity, from pH 1 to pH 7. Results: Mean basal gastrin concentration in the antral vein was 172 ± 23 picograms (pg)/ml; basal pH of the antrum was between pH 4-5 in all dogs. Each change in pH of the antral irrigant was accompanied by a parallel change in gastrin. At pH 7, antral vein gastrin was 340 ± 66 pg/ml, a significant elevation over basal ($p<0.02$). When the pH of the irrigant was between 4 and 5, gastrin level fell to basal, and lowering of the pH to 1.0 decreased gastrin significantly to 107 ± 21 pg/ml. Conclusion: Neutralization of the resting antrum to pH 7 resulted in an augmentation of gastrin release. Decreases in antral pH caused a parallel diminution in gastrin release. Acidification of the resting antrum to pH 1.0 suppressed but did not abolish gastrin release.

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SYMPATHETIC INFLUENCE ON LUNG COMPLIANCE IN CATS: David L. Beckman and Kim F. Mason*. Departments of Anesthesiology and Physiology, Wayne State University, Detroit, Michigan 48201.

It has been shown that lethal mechanical head injury (captive bolt) decreases lung compliance in monkeys by 50% and alters the surfactants in the absence of any attendant gross lung pathology; that this compliance decrease can be prevented by pretreatment with sympatholytic agents (J. Appl. Physiol. 28:807, 1969; 29:631, 1970; 30:394, 1971) but not with isoproterenol or atropine eliminating smooth muscle effects; and that stellate ganglion stimulation and head injury in monkeys causes a 40% in vivo compliance decrease and abnormal alveolar surfactants in the absence of lung edema. In the present experiments 6 cats under ketamine anesthesia were exposed to electrical stimulation of the stellate ganglion. Tracheal pressure swings increased by 25% indicative of a significant decrease in lung compliance. Pulmonary congestion and edema were ruled out as causal factors by normal lung weights, low peak systemic blood pressures (50 to 80 mm Hg) and by the absence of any effect of higher blood pressures on compliance (130 mm Hg induced by carotid artery clamping via the CNS ischemic sympathetic reflex in stellatectomized cats). The compliance decrease was not prevented with Isuprel eliminating airway blockage as a causal factor. The data support the earlier interpretation that alveolar surfactants and lung compliance are in large part under sympathetic control. (Supported by the Detroit General Hospital Research Corporation.)

DYSKINESIAS INDUCED BY LONG TERM ADMINISTRATION OF HALOPERIDOL IN THE MONKEY. Paul Bédard, Louis Larochelle, Jacques De Léan and Jean Lafleur (intr. by Louis J. Poirier). Faculty of Medicine, Laval University, Quebec, Canada.

Monkeys were injected daily with haloperidol (0.3 mg/kg i.m.) during six months. Apart from the usual decrease in locomotor activity, many side effects were observed during treatment including akathisia, choreo-athetoid movements, circling, bucco-facial dyskinesias and postural tremor of the limbs. Three months after cessation of the drug, most of the signs had subsided except for the bucco-facial abnormal movements in one case, and harmaline induced postural tremor in all cases. These motor phenomena were recorded cinematographically.

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A COMPARATIVE STUDY OF FRUCTOSE LEVELS IN SEX ACCESSORY ORGANS OF MALE LABORATORY AND WILD RATS. R. W. Belknap*, E. J. Keenan* and R. V. Andrews. Creighton Univ., Omaha, Nebr.

Seminal vesicle and ventral prostate fructose amounts and concentrations were measured from aliquots of trichloroacetic acid homogenates in breeding and non-breeding laboratory rats and in wild rats. The fructose levels of tissues from non-breeders were significantly lower ($p<0.05$) than those of breeders and wild animals. This observation is supported by the finding that epithelial cell heights (and cytological evidence of activity) were higher in the sex accessory organs of laboratory breeders (prostate cell height = 20.59μ) and wild rats (prostate cell height = 20.41μ) than in non-breeding laboratory rats (prostate cell height = 19.77μ), although these cell height differences were not significantly different in all cases. Gross adrenal weights are highest in the non-breeders and lowest in the breeders, which suggests that reproductive isolation influences adrenal function. No differences in gross testis weights were observed. Gross weights of the seminal vesicle and ventral prostate were higher in both breeders and wild animals, although again not significant in all cases. Failure of organ-body weight ratios to reflect these differences may be attributed to differences in body weights. We conclude that fructose levels in rat sex accessory tissues is correlated with reproductive activity.

SERUM MAGNESIUM AND POTASSIUM CONCENTRATIONS DURING EXERCISE UNDER THERMONEUTRAL AND HOT CONDITIONS. G.A. Beller*, J.T. Maher*, L.H. Hartley, D.E. Bass, and W.E.C. Wacker*, U.S. Army Rsch. Inst. Env. Med. and Peter Bent Brigham Hospital, Natick and Boston, MA.

Serial changes in serum magnesium(Mg^{2+}) and potassium(K^+) were assessed in two groups of healthy males during treadmill exercise in a thermoneutral(21/14C, dry/wet bulb) and hot(49/27C, dry/wet bulb) environment. In both studies venous blood for Mg^{2+} and K^+ determinations were drawn prior to(control), and at 45 and 90 min of exercise. Heart rate(HR) and rectal temperature(T_r) were continuously monitored. In the thermoneutral study, 9 subjects walked at 3.5mph on an 8% grade, and at 90 min had a mean HR increase of 74±4(S.E.) beats/min, rise in T_r of 1.17±0.11C, and a mean weight loss of 1.13±0.04kg. There was a significant($P<0.05$) decrease in mean serum Mg^{2+}(control: 1.99±0.04; 45 min: 1.97±0.04; 90 min: 1.92±0.03), and increase in mean serum K^+ (control: 4.1±0.1; 45 min: 4.6±0.1; 90 min: 4.9±0.1) concentrations (mEq/l). In the heat study, 8 subjects walked at 3.5mph on a 0% grade, and at 90 min of exercise had a mean HR increase of 70±5 beats/min, rise in T_r of 2.06±0.11C, and a mean weight loss of 2.07±0.10kg. There was a significant($P<0.01$) decrease in serum Mg^{2+}(control: 1.87±0.06; 45 min: 1.81±0.07; 90 min: 1.72±0.08) and increase in serum K^+(control: 4.3±0.1; 45 min: 4.8±0.1; 90 min: 4.9±0.1) concentrations(mEq/l). The fall in serum Mg^{2+} was greater($P<0.05$) under hot(9%) than thermoneutral(4%) conditions, whereas the magnitude of serum K^+ rise was not significantly different in the two studies. These data suggest that magnesium depletion might occur during prolonged periods of exertion, particularly in the heat, which may be related to sweat losses of this ion.

Effects of striate lesions and commissure section on the visual response of neurons in inferotemporal cortex. D.B. Bender*, C.E. Rocha-Miranda*, C.G. Gross, S. Volman* and M. Mishkin*. Psychology Dept., Princeton University, Princeton, N.J. 08540

Neurons in inferotemporal cortex of the monkey have visual receptive fields which always include the fovea and, for the majority of neurons, extend well into both visual hemifields (Gross et al, J. Neurophysiol. 35:96, 1972). Inferotemporal cortex receives cortical projections from both prestriate cortices as well as a subcortical projection from the pulvinar. To determine which of these pathways are essential, we recorded from single neurons in inferotemporal cortex in three animals after removal of right striate cortex and in two animals after section of the corpus callosum and anterior commissure. Recording began several months after the lesions were made. The animals were immobilized, anesthetized with nitrous oxide and oxygen and the eyes focused on a tangent screen. Receptive fields were plotted with light and dark slits and edges. Results: In the animals with striate lesions all receptive fields were unilateral and confined to the hemifield ipsilateral to the lesion. In the animals with callosal sections, all receptive fields were unilateral and confined to the hemifield contralateral to the recording site. In all animals, the range of stimulus preferences was similar to that in normal animals. Conclusion: The response of inferotemporal neurons to stimulation in the contralateral field depends on the ipsilateral striate cortex. Their response to stimulation in the ipsilateral visual field depends on both contralateral striate cortex and the corpus callosum.

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THE EFFECT OF ANESTHETICS ON THE GASTRIC SECRETORY RESPONSE TO 2-DEOXY-D-GLUCOSE. Rudy A. Bernard and Massako Kadekaro*. Dept. of Physiology, Michigan State Univ., East Lansing, Mich. 48823, and Dept. Physiology and Pharmacology, Univ. Sao Paulo, Sao Paulo, Brazil.

It has recently been shown that 2-deoxy-d-glucose (2-DG) provokes gastric secretion in cats through a multi-synaptic neuronal circuit originating in the lateral hypothalamus and culminating in the dorsal motor vagus nucleus (DMVN). We decided to test the effect of nembutal, chloralose, and ketamine on the secretory response to 2-DG as an indicator of the probable effect of these drugs on the reflex activation of DMVN through other neural circuits, such as the gustatory. We used 18 cats, each with a chronic gastric fistula, and injected them with 60 mg/kg 2-DG over a 15 min period. Secretion was collected every 15 min during 2 hr and after 18-24 hr fasting. Volume, acid concentration and acid output were determined. The cats were tested 2 or 3 days later under anesthesia. The results were as follows: nembutal decreased and delayed the response (30 mg/kg i.p.) or totally abolished it (40 mg/kg i.p.), chloralose (70 mg/kg i.p.) totally abolished it, and ketamine (30, 40 mg/kg i.m.) maintained it, with a tendency to elevate it above normal. The response was abolished when ketamine (40 mg/kg i.m.) was given after decerebration, indicating that the drug itself did not excite DMVN. Nembutal and chloralose are thus contraindicated in studies of reflex activation of gastric secretion. Ketamine, a newly introduced anesthetic, appears to offer an important advantage in studying the neural control of gastric secretion in animals anesthetized deeply enough to allow extensive abdominal, thoracic and cranial surgery. (Supported in part by grants from NIH (NS 09168) and the Sao Paulo State Research Foundation.)

HEAT DISSIPATION RHYTHMS OF DOGS IN A CONTROLLED ENVIRONMENT. E. L. Besch and J. E. Woods*. Dept. Physiol. Sci., Col. Vet. Med. and Institute for Environ. Res., Col. Engg., Kansas State Univ., Manhattan, Ks. 66506.

Body heat dissipation rates were determined in 4 mature greyhound (23.0 ± 0.3 kg) and 4 mature beagle (10.3 ± 0.2 kg) dogs. Each breed group of 2 dogs was confined, in series, individually, in standard dog cages of equal size in a controlled environment room maintained under conditions of 24°C, 50% relative humidity and fixed ventilation rates. Food and water were available ad libitum. Heat dissipation rates were determined for each group and normalized to an individual dog basis. The ratio of actual heat dissipation to standard metabolic rate -- Standard Heat Ratio (SHR) -- was 2.37 ± 0.22 for greyhounds and 1.67 ± 0.21 for beagles ($P<0.07$). The SHR displays a 24-hour cyclic pattern in which 4 contiguous maximum values differ significantly from 4 contiguous minimum SHR values ($P<0.001$, greyhounds; $P<0.01$, beagles). The hourly dry bulb temperatures for groups of 2 dogs suggest a ΔT of approximately 2.2°C for greyhounds and 1.2°C for beagles in occupied cages compared to chamber temperature. These data suggest that although chamber -- or animal room -- temperature may be optimum, the caged animal within that chamber may be exposed to thermal conditions approaching upper critical temperatures.

(Supported by Animal Resources Branch, Division of Research Resources, NIH, Contract 71-2511).

MORPHOLOGICAL AND PHYSIOLOGICAL PROPERTIES OF THE BODY WALL MUSCLE OF MYXICOLA INFUNDIBULUM. J.A. Besso, Jr.*, J. Wells* and R.L. Parsons. Depts. of Anatomy & Physiology, Univ. of Vermont, College of Medicine, Burlington, Vermont 05401

The pennate body wall muscle of M. infundibulum is composed of longitudinally oriented, obliquely striated muscle fibers approximately 1.5μ x 35μ x 500μ. Sarcomeres contain Z rods, thick filaments approximately 300 Å in diameter and thin filaments approximately 50Å in diameter. The sarcoplasmic reticulum appears to consist of longitudinally oriented systems of interconnected cisternae, which occur immediately beneath the sarcolemma. The resting membrane potential (E_M) of individual muscle fibers determined by standard microelectrode techniques in artificial sea water (10mM KCl) was -38.6 ± 7.8 (mean ± S.D., 91 fibers). E_M decreased linearly with the log $(K^+)_o$ (10-200mM) but was not changed when $(K^+)_o$ was decreased from 10mM to 1mM. Muscle fibers were hyperpolarized at all levels of $(K^+)_o$ in a Na^+-deficient solution and were depolarized in Ca^{2+}-deficient artificial sea water. Normal all or none spikes with overshoots were obtained in artificial sea water containing TTX (10^{-7}-10^{-6} g/ml) or in Na^+-deficient solutions, but were reduced or abolished in a Ca^{2+}-deficient solutions or in artificial sea water containing 20mM Mn^{2+}. (Supported by PHS Grant NS-07740.)

THE KINETICS OF UNIDIRECTIONAL GLUCOSE FLUX INTO THE ISOLATED DOG BRAIN. A.L. Betz* and D.D. Gilboe. Depts. of Neurosurgery and Physiology, Univ. of Wis., Madison, Wis. 53706.

The unidirectional uptake of D-glucose-6-^{3}H was studied in 5 isolated dog brains by means of a single-passage indicator dilution technique using ^{22}Na as the intravascular reference. After a 50μl arterial injection of the isotope mixture, 30 consecutive venous samples were collected at 1 second intervals. Arterial and venous blood was obtained immediately after the 30th sample for glucose analysis by a glucose oxidase method. The average concentration of glucose, $\bar{A}$, presented to the carrier was calculated as the average of the arterial and venous concentrations. The arterial glucose concentration, A, was varied in increments between 25 and 668 mg/100 ml of plasma by addition of unlabeled glucose to the perfusion blood. The fractional extraction of glucose, E, was determined at 4-8 different values of A for each brain by comparing the relative percentage of ^{22}Na and ^{3}H recovered in each sample. Since the fraction of glucose taken up is inversely proportional to the plasma flow rate per unit weight of brain, F/W, the rate of unidirectional uptake, U, is the product of the quantity extracted, $E\bar{A}$, and F/W, i.e. $U=E\bar{A}F/W$. The regression line for the double reciprocal plot of $1/U$ vs. $1/\bar{A}$ was used to calculate a K_m for unidirectional glucose transport of 12.3 mM and a V_{max} of 0.22 mmoles/100 g/min with a correlation coefficient of 0.978. This technique provides a simple and rapid method for describing the effects of various inhibitors and activators on glucose transport in vivo. Supported by Grant NS05961 from the National Institute of Neurological Diseases and Stroke.

PRESSURE-LENGTH-DIAMETER RELATIONSHIPS OF RABBIT URETER. Piero Biancani,* Robert M. Weiss,* Michael Zabinski* and Arthur L. Bassett. Yale Univ. School of Med., New Haven, Ct., Fairfield Univ., Fairfield, Ct. and College of Physicians & Surgeons, Columbia Univ., New York, N.Y.

The ureter in vivo shows both longitudinal and diametral deformation changes with obstruction and vesicoureteral reflux. To evaluate the time course and pattern of deformation we studied the pressure-length-diameter relations of in vitro rabbit ureter. Ureteral segments were perfused with oxygenated Tyrode's solution (37°C). Constant intraluminal pressures of 10, 20, 40, 80 and 200 cm H_2O were applied for periods of 6 hrs. Diametral and longitudinal deformation were recorded photographically at specified time intervals. The ureter increased both in length and diameter after a constant intraluminal pressure was applied. The maximum length increase was approached rapidly (23-57% increase from initial length occurred within 10 min. of applying a loading pressure). Subsequently, length remained constant or decreased slightly. In contrast, diameter increased slowly and gradually over 6 hr. (5-15% increase from initial diameter within 10 min.). The percentage increase in length and diameter were approximately equal at 6 hr. Ureteral length was $\sim$ 40X diameter and actual change in length was much greater than change in diameter. Circumferential and longitudinal wall tensions were calculated from cross-sectional area and wall thickness. Circumferential tension was over 50% higher than longitudinal tension at all times. Our data indicate that the ureter is initially much stiffer and resistant to diameter change than to longitudinal change after a pressure loading and provides some explanation for the clinical finding of ureteral tortuosity during early obstruction. (Supported by NIH Grant AM 13543-03 and NIH Program Project Grant HE 12738-04).

INSTANTANEOUS ALTERATIONS OF THE LEFT VENTRICLE TO ACUTE CORONARY ARTERY OCCLUSION IN CONSCIOUS DOGS. Vernon S. Bishop, Robert L. Kaspar*, George E. Barnes* and Merrill B. Kardon*. The University of Texas Medical School at San Antonio, San Antonio, Texas 78229.

In ten adult mongrel dogs, the response to acute one minute occlusions of the left circumflex coronary artery on left ventricular internal diameter, pressure, and outflow were measured. The immediate response to the cessation of coronary flow was a rapid increase in end-systolic diameter (3.8mm ± 0.56) with little change in end-diastolic diameter (0.37 ± 0.15mm) although filling pressure increased (7.0 ± 0.56 mmHg). The maximal rate of lengthening and the maximal rate of left ventricular pressure declined during diastole and were decreased proportionately greater than their counterpart during systole. Increases in heart rate (45 ± 9 b/min) paralleled the elevation in filling pressure. Stroke volume progressively decreased as the end-systolic diameter rose. The relationship between mean cardiac output and arterial pressure was usually not altered during the occlusion. The decline in cardiac output, and thus arterial pressure, depended upon the tachycardia developed. (Supported by NIH #2 R01-HL12415-04, San Antonio Heart Association and AFOSR-71-2074).

THE CHEMICAL COMPOSITION OF PLASMA AND CEREBROSPINAL FLUID (CSF) IN NORMOTHERMIC & HIBERNATING WOODCHUCKS, *MARMOTA MONAX*. L. Z. Bito* and J.C. Roberts. Dept. Ophthal. Res., Columbia Univ., New York, N.Y.10032.

In hibernation, the plasma concentrations of some constituents are known to be chronically altered and the body temperature is lowered to a point (4-8°C) where most metabolic processes are severely inhibited. The present studies were undertaken to further examine the effects of hibernation on plasma chemistry and to elucidate its effects on CSF composition. In the hibernating vs active woodchuck, plasma [glucose] and [lactate] decreased; [Mg^{++}], [Ca^{++}] and [protein] were increased by 82, 7 and 21% respectively; [Na^{+}], [Cl^{-}] and [K^{+}] were not significantly affected. In the CSF, [Mg^{++}] increased 44% in cisterna magna (CM), 29% in cortical subarachnoid (SA) and only 18% in ventricular fluid; [glucose] and [lactate] were lowered in all regions of the CSF system; [K^{+}] in the CM and ventricular fluids was unaffected by hibernation, and was maintained well below the plasma level; [K^{+}] in the SA fluid was significantly increased; CM [ascorbate] was maintained in hibernation well above that of plasma. The changes seen in plasma composition confirm and extend earlier findings and support the concept that the hibernating animal maintains a controlled internal milieu albeit different from that of the active animal. In general, the composition of CSF of active woodchucks resembles that of other mammals. Since the CSF of hibernating animals remains different from plasma ultrafiltrate, changes seen in hibernation must also represent well controlled, specific alterations rather than a general inhibition of secretory and absorptive transport processes. The increased CSF [Mg^{++}] may play a specific role in the induction and maintenance of hibernation, while the local increase in SA [K^{+}] may be associated with the shutdown of cortical activity in hibernation. (Supported by USPHS Grants FY-00402 & FY-00333).

MODELING OF STEADY STATE PULMONARY TRANSVASCULAR FLUID AND PROTEIN EXCHANGE IN UNANESTHETIZED SHEEP. L. H. Blake* and N. C. Staub. University of California at San Francisco, California 94122.

We are developing a mathematical description of passive transvascular fluid and protein exchange. The transport model includes vascular membrane characteristics, i.e. "equivalent" pore size and distribution and membrane thickness, as well as the physiological variables of microvascular hydrostatic pressure (P_{mv}), perimicrovascular hydrostatic pressure and plasma protein molecular size and concentration. We are using the model to investigate the sensitivity of each of the membrane characteristics and physiological variables upon the pulmonary transvascular exchange in the steady state. For the sheep lung, we measure P_{mv} relative to the left atrium, then assume a linear pressure distribution over the measured height of the lung for constant density and vascular membrane characteristics. Integrated results of the total lymph/plasma concentration ratios of albumin and "globulin" as well as the lymph flow fractions relative to baseline lymph flow rate were obtained from the model as a function of the referenced P_{mv} over the range 10-40 mm Hg. Results have been obtained for three models of membrane characteristics: (1) uniform pore distribution (~ 100 A), (2) two pore distribution (~ 100 A and ~1000 A), and (3) two pore distribution (~100 A and < 35 A). The calculated results of lymph/plasma ratios and lymph flow fractions were compared with the experimentally measured values from unanesthetized sheep. For the P_{mv} range investigated, the theoretical results from the two pore model (#3) showed the best comparison with the experimental results. Further investigation into additional membrane models including vesicular transport as well as other tracer molecules is being continued. (Supported in part by HL-06285 and HL-50003).

The Effects of Hemorrhagic Hypotension on the Mucosal Microcirculation of the Denervated Intestine. H.G.Bohlen*, P.M.Hutchins, and C.E.Rapela. Bowman Gray School of Medicine, Winston-Salem, N. C. 27103

The vasoconstriction of the mucosal microcirculation in the small intestine of the rat during hemorrhagic hypotension has been thought to be caused by increased sympathetic activity. The increased vascular resistance during prolonged hypotension caused a cessation of blood flow and intravascular pooling in the mucosal microcirculation. In this study, the effects of sympathetic denervation on the mucosal microcirculation were studied during hemorrhagic hypotension. The primary responses of the denervated mucosal microcirculation were a generalized vasodilation and a maintained mucosal blood flow without intravascular pooling. The decrease in vascular resistance in the denervated intestine during hypotension is suggested to be a result of autoregulation in response to the hypotension. The absence of intravascular pooling in the microcirculation was result of the maintained blood flow through the dilated vascular channels.

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CHOLINERGIC SENSITIVITY AND INTRINSIC RATE OF CONTRACTION OF ISOLATED ATRIA FROM TRAINED AND SEDENTARY RATS. C. P. Bolter*, R. L. Hughson*, and J. B. Critz. The University of Western Ontario, London, Ontario.

Male rats were exercised for 15 weeks by swimming for one hour/day, five days/week. After 14 weeks exercised rats had significantly lower body weights and resting heart rates than sedentary controls (411±10 and 475±7 g.; 288±6 and 318±7 beats/min.). The intrinsic rate of contraction of isolated atria from exercised rats was considerably lower than that from sedentary controls (128±3 and 146±5 beats/min.). The isolated atria were examined for their chronotropic response to acetylcholine. There was a marked difference in the sensitivity to acetylcholine of atria from exercised and sedentary rats. Over the range -25% to -80% of the maximal chronotropic response, atria from exercised rats demonstrated about one-fifth the sensitivity of atria from sedentary rats. The lower sensitivity of atria from exercised rats may be related to an increase in the tonic release of acetylcholine by vagal cardioinhibitory fibres. It is concluded that the bradycardia of training probably involves at least two mechanisms; a decrease in the intrinsic rate of the sinoatrial node and an increase in cardiac parasympathetic activity.

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MYOCARDIAL FLOW AND OXYGEN CONSUMPTION IN THE CLOSE CHESTED DOG DURING SHOCK INDUCED BY HEMORRHAGE. Robert F. Bond, Eva S. Manning* and Ramon R. Gonzalez, Jr.* Bowman Gray Sch. of Med. of Wake Forest Univ., Winston-Salem, N.C.

Electromagnetic blood flow sensors and arterial occluding devices were chronically implanted on the anterior descending branch of the left coronary artery; and a specially designed catheter was inserted into the coronary sinus of 15 mongrel dogs. Seven to twenty-one days were allowed for surgical recovery, after which they were anesthetized with a combination of fentanyl, droperidol and sodium pentobarbital, and subjected to a modified Wiggers shock protocol, in which they were bled stepwise to a mean aortic pressure of 35 mmHg. Within one to six hours signs of decompensation were apparent at which time they were rapidly reinfused with the blood remaining in the reservoir. All but one animal died within six hours of reinfusion. Myocardial blood flow (ml/min ·100 grams)(M.F.), arterial blood pressure, volume of blood removed and arterial-coronary sinus O_2 difference $(A\text{-}CS)O_2$ were monitored during five critical stages: I, pre-hemorrhage control; II, immediately upon reaching 35 mmHg; III, after 25% blood uptake from the reservoir; IV, immediately following return of blood volume to normal; V, after the arterial blood pressure had fallen below 50 mmHg. Myocardial oxygen consumption (MO_2) expressed as ml O_2/min·100 grams = MF x $(A\text{-}CS)O_2$, ± 1 SEM.

Stages	M.F.	$(A\text{-}CS)O_2$	MO_2
I	70± 6	7.2± .8	5.2±1.1
II	96±14	8.5±1.0	9.0±2.0
III	72±10	8.7±1.0	6.5±1.9
IV	93± 7	6.2± .7	6.2±0.9
V	85±12	7.3±1.2	5.2±1.5

This data suggests that the myocardium does not become hypoxic during any of the five stages studied. (Supported by NIH grants HE-5392 and -00487 and a grant from the N.C. Heart Association).

EFFECT OF CHRONIC SKELETAL MUSCLE DISUSE UPON CYTOCHROME OXIDASE. Frank W. Booth (intr. by Henry B. Hale). Environmental Systems Branch, USAF School of Aerospace Medicine, Brooks AFB, Texas.

Male albino rats weighing about 350g were placed in either a control (CO) or a casted (CA) group for a 4-week period. Both hind limbs of CA rats were casted, with hip, knee and ankle joints at resting angles. The rats were pair fed. Immediately after cutting the cervical spinal cord, corresponding muscles from CO and CA rats were removed, homogenized, and measured manometrically for cytochrome oxidase activity (μl O_2/min/g). The cytochrome oxidase in the red portion of the rectus femoris was significantly less in CA (309±34) (x±SEM) than in CO (461±57) rats ($P<0.005$). Likewise, cytochrome oxidase activity in the red portion of the gastrocnemius was significantly less in CA (322±32) than in CO (481±32) rats ($P<0.05$). Since there was no significant difference between CO and CA rats in cytochrome oxidase activity in the white portion of the gastrocnemius [CO (184±20); CA (171±11)], these results suggest that the loss of cytochrome oxidase activity within red muscles (composed both of fast-twitch red and fast-twitch white fibers) occurs in fibers staining intensely for mitochondrial enzymes. The soleus cytochrome oxidase activity (494±23) in the CO rats was higher than that in the CA rats (427±29). This difference was not significant ($P<0.1$); possibly because with chronic inactivity the soleus proportionately loses slow-twitch fibers and gains fast-twitch red fibers, the fiber type with the highest cytochrome oxidase activity/g. As a result of chronic skeletal muscle disuse, muscle mass is not only smaller, but the decrease in cytochrome oxidase activity suggests smaller aerobic capacity/g of muscle.

THE EFFECT OF CAFFEINE ON SARCOPLASMIC RETICULUM. Edward P. Bornet*, Mark L. Entman*, Arnold Schwartz and Peter Kellaway. Div. of Myocardial Biol., Dept. of Med., Dept. of Pharmacology and Dept. of Neurophysiol., Baylor College of Medicine and the Fondren-Brown Cardiovascular Research and Training Center, Methodist Hospital, Houston, Texas.

Canine cardiac relaxing system (CRS, fragmented sarcoplasmic reticulum) were isolated by the azide-bicarbonate method. The preparation was tested by dual beam spectrophotometry for initial rate of binding (R_B), peak binding (B), rate of release (R_R) and "ease" of release ($R_{R/B}$). Caffeine (5 mM) and Mg^{++} (10 mM), R_B=53% and B=56% of control values. Caffeine (1 mM) under similar conditions R_B=64%, B=66% of control. In both cases $R_{R/B}$ was unchanged from control. At low $[Mg^{++}]$ (<2 mM), 1 or 5 mM caffeine = R_B=B=80-90% of control again with $R_{R/B}$ unaffected. When caffeine was added to CRS after B was maximal, there was a prompt dose-dependent induced release of Ca^{++}. $R_{R/B}$ of the remaining calcium after induced release was normal. On the basis of these data we conclude that caffeine acts at membrane sites sensitive to $[Mg^{++}]$ to decrease the affinity for calcium. This results in a reduction of R_B and B.

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RELATION OF AORTIC DIASTOLIC PRESSURE DECAY AND PERIPHERAL VASCULAR RESISTANCE. M. J. Bourgeois*, B. K. Gilbert*, and E. H. Wood, Mayo Graduate School of Medicine, Rochester, Minnesota 55901.

Large changes in stroke volume and peripheral arteriolar resistance were induced by varying the heart rate and by infusions of acetylcholine or angiotensin II into the ascending aorta of 6 dogs with heart block and electromagnetic flowmeters chronically implanted around the ascending aorta. Variations in stroke volume, aortic and atrial pressures, and calculated peripheral vascular resistance were monitored continuously for periods of 3 to 6 hours during morphine-pentobarbital anesthesia and without thoracotomy, using flowmeter values and multiple indicator-dilution curves. The characteristics of diastolic pressure decay at heart rates ranging from 60 to 200 beats/min, and during transient periods of asystole induced by stopping electrical pacing were studied especially with reference to the presence of distortions of the decay curves resulting from reflected pressure waves within the arterial tree. It was found that the diastolic phase of aortic pressure pulses recorded over a several-centimeter segment of the thoracic aorta centered about 4 cm cephalad to the dorsal insertion of the diaphragm could be represented by a single exponential in spite of large hemodynamic variations. When the aortic catheter was positioned in this "optimal" segment of the thoracic aorta, and under the conditions of these experiments, variations in peripheral resistance could be estimated from changes in the value of the diastolic time constant. This relationship appears to be of practical value for monitoring changes in peripheral systemic vascular resistance, and beat-to-beat changes in stroke volume from continuously recorded aortic pressure pulses. (Supported in part by research grants NIH HE3532, HE4664, FR-7, and AHA CI 10.)

VENOUS DYNAMICS DURING AIR EMBOLISM. A.A. Bove, J.M. Hallenbeck,* D.H. Elliott,* and P.R. Lynch. Naval Med. Res. Inst., Bethesda, Md. and Temple Univ. Med. School, Phila., Pa.

Changes in Right Ventricular (RVP), Central Venous Pressures (CVP), and flow patterns in the vertebral and azygos venous systems were studied after infusion of increasing volumes of air into a peripheral vein of chloralose-anesthetized dogs. Before embolization, a lung inflation alone caused contrast medium injected in the thoracic vertebral veins to flow cephalad and caudad into cervical and abdominal veins not directly subjected to intrathoracic pressure. After embolization, tachypnea, tachycardia and large respiratory swings in CVP developed. A rise in systolic RVP was seen early after embolization. During this phase, blood flow from the vertebral veins into the thorax was either unchanged or slightly increased. As more air was injected, a greater rise in systolic RVP occurred and CVP and end diastolic RVP also rose. Severe tachypnea (70-90/min) was noted at this time and flow from the vertebral system into the thorax was slowed. Contrast medium flowed toward the cervical and lumbar regions from the thoracic vertebral veins seeking alternate pathways to enter the thoracic cavity. Marked reversal of inferior caval flow was seen during expiration and venous return in the IVC was slowed. Since decompression sickness is always associated with endogenous venous air embolism and spinal cord lesions are common in this disease, it is likely that changes in vertebral venous flow in some way contribute to the spinal lesions of decompression sickness.

The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

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EFFECTS OF LITHIUM PRE-TREATMENT ON ISOPROTERENOL-INDUCED MYOCARDIAL NECROSIS IN THE RAT. P. O. Bramante and K. Opitz.* Dept. of Physiology, Univ. of Illinois Coll. of Medicine, Chicago, Ill. and Dept. of Pharmacology, Univ. of Westphalia, Münster, W. Germany.

Information on the cardiocirculatory actions of lithium salts is scarce and controversial; recent findings suggest that this metal stimulates the heart rather than depressing it, as previously believed. Cardiotoxic effects during prolonged lithium therapy have also been reported.

"Light" (b.w. 212 ± 3 g) and "heavy" (b.w. 315 ± 7 g) albino rats, subdivided in 12 subgroups, were treated with daily injections of LiCl (2.5 mEq/Kg b.w., s.c.) for 3 or 7 days, and with a single dose of isoproterenol (40 mg/Kg b.w., s.c.) administered 24 hrs before sacrifice.

Evaluation of the myocardial necrotic lesions elicited by isoproterenol and analysis of the absolute and relative weight changes of selected organs (heart, adrenals, kidneys) revealed a limited but significant degree of protection afforded by the lithium pre-treatment. This was especially evident in the light group after 7 days. Lithium ion concentrations were determined in blood plasma and in some tissues (heart ventricles, skeletal muscle, diaphragm, adrenal glands, kidney). Regression analysis of the lithium levels in the tissues as a function of plasma values, indicated that a condition of acute lithium poisoning, unaccompanied by microscopic evidence of renal damage, can be elicited in the rat early in the course of a mild and presumably "safe" lithium treatment.

Variations of this experimental model, which mimics frequently encountered clinical situations, could contribute to a better understanding of lithium pharmacology and cardiac physiopathology.

EFFECTS OF SODIUM DEPLETION ON ADRENAL STEROID SECRETION IN THE RABBIT. Berton Braverman,* James O. Davis and Addison A. Taylor.* Dept. of Physiology, Univ. of Mo. School of Medicine, Columbia, Missouri 65201.

The pattern of adrenal steroid secretion was investigated in the male, New Zealand white rabbit; the double isotope derivative method was used for steroid analysis. Adrenal venous plasma was obtained by cannulating the renal vein, placing a clamp on the renal vein between the adrenal vein and the vena cava, and collecting a timed 10 ml sample by retrograde blood flow while blood was simultaneously replaced by infusion of dextran into the femoral vein. In nine normal, surgically stressed, thiopental-anesthetized animals, the adrenal steroid secretion rates were as follows: corticosterone (B), 4981±386 mug/min (mean ± SEM); deoxycorticosterone (DOC), 425±103 mug/min; cortisol (F), 116 ±31 mug/min; aldosterone (A), 2.2±.5 mug/min. Rabbits were sodium depleted by feeding them a sodium-deficient diet plus daily injections of mercuhydrin (.1 cc/kg) for 4 to 6 days. When adrenal steroid secretion in nine sodium-depleted rabbits was compared to the above data for normal rabbits, the results were as follows: B, 2519±480 mug/min ($p<.001$); DOC, 170±39 mug/min ($p<.05$); F, 168±33 mug/min ($p>.2$); A, 25.4±5.4 mug/min ($p<.001$). No change was observed in adrenal plasma flow, arterial blood pressure, or the plasma potassium concentration for the two groups, while a significant decrease in plasma sodium concentration was observed from 138±2 mEq/l in normals to 128±1 mEq/l in sodium-depleted rabbits ($p<.001$). These studies showed that the major secretory product of the rabbit adrenal cortex was corticosterone. Aldosterone secretion increased markedly during sodium depletion. Supported by HE10612 and AM41045.

A SELF-PACED INSTRUCTIONAL APPROACH FOR PHYSIOLOGY

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The problem arose to design a course in physiology and basic biophysical sciences which could be presented to both junior biological engineering students and master's candidates from any physical science curriculum.

The design of the course required:

1. A statement of final objectives in behavioral terms.
2. A detailed list of all of the skills and units of information which would be required to achieve the stated objectives.
3. Construction of a flow sheet describing the logical hierarchy of the information units.
4. Preparation of detailed instructions for each unit as well as study questions and post test materials.
5. Preparation of proctors responsible for contact with students.
6. Design of pretest to determine students' readiness for the material.

The basic texts for the course were the Yearbook Medical Publishers "Physiology" series. These texts were supplemented by texts in physical, organic, and biochemistry. Students were not allowed to proceed to a more advanced unit until the preceding unit was completed with perfection. The course was entirely self-paced, after the method of Keller (J. Applied Behavior Analysis, 1, 79-89, 1968). Lectures were used only as motivational devices. A student evaluation of the course was conducted and analyzed.

The Functional Residual Capacity by (N_2) Gas Dilution: Alinear Increase with Age & A Rapid, Clinically Useful, Graphic Method for Solving The Dilution Equation. Brody, Alfred W., Herrera, Henry R. Snider, Donald J. Campbell, J. Clayton Zarlengo, Marco Knox, William J. Johnson, J. Raymond.

Replotting previously published normal values of Other authors for the Residual Volume (RV) and the Functional Residual Capacity (FRC) against age, suggests a progressively more rapid increase in RV with age after 45 than before. Our findings inthis investigation are corroberative. Our FRC measurements in 101 normal subjects were by closed circuit N_2 dilution using the N_2 meter (performed in conjunction with measurements of the distribution of ventilation; three measures ofdistibution are recorded early during equilibration). The two primary variables measured for calculation of FRC using the Equation forthe Closed Circuit Equilibration Process are: (V) Volume (of oxygen) in the spirometer + dead space prior to rebreathing, and (P) Nitrogen percentage in system after rebreathing. Secondary variables like; (TN) theNitrogen Volume released by the subjects blood and tissues, (G) initial Lung Volume above the FRC, (Δ)Volume of O_2 utilized by the subject and (A) the % N_2 initially in the spirometer are each expressed as a correction for the measured P or V. The corrected Initial Volume and the corrected Equilbrated % N_2 are then interpollated on a V-P graph containing iso-FRC lines for direct readout of the Dilution Equation; $78(FRC+G) + A \cdot V + (TN) = P(FRC+V-\Delta)$. The FRC of normal lung like the inert connective matrix in other tissues, increases rapidly as a % of Total Organ Mass with age beyond 40. The normal FRC predictions are in error over 60; thus fewer patients with emphysem have abnomalities in the FRC than is the traditional view. (Partially supported by USPHS HL 9099 & TO1-HL5506, & Neb TB & Resp Dis Assoc.).

CORTICAL AND PERIPHERAL CONTROL OF PRESYNAPTIC POLARIZATION IN THE CUNEATE NUCLEUS OF CHLORALOSE ANESTHETIZED CAT. M.B. Bromberg* and D. Whitehorn. Dept. Physiol. & Biophys., Univ. of Vermont, Burlington, Vt. 05401

Changes in excitability of terminal branches of cutaneous primary afferents (90-50m/sec) were measured by observing changes in the area of the antidromic response recorded in the ulnar nerve following electrical stimulation in the cuneate nucleus. Stimulation of the ipsilateral superficial radial nerve (SR), the contralateral forepaw (CFP) or the contralateral peri-cruciate cortex (COR) produced terminal depolarization (PAD). SR stimulation produced maximal changes at condition-test intervals of 10-20 msec. In most preparations, PAD declined smoothly over the next 150-200 msec. Nearly maximal PAD was produced by SR volleys containing half the alpha fibers, but PAD continued to grow as more alpha fibers were recruited. COR or CFP stimulation produced less PAD than did SR stimulation and peak PAD occurred at condition-test intervals of 40-60 msec. PAD produced by simultaneous COR and SR volleys did not differ from that produced by SR alone. In some cases, continuous COR stimulation at 30-200 Hz did effect SR produced PAD. Both increases and decreases were observed. Interaction of COR and CFP produced similar results. Cooling or ablation of COR had no consistant influence on SR evoked PAD. The results indicate that, under chloralose, ipsilateral peripheral nerves are the dominant factor in determining presynaptic polarization at the cuneate nucleus. No evidence for a cortically mediated feedback loop was found. (Supported by grant #PHS 09472).

LEFT VENTRICULAR DIAMETER DURING HYPOXIC HYPOXIA. B. G. Brown*, H. L. Stone, and H. H. Erickson. USAF School of Aerospace Medicine, Brooks AFB, Texas.

This study was designed to determine the effects of hypoxic hypoxia on the left ventricular chamber diameter and pressure. In eight mongrel dogs, piezoelectric crystals were implanted across a major internal diameter of the left ventricle through small stab wounds. A solid state pressure cell was implanted in the apex of the left ventricle and a catheter was placed in the left atrium. Hypoxia was produced by breathing the animals on mixtures of 10% and 5% oxygen through permanent tracheostomies for four minutes. Sympathetic activity to the heart was blocked in some experiments using propranolol (1mg/kg). When the animals were exposed to 5% oxygen the left ventricular end diastolic diameter (LVEDD) did not change but the end systolic diameter (LVESD) decreased by an average of 1.1 mm while heart rate and dp/dt both increased. Mean left atrial pressure did not change. Using the diameters squared, an index of ejected and residual fractions was determined. A significant increase in ejected fraction with a decrease in residual fraction was observed. Beta-blockade produced a significant increase in LVEDD and LVESD compared to the controls. The response to 5% oxygen was similar to that found during the control period except from a larger chamber dimension. Heart rate and dp/dt increased but were below control values. Index of ejected and residual fractions did not change. The increase in sympathetic activity to the heart with hypoxic hypoxia increases the pumping efficiency of the heart by decreasing the end systolic volume. A decrease in parasympathetic tone alone can produce an increase in rate but not the increase in pumping ability as typified by the intact animal.
SUPPORTED BY NASA CONTRACT #A94544.

EFFECT OF IONIZING RADIATION ON RENAL FUNCTION. John E. Buerkert*, James Doyle* and Siegmund J. Baum. Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20014

Urinary output is known to increase greatly after the kidney is exposed to more than 1500 rads of ionizing radiation. The present experiments were performed to characterize more clearly renal function postirradiation. The left kidney of 5 dogs with operationally prepared split bladders was exposed to 2000 rads of x-irradiation while the rest of the body was lead shielded. Clearance measurements were used to determine the response to a water load and to antidiuretic hormone (ADH) by the irradiated (IK) and the control kidney (CK), on days 1, 7 and 14 postirradiation. No changes in glomerular filtration rate (GFR) and renal blood flow (RBF) in the two kidneys was observed. In water diuresis urinary excretion was 37 percent greater from the IK ($p < .05$) within 24 hours postirradiation and this difference persisted throughout the time of study. At 24 hours urinary sodium ($U_{Na}V$) and potassium (U_KV) excretion on the irradiated side was increased by 61 percent and 48 percent of control respectively and tended to remain elevated through 14 days. On days 1, 7 and 14 the clearance of free water by the IK increased by 37 percent, 68 percent and 98 percent respectively. When ADH was administered (50 milliunits/kg/hr) urinary excretion fell on both sides but was still higher from the IK on days 1 and 7. $U_{Na}V$ and U_KV were higher on the irradiated side. The clearance of solute from the IK was 48 percent and 20 percent greater at 24 hours and 7 days respectively. It appears that ionizing radiation significantly alters the reabsorption of water and electrolytes by the renal tubule at a time when GFR and RBF are apparently unchanged.

The Effect of Denervation and Immobilization on Muscle Membrane Phospholipids. Wilton Bunch and Jenny Plesums* University of Virginia, Charlottesville, Virginia.

Many membrane changes of denervation are well documented, however, some nerve dependent properties are difficult to seperate from simple disease. The turnover of 32_P phospholipids of denervated and immobilized rat skeletal muscle was studied at 3-30 days. The mean ratios of specific activity of the treated/normal side are:

		Time (Days) 3	6	10	13	20	30
phosphatidyl choline	D/N	1.9	2.4	2.4	3.0	3.2	2.8
	I/N	1.3	2.0	1.9	2.1	2.0	1.7
phosphatidyl ethanolamine	D/N	1.6	2.8	3.1	3.9	3.5	3.1
	I/N	1.2	2.1	2.2	2.3	2.2	2.0
phosphatidyl serine	D/N	1.8	2.5	3.1	3.5	3.3	3.3
	I/N	1.6	1.7	2.0	2.2	2.0	1.7
phosphatidyl inositol	D/N	1.7	2.4	2.7	2.9	3.3	3.7
	I/N	1.3	1.9	2.2	2.1	2.5	1.8

This data suggests direct nerve control of membrane phospholipid metabolism rather than a non-specific effect of disuse.

ROENTGEN VIDEODENSITOMETRIC DETERMINATION OF THE RESIDUAL FRACTION OF THE NORMAL LEFT VENTRICLE AND REGURGITANT FRACTION IN EXPERIMENTAL AORTIC REGURGITATION. J. H. Bursch, P. H. Heintzen, and R. Simon, (intr. by E. H. Wood), Department of Pediatric Cardiology, University of Kiel, Germany, and Department of Physiology, Mayo Graduate School of Medicine, Rochester, Minnesota 55901.

Roentgen contrast medium injected into the left ventricle was used as an indicator of blood flow and volume. Changes in roentgen opacity over the entire ventricle following such injections were used to measure the amount of indicator in the ventricle and to calculate changes in its fractional volume. The reproducibility and accuracy of the method were studied in 30 pigs weighing 17-23 kg. The residual fraction of the left ventricle determined following 96 diastolic injections of small volumes (0.4 ml/kg) of contrast medium into this chamber averaged 0.49, standard deviation, 0.08. The method of Chapman et al. for determination of residual fraction gave lower values (mean, 0.43; standard deviation, 0.07). Calculations of ventricular volumes by density measurements of opacified blood were also used to determine the regurgitant fraction in the presence of aortic regurgitation. The densitometric results were compared with values obtained by an electromagnetic flowmeter encircling the ascending aorta. A good correlation ($r = 0.91$) was found in 48 simultaneous measurements. The standard deviation of the differences between simultaneous values for the regurgitant fraction was 5.2%. Possible errors in this roentgenological method due to the physical characteristics of the contrast medium and superposition of opacified myocardium are discussed. (Supported by research grant from Volkswagen Foundation, Germany.)

THE INFLUENCE OF ETHANOL ON MYOCARDIAL dp/dt/P. John W. Burns*. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas, 78235.

Seven mongrel dogs ranging in weight from 14.3 to 19.3 kg were anesthetized with either 100 mg/kg of alpha chloralose or 30 mg/kg of sodium pentobarbital. Left ventricular pressure (LVP) was measured with a high frequency catheter-tip pressure transducer by way of femoral artery catheterization. The first derivative of LVP (dp/dt) was obtained by active electronic differentiation. Aortic root pressure and ECG were also monitored. Control data were collected, and then 2 gm/kg of 95% ethanol in a 40% solution were administered intraperitoneally. Data were again collected at one and two hr. after ethanol administration, along with arterial blood samples for alcohol determination. Control peak dp/dt/P and maximum (max.) dp/dt/P (the linear extrapolation of dp/dt/P vs. P to zero P) were 26.7 ± 2.3 (SEM) and 56.4 ± 9.5 $sec.^{-1}$, respectively. At one hr. after ethanol administration when blood alcohol conc. was 192.9 ± 12.6 mg %, no significant change was seen in peak dp/dt/P or max. dp/dt/P over control. Peak dp/dt/P averaged 29.7 ± 1.7 and max. dp/dt/P averaged 59.0 ± 7.8 $sec.^{-1}$. However, at two hr. after ethanol when blood alcohol conc. was 153.2 ± 11.9 mg %, a significant ($P < .005$) increase of peak dp/dt/P was seen over control. At this time, peak dp/dt/P averaged 36.4 ± 1.7 $sec.^{-1}$; and although max. dp/dt/P averaged 70.6 ± 8.7 $sec.^{-1}$, an increase over the control value, it was not significant. At one hr. after ethanol, heart rate (HR) was significantly increased ($P < .01$) from a control level of 85.9 ± 3.8 to 137.9 ± 7.1 b/m. HR further increased ($P < .025$) to 155.2 ± 6.7 b/m at 2 hr. after ethanol administration. The significant increase in HR observed here indicates an increased sympathetic tone and could explain the augmented peak dp/dt/P at 2 hr. after ethanol. The findings of this study do not support recent reports of cardiac depression due to ethanol. (Paper sponsored by R.R. Burton).

CARDIOVASCULAR RESPONSES OF MINIATURE SWINE TO $+G_Z$ ACCELERATION. R. R. Burton. Environmental Sciences Division, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

Five conscious adult miniature swine, 2 males and 3 females, were exposed to +2 to +8 G_Z accelerations of 15-sec. duration. Arterial and venous pressures, heart rates, and electrocardiograms were determined prior to, during, and following increased accelerations. Arterial pressures at eye level were inversely and rectilinearly correlated with increasing $+G_Z$ and were significantly increased with intrathoracic pressure changes associated with a voluntary forced exhalation ("grunt") --an arterial vascular response not unlike that found in man resulting from the "Valsalva" or "M-1" effort. Arterial pressure increases also occurred during G--apparently, a response to the baroceptor reflex. Pulse pressures were inversely correlated also with increasing $+G_Z$. Heart rate, however, was significantly increased during G and reached a peak of 230 beats/min. A standard human bladder type inflated G suit significantly increased arterial pressures although remaining a function of increasing $+G_Z$. Pulse pressures remained constant during increasing G, yet heart rates were unaffected by the inflated G suit. Following acceleration exposures, systolic arterial and pulse pressure "overshoots" occurred, the magnitudes of which were independent of prior G intensity yet their occurrences were significantly delayed following higher acceleration levels. Consequently, cardiovascular recovery duration was directly correlated with the level of prior G intensity. G suit inflation during acceleration had no significant effect upon physiological recovery.

MODIFICATION OF REPRODUCTIVE ORGAN ATROPHY IN BLINDED MALE HAMSTERS TREATED WITH HUMAN CHORIONIC GONADOTROPHIN (HCG), LUTEINIZING HORMONE (LH), AND CLOMIPHENE. Francis M. Bush, Hugo R. Seibel* and William L. Poteat.* Dept. of Anatomy, Med. Col. of Va., Va. Commonwealth Univ., Richmond, Va. 23219.

The effects of HCG, exogenous LH, and clomiphene citrate on the reproductive and endocrine organs of 120-day-old normal hamsters and of hamsters the same age subjected to bilateral blinding, pinealectomy, and both blinding and pinealectomy, were studied. Five I.U. of HCG/hamster, injected i.p. daily between 9:00 and 11:00 AM for six weeks, nullified the atrophic effect of blinding upon the reproductive organs. The weights of reproductive organs in hamsters treated with HCG were similar, but blinded hamsters treated with HCG had significantly larger reproductive organ weights than found in the blinded hamsters receiving saline. Significantly larger reproductive organ weights were found in blinded hamsters given 1.0 mg LH/day i.p. for seven days after 24 days of blinding than in blinded hamsters receiving saline. LH did not completely prevent the atrophy when given 0.5 mg/day for 25 days after 42 days of blinding. Daily s.c. injections of 0.1 mg clomiphene/kg b.w. for six weeks concomitant with blinding partly prevented the atrophy. The results with HCG suggest that the putative pineal antigonadotrophic substance does not inhibit the stimulatory effect of exogenous gonadotrophin on the reproductive organs. The findings with LH show that the atrophic effect is delayed if LH is given soon after blinding. Clomiphene appears to be gonadotrophic in blinded hamsters, and probably exerts its effects via the hypothalamus by impinging on brain receptors that control gonadotrophin secretion.

SURVIVAL TIME OF HYPOXIC DOGS GIVEN EPINEPHRINE OR PROPRANOLOL. S. M. Cain. Univ. of Alabama Medical Center, Birmingham, Alabama.

Sympathoadrenal stimulation by severe hypoxia increases energy utilization because of the calorigenic action of catecholamines. With prolonged hypoxia severe enough to depress $\dot{V}_{O_2}$, calorigenesis enhanced by epinephrine IV or inhibited by a β-blocking agent, propranolol, should alter survival time by the difference in energy deficit incurred with limited aerobic metabolism. This hypothesis was tested in anesthetized paralyzed dogs ventilated at a constant rate with 9% O_2 in N_2. Survival time was taken as the time in hypoxia at which mean systemic arterial pressure decreased below 70 mm Hg. Comparisons were made of survival time, net O_2 deficit (NOD) and excess lactate (XL) in three groups of dogs: (A) no treatment, (B) single IV dose of epinephrine, 1 μg/kg, (C) propranolol IV, 1 mg/kg/hr. Survival time was decreased significantly ($P < .001$) in group B, 40.9 min vs. 93.3 min (Gp A) and 111.4 min (Gp C), the latter groups not differing significantly. NOD was significantly different between all 3 groups: 146 ml/kg (Gp A), 72 ml/kg (Gp B) and 236 ml/kg (Gp C). XL at end of hypoxia was not different between Gp A and Gp C, 8.4 mM vs 10.8 mM, nor between Gp A and Gp B which averaged 6.9 mM but Gp B was marginally less ($P < .05$) than Gp C. The best correlate to survival time was the rate of XL accumulation in that dogs of all three groups fitted a common regression line having a negative slope and correlation coefficient of -0.77. Epinephrine was detrimental to survival of anesthetized dogs in hypoxia because of the increased energy demand reflected as a higher rate of anaerobic metabolism. (Supported by Nat. Heart and Lung Inst. Grant HE-14693.)

COMPRESSION OF AIRWAYS DURING EXPERIMENTAL BREATH-HOLD DIVING IN ANIMALS. Enrico M. Camporesi* and Albert B. Craig, Jr. Dept. of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, New York 14642.

Anesthetized rats and rabbits were placed in a pressure chamber and subjected to different pressures to simulate breath-hold diving. As the ambient pressure increased, the pressure in the occluded trachea initially increased, indicating gas volume compression during the first part of the descent. At a definite chamber pressure the tracheal pressure showed no increase despite the additional increase of the ambient pressure. The system appeared to change from a collapsible to a relatively rigid condition. With such pressure differences the animals developed a "lung squeeze" with pulmonary congestion, rupture of small pulmonary vessels and extravasation of blood into alveoli and airways. As predicted by Boyle's Law, the external pressure at which the system becomes relatively rigid is directly related to the initial gas volume. However, a rapid increase in pressure simulating a fast descent causes the respiratory system to become relatively rigid at a lower pressure than the slow application of pressure. Blocking the major portion of the venous return by tying off the jugular veins and inflating a balloon in the inferior vena cava causes the system to become rigid at a pressure which is independent of the rate of descent. These observations support the hypothesis that a shift of blood from the extra- to the intrathoracid vessels is an important factor in determining the depth limit of breath hold diving. (Supported in part by USPHS, NIH Grant HL09676).

SODIUM EXCRETION AND INTRARENAL DISTRIBUTION OF BLOOD FLOW DURING NOREPINEPHRINE INFUSION AND REDUCED PERFUSION PRESSURE. J.R. Cant*, J.M. Cunningham*, M.D. Johnson*, and H.V. Sparks, University of Michigan, Ann Arbor, Michigan 48104.

Intrarenal distribution of blood flow was measured (^{85}Kr clearance) in two states of reduced sodium excretion (Na^+ex) to see if redistribution from outer cortical (OC) to juxtamedullary and outer medullary (JM+OM) regions could explain the lowered Na^+ex. A flow probe and small adjustable clamp were placed on the left renal artery in 13 anesthetized dogs; renal artery catheters were inserted for ia infusion and monitoring perfusion pressure (PP). Creatinine in saline was infused iv at 2-3ml/min after a loading dose in 150 ml. After a 1 hr control period, either PP was lowered to about 70mmHg or norepinephrine (NE) was infused until flow fell by 20-40%; the other maneuver followed a second control period. During each hour, ^{85}Kr washout and renal clearances were measured. Autoradiographs were prepared. GFR was reduced by both NE (26%) and↓PP (15%) but Na^+ex fell more with ↓PP (75%) than with NE (38%). (p values for the paired differences between maneuvers are .62 for GFR and .03 for Na^+ex.) NE increased flow in JM+OM regions by 27% (89 to 102 ml/min/100g) and also reduced flow in patches of cortex from the OC rate (502 ml/min/100g) to a rate comparable to that of the JM+OM area; thus a larger fraction of total flow perfused the JM+OM region. ↓PP increased JM+OM flow 44% without a change in OC flow. (p values for the change of JM+OM flow during NE compared with ↓PP is .47.) Therefore the much greater reduction of Na^+ex with ↓PP cannot be explained by a shift of flow from OC to JM+OM areas (or a greater fall in GFR). It is unlikely that the increased flow rate *per se* in the JM+OM region accounts for the reduced Na^+ex since this reduction is 2X greater with ↓PP than with NE whereas the change in flow is not statistically different ($P=.47$). USPHS grants GM-00353 and HE-13538.

INNERVATION OF APLYSIA GILL MUSCLE FIBERS BY TWO IDENTIFIED EXCITATORY MOTOR NEURONS USING DIFFERENT CHEMICAL TRANSMITTERS

T. Carew*, J.H. Schwartz* and E.R. Kandel. N.Y.U. Med. Sch., N.Y.

The gill-withdrawal reflex of Aplysia is mediated by several identified motor neurons located in the abdominal ganglion. Two of these, L7 and LDG, contribute substantially to the total reflex response. These two motor neurons directly innervate gill musculature. Action potentials initiated by injection of depolarizing current pulses into LDG and L7 produce excitatory junctional potentials (EJPs) which can be recorded intracellularly in individual gill muscle fibers. The latencies of these EJPs are unaltered in high Ca^{++} solution. EJPs from both L7 and LDG can be recorded from the same muscle fibers in the efferent vein of the gill. This indicates that both neurons innervate the same muscle fiber or, alternatively, different fibers which are electrically coupled. EJPs from both LDG and L7 show marked facilitation. Also, gill contractions produced by either neuron are blocked reversibly by high Mg^{++} solutions. We therefore conclude that the junctional actions of both motor cells are mediated by chemical transmission. We have found, however, that the transmitters of the two motor neurons are different. Extracts of cell bodies of both cells were assayed for choline acetyltransferase; in independent experiments, ^{3}H-choline was injected intracellularly into LDG and L7, and the conversion of the labeled choline to acetylcholine was determined. Both of these tests indicate that LDG is cholinergic and that L7 is not. This distinction is further supported by the finding that gill contractions produced by direct stimulation of LDG are blocked selectively by the excitatory cholinergic blocking agent, hexamethonium, while gill contractions from L7 are unaffected. Thus, Aplysia seems to use at least two different transmitter compounds for neurally mediated excitation of gill musculature.

PHASIC CORONARY BLOOD FLOW IN THE INTRAVENTRICULAR SEPTAL ARTERY IN DOGS.

Thomas E. Carew* and James W. Covell, Sch. of Med., UCSD, La Jolla, Cal.

Although the factors influencing flow velocity in epicardial coronary arteries have been extensively investigated, there is scant information on flow in intramyocardial coronary arteries. Accordingly, in the present study in 7 open chest dogs, flow was measured at the proximal portion of the intraventricular septal artery (ISA) and left circumflex artery (LCC) with electromagnetic flow probes. Right ventricular pressure (RVP) and left ventricular pressure (LVP) were selectively adjusted by partially occluding the pulmonary artery or aorta. Average resting ISA flow in 4 dogs was 19.7 ml/min (range 14-28 ml/min) compared to an average LCC flow of 41.4 ml/min (range 24-61 ml/min). Diastolic stroke flow in the ISA averaged .11$\pm$.02 ml and was 79% of total stroke flow. Diastolic stroke flow in the LCC was .21$\pm$.05 ml (75% of total stroke flow). Peak diastolic flow averaged 38$\pm$5 ml/min in the ISA and 79$\pm$21 ml/min in the LCC. The systolic decrease in ISA flow preceded the systolic decrease in LCC flow by 10-20 msec. However, this earlier decrease in ISA flow was abolished by ventricular pacing indicating that this timing relationship reflects earlier activation of the intraventricular septum. When RVP was increased from an average control level of 23 to 51 mmHg, LVP fell an average of 20 mmHg and peak ISA flow rate increased by 11% while LCC diastolic flow rate was unchanged or decreased. When LVP was increased 25 mmHg, peak ISA diastolic flow increased 9% and peak LCC diastolic flow increased 12%; ISA diastolic stroke flow increased 21% compared to 24% in the LCC. With this increase in LVP systolic stroke flow increased 24% in the ISA and 42% in the LCC. It is concluded that phasic ISA flow is similar to phasic flow in the large epicardial vessels and that it is influenced by alterations in both RVP and LVP. Moreover, the phasic ISA flow pattern is influenced by the timing of septal activation.

A DIFFERENTIAL EFFECT OF ETHINYL ESTRADIOL UPON PLASMA FSH AND LH RELATING TO TIME OF ADMINISTRATION IN THE MENSTRUAL CYCLE. C.M.Cargille, J.L.Vaitukaitis*, J.A.Bermudez*, and G.T.Ross*. Reproduction Research Branch, National Institutes of Health, Bethesda, Maryland, 20014.

The hypothesis that orally administered exogenous estrogen might exert differing effects upon circulating levels of plasma FSH and LH depending upon the time of administration during the menstrual cycle was investigated. Ethinyl estradiol (EE), 100µg day, was administered to 7 normal volunteers from day 9 to 18 of the cycle and plasma FSH and LH concentrations were compared to those from 7 matched controls. These results were also contrasted to those observed when the same dose of EE was administered from cycle day 0 to 7 (Vaitukaitis,J.L. et al, J.Clin. Endocr. 32:503, 1971). FSH and LH were measured by double antibody radioimmunoassays. Data was analyzed by aligning the cycles in each group on the first day of menses (day 1) and determining mean FSH and LH values on each day. During EE from days 9 to 18 levels of FSH underwent a transitory elevation at a time when FSH in the controls was declining. Subsequently, a proportionately greater decline than that seen in the luteal phase of the controls occurred and reached its nadir 6 days prior to the luteal nadir in the control group. Cessation of treatment was followed by a prominent elevation of FSH not seen in the untreated women. A tall but widened peak of LH occurred during EE treatment and a sustained elevation from day 10 to 22 was apparent. In contrast to women receiving EE on cycle day 9-18, mean levels of both FSH and LH were suppressed, no peaks occurred during therapy, and no significant rebound followed cessation of EE in women treated with EE from cycle day 0 to 7. These results provide evidence that the effect of orally administered estrogen upon plasma gonadotropins varies with the time of administration in the menstrual cycle.

RADIOTELEMETRY OF GASTRIC ANTRAL AND DUODENAL CONTRACTILE ACTIVITY IN THE UNANESTHETIZED DOG. G. M. Carlson, C. C. Hug, Jr. and P. Bass (intr. by S. Y. Botelho). Dept. of Pharmacology, The Univ. of Michigan School of Medicine, Ann Arbor, Michigan.

Contractile activity patterns of the canine gastric antrum and duodenum were monitored continuously during 24 hr periods. Contractile activity was measured with extraluminal strain gage force transducers. Signals from the force transducers were transmitted from a chronically implanted four channel PAM-FM radiotelemetry unit. Studies were performed with the dogs in their "home cage" holding quarters, and recording equipment was located outside the animal room. The only human contact with the animals was for feeding. Interdigestive and digestive contractile patterns could be readily distinguished. The interdigestive patterns were cyclical in nature, and consisted of sequentially occurring periods of basal, preburst, and burst activity patterns (Carlson et al., J. Pharmacol. Exp. Ther. 172: 367, 1970). The average duration of each cycle was 1 hr, 41 min. The interdigestive activity patterns occurred simultaneously in the antrum and duodenum. Digestive activity began immediately after the feeding of a standard laboratory diet, and continued for periods of 14 to 19 hr postprandial. Digestive activity ended with a burst activity pattern, and was followed by the characteristic interdigestive pattern sequence. Contractile activity patterns recorded from the undisturbed dog by radiotelemetry were similar to those previously recorded with hard wire cables from dogs in a routine laboratory environment. It is apparent that the radiotelemetry units would be useful in studies requiring prolonged, uninterrupted recording sessions and in studies utilizing animals not adaptable to regular laboratory procedures. (Supported by a grant from the AMA-ERF.)

EFFECTS OF HYPOXIC HYPOXIA AND CARBON MONOXIDE HYPOXIA ON CORONARY CIRCULATION. Susan Carlson and Ray Gilbert (intr. by B. Bromberger-Barnea). The Johns Hopkins University, Baltimore, Maryland 21205.

Experiments were carried out to compare the effects of hypoxic hypoxia and carbon monoxide (CO) hypoxia on oxygen extraction in the coronary circulation. In one series of dogs coronary sinus P_{O_2} and oxygen content were higher during CO hypoxia than during hypoxic hypoxia (compared at equivalent arterial oxygen contents). For example, at an arterial oxygen content of 12 vol%, coronary sinus P_{O_2} was 2mmHg higher and coronary sinus oxygen content 2 vol% higher during CO hypoxia than during hypoxic hypoxia. In contrast this difference in P_{O_2} and oxygen content, comparing hypoxic hypoxia and CO hypoxia, was not found in mixed venous blood of the systemic circulation. To determine if the higher coronary sinus oxygen content during CO hypoxia was the result of a higher coronary blood flow or lower cardiac oxygen consumption, anterior descending coronary artery blood flow was measured and oxygen consumption calculated in a second series of dogs. We found that during CO hypoxia flow was higher (30% at an arterial oxygen content of 9-10 vol%) than during hypoxic hypoxia, while oxygen consumption was not different in the two states. We conclude that while flow is increased in both states, the heart maintains its oxygen consumption during CO hypoxia by a greater increased flow, while during hypoxic hypoxia oxygen consumption is maintained primarily by an increased oxygen extraction. The mechanism for this phenomenon is still under investigation.

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URINARY KALLIKREIN EXCRETION IN DOCA TREATED DOGS. O.A. Carretero, M. Marin-Grez*, and N.B. Oza*, Department of Medicine, Henry Ford Hospital, Detroit, Michigan.

The explanation for the renal "escape" from the sodium retaining effects of the mineralocorticoids is a matter of speculation. The presence of a natriuretic hormone has been suggested. Since we have observed a relationship between urinary kallikrein (UK) and natriuresis in sodium loaded rats and dogs, it seemed of interest to study this enzyme in DOCA treated dogs. Seven dogs were placed in metabolic cages and received a constant sodium diet (5.5 mEq/Kg/day). After a habituation period of 72 hours, urine was collected for two 24 hour periods. DOCA (25 mg/day) was then given for 5 days. Urine was collected daily during this period and for two additional 24 hour periods. The UK increased from 251.9 ± 34.8 (Mean ± SEM) to 639.8 ± 110.1 µg/day ($P < .01$) by the third day of treatment. The UK remained elevated even 2 days after the DOCA was discontinued. The sodium excretion decreased significantly on the first day of treatment, returning to the previous value thereafter. The urinary volume tended to increase slightly, though not enough to account for the increased kallikrein excretion. Protein excretion remained unchanged throughout the experiment. The enhanced UK during the "escape" suggests that the kallikrein system could be involved in the regulation of sodium metabolism by acting as a natriuretic hormone or perhaps by regulating the renal blood flow. (Supported by the Michigan Kidney Foundation)

STUDIES ON RESTING METABOLIC RATE (RMR), NONSHIVERING THERMOGENESIS (NST) THERMONEUTRAL ZONE (TNZ) AND SURVIVAL TO TEMPERATURE EXTREMES IN COLD AND HEAT-ACCLIMATED MACACA MULATTA.

R.R.J. Chaffee and J.R. Allen* Dept. of Ergonomics, U. Cal., Santa Barbara 93106.

Adult male M. mulatta were acclimated for 14 to 40 months at three different environmental temperatures, 25C (Controls), 5C (Cold), and 35C (heat-acclimated). RMRs were measured at -6, 2, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, and 40C. The TNZ was the same for all (between 10 and 31C). The mean RMR at the TNZ of the heat-acclimated animals were 672 $ml O_2/kg^{0.7}/hr$, of controls, 936, and of cold-acclimated animals, 1380. The norepinephrine response in the TNZ was greater in cold-acclimated than in control monkeys and completely absent in the heat-acclimated monkeys. When exposed to 40C, the heat-acclimated animals and controls did not develop symptoms of heat stroke, whereas the cold-acclimated animals did, and had to be removed. Some of the latter died as a consequence of the heat exposure. When exposed to -6C the heat-acclimated animals and controls showed a continuous decline in rectal temperature (RT) and had to be removed after three or four hours to prevent body temperature from reaching lethal levels (ca 30C). The rate of drop in RT of the controls was less than that of the heat-acclimated animals. The cold-acclimated animals at -6C were able to maintain body temperature at 37C. Thus the data clearly indicate that there are fundamental differences in the thermo-regulatory abilities of control, cold and heat-acclimated monkeys and support the concept that cold increases the nonshivering thermogenic potential, whereas heat acclimation depresses it. It also shows that cold acclimation increases cold resistance but lowers heat tolerance, whereas the converse is true in heat-acclimated primates.

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EFFECT OF FERTILIZATION ON THE Na^+ AND K^+ CONTENT, AND Na^+ FLUX IN THE SEA URCHIN EGG. E.L. Chambers, University of Miami School of Medicine, Miami, Fla.

Following insemination of Lytechinus variegatus eggs at 22.4°C a sharp increase in Na^+ content occurs amounting, on the average, after correcting for wash-out during the analytic procedure, to 4.8 µm Na/ml eggs or 21.5% of the initial Na^+ content in the first 5 minutes, with return to the unfertilized level by 13 minutes. The Na^+ content of the unfertilized eggs immediately prior to insemination amounted to 22.1 µm Na^+/ml eggs; in the unfertilized eggs the Na^+ content increases exceedingly slowly and linearly at a rate of 2 to 4% of the initial content per hour. In contrast to the unfertilized eggs where Na^+ influx amounts to 0.6 pmoles cm^{-2} sec^{-1}, and efflux to 0.4 pmoles cm^{-2} sec^{-1}, in the fertilized eggs during the first 5 minutes after insemination Na^+ influx increases 90-fold, and efflux 60-fold. During the interval 15 to 60 minutes after insemination Na^+ influx balances Na^+ efflux at 23 pmoles cm^{-2} sec^{-1}. In the eggs of Strongylocentrotus purpuratus at 15°C, a 2.7% decrease of the K^+ content (initially 172 µm K/ml eggs) amounting to a loss of 4.7 µm K^+/ml eggs occurs during the first 8 minutes after insemination, followed by a return of the K^+ content to the unfertilized level by 25 minutes after insemination. The K^+ content of the unfertilized eggs remains essentially constant. The data indicate that fertilization is followed by (1) an increase in permeability of the egg to Na^+ and K^+ and (2) activation of $Na^+ + K^+$ pump.

EFFECTS OF SIMULATED OBSTRUCTIVE AIRWAY DISEASE IN DOGS ON REGIONAL VENTILATION AND PERFUSION. W.J. Chen*, D.G. Hess*, and K.C. Weber. ALFORD, NIOSH, USPHS, DHEW, and Department of Physiology and Biophysics, West Virginia University Medical Center, Morgantown, W.V. 26506.

Dogs breathing spontaneously and in the supine position were anesthetized with Pentobarbitol (35 mg/kg). The right and left lungs were separated by means of a modified endobronchial catheter. An apparatus was constructed to allow either lung to breathe independently from the air or a spirometer. Three different resistances (1,2 & 3 cm H_2O/L/min) were added in series with the expiratory airway of the right lung. With each resistance, regional ventilation and perfusion were studied using a scintillation camera and $Xenon^{133}$. In 8 complete experiments on 6 dogs the washout half times, at the highest resistance level, increased from 12.9 $\pm$ 1.3 to 24.0 $\pm$ 1.5 sec ($P<0.05$) and from 12.9 $\pm$ 1.9 to 15.8 $\pm$ 0.7 sec for the right and left lung, respectively. The ventilation index ($\dot{V}\%/V\%$) decreased in the right lung from 0.96 $\pm$ 0.04 to 0.85 $\pm$ 0.03 ($P < 0.05$) and increased in the left lung from 1.05 $\pm$ 0.04 to 1.25 $\pm$ 0.05 ($P < 0.05$). The perfusion index ($\dot{Q}\%/V\%$) decreased from 0.99 $\pm$ 0.02 to 0.81 $\pm$ 0.05 ($P < 0.05$) in the right lung and increased from 1.03 $\pm$ 0.03 to 1.36 $\pm$ 0.09 ($P < 0.05$) in the left lung. The ventilation perfusion ratio ($\dot{V}/\dot{Q}$) increased significantly in the right lung and remained constant in the unobstructed (left) lung. In addition, arterial and venous O_2 tension and cardiac output decreased significantly while CO_2 tension, pH and respiratory rate remained unchanged at the highest resistance level. Under the same conditions, the right and left wedge pressure and esophageal pressure were increased. These experiments indicate that the respiratory and cardiovascular regulation in obstructive airway disease may attempt to maintain a constant $\dot{V}/\dot{Q}$ in the normal areas in spite of changing ratios in the obstructed areas. Supported in part by a NASA Grant NGR 47-001-048.

EVIDENCE FOR PARTICIPATION OF ATP IN ACTIVE HYPEREMIA OF HEART DURING STELLATE GANGLION STIMULATION. W.T. Chen*, C.C. Chou, J.B. Scott, and F.J. Haddy. Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

The role of adenine nucleotides in local regulation of blood flow is controversial. Forrester and Lind found increased ATP in venous plasma from activated skeletal muscle; but Dobson et. al. did not. We have reported recently increased ATP & AMP concentrations in venous plasma during active hyperemia (AH) of canine skeletal muscle (Fed. Proc. 31: 379, 1972). The present study examines the role of ATP & AMP in AH and reactive (RH) hyperemia of the canine heart by using our recently developed enzymic-radiometric assay technique. The coronary sinus (CS) was cannulated in naturally perfused hearts. CS blood was analyzed for plasma ATP & AMP before and during stellate ganglion stimulation (AH) (30 V, 1.6 ms, 12 cps) and after 10-20 seconds left common coronary arterial occlusion.

	Control	AH (N=14)	Control	RH (N=11)
H.R. beats/min	134	203*	-	-
CS flow ml/min	67	138*	62	144*
CVR mmHg/ml/min	1.38	1.02*	1.38	0.53*
CS ATP ng/ml plasma	108	267*	72	87
CS AMP ng/ml plasma	23	68	10	10

(CVR = coronary vascular resistance. *$p<0.05$ compared to control.) Thus, ATP concentration in CS significantly rose during AH but not during RH. In three other dogs, left common coronary artery was cannulated and perfused at constant flow. ATP was infused intra-arterially to achieve a plasma concentration comparable to that seen during AH. At this infusion rate ATP produced a significant fall in CVR. Thus, the present study indicates that ATP may participate in AH of the heart but not in RH. The increased ATP might come from the myocardium, nerve or blood.

CARDIAC OUTPUT AND BODY FLUID CHANGES IN RENAL HYPERTENSION AFTER CARDIAC DENERVATION. J.C. Chessar*, C.M. Ferrario and J.W. McCubbin. Research Division, Cleveland Clinic, Cleveland, Ohio 44106.

The initial increase in cardiac output (CO) that preceeds onset of experimental renal hypertension might be due to increased myocardial contractility resulting from enhanced sympathetic discharge; if so, it would be prevented by removal of the sympathetic chain from T1 to T7. In conjunction with cardiac denervation, flowmeters were implanted around the ascending aorta and measurements of flow and pressure were made daily. Within a week after wrapping one kidney in cellophane, both stroke volume and CO rose, as in dogs not subjected to cardiac denervation. Hypertension appeared only when the normal kidney was removed and was due to further increase in CO and lack of any further compensatory fall in PR. With time, increase in PR became entirely accountable for rise in MAP while CO fell to control levels. An unexpected finding was that serial measurements of plasma (Evan's blue) and extracellular fluid (82Br) volumes showed startling changes after wrapping one kidney in cellophane. Plasma volume increased 30 to 50% during the early rise in cardiac output, hematocrit fell, and there was a significant fall in volume of the interstitial fluid. After contralateral nephrectomy, plasma volume began to decrease as MAP and PR rose and interstitial fluid volume returned to control levels. The experiments indicate that though removal of the thoracic sympathetic outflow to the heart and adjacent viscera does not modify the hemodynamic changes that accompany onset of renal hypertension, it permits a presumably humoral substance of renal origin to exert a dramatic effect on body fluid volumes. (Supported in part by grant HL-6835 from the NHLI and the American Heart Association.)

TRANSPORT OF LITHIUM BY FROG SKIN. Dante Chiarandini* and Oscar A. Candia. Dept. of Ophthal. Mount Sinai School of Medicine, New York.

Isolated frog skin bathed with Li-Ringer (Na-free) on the outside and Na-Ringer on the inside, can maintain a normal potential difference (PD) and short-circuit-current (SCC) for more than 6 hours. The SCC corresponded to the unidirectional out→in Li flux. The in→out Na flux was 5% of the SCC. Ouabain 10^{-5} M depressed and amiloride 10^{-5} M abolished the Li transport (measured as SCC), while oxytocin 0.1 U/ml stimulated it. When the inside of the skin was bathed with Li-Ringer, PD and SCC fell to zero within 2 hours. The oxygen consumption of skin slices bathed in Li-Ringer was 26% lower than controls bathed in Na-Ringer.

The isolated frog skin shows electrical rectification when bathed in Na_2SO_4-Ringer. This rectification has been correlated with the active transport of Na, (Candia. 1970. Biophys. J. 10: 323.) In skin transporting Li (Li_2SO_4 outside, Na_2SO_4 inside), rectification characteristics are similar to those previously described for Na transport. When the inner face of the skin is bathed with Li-Ringer, rectification, PD and SCC decline in a parallel fashion.

It is concluded that: 1) Li can be transported when Na is present at the inner face. 2) Amiloride, ouabain and oxytocin affect Li and Na transport in a similar manner. 3) Li transport, like Na transport, is associated with rectification. 4) Active transport of Na and Li seem to depend on two different but associated processes: one taking place at the external barrier (where rectification occurs), as shown by the effect of amiloride; and the other at an inner site related to energy requirements and affected by ouabain and Li.

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PHYSICAL TRAINING AND INTERSTRESS ADAPTATION TO COLD. A. K. Chin* and R. Seaman*. (intr. by - E. Evonuk). Applied Physiology Laboratory, York University, Toronto, Canada, and Defence and Civil Institute of Environmental Medicine, Toronto, Canada.

Male adult rats were randomly divided into a non-exercised environmental control, a non-exercised cold control and three exercised groups. The light, moderate and heavy exercise programmes were administered for three weeks. Following the exercise programmes, the non-exercised cold control and the three exercised groups were administered a cold-tolerance test at -20°C for three hours. The colonic temperature of all three exercised groups dropped only slightly; whereas the colonic temperature of the non-exercised cold control group decreased very markedly ($P < 0.01$). All groups exposed to -20°C showed significant increases in plasma norepinephrine, epinephrine, total catecholamine and corticosterone levels when compared to the non-exercised environmental control group ($P < 0.01$). However when the exercised groups were compared to the non-exercised cold control group, the exercised animals exhibited concentrations that were 23.3 to 31.4% lower in plasma norepinephrine, 39.5 to 52.4% lower in epinephrine, 29.0 to 36.1% lower in total catecholamines and 25.6 to 32.2% lower in corticosterone ($P < 0.01$). This decreased sympathoadrenal activity may be attributable to a less severe stressing effect of cold in the exercised animals. It is possible that the physical activity may have stimulated a nonspecific response to exercise stress which increased the metabolic capacity of the animal sufficiently to delay hypothermia. Thus it appears that physical training may produce an interstress adaptation to cold.

BIORHYTHM ALTERATIONS IN HEAT STRESSED RHESUS MONKEYS. B. J. Chou* and E. L. Besch. Dept. Physiol. Sci., Col. Vet. Med., Kansas State Univ., Manhattan, Ks. 66506.

Urine output and deep body temperature rhythms were measured in 6 adult, male, Rhesus monkeys (av. body wt. 7.7 ± 0.9 kg) housed in a controlled environment room. These animals were exposed (2 per group) to one photoperiod (12L:12D) but two thermal conditions -- a control (21.5°C) followed by an experimental (36.5°C). Food and water were available *ad libitum*. The heat stress resulted in 100% mortality in 11 ± 2 days. Relative urine output of 18.1 ± 6.1% and 13.0 ± 5.8% (N.S.) were observed during the dark period under control and heat stress temperatures respectively. In the 2-day period immediately preceding death, compared to control values, there was a significant (<0.001) increase in relative urine output to 53.7 ± 1.3% during the 12-hours of dark. In the 2-hour period preceding death the mean body temperature increased from 40.2 ± 0.8°C to 43.5 ± 0.4°C (<0.001). Analyses of these data with appropriate mathematical transformation techniques (Fourier) revealed changes in both shape and amplitude of the urine output and body temperature rhythms not unlike those previously reported for heat stressed rats (Physiologist 14:122, 1971). Thus, it appears that physiological deterioration of heat stressed monkeys may be detected from analyses of urine output and body temperature rhythms.

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LOCAL EFFECTS OF G-I HORMONES ON DUODENAL, JEJUNAL, SPLEEN, SKIN AND MUSCLE VASCULAR RESISTANCE. C.C. Chou, C.P. Hsieh*, and J.M. Dabney. Depts. of Physiol. and Med., Mich. State Univ., E. Lansing, Michigan

Effects of local intra-arterial infusions of secretin, cholecystokinin (CCK) and pentagastrin on vascular resistance (R) of pump-perfused duodenal segment, jejunal segment, spleen, forelimb and naturally perfused forelimb were studied in anesthetized dogs. In naturally perfused forelimb, blood flow from the brachial and cephalic veins (an index of muscle and skin flow respectively) were measured. The weight of the spleen was also measured. The solvent of these hormones was infused as volume control. Secretin decreased R of all organs studied if local blood secretin concentration was raised by 0.01 u/ml or above (-10% in R at +0.01 u/ml and -35% at +0.07 u/ml). CCK decreased R of duodenum and jejunum when its concentration was raised by 0.006 u/ml or above (-20% in R at +0.006 u/ml and -40% at +0.03 u/ml). CCK also decreased splenic R when its concentration was raised by 0.05 u/ml (-20% in R at +0.05 u/ml and -22% at +0.1 u/ml). CCK did not alter R of forelimb, skin or muscle. Gastrin decreased R of duodenum and jejunum when its concentration was raised by 0.04 μg/ml or above (-14% in R at +0.04 μg/ml and -23% at +0.2 μg/ml). Gastrin did not alter splenic R. Splenic weight was decreased by CCK and gastrin but not by secretin. While secretin produced relatively linear dose-response curves, gastrin at +0.1 μg/ml and CCK at +0.03 u/ml caused near maximum dilation followed by a relatively small fall in R with increasing dosages. These studies indicate that the vasodilator action of secretin is equipotent in the duodenum, jejunum, spleen, skin and muscle. But CCK is more potent on the gut than on the spleen and has no effect on the forelimb. Gastrin dilates the gut vasculature but has no effect on the spleen. However, on unit basis, CCK appears to be more potent a dilator than secretin in the gut.

THE EFFECT OF ACID-BASE CHANGES ON SERUM INORGANIC PHOSPHORUS. Enrique Cipriani* and Robert Fitzgerald. The Johns Hopkins University, Baltimore, Maryland 21205.

Hypocapnia has been observed to produce a decrease in serum inorganic phosphorus (Pi) while hypercapnia has been reported to increase Pi. The present experiments were undertaken to determine if CO_2 and H^+ ion exerted separate effects on the level of Pi. Female dogs were anesthetized, paralyzed, and made acidotic or alkalotic either by 1 hr of 10% CO_2 in air or hyperventilation. In a second set of experiments these two conditions were compensated by an infusion of 0.3N $NaHCO_3$ or 0.2N HCl respectively. In a third set of experiments animals were made metabolically acidotic or alkalotic at constant $PaCO_2$ (control value) by an infusion of one or the other of the above two solutions. At 15 minute intervals arterial samples were measured for pH, $PaCO_2$, PaO_2, serum Ca and Pi. During respiratory, compensated respiratory, and metabolic acidosis the mean increase in Pi (% of control)/10 mmHg or 10 nmolsH^+ was 21.7, 6.5, 3.6. During respiratory, compensated respiratory, and metabolic alkalosis the mean decrease in Pi (% of control)/10 mmHg or 10 nmolsH^+ was 17.6, 2.3, 13.4. These results suggest that during acidosis H^+ per se has little effect on the level of Pi. During alkalosis the interpretation of the results is less clear. Respiratory alkalosis (with a drop in HCO_3^-) has about the same effect on Pi as does metabolic alkalosis at constant $PaCO_2$. (Supported in part by PHS Grant HL 17417.)

PRODUCTION OF GASEOUS NITROGEN DURING HUMAN STEADY STATE EXERCISE.
John H. Cissik*, Robert E. Johnson, and Bruce A. Hertig. University of Illinois at Urbana-Champaign, Urbana, Illinois 61801

Our studies of respiratory gaseous nitrogen (VN_2) balance (J. Appl. Physiol. 32:155-159, 1972) have been extended to exercising subjects. Nine volunteer subjects (six males, three females) marched on a level treadmill at 4.8 km/hr for one hour in the post-absorptive state, or following ingestion of meals of variable protein content (22%, 31%, and 67%; 21, 35, and 61 gms protein, respectively). In every case, VN_2 expired exceeded VN_2 inspired. Average values for the N_2 difference were: post-absorptive, 217 ml/min; 22% protein, 319 ml/min; 31% protein, 409 ml/min; and 67% protein, 509 ml/min. The differences were linearly related to the protein content of the meals ($r = 0.86$). Sensitivity of the measuring system yielded a ± 2 S.E.M. of 25.6 ml N_2/min, which is an order of magnitude less than the smallest difference observed. The Haldane transformation assumes $VN_{2\ insp} = VN_{2\ exp}$. Correcting for the observed N_2 differences leads to values of oxygen consumption substantially less than those calculated by the Haldane equation; as much as 31% in our studies. The magnitude of $VN_{2\ exp} - VN_{2\ insp}$ we have observed during exercise suggests that N_2 is evolved in substantial quantities both following intake of protein and during fast by some unidentified intermediate metabolic pathways.

RESPONSE OF MUSCULAR AND CUTANEOUS VESSELS TO STIMULATION OF MUSCLE AFFERENTS.
D. L. Clement* and J. T. Shepherd.
Mayo Foundation, Rochester, Minnesota.

The effect of stimulation of muscle afferents on the cutaneous and muscular vessels was studied in eight anesthetized dogs. The vagi were cut and the carotid sinuses kept at constant pressure. The left gracilis muscle, hind paw and saphenous vein were perfused at constant flow. Muscle afferents of the right hind limb were electrically stimulated for one minute, either by stimulation of the central end of the cut femoral nerve or by direct stimulation of the muscles of the thigh. Each stimulus lasted 5 msec. Femoral nerve stimulation at 5 cps and 1 volt (at the electrodes) caused a decrease in perfusion pressure of 28 ± 4 mm Hg (mean ± SE) in the gracilis muscle, of 28 ± 7 mm Hg in the paw and an increase in perfusion pressure of 13 ± 2 mm Hg in the saphenous vein. At 40 cps and 5 V, stimulation caused an increase in perfusion pressure of 20 ± 3 mm Hg in the gracilis muscle, of 21 ± 4 mm Hg in the paw and a decrease of 10 ± 3 mm Hg in the saphenous vein. The responses were not prevented by atropine but were markedly attenuated by phenoxybenzamine. In four of the eight dogs, muscle stimulations were performed with electrodes inserted into the thigh muscles; with muscular contraction comparable results were obtained as with nerve stimulation. Paralysis of the stimulated muscles prevented the vascular responses to stimulation at 40 cps, but not to stimulation at 5 cps. Thus, muscle contraction can lead to activation of receptors in the limbs, which cause constriction of the resistance vessels in skin and muscle and dilatation of the cutaneous veins; such contraction is not necessary to activate the receptors which cause dilatation of the resistance vessels and constriction of the cutaneous veins. (Supported in part by NIH grant HL-5883).

CYANIDE (CN) AND 2-4 DINITROPHENOL (DNP) CONTRACTURES IN CANINE TRACHEALIS MUSCLE. R.F.Coburn and T. Tomita*. Dept. of Physiol., Fac. of Med., Kyushu University, Fukuoka,Japan.

CN(0.04-3mM) and DNP (0.08-3mM) resulted in sustained contractures occasionally preceded by a small relaxation (latent period 2-15 sec., max.tension 10-60% of max.tension with field stimulation) of canine trachealis muscle in 37° C Krebs solution equilibrated with 97% O_2 and 3% CO_2. These contractures were not influenced by hyoscine ($1\text{-}4 \times 10^{-6}$ g/ml), but were abolished by 20 min. exposure to "No Ca^{++}" Krebs solution containing 2 mM EGTA, and after depolarization of the membrane potential (Vm) with 126 mM external K^+. DNP or CN caused 2-12 mV depolarizations of Vm and marked decreases in membrane resistance(Rm) with the double sucrose gap method. Although ouabain (10^{-6}-10^{-5} g/ml) resulted in diphasic contractures and 0-6mV depolarizations, CN or DNP contractures and Vm and Rm changes persisted after pretreatment with this agent. Low Na^+ (16.6 mM) Krebs (NaCl replaced with isosmotic sucrose, Tris Cl or Choline Cl) resulted in a contracture; in this solution CN or DNP contractures and Vm and Rm changes were inhibited or abolished. The data suggest that CN and DNP contractures are a result of membrane effects of inhibition of aerobic metabolism. Inhibition of a ouabain sensitive electrogenic pump can not completely explain the data. CN and DNP may result in an increase in membrane Na^+ conductance or inhibition of a membrane electrogenic Ca^{++} pump. It seems unlikely that the primary event was release of Ca^{++} from intracellular stores and that the membrane changes resulted from increases in intracellular Ca^{++}.

MYOCARDIAL EFFECTS OF ANGIOTENSIN. Bernell Coleman and Marva Watts* Dept. of Physiol. and Biophysics, The Chicago Medical School, Chicago, Ill. 60612

The effects of angiotensin infusion (0.1-1.0 μg/kg/min.) on myocardial performance were examined in 20 open chest, vagotomized or atropinized (0.2 mg/kg) dogs under morphine-chloralose anesthesia, before and after beta adrenergic blockade (propranolol 1 mg/kg). Angiotensin caused a marked increase in left ventricular systolic pressure (LVSP) and its first derivative (dp/dt), while time to peak tension decreased. Myocardial oxygen consumption increased both as a result of augmented coronary blood flow and a widened myocardial A-V oxygen difference. Left ventricular end-diastolic pressure (LVEDP) was relatively unchanged. The rate of change of left ventricular circumferential dimension increased while the absolute values for systolic and diastolic dimensions remained about the same. The diastolic interval was consistently lengthened despite a relatively constant heart rate. Beta adrenergic blockade had no appreciable effect on the response of the heart to angiotensin, suggesting that the indicated results were due to a direct action of the hormone on the contractile mechanism. The results of these studies indicate that angiotensin enhances myocardial contractility by increasing the degree of activation of the contractile element, i.e. by shifting the force velocity relationship to the right. (Supported by Grant HE-12285, from the National Heart and Lung Institute, National Institutes of Health, Bethesda, Md.)

CARDIAC OUTPUT IN THE RAT BY DYE-DILUTION. Thomas G. Coleman, R. Davis Manning, Jr.* and Roger A. Norman, Jr.* (with technical assistance of Milton H. Davis, Jr.) Dept. of Physiology & Biophysics, University of Mississippi School of Medicine, Jackson, Mississippi, 39216.

The feasibility of using dye-dilution to measure cardiac output(CO) in rats was demonstrated with a low-volume, flow-thru system. Blood, driven by arterial pressure, flowed continuously at an average of 4 ml/min from carotid artery to jugular vein thru a Gilford 103-IR cuvette and a combination of .85 mm I.D. and 1.0 mm I.D. tubing having a total length of 40 cm. The system had a volume of .5 ml and was primed with half-strength Dextran 40 (Pharmacia Lab.) containing 500 units heparin /ml. Boli of .035 mg Cardio-Green (Hynson, Westcott & Dunning) in .07 ml H_2O were injected into the venous arm of the flowing system via a T connector. Calibration at 10 mg/liter was achieved by adding .02 ml of .5 mg/ml dye to 1 ml blood, which was then reinfused into the animal. The data was analyzed using standard techniques. Ten large rats (9 male & 1 female) weighing an average of 428 grams (Range = 267 to 582) were used in this study. Mean CO in the animals, anesthetized with 60 mg/kg sodium pentobarbital, was 179 $\pm$ 24 ml/min/kg. Mean arrival time of the dye was 2.75 $\pm$ .17 seconds. The sensitivity of the technique was demonstrated by measuring CO after infusing .1 mg/kg isoproterenol (Winthrop Labs) and 10 cc/kg Dextran 40 over 5 minutes. CO increased to 478 $\pm$ 34 ml/min/kg. Subsequent hemorrhage of 16 cc/kg over 5 minutes decreased CO to 163 $\pm$ 14 ml/min/kg. Absolute accuracy of the technique was estimated using identical procedures on a properly scaled hydraulic analog operated at 37° C. Regression analysis showed that in the analog: Dye-Dilution Flow (ml/min) = .96 Actual Flow + .2 ml/min. Dye-dilution, in this instance, underestimated flow by 4.2 $\pm$ 1.2%. All statistics are mean $\pm$ standard error. Supported by NIH Grant HE-11678.

OBSERVATIONS ON THE NEUROTRANSMITTER CHARACTERISTICS OF GLUTAMATE AT THE LOBSTER NEUROMUSCULAR JUNCTION. Carol Colton* and Alan R. Freeman. Depts. of Psychiatry and Physiology, Indiana Univ. School of Med., Indianapolis, Ind., 46202.

The putative neurotransmitter glutamate exerts significant actions on nonsynaptic as well as synaptic membranes. When studied at 18°C, glutamate added at 5×10^{-4}M to the bathing medium (5 meq. K^+, artificial sea water) surrounding the lobster neuromuscular junction induces a membrane depolarization which is accompanied by a 20-40% increase in effective membrane resistance (Reff). Single surface fibers were impaled with two closely spaced microcapillaries for the purpose of voltage recording and current passing. Voltage-current relationships were plotted and the resistance calculated. Each fiber served as its own control. The induced increase in Reff remains as temperature is reduced until a phenomenological null point is reached at about 6°C. Below this value glutamate application results in both a diminution in Reff ranging from 10-50% of control and also a marked increase in sensitivity to the compound; i.e., 5×10^{-5}M below 6°C is as effective in changing Reff as 5×10^{-4} at 18°C. In separate control experiments effective membrane resistance was found to progressively increase when temperatures were lowered from 18°C through 0°C, possibly due to K^+ inactivation. In this respect, preliminary experiments showed a temperature induced change in the slope of the E_m vs. K^+_{out} relation, i.e., a 56 mV per decade response at 18°C shifted to approximately 40 mV per decade at lowered temperatures. These studies reveal that synaptic and nonsynaptic actions of glutamate may be differentially investigated in an effort to gain a more complete understanding of the actions of this putative neurotransmitter.

THE PHOTOMYOCLONIC RESPONSE IN EPOCH EEG AVERAGING. Robert C. Conroy* and Samuel M. Peacock, Jr. Division of Electroencephalography and Clinical Neurophysiology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, Pa.

Simultaneous multichannel averaging of EEG epochs in response to trains as well as continuous stimulation has demonstrated the responsivity to photic stimulation of the entire accessable cortex. Parametric sensitivity, however, suggests differences in organization. The possibility that such differences might be due to contamination by the photomyoclonic response was investigated. It was concluded that photomyoclonic potentials under certain conditions can contaminate the averaged record but this does not account for the cortical areal response differences observed.

LYSOSOMAL DEGRADATION OF LABELED PARTICULATE LIPID WITHIN MACROPHAGES. Robert P. Cornell*and Thomas M. Saba. Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago, Illinois 60612.

An ^{131}I-triolein lipid emulsion administered intravenously to dogs and rats at a dose of 300 mg/kg was selectively phagocytized by macrophages of the reticuloendothelial system (RES) with 90% of the injected dose localized in hepatic Kupffer cells. Intracellular degradation of this particulate lipid was studied both in vivo and in vitro utilizing a technique (Am. J. Physiol. 221:1511-1516, 1971) to separate the free ^{131}I and lipid-bound ^{131}I activity of tissue homogenates. In vivo degradation of ^{131}I-triglyceride (TG) with the formation of free ^{131}I within the liver, spleen, and lungs, three major RE cell-containing organs, followed Michaelis-Menten kinetics implicating an enzyme-catalyzed reaction. The maximal reaction velocities (V_{max}) calculated from Lineweaver-Burk plots relative to particle degradation in the liver, spleen, and lungs were 42.1, 21.1, and 0.42 µg TG deiodinated/g/min, respectively. Incubation in vitro of the labeled lipid with different hepatic subcellular fractions (whole homogenate, 10,000 g supernate, large-granule fraction [LGF]), revealed a significant ($p<0.01$) correlation between the subcellular deiodinative and acid phosphatase activities. The highest specific deiodinative activity of 40.3 µg TG deiodinated/10 mg protein/180 min was manifested by the lysosome-rich hepatic LGF. Prior disruption of the hepatic LGF and an acid pH enhanced the degradation of the particulate lipid indicating an intimate role for lysosomal enzymes in the macrophage digestive activity relative to this substrate. The data suggests that quantitation of the kinetics for RE cell degradation of this substrate may provide an in vivo technique to assess the digestive activity of macrophages. (USPHS-AM-14382).

EFFECTS OF THEOPHYLLINE ON TRIGLYCERIDE UTILIZATION, GLYCOGENOLYSIS AND CONTRACTILITY IN THE PERFUSED WORKING HEART. M. F. Crass III and J. C. Shipp, Depts. of Biochem. and Med., Univ. of Nebraska Med. Ctr., Omaha, Nebr.

Hearts from normal fed rats with lipids prelabeled in vivo with palmitate -1-^{14}C, were perfused with oxygenated bicarbonate buffer containing 5.5 mM glucose, with or without added theophylline (THEO), in a closed recirculated working system at 10 cm H_2O left atrial filling pressure for 30 min. A 5 min non-recirculated perfusion preceded the addition of THEO (2.5×10^{-5} to 1.0×10^{-3}M). Heart rate and pressure development were monitored continuously. Initial and final (30 min) values for total and labelled triglycerides (TG) and phospholipids (PL), $^{14}CO_2$, and glycogen content were determined. THEO produced a concentration-dependent increase in the rate of triglyceride mobilization and oxidation ($^{14}CO_2$ production). Maximal stimulation of TG utilization (3-fold) was observed at 2.5×10^{-4}M. Content and labeling of PL were unchanged in the presence of THEO. Rates of glycogenolysis were not different from controls, even at the highest THEO concentration tested (1.0×10^{-3}M). No inotropic effects were observed with THEO at the concentrations employed, but a positive chronotropic effect was observed at 1.0×10^{-3}M. The selective stimulation of myocardial triglyceride utilization and the absence of enhanced glycogenolysis in the intact working heart were unexpected. The observed effects of THEO, if due to an increase in cyclic AMP via inhibition of phosphodiesterase (PDE), suggested that the lipolytic and glycogenolytic systems have differential sensitivities. Alternatively, the lipolytic effects of THEO could be explained by mechanism(s) other than PDE inhibition. (Supported by NIH AM 14986 and Nebr. Ht. Assn.)

SHORT-CIRCUIT CURRENT AND ACTIVE Na AND Cl TRANSPORT ACROSS ISOLATED RABBIT BLASTOCYSTS. M. H. Cross (intr. by R. L. Brinster). University of Pennsylvania, Philadelphia.

Ion transport processes of the 6-day rabbit blastocyst were examined in vitro by measuring fluxes of ^{22}Na and ^{36}Cl across the short-circuited preparation. When Eagle's medium (20% calf serum) containing 25 mM HCO_3 bathed both sides of the blastocoele and the transmural potential difference was reduced to zero, there was a net Na flux (0.58 ± 0.158 $\mu Eq/cm^2/hr$) and a net Cl flux (0.59 ± 0.149 $\mu Eq/cm^2/hr$) from the outside bathing solution to the blastocoele. Net Na and net Cl fluxes were both three times larger than the short-circuit current and accounted for only 5% of the short-circuit current. Changing the outside bathing medium to a HCO_3-free solution greatly reduced the potential difference and short-circuit current, while removal of the transportable ions (Na and Cl) from the outside solution had no effect. It is concluded that Na and Cl are actively transported into the rabbit blastocoele, and the presence of an appropriately directed unidentified component of short-circuit current which is greatly reduced in HCO_3-free solutions suggests that the rabbit blastocyst also actively transports HCO_3. Supported by NIH Contract 69-2141.

THE EFFECTS OF HYPERBARIC OXYGEN TREATMENT FOR BLAST INJURY IN THE BEAGLE. Edward G. Damon and Robert K. Jones*. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico.

The effects of hyperbaric oxygen treatment for primary blast injury was explored in Beagle dogs. The animals were exposed in pairs on the end plate of a 42-inch diameter shock tube to reflected shock pressures. One member of each pair was then treated in a hyperbaric chamber and the other was retained as an untreated control on each shot. Three modes of hyperbaric treatment were investigated. In the first experiment, dogs were pressurized with air at 72 psig (P_{O_2} = 17.5 psia) for 3 hours followed by a 26 hour decompression schedule. In the second experiment, the animals were pressurized with 100 percent oxygen for 3 hours at 12 psig (P_{O_2} = 24 psia) followed by a 25 hour decompression schedule. In the third experiment, the animals were treated with 100% O_2 for 24 hours at an anitial chamber pressure of 27 psia followed by an additional 24 hours with 60% O_2 at a chamber pressure of 14 psia. The first two experiments resulted in an increase in the survival time of the treated animals with no overall increase in survival and recovery compared to the untreated controls. In the third experiment, the mortality at 7 days was 30% in the treatment group and 60% in the untreated control group. The effects of the treatment on the pathophysiology of blast injury was discussed. (Supported by Contract DASA-01-70-C-0075, Defense Nuclear Agency of the Department of Defense.)

RELATIONSHIP OF RESPIRATORY MUSCLES ELECTROMYOGRAMS TO PRESSURE AND VOLUME DURING STATIC EXPIRATORY EFFORTS. **J. Danon*, W. S. Druz*, W. Machnach* and J. T. Sharp. U. of Illinois Med. Coll. & VAH Hines, Ill.**

The integrated electromyogram is known to bear a nearly linear relationship to the tension generated by muscle contracting isometrically. Therefore, we have used the integrated EMG as an almost quantitative indicator of the number of muscle fiber contracting and the frequency of contraction in the respiratory muscles during quasi-isometric (static) expiratory maneuvers. Normal subjects generated varying degrees of expiratory (positive) airway pressure against a closed airway at volumes varying from residual volume to total lung capacity. Electromyograms from several inspiratory and expiratory muscles were rectified, integrated and recorded with airway pressure and lung volume. The various lung volumes were attained and maintained passively by applying negative pressure to the body surface. The relationships of the integrated EMG's to expiratory pressure at constant lung volume and to volume at constant expiratory pressure were evaluated. The major findings were the following: 1) Inspiratory muscles such as the scalenus and sternomastoid participated in the expiratory efforts, the amount of activity increasing non-linearly with the degree of expiratory pressure. In maximum expiratory maneuvers they contracted to the same degree as in maximal inspiratory activity. 2) In a similar study done during inspiratory efforts (The Physiologist 14:128, 1971) the inspiratory muscle EMG's at constant inspiratory (negative) pressures were found to increase with increasing volume in accordance with the length-tension relationships of inspiratory muscles. During expiratory efforts, however, the EMG of both inspiratory and expiratory muscles bore little relationship to volume.

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THE EFFECTS OF ACETAZOLAMIDE AND OUABAIN ON THE D-C POTENTIAL DIFFERENCE BETWEEN CSF AND BLOOD. D. G. Davies*and R.E. Dutton.

A positive correlation between the bicarbonate ratio (CSF/blood) and the ΔPco_2 (CSF-blood) has been demonstrated (Fed. Proc. 30:1668, 1971). The fact that the D-C potential difference between CSF and blood changes in the same direction as the bicarbonate ratio suggests that the charged membrane effect might be involved in its generation. This could be true if the potential were a diffusion potential related to the bicarbonate differences. We have used Goldman's derivation of the diffusion potential to calculate that the permeability coefficient for H^+ must be of the order of 10^7 for any bicarbonate differences to occur, a possibility if there is facilitated or carrier mediated diffusion of HCO_3^- and H^+ with CO_2 as the carrier. Carbonic anhydrase must be present for this to occur since the ΔPco_2 (CSF-blood) was abolished by acetazolamide (Physiologist 14:129, 1971). Therefore, in order to test this hypothesis we measured the effect of carbonic anhydrase inhibition on the D-C potential. When acetazolamide was administered i.v. and intracisternally the slope of ΔE (CSF-blood) vs. pHa was reduced by approximately 60 %. Since Held et al. (J. Neurophysiol. 27:942-959, 1964) demonstrated a similar decrease in this slope when ouabain was added to the CSF perfusion we administered acetazolamide and ouabain together. Following this the slope of ΔE vs. pHa was not significantly different from zero, although there was still a small potential remaining. We suggest that the electrical potential difference between CSF and blood can be accounted for on the basis of three phenomena: 1) the charged membrane effect; 2) ouabain sensitive active transport mechanisms and 3) the Gibbs-Donnan equilibrium potential.

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THE RESPIRATORY RESPONSE OF FROG SARTORIUS TO CONTRACTURE-INDUCING AGENTS: EFFECTS OF CYCLIC AMP AND PROSTAGLANDINS. M. Joan Dawson* and C. P. Bianchi, Dept. of Pharmacology, Univ. of Pa., Phila., Pa. 19104.

When exposed to caffeine or high concentrations of potassium, skeletal muscle responds with a delayed increase in its rate of oxygen consumption, as well as with contracture. While the mechanism of this excitation-respiration coupling is not clear, earlier studies have indicated that calcium is involved, just as it is in excitation-contraction coupling. Our own studies with glycerol-treated muscles indicated that in addition to calcium, there is a requirement for cyclic AMP if a respiratory response is to occur (FASEB, Abst. 1939, 1972). In these experiments, isolated frog sartorii were used to confirm the effects of cyclic AMP on the respiratory response of normal tissue to contracture-inducing agents. Dose-response curves to potassium and to caffeine were obtained, with both tension and respiratory responses being measured. Paired muscles were exposed to drugs which interact with the cyclic AMP system before the responses to caffeine or K-depolarization were obtained. At concentrations which caused no observable effects themselves, cyclic AMP, epinephrine and prostaglandin E_1 potentiated the respiratory response to both K-depolarization and to caffeine. Although respiratory responses were potentiated by these drugs, tension responses were not affected. The prostaglandin inhibitors, acetylsalicylate and polyphloretin phosphate, markedly decreased the respiratory response to both caffeine and to potassium, again without decreasing contracture tension. We conclude that cyclic AMP, and agents which interact with cyclic AMP, have a marked effect on the respiratory responses of skeletal muscle to contracture-inducing agents, and that these effects are independent of effects on the contracture itself.

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A WAVE-SPEED THEORY OF FLOW LIMITATION DURING FORCED EXPIRATION.
Stanley V. Dawson (intr. by J. Mead). Harvard School of Public Health, Boston, Massachusetts 02115.

The basic mechanism of the limitation on air flow from the lung during forced expiration appears to be the progressive reduction of airway cross-section as parenchymal pressure is increased. The present work develops a mathematical model of the physics of this phenomenon in such a way as to predict the flow-pressure ($\dot{V}$,P) relationship and the area (A) of a tube cross-section. The most striking result is that the bulk velocity of flow in a collapsible tube is shown to be limited by a speed of wave propogation in the tube at a critical area (A_c) to be calculated. This wave speed, which has been used in the theory of blood flow, is given essentially by a formula involving compliance of the tube (dA/dP) and the inertance of the gas (ρ/A). The formula for flow limitation is

$$\dot{V}/A_c \leq (\rho^{-1} A_c \, dP/dA_c)^{1/2}$$

The present theory proceeds from equations for conservation of axial momentum and of mass of fluid in a tube with an elastic wall. A differential equation for area of cross-section as a function of axial co-ordinate is derived and solved. A critical point of the differential equation fixes the critical area, which in turn fixes the critical flow. An increase of pressure beyond the value which is just required to attain critical flow causes the solution for area to jump down from the higher-area branch of the solution curve to the lower-area branch. The jump is located at a point that results in the exact dissipation of the increase in flow energy due to increased driving pressure. The jump appears to correspond to the equal-pressure point observed in experiments on forced expiration, and the lower branch appears to correspond to the collapsed segment.

EFFECTS OF CHRONIC EXPOSURE TO LOW LEVELS OF CARBON MONOXIDE ON THE HEMATOLOGIC AND CARDIOVASCULAR SYSTEMS OF THE CYNOMOLGUS MONKEY.
D.A. DeBias, C.M. Banerjee, N.C. Birkhead, L.A. Kazal, R.R. Holburn, W.V. Harrer* and C.H. Greene*. Department of Physiology, Thomas Jefferson University, Philadelphia, Pa.

This study was undertaken to obtain quantitative correlations between chronic carbon monoxide exposure and physiologic parameters of the cardiovascular system and blood of normal cynomolgus monkeys, and monkeys with myocardial infarction. Experimental infarctions were induced using a closed-chest technique by depositing polystyrene microspheres selectively into the left coronary artery using direct coronary catheterization with the aid of image intensifying fluoroscopy. Successful infarction was reflected by characteristic changes in the ECG, blood pressure, leucocyte count, and serum enzymes (LDH, CPK, GOT). Normal and infarcted animals were exposed continuously (23 hours/day) in a chamber in which the carbon monoxide level was maintained at 100 PPM. Air breathing controls were housed in separate quarters removed from the chamber area. COHb levels of CO breathing animals averaged 12.4%. Significant and characteristic increases in the Hct, Hb and RBC levels were observed after three weeks of CO exposure and persisted until sacrifice three or six months later. A concomitant increased P wave amplitude and T wave inversion were observed in the ECG as well as bradycardia. Gross and microscopic observations on the heart (and other body organs) taken at sacrifice did not reveal changes which could be attributed to CO.

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CALCIUM ACTION POTENTIAL IN FROG ATRIUM. J.F. Delahayes (intr. by E. Bozler). Dept. of Physiology, The Ohio State University, Columbus, Ohio 43210.

Electrical activity of frog atrial preparations immersed in solutions in which part of all Na^+ was replaced isosmotically by Ca^{++} was recorded by means of microelectrodes. In 45 mM Ca^{++} solution action potential had a shorter duration and an increased amplitude due to an increase in both resting potential and overshoot. In Na-free solution responses were usually local but became conducted when epinephrine (5.10^{-6}M) was added or when the potassium concentration was raised from a control 3 mM to 10 mM. Action potentials had then a much larger amplitude reaching 185 mV and were insensitive to tetrodotoxin (10^{-7} g/ml). These results clearly demonstrate an influx of Ca^{++} during the cardiac response, strong enough for conduction to take place in absence of Na. The fact that epinephrine facilitated the development of the responses and also increased the amplitude and duration of the plateau supports the assumption that the drug increases P_{Ca}.

CARDIOVASCULAR AND PULMONARY FUNCTION DURING ESTIVATION OF THE AFRICAN LUNGFISH, PROTOPTERUS AETHEOPICUS. R.G. DeLaney*, S. Lahiri and A.P. Fishman. Depts. of Med. and Physiol., University of Pennsylvania, Philadelphia, Pa.

During the dry season the African lungfish burrows into the mud, forms a moisture-conserving cocoon and remains viable despite partial desiccation, lack of food intake, loss of gill-skin gas exchange and excretory function. It relies entirely on air breathing through a vent to the surface for respiratory gas exchange until the waters return. The present study was undertaken to elicit the temporal sequence of cardiovascular and pulmonary function during estivation. Seven lungfish (2-6 kg) with ECG electrodes and third branchial arch arterial, buccal and lung cannulae, were successfully studied for 1½ to 9½ months while estivating in mud (4 fish) or in artificial cloth bag nests (3 fish) at 24-26° C. Arterial P_{CO_2} (aquatic 25-30 mm Hg) increased to 40-55 mm Hg and pH (aquatic pH 7.60) decreased to 7.30 as the cocoon was formed within 20 days. Lung P_{CO_2} paralleled arterial increase and remained between 40-69 mm Hg for up to 165 days of observation. Lung breath frequency (aquatic 2-10/hr.) transiently increased 2-5 fold during the first 30 days in estivation and then stabilized at 5-11 breaths/hr. over the next 30 days. Arterial blood pressure (aquatic 22-28 mm Hg) gradually decreased to a stable value of 12-15 mm Hg during the first 20 days in estivation but heart rate (aquatic 22-30 beats/min) dropped more gradually and reached a steady state range of 10-15 beats/min. in 60 days (285 days of observation). These sequential cardiopulmonary changes are associated with the altered metabolic and environmental states during estivation of Protopterus. Deep torpor did not account for the changes during estivation. (Supported by NIH grant HE-08805.)

MECHANICAL INTERACTIONS BETWEEN PARALLEL MOTOR UNITS. Henri N. Demieville* and Lloyd D. Partridge. Med. Units, Univ. of Tenn, Memphis, Tn.

Most effective activities of vertebrate muscles involve asynchronous contraction of several motor units. When the load is movable the activity of one unit usually modifies the working length and shortening velocity of other units in the same muscle. We are reporting analyses of effects of this physical relationship in the case of two parallel motor units. In one analysis two isolated muscles (artificial motor units) were connected to separate force transducers and in parallel to a single load. The load was equipped with position, velocity, and acceleration transducers. Contraction of one muscle usually markedly altered power (force x velocity) delivery by a twitch of the other muscle. The magnitude of these power changes was dependent on the relative timing of the stimuli to the two muscle units, on initial length of the muscles and on load. A second analysis of the problem was developed on theoretical grounds. This analysis showed that a large part of the observed interaction should be anticipated from length-tension and force veolcity effects. It is concluded that in normal activity of muscle, output is probably not determined simply by algebraic superposition of the responses of the individual units but represents effects of an appreciable interaction through the mechanical coupling of the motor units. This might be considered to be a peripheral integrative process.

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EFFECT OF LOCALLY INDUCED HYPOTHERMIA UPON MAMMARY CIRCULATION AND ENERGY METABOLISM. Thomas DeMott* and Monica Reynolds. Dept. of Animal Biology, School of Veterinary Medicine, U. of Pa., Phila., Pa.

The relationship between mammary temperature, mammary blood flow and oxygen consumption was studied. Lowering of ambient temperature around the mammary glands of conscious lactating goats was effected by an encompassing water jacket featuring thermostatic control and continuous circulation for maintenance of uniform temperature. Water, udder and body temperatures were monitored by thermistors, and mammary blood flow was monitored from an electromagnetic flow probe of the gaited-sine wave type (Medicon) chronically implanted around the mammary artery. Oxygen consumption was calculated from the blood flow and arterial and mammary venous oxygen concentrations. In approximately 10 experiments with an average cooling time of 90 min, cooling from 25° to 5° C, a gradual decrease in blood flow was always found. Recovery to control mammary blood flow values required 38 to 50 minutes. Mammary blood flow then continued to increase for some time in what appeared to be a compensatory hyperemia and at maximum reached values considerably above control levels. Oxygen consumption in general followed the mammary blood flow changes, decreasing during cooling and increasing during the hyperemic recovery phase. Since milk secretion is directly related to mammary blood flow, these results emphasize the importance of avoiding extreme lowering of mammary temperatures for considerable lengths of time if good milk production is to be maintained. (Supported by U.S. Public Health Service Grant #HE-04121-12 and -13)

PHYSIOLOGICAL CONSEQUENCES OF HYPERVENTILATION DURING EXERCISE IN HYPOXIA. J.A.Dempsey,J.Thomson,*J.Thoden,*W.G.Reddan,*H.V.Forster,* S.C. Alexander. Pulmonary Physiol.Lab.,Univ. of Wis.Med. School,Madison,Wis.

In the healthy sojourner at work, after 2-8 wks. at 3100m altitude, $\dot{V}_E$ increases ~50-120% over sea-level normoxia. The hyperventilation achieved in prolonged, submaximal work at 3100m is severe - Pa_{CO_2}<20 torr,pHa>7.45. The majority of this hypervent. is attributable to mechanisms operating during altitude sojourn, per se,i.e. it occurs between acute(mins) and chronic(days or wks.) exposures to hypoxia(P_{IO_2}~100 torr). A series of 4 studies has revealed a variety of consequences to the working sojourner attributable to his hypervent. and respiratory alkalosis: 1.The hypervent.permits Sa_{O_2} to be maintained at resting levels even during prolonged exhaustive exercise, because of:a)a high overall $\dot{V}_A:\dot{Q}_c$, $P_{A_{O_2}}$ & P_A-$P\bar{v}_{CO_2}$ gradient; and b)an effect of resp.alk. on arterial HbO_2 association. 2.Alkaline femoral venous pH inhibits O_2 offloading to working skeletal muscle,in the absence of an exercise-induced shift in (in vitro)P_{50};3.Resp.Alk.reduces cerebral blood flow during exercise and cerebral O_2 transport falls despite a rise in Ca_{O_2}; 4.Total ventilatory work increases 40-60%,secondary to increased flow-resistive work. In total, the hypervent. attained by the working sojourner at 3100m must be viewed as a truly maladaptive process,and is manifested in severe exertional dyspnea,marked tissue hypoxia, & the need for extended recovery periods following exercise. On the other hand, the native or long-term resident of 3100m avoids hyperventilation,resp.alk. and its consequences during exercise in hypoxia, without compromising arterial SO_2 or tissue O_2 transport. The efficiency achieved in the pulmonary response to muscular work clearly denotes the attainment of "steady-state" physiologic acclimatization to environmental hypoxia.

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COMPARATIVE PROPERTIES OF CHYMOTRYPSIN FROM THE DIGESTIVE FLUID OF THE POLYCHAETE APHRODITE JAPONICA. E.J. DeVillez. Miami University, Oxford, Ohio.

Digestive fluid samples of the sea mouse were assayed for chymotryptic activity based on the hydrolysis of BTEE in 0.1 M Tris at pH 6-9. The pH optimum for BTEE activity was pH 8.0. Digestive fluid extracts were allowed to stand for 24 hours at 22°C in 0.1 M acetate, phosphate or Tris buffer at pH 3-9 followed by the assay for residual chymotryptic activity. The BTEE active components were stable from pH 9-5 but only 42% of the original BTEE activity remained after 24 hours at pH 3. Samples were subjected to slab acrylamide gel electrophoresis at pH 8.1. After electrophoresis, proteolytic digestive enzymes were identified by incubation of the gels on agar-gelatin or agar-casein at pH 7 for 2 hours. Gel fractions(5mm) were eluted in H_2O at 4°C for 24 hours and fractions of eluate were assayed for chymotryptin in the presence of BTEE at pH 8. As many as 9 proteolytic components were identified on agar-gelatin whereas 4 major peaks of protease activity were evident when fractions were incubated with casein. Three of the 4 caseinase peaks demonstrated BTEE activity and included a cathodal component(C_1), a slow moving anodal component(C_2) and a fast moving anodal component(C_3). The molecular sizes of the BTEE components as determined by Sephadex G-75 chromatography were 13,500(C_1), 17,300(C_2) and 18,900(C_3). The BTEE components were incubated in the presence of the inhibitors PSMF, TPCK and TLCK. C_1 was inhibited by PSMF and TPCK whereas C_2 and C_3 were inhibited only by PSMF. TLCK was not inhibitory. It would appear that C_1 is the only chymotryptic component.

RESPIRATORY FUNCTIONS OF BLOOD OF KILLER AND BELUGA WHALES. D. S. Dhindsa, J. Metcalfe, A. S. Hoversland* and R. A. Hartman*. Heart Research Lab., Dept. of Med., Univ. of Oregon Med. School, Portland, Ore. 97201, and Vancouver Aquarium, Vancouver, B.C., Canada.

The respiratory characteristics of blood from killer whales (Orcinus orca) and beluga whales (Delphinapterus leucas) were studied. One young male and one adult female of each species were studied and no differences attributable to age or sex were detected. All animals were studied on two occasions, 6 months apart. Oxygen dissociation curves were constructed at 37°C and corrected to a plasma pH of 7.40 using the Bohr factors determined in this study for each species. The mean oxygen capacity for killer whale blood (21.8±0.5 vol%) was significantly lower ($P<0.01$) than that for beluga whale blood (25.8±0.6 vol%). The Bohr factor ($\Delta \log P_{O_2}/\Delta pH$) for killer whale blood (-0.602±0.148) and beluga whale blood (-0.782±0.073) were not significantly different ($P>0.05$). The mean partial pressures of oxygen required to half-saturate the hemoglobin in the whole blood (P_{50}) were 25.2±0.5 mm Hg (n=6) and 24.4±0.1 mm Hg (n=3) for killer and beluga whales, respectively, and these values are significantly different ($P<0.05$). Completely deoxygenated blood combines with more CO_2 than oxygenated blood at the same P_{CO_2}; this is called the Haldane effect and its values at a P_{CO_2} of 40 mm Hg were 7.0 and 9.4 vol% for killer and beluga whale blood, respectively. The concentration of 2,3-diphosphoglycerate in killer whale blood (15.12 μmol/g Hb) was significantly higher ($P<0.01$) than in beluga whale blood (11.49±0.63 μmol/g Hb). Starch gel electrophoresis showed that hemoglobin from killer whales had two major components, while hemoglobin from beluga whales had a single major component. (Supported in part by USPHS NIH Grants HL 05499 and HL 06042, and the Oregon Heart Association.)

EFFECT OF PROSTAGLANDIN AND INDOMETHACIN ON CORTICOSTEROIDOGENESIS IN THE ISOLATED PERFUSED RAT ADRENAL. E.J.Diamond*, C.R.Martin and C. Monder* Hunter College(CUNY) and Res.Inst.,Hosp.for Joint Diseases,N.Y.

The effects of prostaglandin and indomethacin on the rat adrenal gland were studied using a technique for in situ perfusion recently developed in our laboratory. Male hooded rats (300-450g) were anesthetized with urethane and the arterial and venous circulations of the left gland isolated. Oxygenated Krebs Ringer Bicarbonate (KRBG) at 38°C was perfused within 60 sec after interruption of circulation. X-ray studies of glands perfused with Thorotrast or $BaSO_4$ confirmed that the perfusate passed through the adrenal and was present in the venous effluent. Flow rate was maintained at 1.0-4.5 ml/hr with a peristaltic pump. An output of 1.9 + 1.1 μg corticosterone (B) during the first 30 min declined to 0.74 ± .82 μg B after 6 hrs of perfusion. With unsupplemented KRBG, a transient spontaneous increase in B output frequently occurred without a significant change in flow rate. The increase was eliminated or greatly diminished by indomethacin (5 μg/ml KRBG), an inhibitor of prostaglandin synthetase. Addition of prostaglandin E_2 (5μg/ml KRBG) to the indomethacin-containing medium resulted in a transient stimulation of B output with no concomitant increase in flow rate. The spontaneous transient increase in B output may represent a response to increased endogenous adrenal prostaglandin synthesis. (Supported by grants from The National Science Foundation and The U.S. Public Health Service).

PLASMA ENZYMES IN QUAIL FED GRADED LEVELS OF PESTICIDES OR POLLUTANTS. M.P. Dieter (intr. by R.P. Breitenbach). Bureau of Sport Fisheries and Wildlife, Patuxent Wildlife Research Center, Laurel, Maryland 20810.

Multiple enzyme analysis of blood from repetitively sampled birds was used to monitor contaminant exposure. Japanese quail were maintained 12wk on diets containing 5, 25 or 100 ppm DDE or Aroclor 1254, 8, 35 or 160 ppm malathion, or 2, 4 and 8 ppm mercuric chloride. They were sampled before exposure and at 2, 4 and 12wk. Abnormal levels of plasma enzymes were detected in all groups as early as 2wk. At 12wk it was possible to distinguish which class and what amount of contaminant the birds had been exposed to by comparing the differences in enzyme responses. In birds fed DDE or Aroclor there was a 2-5 fold increase in creatinephosphokinase (CPK), aspartate aminotransferase (AAT), aldolase (Ald) and cholinesterase and a 20 fold increase in lactic dehydrogenase (LDH). These changes were linearly related to the log dose of the fed contaminants. The slopes of the AAT and Ald responses were greater in birds fed DDE and that of CPK greater in birds fed Aroclor. However in birds fed malathion there was a log dose related linear decrease in cholinesterase activity that fell to half that in controls, no changes in CPK or Ald, and only a 25% increase in AAT and a 6 fold increase in LDH. The birds fed mercuric chloride showed a 4 fold increase in LDH that was unrelated to dose and no change in activities of the other enzymes. The elevation in plasma enzyme activities indicated cellular membrane permeability was altered by each of the four contaminants. Inspection of the pattern of enzyme responses and LDH isoenzyme analysis suggested that Aroclor more greatly altered membrane permeability in the muscle, DDE that in the liver, mercuric chloride that in the heart, and malathion that in the nervous system.

EFFECT OF CALCITONIN ADMINISTRATION ON GROWING TURTLES. Marie T. Dimond, L.F. Bélanger*, Joan Rogers*, and D.H. Copp. Trinity Col., Washington,DC; Univ. of Ottawa, Canada; Univ. of British Columbia, Vancouver, Canada.

Pure salmon calcitonin (CT) (4 µg/kg) was injected 3 times weekly into hatchling turtles (Chelydra serpentina serpentina, Graptemys kohni, Pseudemys scripta elegans). Some specimens of P. s. elegans were similarly injected with parathyroid extract (PTE) (4 µg/kg) alone or in combination with CT. With a high calcium diet CT had no significant effect on growth up to 15 weeks of treatment, but by 18 weeks (March-July) the controls of C. s. serpentina showed a significantly higher weight regression curve. A second series of C. s. serpentina (January-May) was divided into 2 groups, one maintained on a low calcium diet and the other on high calcium. In the high calcium group CT had no significant effect on growth rate or morphology up to 18 weeks. CT-treated specimens with low calcium intake grew comparably to those on high calcium, but their carapace was markedly softer. Untreated turtles on the calcium-deficient diet were significantly smaller after 12 weeks. There were no external differences in the 2 other species (maintained on high calcium) after 11 weeks (May-July) of treatment with CT, PTE, or CT+PTE. In all 3 species CT-administration resulted in increased epiphyseal cartilage as well as other histological changes in the tibia. The typical effects of PTE on bone histology were prevented by simultaneous administration of CT. CT apparently enhances growth under conditions of calcium deficiency by stimulating changes in bone structure. It has an inhibitory effect on growth after prolonged treatment during a seasonal phase of rapid growth. (Supported by USPHS Grant AM 01766 and grants from the Medical Research Council of Canada.)

EXPRESSION OF BLOOD FROM THE SPLEEN; AN ACTIVE PROCESS. D. E. Donald and G. A. Brooksby* Mayo Clinic and Mayo Foundation, Rochester, Minn.

Previous studies in anaesthetized dogs showed that 65% of the change in splanchnic blood volume resulting from electrical stimulation of the thoracic splanchnic nerves could be regarded as "passively" released as a result of the decrease in arterial inflow. In the present study isolated dog spleens were autoperfused and measurements made of change in splenic weight (isometric force tranducers), splenic inflow and outflow (cannulating electromagnetic flow transducers), and inflow and outflow pressures (strain gauge manometer systems). Supramaximal electrical stimulation of the splenic nerves (20v., 10 cps) or occlusion of arterial inflow was carried out during changes in 1) splenic venous pressure and 2) splenic inflow. Stimulation or occlusion was maintained until splenic weight was constant at the new value. With increase in venous pressure there was an increase in splenic weight and in the amount of blood expressed during nerve stimulation, but a reduction in the amount released during inflow occlusion. At venous pressures of 5 10 15 and 20 cms H_2O the average change in splenic weight during occlusion was 24 13 7 and 6% respectively of the weight change during nerve stimulation. At constant splenic venous pressure (12 cms H_2O) increase in inflow was associated with a small increase in the weight change both during nerve stimulation and inflow occlusion. Over the range of flows used (16 to 100 ml/min.) the "passive" weight change was on the average 10% (range 3-14%) of that evoked by nerve stimulation. Thus in contrast to the total splanchnic circulation, expulsion of blood from the spleen is almost wholly an active process. (Supported in part by Research Grant HLO 6143).

EFFECT OF PERFUSION PRESSURE ON TRANSMURAL DISTRIBUTION OF CORONARY COLLATERAL BLOOD FLOW. H. F. Downey and F. A. Basnour. Cardiopulmonary Institute, Methodist Hospital and University of Texas Southwestern Medical School, Dallas, Texas.

Following ligation of the anterior descending coronary artery of anesthetized dogs, regional coronary flow was estimated by tissue uptake of radioactive rubidium, potassium and labelled microspheres. Subepicardial (Epi) and subendocardial (Endo) tissue samples were taken from ischemic and control left ventricular myocardium under the following perfusion conditions: normal aortic pressure (80-130mmHg, n=19), low (50-60mmHg, n=6), and high (150-175mmHg, n=6) pump perfusion and during the hypotensive period of nitroglycerine (55-70mmHg, n=6). Collateral flows to the ischemic tissues are expressed below as percentages of the flows to non-ischemic, control sections of the left ventricle. ( ) = S.E.

	Aortic	NTG	Low	High
Endo	17.5 (3.9)	11.8 (2.5)	8.6 (1.8)	22.5 (3.3)
Epi	27.7 (5.3)	22.4 (6.4)	7.9 (2.9)	51.6 (7.7)

Ischemia following coronary occlusion was more pronounced in the subendocardium. Hypotension of NTG further accentuated this difference. Mechanical low perfusion pressure reduced uniformly flows to the ischemic left ventricle. High perfusion pressure increased collateral flow preferentially to the subepicardium.

CHEMOSENSORY FUNCTION OF THE OSPHRADIUM IN APLYSIA. Paul Downey* and Behrus Jahan-Parwar, Clark Univ., Biol. Dept., Worcester, Mass., and Worcester Foundation, Shrewsbury, Mass.

Special techniques were used to allow localized application of chemosensory stimuli to the osphradial epithelium and to prevent direct stimulation of neurons in the osphradial area. Excitatory, inhibitory or mixed responses were obtained from 37 out of 187 cells recorded in the abdominal ganglion. The majority of responsive units were affected by seaweed extract (Rhodymenia palmata), and 2 amino acid constituents of this seaweed (glutamic acid and aspartic acid). These amino acids were effective in concentrations as low as 10^{-5}M (glutamic acid) and 10^{-4}M (aspartic acid). Response to stimulus solutions did not result from a change in osmotic pressure or mechanical stimulation associated with application of stimulus solutions. None of the 37 responsive units were affected by mechanical stimulation of the osphradium with plain seawater, and only 2 cells responded to a change in osmotic pressure at the osphradium. The 37 chemosensory units included identified and unidentified units, and both white cells and pigmented cells, and the majority (26 cells) were located in the right caudal quarter ganglion. This experiment represents direct evidence for the presence of chemoreceptors in the osphradial organ. Supported by NIH Research Traineeship MH 10625 to P. Downey and by PHS Grant No. NSO8868 and Career Development Award No. K4-HD-5178 to B. Jahan-Parwar.

SINGLE TRIGEMINAL AFFERENT FIBERS SENSITIVE ONLY TO WARMING OR COOLING OF THE HAIRY SKIN OF THE MONKEY'S FACE. R. Dubner and R. Sumino*. National Institute of Dental Research, NIH, Bethesda, Md.

Single unit activity of thermoreceptive afferent fibers was recorded from isolated strands of the infraorbital nerve of anesthetized rhesus monkeys. Single fibers which increased their activity during warming of the skin (warm fibers) had receptive fields (single spots, <1 mm in diam.) located on the hairy skin of the face, with the highest density found below the nose. On the basis of conduction velocity measurements (range of 1.2 to 5.4 m/sec, mean=3.2 m/sec), at least some of these were small (A delta) myelinated axons. Warm fibers usually were active during the application of constant temperature stimuli ranging from 30 to 50°C. Peak firing rates occurred at higher constant temperatures (between 40 and 47°C), and reversible, irregular discharge patterns often were found in the noxious heat range (above 45°C). Rapid temperature shifts produced increases in firing rate which were dependent on the size of the temperature change, the adapting temperature, and the time between stimuli. Single fibers which increased their activity during cooling (cold fibers) had receptive fields (single spots, <1 mm in diam.) distributed throughout the infraorbital region, and had conduction velocities in the range of 2.1 to 11.7 m/sec (mean= 6.9 m/sec). Cold fibers responded to constant temperature stimuli over a range from less than 20°C up to 40°C, with some fibers also active at temperatures above 45°C. Compared to warm fibers, their activity following rapid temperature changes was more dependent on the size of the temperature shift, and less sensitive to previous stimuli and the adapting temperature. The data indicate that A delta thermoreceptive trigeminal fibers are responsive to warming or cooling, and that many are sensitive to stimuli in the noxious heat range.

MYOCARDIAL SUBSTRATE UTILIZATION CHANGES DURING GLUCAGON INFUSION IN CONSCIOUS DOGS. Beatrice C. Durham* and Harvey I Miller, Division of Research, Lankenau Hospital, Philadelphia, Pennsylvania 19151

It is known that glucagon (GLG) injection increases plasma glucose (G) while decreasing FFA. We have shown that GLG infusion (2-4ug/kg min for 4 hr) produces cyclic variations in plasma concentrations of these substrates. During the first 15 min of GLG infusion into unanesthetized fasted dogs the G level increased to over 200 mg%. Thereafter it fell to control levels at 3 hr and rose again at 4 hr. Plasma FFA, although lower at 15 min, reached its lowest value at 3o min, rose to the control level at 2 hr. Myocardial FFA uptake was barely detectable at 30 min and then rose to control level at 4 hr. Significant G uptake by the heart was not seen until 60 min after the start of infusion or 45 min after the peak G level and while immunoreactive insulin concentration was high. With the fall of G level at 2 hr, uptake by the heart was again undetectable and remained so. At no time did the heart extract enough G to balance the decreased FFA extraction. Lactic acid (L) extraction, on the other hand, increased about 2-1/2 fold by 15 min, possibly supplying most of the energy deficit. Although no change in myocardial O_2 consumption was observed due to GLG, the percent for FFA oxidation decreased sharply at 15 min and remained depressed for the first hour during which time L uptake decreased and the percent of O_2 consumption for FFA oxidation returned to normal. L uptake decreased rapidly by 2 hr, there was no A-CS difference at 3 hr, and an output of L by 4 hr. During the early phase of GLG infusion when G level was high and L level was slightly elevated, L appeared to be preferred to G as an energy source for the myocardium. Later, when FFA level had returned to control values, FFA once again was the major energy substrate. (Supported in part by USPHS, NIH grants HE12636 and FR5585. Dr. Miller is an Established Investigator of the American Heart Association).

DYNAMIC RESPIRATORY CONTROL DURING RECOVERY FROM CO_2 BREATHING IN INTACT AND CHEMODENERVATED AWAKE DOGS. R.E. Dutton, J.A. Krasney, and A.J. Berger*. Albany Medical College, Albany, N.Y. and Rensselaer Polytechnic Institute, Troy, N.Y.

Recently, Gelfand et al. (Fed. Proc. 30: 270, 1971) have reported that by analyzing the recovery transients from CO_2 breathing in awake intact dogs, a peripheral chemoreflex component could be isolated from the central chemoreceptive drive. However, their association of only the fastest of 3 components of these respiratory transients with the peripheral contribution did not appear to be definitive, since their ventilatory studies were performed on intact dogs only. In this present study, respiratory transients following abrupt removal to room air after 10 min of CO_2 inhalation (end-tidal CO_2 = 8%) were recorded in 5 awake dogs before and after denervation of carotid and aortic bodies. By comparing intact with denervated responses, it was calculated that the peripheral chemoreceptors contribute 18% (range 8% to 35%) to the dynamic ventilatory response, and have a mean time constant of 4 sec with no measurable delay in onset of the decline in ventilation (V_E). In denervated animals, two central time constants of 20 sec and 118 sec were calculated by standard curve peeling techniques. Respectively, these had amplitudes of 56% and 44% of the total central contribution. Recovery of V_E was initiated after an average 4 sec delay. These results support the suggestion by Gelfand et al. that the first time constant of tidal volume during recovery from hypercapnia in awake intact dogs represents the peripheral chemoreceptor contribution, and that the second and third time constants are centrally mediated. (Supported by U.S. Public Health Service Grants HL 12564 and HL 11982.)

POTASSIUM ACCUMULATION NEAR PACEMAKING CELLS OF APLYSIA. D. C. Eaton (intr. by S. Hagiwara). Dept. of Physiology, UCLA Medical School, Los Angeles, Calif.

A delayed current decrease similar to that observed in several other preparations is present in certain cells of Aplysia. The pacemaking cells, in particular R_{15}, display this delayed current decrease while non-pacemakers such as R_2 do not. The current voltage relationship obtained by voltage clamp methods for long duration command pulses (3 sec) displayed a time dependent decrease in outward current going from a maximum near 100 msec to a steady state minimum level 20-30% of maximum at 1.5 to 2.5 seconds after the beginning of the voltage command. Double step voltage clamps showed that this current decrease was associated with a large shift of EMF. Measurements of conductance, on the other hand, failed to show any significant difference between conductance at the times of peak and steady state current. Three possible explanations of this phenomenon were offered: (a) accumulation of K^+ near the membrane surface, (b) compensating conductance changes which produce an apparent change in EMF but no apparent change in membrane conductance, and (c) metabolic processes producing electrogenic effects. These possibilities were tested by (1) application of Na^+ and Cl^- free ringer. There were no changes in the I-V relations which could account for the observed effects, so (b) was ruled out. (2) Application of metabolic inhibitors, ouabain, K^+ free, Li^+, or low temperature. There were no noticeable effects so (c) was excluded. To test for accumulation, high K^+ and TEA salines were applied to the cell. These solutions produce dramatic reductions in the delayed current decrease, lending support to this possibility. From anatomical and electrophysiological considerations, the conclusion is reached that the accumulation takes place in extensive invaginations of the cell membrane.

THE ADAPTATION OF CORONARY AND SYSTEMIC CIRCULATION IN UNANESTHETISED DOGS TO PACED HEART RATE INCREASE COMPARED WITH THE CIRCULATORY ADAPTATION TO EXERCISE. Walter Ehrlich, Francine Schrijen*, David T. Krausman*, Paolo Caldini and Joseph V. Brady*. Johns Hopkins Univ., Sch. of Medicine and Sch. of Hygiene, Baltimore, Md. 21205.

The changes of coronary and systemic circulation during the transition from normal heart rate to electrically-paced increase of heart rate were investigated in 30 trials with 3 unanesthetised dogs. These changes were compared with the changes of circulatory functions during 56 trials of adaptation to treadmill exercise accompanied by a similar heart rate increase with the same animals. With the onset of pacing, the heart rate and the cardiac output increased more suddenly than with exercise. With pacing, the cardiac output increased by 1L./min; with exercise by 4L./min. With pacing, the stroke volume decreased; with exercise, it increased. With pacing, the systolic blood pressure fell, and the diastolic b.p. rose; with exercise, the systolic b.p. rose, and the diastolic b.p. fell for 8 seconds and returned subsequently to the rest values. The right atrial pressure fell in both situations. The total peripheral resistance during pacing was higher than with exercise.--The coronary flow decreased for the first four seconds of exercise before it increased steeply, as was described previously. With pacing, however, the coronary flow increased immediately. This does not support the explanation that the initial decrease in coronary flow during adaptation to behavioral activities is caused by extravascular pressure changes. The steady state values of coronary flow reached with pacing were half of those reached with exercise. This is compatible with the hypothesis that steady state values of coronary flow are regulated mainly by myocardial oxygen needs.

DIRECT IN VITRO EFFECTS OF MELATONIN ON STEROID BIOTRANSFORMATION BY RAT TESTICULAR TISSUE. LeGrande C. Ellis and Ronald L. Urry*. Utah State University, Logan, Utah.

A series of investigations on steroid biotransformations by rat testicular tissue were undertaken to establish the fact that melatonin has a direct effect on the testis in vivo. Hypophysectomy and subsequent daily injection of either 1 or 2 mg of melatonin resulted in a decrease in synthesis of androstenedione and testosterone from progesterone-4-^{14}C. The 5α-reductase activity for progesterone was similarly elevated. Irradiation of rats with 450 R increased androgen synthesis 24 hrs. after treatment, but decreased it afterwards. 5α-Reductase activity was similarly affected. Melatonin synthesis was decreased 24 hrs. after irradiation, but was increased afterwards. Senescence of the testes with respect to androgen synthesis by both control and irradiated animals was observed after 15 weeks of age. Melatonin specifically increases the 5α-reductase of seminiferous tubules for both progesterone and testosterone. It also decreases androgen synthesis by both the interstitial cells and the seminiferous tubules. Similarly, melatonin and the pineal gland were observed to be responsible for the high 5α-reductase activity of the rat testes in the prepubertal rat previously reported by other workers. Thus, melatonin and the pineal gland do affect the testis in the absence of a pituitary and do have a functional relationship to aging and irradiation. Melatonin is very effective as an antigonadal agent since it decreases testosterone synthesis, but increases its inactivation at the tubular level. Additional studies with animals subjected to changes in environmental lighting show similar effects on steroid biotransformations. Supported by the U. S. Atomic Energy Commission Grant No. AT(11-1)-1602.

CEREBRAL HEMONDYNAMICS DURING ENDOTOXIN SHOCK IN THE DOG. T.E. Emerson, Jr. and J.L. Parker*. Dept. of Physiol.,Mi.State Univ., E.Lansing, Mi.

This study describes the effects of severe endotoxin shock on cerebral blood flow (CBF), cerebral vascular resistance (CVR) and systemic arterial blood pressure (ABP). 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. Three groups were studied: 1) artificially respired, shock (N=10); 2) artificially respired, controls (N=11); 3) spontaneously respired, shock (N=7). Results after endotoxin administration in group 1 are shown below (* = $P < 0.05$):

Time	0	15'	30'	60'	120'	180'	240'
ABP (mm Hg)	115	50*	61*	53*	58*	64*	55*
CBF (ml/min)	27	18*	20*	17*	18*	16*	11*
CVR (PRU)	4.3	3.4*	3.5*	3.7*	5.0	5.9	7.4
$PaCO_2$ (mm Hg)	30	-	30	32	34	34	30
pH (units)	7.27	-	7.21*	7.19*	7.17*	7.14*	7.20*

Calculation of per cent change at 240' post-endotoxin shows that CBF fell an average of 60% and CVR increased 72% ($P \approx .05$). These changes were different than those in the control group. Four of the 7 spontaneously breathing dogs died from 60-180 min after endotoxin. CBF decreased an average of 56% and CVR changed irregularly at the time of death or at 240' post-endotoxin. Changes in pH were similar to those in group 1 but $PaCO_2$ fell as a result of hyperventilation. Autoregulatory curves were run when possible and were unaffected during shock. Our preliminary data suggest that a marked depression of CBF during the latter phase of endotoxin shock may be involved in the pathogenesis of this shock state. (Supported by grants from NIH, HE14774, and the Mich. Heart Assoc.)

INEFFECTIVENESS OF OSMOTIC STIMULI TO INDUCE WATER INTAKE IN RATS WITH LESIONED THALAMIC TASTE NUCLEUS. R. Emmers and P. Passamonte*. Department of Physiology, College of Physicians and Surgeons, Columbia University, New York, N. Y.

Recent electrophysiological studies (The Physiologist 14:139, 1971) have revealed that hypothalamic thirst neurons are not osmoreceptors; their response to hypertonic NaCl is mediated via the thalamic taste nucleus (thtn). The present study was designed to test whether a bilateral destruction of this nucleus would abolish the effectiveness of extracellular NaCl to induce water intake. A subcutaneous injection of 1 ml of 15% NaCl was administered to 21 rats once a day and their individual water intake was measured at 1 and 24 hrs post-injection. Five days later, lesions were placed in the thalami of all rats to produce a total, a partial, or no electrocoagulation of the thtn. The injections and measurements were resumed a day later. Lesions were reconstructed histologically. - A total bilateral destruction of the thtn decreased the mean water intake during the 1st hr of post-injection from 8.3 ml to 1.2 ml, whereas a partial or no damage to this nucleus resulted in a decrease from 7.5 ml to 7.3 ml ($P < 0.01$ of a t-test). Water intake during the post-injection period between 1 and 24 hrs had a mean decrease from 1.9 to 0.7 ml/hr and from 2.0 to 1.9 ml/hr with a total destruction of the thtn and control rats, respectively. Rats with total thtn lesions remained permanently hypodipsic; for some this was inadequate to maintain life. (Aided by grant NS-03266 from NINDS)

Influence of calcium, sialic acid and pH on the surface tension measurements of lung surfactant. R. L. Engen, R. F. Henderson* and R. C. Pfeger.* Iowa State University, Ames, Iowa and Lovelace Foundation, Albuquerque, New Mexico. Canine lung surfactant material, obtained by pulmonary lavage, was concentrated by centrifuging the recovered lavage fluid to remove the cellular matter and then recentrifuging at 1.2×10^6 g-min. to obtain a white, acellular, and amorphus precipitate which was then dialyzed and lyophilized. The high speed precipitate was weighed and dissolved in hexane: ethanol (4:1, v/v). The H:E solution, 10 ul containing 10-12 ug surfactant lipids, was layered over either a saline or mammalian Ringers solution (with and without calcium) in the trough of a "Wilhelmy" balance. The pH was changed by varying either the H^+ concentration or sialic acid (a normal constituent of cellular membranes and sialomucin) in the subphase. The presence of calcium in the subphase lowered the surface tension of the film during the expansion phase of the hysteresis cycle. Either an increased sialic acid concentration or an acid pH reduced the total hysteresis area and lowered the surface tension during the expansion cycle, which caused the expansion curve to approach the compression curve. Calcium and sialic acid appear to decrease the rate at which the compressed film returns to the liquid state.

DIFFERENCES BETWEEN CALCIUM BINDING AND UPTAKE BY SARCOPLASMIC RETICULUM: SPECIFIC EFFECTS OF ANTIBIOTIC IONOPHORE X537A. Mark L. Entman * and Arnold Schwartz. Div. of Myocardial Biology and the Dept. of Medicine, Baylor College of Medicine and the Fondren-Brown Cardiovascular Research and Training Center, Methodist Hospital, Houston, Texas.

The sarcoplasmic reticulum (CRS) is thought to play an important role in excitation-contraction coupling and relaxation through accumulation and presumed release of calcium. Two different methods have been used for the measurement of calcium accumulation. These are "binding" in the absence and "uptake" in the presence of a precipitating anion (oxalate or phosphate) in the reaction. With the use of a dual beam spectrophotometer an initial binding "burst" was observed before linear uptake ensued. Uptake per se required low Mg^{++} (Km<1 mM) while binding and the initial binding burst required higher Mg^{++}. The Mg^{++} response of binding suggested two classes of sites with Km for Mg^{++} of 3 mM and < 1 mM respectively. An ionophore antibiotic (X537A) partially dissociated binding and uptake processes; the data also suggest, however, that they may share an initial binding process or site. X537A at 5 µg/mg inhibits binding and uptake similarly and induces prompt calcium release when added at peak binding; it does not induce release after calcium uptake. At higher concentrations, "uptake" is virtually eliminated while "binding" (I50-16 µg/mg) remains >50% suggesting an additional action of X537A on a step unique to uptake. The data suggest two classes of Ca^{++} binding sites in CRS, one of which is related to transport (uptake), and that X537A may be a specific releasing agent affecting them. X537A does not affect CRS ATPase or NaK-ATPase.

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DRINKING INDUCED BY LOW DOSES OF INTRAVENOUS ANGIOTENSIN. Alan N. Epstein, Department of Biology & Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, PA

The high doses of angiotensin that are necessary for the induction of thirst by intravenous infusion are an obstacle to acceptance of the hormone as a natural dipsogen. In previous studies (Fitzsimons & Simons, J. Physiol. 203:45, 1969) rats drank to 10 µg/rat. We have reduced the effective dipsogenic dose by 1) using isoproterenol (100 µg/kg, sc) several days before infusion to stimulate drinking with the renal dipsogen (Houpt & Epstein, Physiol. Behav. 7:897, 1971), 2) testing the animals in their home cages the morning after ether anesthesia and catheterization, and 3) using angiotensin I (Schwarz-Mann). Using the decapeptide for intravenous infusion more closely imitates the physiological geography of the renin-angiotensin system in which angiotensin I reaches the right heart from the kidneys and newly converted angiotensin II enters the arterial circulation from the lungs, and it avoids the hazard of pulmonary degradation of the octapeptide. With these improvements in method, 7 rats (350-400g, ♂) with catheters in the right superior vena cava drank an average of 2.0 ml (R=0.2-3.3) to an average cumulative dose at the initiation of drinking of 359.0 ng/rat (R=164.8-658.0) of angiotensin I infused at 40 ng/min, 4 others drank 3.4 ml (R=2.7-4.0) to 3278 ng/rat, at 400 ng/min. Angiotensin I was 2.1 times more effective than angiotensin II when compared in the same rats (N=4, 6 comparisons). Peripheral angiotensin is a potent dipsogen at doses that approximate those for other effects of the hormone in intact, unanesthetized rats.

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CORONARY BLOOD FLOW AND MYOCARDIAL FUNCTION DURING EXPOSURE TO 100 PPM CARBON MONOXIDE. Howard H. Erickson and Delwin K. Buckhold*. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

The objective of this study was to determine the effects of 100 ppm carbon monoxide (CO) on both coronary blood flow and left ventricular function in the conscious dog. Mongrel dogs were surgically instrumented to measure coronary blood flow through the circumflex branch of the left coronary artery with a Doppler ultrasonic flowmeter. A solid-state pressure transducer was implanted within the chamber of the left ventricle in order to measure pressure and compute left ventricular dP/dt. Catheters were placed in the carotid artery and pulmonary artery in order to measure arterial pressure and to determine blood gases, pH, oxygen saturation, and carboxyhemoglobin saturation in arterial and mixed venous blood. Seven dogs were exposed to a 100 ppm CO-air mixture, introduced through an endotracheal tube in a permanent tracheostomy. Five dogs were exposed to CO in an environmental chamber. Three hours' exposure to CO increased the COHb from 0.9 to 7.1%. The arterial oxygen saturation decreased by 7.1% and the mixed venous oxygen saturation by 7.3%. Coronary blood flow increased by 18%, heart rate by 3%, and maximum left ventricular dP/dt by 11%. The results suggest that low levels of carbon monoxide result in significant changes in coronary blood flow and myocardial function.

ACUTE STRESS STIMULATION OF SERUM LH AND PROLACTIN. J. Euker*, G. Riegle, C. Shaar* and J. Meites. Michigan State University, East Lansing, Michigan 48823.

The effect of the acute stress of animal handling, anesthesia and blood sampling on serum LH and prolactin was tested in male Long-Evans rats. Blood samples were collected by orbital sinus puncture under light ether anesthesia. Serum LH and prolactin were measured by radioimmuno techniques. Serum LH and prolactin in samples taken within 1 min after initial animal disturbance (13.8 and 17.3 ng/ml respectively) were similar to levels measured after decapitation with minimal animal handling. Serum LH and prolactin were increased in serial blood samples taken at 4, 8 and 15 min after animal disturbance. Serum LH and prolactin in individual blood samples taken 2, 5, 10 or 15 min after placing rats in transfer cages for transport to the blood sampling area were also higher than the levels in either the orbital sinus 1 min or the decapitation sample. Serum LH and prolactin levels remained elevated in rats serially bled at 15, 45 and 90 min after animal disturbance. Serum LH and prolactin levels were increased 2 to 10 fold following acute stress. Dexamethasone suppression of adrenocortical secretions (50 ug/100 g bw for 8 days) suppressed serum LH and prolactin levels in rats subjected to serial bleeding at 1, 4, 8 and 15 min after initial handling. Although the stress of serial bleeding increased serum prolactin levels in castrate males the elevated serum LH values in these rats were reduced by the stress of serial blood sampling. These data suggest that acute stress can result in increased serum LH and prolactin levels which must be of concern to the investigator. The biological significance of these elevations needs further study. (Supported in part by NSF grant No. 8687 and NIH grant No. AM 04784)

ANALYSIS OF THE STATIC CHARACTERISTICS OF IN VIVO CAT DIAPHRAGM

Myron J. Evanich, Micheal J. Franco* and Ruy V. Lourenço, Univ. of Illinois College of Medicine, Chicago, Ill. 60680

We used transdiaphragmatic pressure (Ptd), as a measure of the force output of the diaphragm, during electrical stimulation of the phrenic nerves with a physiological range of pulse rates of 1 to 50 pulses per second (pps). We obtained, in cats, under isovolumetric conditions, values of Ptd at functional residual capacity (FRC) and at higher and lower volumes. At stimulus rates less than 5pps, the response was a series of single pressure twitches with amplitude inversely related to lung volume. Also, when lung volumes were increased above FRC there was a decrease in the rate of rise and rate of decay of the pressure twitch, and when they were decreased below FRC there was an opposite effect. The tetanic pressure-pulse rate curve had a sigmoid form with a middle range (10-30pps) where the change in pressure produced per unit change in pulse rate was steep. Further increases in rate resulted in a decrease of the slope of this curve which asymptotically approached a maximum value between 50 and 100pps. The pressure-pulse rate curve is significantly altered by changes in volume: at lung volumes above FRC, the slope and maximum pressure decreased, while at volumes below FRC, this slope and maximum pressure increased. This effect was not symmetrical, volumes below FRC having a greater effect than those above. These results indicate that: 1) the rate of phrenic motor nerve firing with the most effective transfer of neural to diaphragmatic mechanical information corresponds to that found during normal breathing, 2) diaphragm muscle "gain" is a function of lung volume, and 3) the "effective resting length" of the diaphragm is below FRC. Supported by NIH Grant HL 14735

EFFECT OF ANESTHESIA ON GASTRIC SECRETION AND CIRCULATING GASTRIN.

J.C.W. Evans*, D.D. Reeder* and J.C. Thompson. Univ. of Texas Med. Branch, Galveston, Texas.

The effects of anesthesia on gastric secretion are not well understood. We have studied the effect of pentobarbital anesthesia on circulating gastrin and on the gastric secretory response to both endogenous and exogenous gastrin. Method: Paired studies were performed in dogs on alternate days with the animals either awake or anesthetized with pentobarbital sodium, 25 mg/kg i.v. In 10 dogs, endogenous gastrin release was achieved by irrigation of the isolated antral pouch with 0.5% acetylcholine (Ach), and acid secretions were collected every 15 min. from a gastric fistula for 3 hours. Serial serum samples were obtained for radioimmunoassay of gastrin. In five additional dogs, a 90 min. infusion of synthetic human gastrin (1.25 μg/kg/hr) was given i.v., and acid secretions were measured. Results: In the 10 dogs that received antral Ach, acid secretion with the animals awake was 2.74 mEq/15 min. and during anesthesia was 1.0 mEq/15 min. ($p < 0.05$). Mean serum gastrin in the awake animals was 277 ± 21 pg/ml. During anesthesia, gastrin levels were consistently significantly higher (mean 476 ± 41 pg/ml) than during the studies awake. In the five dogs receiving exogenous synthetic gastrin, mean acid output was 4.36 mEq/15 min. awake and was unchanged from acid output during anesthesia (4.42 mEq/15 min.). Conclusions: Pentobarbital anesthesia caused a decreased acid output in response to endogenous gastrin (although gastrin release was enhanced) and caused no change in acid response to exogenous gastrin. These results suggest that anesthesia causes the parietal cell to differentiate between gastrins of different molecular sizes.

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EFFECT OF HEMORRHAGIC AND ENDOTOXIC SHOCK ON CIRCULATING SERUM GASTRIN. J.C.W. Evans*, D.D. Reeder* and J.C. Thompson. University of Texas Medical Branch, Galveston, Texas

Experimental studies on the metabolism of hormones are often associated with significant hemodynamic changes. To test the possible significance of these changes, we have studied the effect of hemorrhagic and endotoxic shock on circulating levels of gastrin. Method: In seven anesthetized dogs, the mean arterial blood pressure was lowered to 40-50 mm Hg by rapid arterial bleeding and was maintained at that level for 2 hours. Normal blood pressure was then restored by transfusion. Five additional anesthetized dogs were given i.v. injections of 6 mg endotoxin (E.coli) which resulted in an immediate fall in mean arterial pressure to 35-50 mm Hg. This level of hypotension persisted during the remaining 3 hours of the study. Serum concentrations of gastrin were measured by radioimmunoassay in blood samples obtained at 15 min. intervals throughout the experiments. Results: Basal serum gastrin levels were 38 ± 8 picograms (pg)/ml. There was no change in circulating gastrin during hemorrhagic shock or after restoration of normal blood pressure by transfusion. After endotoxin, gastrin rose transiently to 65 ± 27 pg/ml but was not significantly elevated over basal ($p > 0.2$). Conclusion: Major alterations in blood pressure and blood volume did not change circulating gastrin. The homeostatic mechanisms responsible for maintenance of constant levels of circulating gastrin are apparently capable of compensating for changes in tissue perfusion.

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FETAL BLOOD VOLUME AS A DETERMINANT OF FETAL PLACENTAL BLOOD FLOW. J. Job Faber+, Thomas J. Green*, Charles Gault*, Kent Thornburg. Department of Physiology, University of Oregon Medical School, Portland, Oregon 97201

Nine sheep fetuses were prepared with electromagnetic flow sensors on the distal aorta and studied 2-7 days later. The sensors were calibrated in vitro (SEM ≤2%). In vivo, flows measured electromagnetically and by the microsphere technique differed by 5.3% (N.S.). Placental flow was found to be 84 (± 2, SEM) % of distal aorta flow. This distribution did not depend on fetal blood volume, which was changed by blood letting ($r = -0.15$, N.S.). Mean placental flow 3 days after surgery was 177 (± 9.3 SEM) ml min^{-1} kg $fetus^{-1}$.

Blood volumes (75-115%) and placental flows (50-115%) were recorded 63 times in six fetuses: Flow (%) = -70 + 1.7 (±0.1, SE)·Blood volume (%); $r = 0.85$; $P << 0.01$. This dependency was not a function of time after blood letting, the recovery of flow being paralleled by hemodilution. Blood volumes were reduced to 87% in three fetuses by infusion of hyperosmolar mannitol into the ewes. Distal aortic flows were recorded for periods of 3 hours. The results were virtually identical to those obtained by blood letting.

Fetal placental blood flow depends strongly on fetal blood volume, independent of time and hemoglobin concentration over the ranges studied in these experiments.

+ Established Investigator of the American Heart Association.

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FAILURE OF AMINERGIC BLOCKING DRUGS TO INHIBIT THE ACTH RESPONSE TO KETAMINE. E. Edwin Fahringer*, Arnold S. Lippa*, Seymour M. Antelman*, and Edward S. Redgate. Depts. of Physiology and Psychology, University of Pittsburgh, Pittsburgh, Pa. 15213.

Ketamine HCl (K)--a phencyclidine derived, nonbarbiturate, short acting anesthetic -- stimulates the pituitary adrenal system in intact male rats. We have previously shown that the corticosterone response to K is abolished in 24 hr. hypophysectomized rats, is blocked by dexamethasone, is reduced by pentobarbital, and is not altered by either atropine or nialamide (Fed. Proc. 31: 811, 1972). In the current study intact male rats were pretreated with an α or β or dopa aminergic blocker one hour before injection of K (120 mg/kg IP) or K vehicle (V). Blood samples were taken 45 min after K or V injection and the plasma fluorometrically assayed for corticosterone. All injections were given IP except haloperidol which was given SC.

DRUG PRETREATMENT (mg/kg)		PLASMA CORTICOSTERONE (μg%) 45 min post ketamine	45 min post vehicle
Phentolamine	5.0	30.1 ± 2.8 (4)	15.0 ± 2.4 (4)
Haloperidol	0.2	24.9 ± 1.5 (5)	8.6 ± 2.7 (4)
Pindolol	5.0	23.3 ± 3.4 (3)	9.8 ± 1.1 (4)
Propranolol	6.5	32.6 ± 2.6 (4)	11.9 ± 0.9 (3)
	10.0	33.2 ± 3.9 (8)	
Saline		29.8 ± 2.6 (6)	11.9 ± 1.5 (4)

None of the aminergic blockers abolished the corticosterone response to K. Furthermore the drugs by themselves did not change resting levels (saline + V = drug + V), suggesting that under the above conditions aminergic neurotransmitters do not tonically inhibit ACTH release.

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ENZYMATIC ASSESSMENTS OF THE PINEAL GLAND DURING PROLONGED PSEUDOPREGNANCY. Anthony V. Fasano*, Frances A. Kovarik*, Barbara A. Kasprow*, and Joseph Thomas Velardo. Department of Anatomy, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois.

In an effort to establish semi-quantitative histochemical assessments of the pineal gland in Sprague-Dawley derived adult albino rats, it appeared of interest to determine the relationships between certain enzymatic activities within the gland during prolonged pseudopregnancy, i.e., in pseudopregnant rats bearing decidual reactions. Rats were housed in suspended, stainless steel cages and fed Purina Rat Chow and water ad libitum. A light-dark cycle of 12:12 was maintained. Pseudopregnancy was initiated by vibratory stimulation of the cervix during estrus and the endometrium was surgically traumatized by scratching with a burred needle five days after the onset of pseudopregnancy. The animals were necropsied on days 6, 10, 13, 15, 18, 20, and 21 of prolonged pseudopregnancy and four enzymes (succinic dehydrogenase, lactic dehydrogenase, alkaline phosphatase and acid phosphatase) were studied. Comparative histochemical assessments in the pineal gland revealed the following for succinic dehydrogenase: Day 18>10>13>20> 6 and 21 (similar)>15; lactic dehydrogenase: Day 13>10>6>18>20>15 and 21 (similarly minimal); alkaline phosphatase: Day 15>6 and 13 (similar)>10>18 and 20 (similar)>21; and acid phosphatase: Day 15>6 and 13 (similar)>10 and 18 (similar)>21>20. These data form workable standard reference base-lines for several of the important reactions associated with the pineal gland which can be effectively utilized in subsequent hormonal studies. (Supported by U.S.P.H. Service grants to Professors Kasprow and Velardo).

CONTRACTILE RESPONSE OF ISOLATED SMOOTH MUSCLE FIBERS TO FIELD AND LOCAL ELECTRICAL STIMULATION. Fredric S. Fay and Claudio M. Delise.* Physiol. Dept., UMass Med. Sch., Worcester, Mass.

The present studies were undertaken to determine what structural changes are associated with contraction of isolated smooth muscle cells from Bufo marinus. Isolated fibers were obtained from the stomach wall by proteolytic digestion according to Bagby, et al (Nature 234:356). Isolated fibers suspended on a glass slide were observed using a differential interference contrast microscope and cinematographic recordings simultaneously performed. The cells were electrically stimulated (100 volts, 10 pps, 1 msec. duration) through a microelectrode adjacent to the cell membrane. Localized contractions were induced when electrical stimulation was through a high impedance electrode (10 mΩ) but synchronous contraction along the entire fiber resulted when the impedance of the stimulating electrode was low (1KΩ). In both cases fibers spontaneously relaxed after stimulation, and could be restimulated to contract thereafter. In the absence of Ca^{++} in the suspending medium electrical stimulation produced no contraction. The surface membrane in the area of contraction exhibited large evaginations which retracted upon relaxation. Contraction resulted in a change in length to 33±2%(S.E.) of rest and an apparent change in volume to 81±4%(S.E.) of rest. The observations are consistent with a model for smooth muscle contraction in which force of the contractile apparatus is exerted between sites on the cell membrane that are closely spaced. A motion picture demonstrating these effects will be shown.

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A NEW APPROACH TO ACTIVE STATE MEASUREMENT. Theodore S. Feit and Berl G. Bass (intr. by N. M. Buckley). Albert Einstein College of Medicine, New York.

Quick release and quick stretch techniques are subject to question because the experimental intervention may in itself alter the contractile state. A method has been developed for computing the time course of the active state directly from mechanical data without applying perturbing step forces to the muscle. A. Huxley's sliding filament theory has been extended to include the kinetics of time-varying cross-bridge attachment and variable contractile element velocity. The active state was defined as the time variation in the rate constant for cross-bridge attachment. Integral equations describing isometric, isotonic, and delayed isometric contractions were derived. The time course of tension and shortening was recorded for families of isometric, isotonic, and delayed isometric contractions at various preloads in isolated cat papillary muscle preparations stimulated at 30/minute. The mathematical model was used to compute the time course of the active state from the experimental length-extension curve of the series elastic element, the length-active tension plot, and the time course of the length and tension changes during the contraction. The computed active state reached a rounded peak 250-350 msec. after the stimulus; by the time of peak tension the active state was decreasing rapidly. Relaxation was marked by a rapid fall-off in active state followed by a much slower decay, in contrast to results obtained by others using the quick-release method. Supported by grants NYHA & NIH 5T5 GM 1674.

MECHANISM OF LEAD SENSITIZATION TO ENDOTOXIN SHOCK. James P. Filkins and Bernard J. Buchanan.* Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Lead acetate iv sensitized rats to the lethal effects of endotoxin as reflected in a 2000-fold decrease in the LD_{50} to Salmonella enteritidis endotoxin (Proc. Soc. Exp. Biol. & Med. 134: 610, 1970). Lead also sensitized rats to shock induced by hind-limb ischemia, superior mesenteric artery occlusion, or Noble-Collip tumbling trauma. In order to elucidate the mechanism of lead sensitization to endotoxin the intravascular removal, hepatic detoxification, and select metabolic responses to endotoxin were evaluated in lead-treated rats. The intravascular clearance of a test dose of 500 micrograms of endotoxin was evaluated via shock bioassay in control rats and in rats receiving 5 milligrams of lead acetate iv. No significant difference in endotoxin removal from the blood was measured. In contrast, the blood clearance of colloidal carbon was depressed at 1,2 and 4 hours after lead treatment. Lead had no effect on the ability to the liver to detoxify endotoxin after either the in vitro addition of lead to liver homogenates or at 1/2, 1, 3 or 8 hours after in vivo lead administration. The death syndrome in lead-treated rats exposed to endotoxin was marked by profound hypoglycemia, lactacidemia, and hepatic glycogen depletion. Hepatic gluconeogenesis was depressed by endotoxin. The sensitization of the rat to endotoxin by lead is therefore probably not related to either the rate of intravascular clearance of endotoxin or a defect in the hepatic detoxification system; rather, lead may obviate the hepatic gluconeogenic response to endotoxemia and thus jeopardize the metabolic basis of shock resistance. (Supported by HL 14540 and HL 08682).

LOCAL EFFECTS OF K^+, Mg^{++} and Ca^{++} ON SPLENIC VASCULAR RESISTANCE AND WEIGHT. L.R. Fine* and C.C. Chou. Depts. of Physiol. and Med., Mich. State University, East Lansing, Michigan

Local effects of K^+, Mg^{++} and Ca^{++} on the vascular resistance (R) of various peripheral vascular beds have been studied. But their effects on splenic R and volume have not been studied. In in situ, pump perfused, collateral-free canine spleens, we measured perfusion pressure, large vein pressure, venous outflow and weight (W) of the spleen and aortic pressure as an isotonic solution of NaCl, KCl, $MgCl_2$ or $CaCl_2$ was infused intra-arterially. The mean splenic blood flow was 74.3 ml/min and weight 194 gm. The mean R and changes in W (gm) at various infusion rates (0.2-7.75 ml/min) are shown below. (N=10-13).

		0	0.2	0.38	0.97	1.94	3.38	7.75
NaCl	R	1.85	1.85	1.76	1.82	1.81	1.76	1.68
	W	-	+1.2	+2.7	+3.2	+3.9	+3.9	+3.9
KCl	R	2.20	2.23	2.29	2.40	2.76	3.44	-
	W	-	-0.8	-3.8	-8.5	-19.5	-43.2	-
$MgCl_2$	R	2.23	2.29	2.15	1.85	1.63	1.41	1.28
	W	-	-1.2	-4.4	-13.0	-16.8	-20.9	-26.1
$CaCl_2$	R	1.45	1.45	1.49	1.58	1.46	1.55	1.93
	W	-	-2.0	-3.2	-7.6	-14.6	-35.2	-79.6

Thus, using isotonic NaCl as volume control, splenic R was significantly and progressively raised by K^+ and lowered by Mg^{++}. Ca^{++} did not significantly affect R until infusion rates were 3.38 ml/min or above. All three ions decreased splenic W. While NaCl and $MgCl_2$ did not alter aortic pressure, KCl (8 out of 11 dogs, +9 mmHg) and $CaCl_2$ (5 out of 10 dogs, +7 mmHg) raised aortic pressure as R rose and W fell. It is concluded that local effects of these ions on splenic R are in some respects different from that on other vascular beds. Splenic W, i.e., its reservoir capacity, can be altered by these ions.

AN ANALYSIS OF THE BETA-ADRENERGIC FACILITATION OF THIRST. A.E. Fisher*, S.M. Antelman*, J.M. Tarter*, and E.S. Redgate. Psychobiology Program and Depts. of Psychology and Physiology, Univ. of Pittsburgh, Pgh.,Pa.15213.

Lehr,et al (J. Pharmacol. Exp. Therap. 158, 150, 1967) first reported that systemic injections of isoproterenol, a β-adrenergic agent, induced thirst in the rat. Lehr, and later Liebowitz suggested that the drug was acting centrally, and Liebowitz reported β- adrenergic facilitation and α-adrenergic inhibition of thirst following hypothalamic injections and proposed a model for the central regulation of water intake by adrenergic neurons (Liebowitz, S.F., Proc. Nat. Acad. Sci., 58:2, 332, 1971). In studies reported here we show that 1)the threshold dose of isoproterenol to elicit drinking is generally higher for central than for peripheral injections, 2)central isoproterenol drinking is blocked by nephrectomy, while central angiotensin and cholinergic drinking survive nephrectomy, 3)cord transection at T-1 eliminates drinking to isoproterenol following hypothalamic injection, 4)drinking to isoproterenol following dorsal hippocampal injection survives T-1 cord section in some cases, 5) studies with tritiated isoproterenol indicate that leakage of radioactivity into the periphery following hippocampal injection is 3-5 times that observed after hypothalamic injection. The argument will be presented that 'central' isoproterenol induced drinking probably does not reflect direct mediation of thirst-related behavior by adrenergic neurons. Instead, the drinking behavior appears to be mediated by two other pathways a)via a sympathetic signal (eliminated by transection) which leads to renin release, the formation of angiotensin, and the direct action of this compound on thirst-related central neurons, b)via leakage of isoproterenol to the periphery and the subsequent activation of the renin-angiotensin system.

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Contractile Properties of Skeletal Muscle in Trained Miniature Pigs. R. H. Fitts, D. R. Campion, R. G. Cassens, F. J. Nagle (intr. by B. Balke) Muscle Biology Lab., Univ. of Wisconsin, Madison.

To determine if the type of exercise alters the contractile properties of skeletal muscle, an in situ preparation of the tibialis anterior muscle of 4 control, 6 anaerobically trained and 4 aerobically trained miniature pigs was tested for time to peak tension, half-relaxation time, twitch tension, tetanus tension, and twitch tetanus ratio. The only significant difference found was that trained groups had a shorter contraction time than the controls. When the preparations were stimulated at 4/sec over a period of 45 min a significantly higher level of isometric tension was maintained by the two trained groups for each measurement between 5 and 45 minutes. Histochemically the tibialis anterior of the miniature pig is classified a heterogeneous muscle dominated internally by the slow twitch resistant red fiber and externally by the fast twitch resistant red and non-resistant white fibers. The more rapid contraction times after training may indicate adaptation of the contractile filaments and/or the supporting structures of contraction in these fibers. The greater time spent in relaxation during each contraction cycle as well as an increase aerobic energy supply in all fiber types may explain the increased endurance of the trained pigs.

THE RESPIRATORY EFFECT OF METABOLIC ACIDOSIS AT CONSTANT $PaCO_2$ IN THE DEAFFERENTED CAT. Robert Fitzgerald, Gail Gurtner and Barry Burns*. The Johns Hopkins University, Baltimore, Maryland 21205.

These experiments were performed to determine the response of some index of ventilation to metabolic acidosis at constant $PaCO_2$ in vagotomized-carotid body denervated cats, i.e. to see the rapidity and magnitude of change in this index in response to increased arterial H^+ alone affecting presumably only the medullary chemoreceptor. The index ("V_T") was the rate of phrenic nerve activity per burst which we have previously found to be highly correlated with V_T. Cats (3.0-3.5 kg) were anesthetized, vagotomized, and carotid body denervated. They were paralyzed and artificially ventilated to keep $P_{ET}CO_2$ at a fixed level. Neural activity in the transected left phrenic nerve was recorded, rectified and integrated. After a control period 0.2 N HCl was infused into the abdominal aorta (1.23 ml/min). The onset of the response appeared after 2.5-3.0 minutes. In one cat pH_a had fallen from 7.395 to 7.295 and "V_T" increased by 26.5% (31% by 26 minutes); in another animal the pH_a change (7.345 to 7.180 at 17 minutes) had increased "V_T" by 43.3% (73.5% at 26 minutes). Other observations (Davies et al., The Physiologist 13:76, 1970; Mitchell et al., The Physiologist 7:208, 1964) would suggest a slower response to metabolic acidosis. There are, however, several possible explanations to the relatively rapid onset of the increase in phrenic neural activity: 1) another receptor is acting; 2) an apparently very small change in the arterial-CSF HCO_3^- gradient (about 1 mEq) is sufficient to stimulate the central receptors; 3) even at constant $PaCO_2$ the PCO_2 of brain interstitial fluid is increased as postulated in the charged membrane hypothesis (Resp. Physiol. 6:173-187, 1969), which increase eventually appears in the CSF as observed by Davies et al. (see above reference). (Supported in part by PHS Grant HL 17417.)

STEROID METABOLISM IN MALE RATS CHRONICALLY EXPOSED TO HIGH ALTITUDES. C T Fletcher and Judith A. Ramaley. Dept. of Anatomy and Physiology, Indiana University, Bloomington, Indiana, 47401.

Groups of ten male Sprague-Dawley rats (E series) were exposed to 18,000 feet simulated altitude for 3, 6, 9, and 12 days, following a 3 day exposure of stepwise increases to lower altitudes. Two control groups of the same size and housed in identical living quarters represented Bloomington altitude controls (C series) and Bloomington level starvation controls (SC series). Rats in each group were 40 days old on day 1 of high altitude. Endocrine organ weights and histology, serum corticosterone concentrations and liver microsomal metabolism of estradiol-17,β-6,7-H^3 and corticosterone-1,2-H^3 were determined. Adrenal weights in the E series rats were approximately twice those of the C series through day 9, while adrenal weights in the SC series were intermediate. Serum corticosterone levels in the E series rats were least on day 9, at which time the C series rats showed their peak concentration. In the estradiol study the percent of the steroid metabolized did not vary significantly between groups. The E series rats metabolized a significantly greater fraction of corticosterone through day 6 (p level for mean differences between chromatogram area peaks $<.05$), the difference being represented by greater quantities of non-polar metabolites separated by paper chromatography and quantitated by liquid scintillation spectroscopy. The pattern of steroid inactivation did not vary significantly between the SC and C groups in either study. The increase in corticosterone inactivation through day 6 parallels the decreasing serum level observed during the same period. These results indicate an induction of the liver steroid hydroxylase system for corticosterone during the initial days at high altitude. (Supported in part by Ind. Acad. Sciences Grant # 74 and IU-Faculty Grant-in-Aid 26-234-71).

HUMAN CARDIOVASCULAR RESPONSE TO APNEIC IMMERSION IN COOL AND WARM WATER. L.J. Folinsbee* and L.D. Carlson, Univ. of Calif., Davis.

It has been reported that the bradycardia and peripheral vasoconstriction of breath-hold diving in man is due to a combination of stimuli resulting from apnea, position of the thorax, water temperature, esophageal pressure, and immersion of the face. Several of these stimuli were compared in healthy swimmers during body immersion and apnea (90 sec. duration) with and without face immersion in a thermoneutral (T_w=35°C) and a cool (T_w=31°C) water bath. Immersion of the face did not alter the bradycardia and peripheral constriction observed during apnea. The decrease in calf blood flow (1.2 - 1.3 ml/100 ml·min) was the same at both water temperatures despite a significantly lower resting calf blood flow in cool water. The vasoconstriction occurred more rapidly in warm water particularly with a full inspiration. The heart rate (HR) decreased at a more rapid rate in cool water but was of the same magnitude (ΔHR = 7-8/min) after 40 sec. of apnea at both water temperatures. These data show that the magnitude of the cardiovascular response to apnea and immersion is unaffected by pre-existing bradycardia and vasoconstriction due to cold, although some differences were observed in the rate at which the responses occurred.

HYPOPHAGIA FOLLOWING ADRENERGIC AGONISTS AND ANTAGONISTS INJECTED INTO THE LATERAL HYPOTHALAMUS OF SHEEP. J. M. Forbes* and C. A. Baile, U. of Penn., Phila., Pa. and SK&F Labs, 1600 Paoli Pike, West Chester, Pa.

Recent work in this laboratory showed that α and β adrenergic agonists injected into the medial hypothalamus caused increased feeding in sheep. The effects were blocked only by the corresponding antagonists. Because of the importance of the lateral hypothalamus (LH) in the control of feed intake, we have now injected these drugs into the LH. Six sheep (wethers), prepared with cannula guides directed toward the medial and on the contralateral side toward the lateral area of the hypothalamus, were fed a concentrate diet ad libitum. Feed and water intakes were recorded at 15, 30, 60 and 120 min after intrahypothalamic injections (1 μl). It was first confirmed that 8 nmoles dl-isoproterenol HCl, a β adrenergic agonist, injected into the medial hypothalamus resulted in feeding in fully satiated sheep (135g in 60 min vs 33g for carrier, $P < .01$). Isoproterenol was then injected into the LH of sheep after fresh feed was available for one hour but then withheld for 30 min to synchronize feeding. Doses from 8 to 512 nmoles had no significant effect on feeding. In contrast, l-norepinephrine bitartrate (l-NE), an α adrenergic agonist, depressed feed intake(137, 89, 111, 77 ($P < .05$) and 73g ($P < .05$) in 60 min for 0, 30, 60, 120 and 240 nmoles l-NE, respectively). 20 nmoles phentolamine HCl, an α antagonist, caused a further decrease in feed intake (to 46g in 60 min, $P < .05$) when injected 5 min before 120 nmoles of l-NE. Water intake was increased by this treatment (327 ml in 60 min vs 156 ml for control). Intraperitoneal temperatures were not affected by these treatments. In sheep injections into the LH of l-NE, but not isoproterenol, suppress feeding; in contrast, similar doses of isoproterenol injected into the LH of rats suppress feeding whereas l-NE does not. Supported in part by a grant from the NSF, Grant #GB 28836.

ELECTROPHYSIOLOGICAL CHARACTERISTICS OF THE DESCENDING SYMPATHETIC SPINAL PATHWAYS. Robert D. Foreman* and Robert D. Wurster. Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Previous work in this laboratory described descending sympathetic pathways localized on the surface of the spinal cord, approximately 1 to 2 mm below the dorsolateral sulcus. The purpose of the present experiments was to characterize these pathways by electrophysiological techniques. Laminectomies were performed on anesthetized cats (phencyclidine hydrochloride and α-chloralose) at the C_2 to C_3 and the T_1 to T_3 segments of the spinal cord. One hundred evoked responses, averaged on a transient averaging computer, were recorded from the T_2 preganglionic fibers by stimulating either the C_2 or the T_2 segment. The calculated conduction velocity of this pathway was 5 m/sec with a range of 3 m/sec to 7 m/sec, indicating that fibers transmitting sympathetic responses are small. Conduction times from the T_2 segments in these experiments were approximately 17 msec. With antidromic stimulation of the preganglionic fibers and recording from the extracellular potentials of the intermediolateral cell column, conduction times of 5 to 9 msec were observed. Thus a calculated central delay of 8 to 12 msec may be occurring between the site of T_2 stimulation and the preganglionic cell. Cross over patterns were also studied by placing stimulating electrodes on the bilateral descending sympathetic tracts at the C_2 segment and recording from the T_2 preganglionic fibers on the right side of the animals. The experiments indicated no crossing over of the bilateral tracts occurred between the C_2 and T_2 segments of the spinal cord. (Supported by NIH Grants HE 08682 and GM 999).

EFFECT OF VARIOUS DURATIONS OF HYPOXIC EXPOSURE ON EXCITABILITY OF VENTILATORY CONTROL MECHANISMS. H.V.Forster,*J.A.Dempsey,E.Vidruk,G. doPico.* *Pulm Physiol.Lab.,Univ. of Wis.,Med. School,Madison,Wis.

It has been demonstrated that: a) acute hypoxia potentiates the ventilatory($\dot{V}_E$) response to CO_2,exercise, and to nor-epinephrine;b) sojourn at altitude results in an increased $\dot{V}_E$ at rest and work, during CO_2 breathing, and during isocapnic hypoxia even though arterial and CSFpH are .03 alkaline: and c) altitude natives have a blunted $\dot{V}_E$ response to hypoxia and hypoxic work and a normal response to CO_2. The regulation of $\dot{V}_E$ during these 3 conditions was further investigated in the present study by measuring the ventilatory response to a pharmacological $\dot{V}_E$ stimulant, doxapram hydrochloride, on 8 healthy sea level residents during: 1) normal rest,2) acute respiratory acidosis-R.A.,3) 5 days of metabolic acidosis-M.A.,4) light work,5) acute hypoxia-A.Hyp. (PaO_2=46mmHg for 15 min) and 6) after 2 wks. of chronic hypoxia-Ch.Hyp. (PaO_2=58mmHg). Measurements were also made on 7 natives of 3100m altitude-alt. (nat.).Doxapram was infused for 25 min(7mg/min) during isocapnic hyperoxic conditions($P_{ET\,O_2}$≥200mmHg,except A.Hyp.). Results:1)The $\dot{V}_E$ response to doxapram was virtually identical over 5 conditions(normal, R.A., M.A., work, and Alt. Nat., 8-12 l/min, P> .10).,2)The response was markedly elevated during both A. and C. Hyp.(26.0 l/min-P< .03). It is concluded that: 1) separate and distinct increases in excitability of ventilatory control mechanisms occur with A. and C. hypoxia, 2) This change appears unrelated to the acid-base status of arterial blood, cerebral spinal fluid, or the intra-cellular environments, and 3) a control mechanism specific to hypoxia is altered with lifelong hypoxia. It is postulated that both A. and C. hypoxia result in a "facilitation" of the medullary ventilatory control center by the reticular activating system. Supported by A.H.Robbins Co.,NIH and the Wis. Heart Association.

THE STANDARDIZATION OF A PHYSIOLOGICAL HEMOGLOBIN PROCEDURE BY ATOMIC ABSORPTION SPECTROPHOTOMETRY. William C. Foster and Robert A. Donato*
Clinical Labs. Jeanes Hosp., Philadelphia, Pa. 19111.

The oxyhemoglobin method for the determination of blood hemoglobin is accurate, simple and more physiological, but due to the ease of standardization the cyanmethemoglobin procedure is in greater use. Zettner et al[1] reported the employment of atomic absorption spectrophotometry (A.A.S.) in the standardization of hemoglobin. However, in our present studies, a modification was found important. Pooled samples of venous blood were well-mixed and aliquots diluted 100 times with deionized water for hemolysis. Standards were prepared from iron wire in dilute HCL to which albumin was added. The iron contents of both standards and dilute hemolyzed blood were determined by A.A.S. The results were compared with those obtained by measuring to oxygen capacity of pooled blood samples and by Hainline's[2] modification of Wong's iron method. In 197 pooled samples hemoglobin standardization by measurement of the oxygen capacity showed a mean of 14.6, and range from 11.5 to 16.5 grams per 100 ml. blood. Standards by A.A.S. gave a mean of 14.9 and range from 14.3 to 15.9. The latter method is more accurate, simpler, and presents fewer technical difficulties.

1. Zettner et al: Am. J. Clin. Path. 48:225-228 (1967)
2. Hainline: Standard Methods Clin. Chem. II, 49-60 (1958).

PREDICTION OF MAXIMAL AEROBIC POWER BEFORE AND AFTER PHYSICAL TRAINING. E. L. Fox, Exercise Physiol. Lab., Ohio State Univ., Columbus, O. 43210.

The purpose of this study was to determine the feasibility of predicting maximal aerobic power (VO2max) from submaximal heart rate (HRsub) before and after physical training. A nomogram for predicting VO2max was constructed from data gathered on 87 untrained college males (age, 17-27yrs; ht, 159-191cm; wt, 53-122kg; VO2max, 2.32-4.29l/min or 27.9-55.5ml/kg-min). Prediction was based on a linear relationship between measured (meas) VO2max (open circuit spirometry) and HRsub (EKG) recorded during the 4th to 5th min of bicycle exercise at 150 watts (900kg-m/min). The regression equation, standard error of estimate (syx) and the correlation coefficient (r) were as follows: VO2max l/min = 6.3 - 0.0193HRsub; syx = 246 ml/min; r = -0.762 ($p<.001$). With this equation, VO2max was predicted (pred) on a group of subjects (n = 24) taken from the literature. Prior to training, the $\bar{X}\pm SD$ for VO2max(pred) was 3.09 ± 0.32 l/min compared to VO2max(meas) of 3.15 ± 0.32 l/min (r = 0.78). The difference of 0.066 ± 0.21 l/min was not statistically significant. On 19 of the same subjects after training, VO2max (pred) was 3.42 ± 0.34 l/min and for VO2max(meas) 3.51 ± 0.37 l/min (r = 0.67). The difference of 0.086 ± 0.29 l/min was not significant. For all 43 comparisons (before + after training) VO2max(pred) was 3.31 ± 0.38 l/min and VO2max(meas) 3.23 ± 0.36 l/min (r = 0.79). The difference of 0.075 ± 0.25 l/min was not significant. The change in VO2max after training was 0.37 ± 0.24 l/min when measured and 0.35 ± 0.17 l/min when predicted. Neither the difference of 0.016 ± 0.28 l/min nor the correlation (r = 0.16) were significant. Conclusions: 1) Prediction of VO2max from HRsub before and after training is reliable on an individual and group basis; 2) Predicted changes in VO2max due to training are reliable only on a group basis. (Supported by US Army Med Res Devel Comm).

The Effect of Intraperitoneal Norepinephrine on Gastrointestinal Blood Flow. Martin S. Frank*, Abraham D. Merav*, Stanley S. Siegelman*, and Scott J. Boley. Departments of Surgery and Radiology, Montefiore Hospital and Medical Center and Albert Einstein College of Medicine, Bronx, New York.

Intraperitoneal norepinephrine has been suggested for the treatment of gastrointestinal bleeding. This hypothesis was tested in anesthetized dogs weighing 20-25 kg by measuring blood flow to the stomach and small intestine with nonocclusive electromagnetic flow probes placed on the celiac and superior mesenteric arteries (SMA). Systemic blood pressure was measured via the femoral artery. In a group of 9 dogs, 300 ml of saline containing 4.8 mg of norepinephrine was introduced intraperitoneally. This amount filled the abdominal cavity. Immediately following administration, celiac arterial flow fell an average of 18%, SMA flow fell an average of 10%, and systemic blood pressure rose an average of 15%. The average maximum fall in celiac flow was 21%, occurring within 1½ hours, and the average maximum fall in SMA flow was 19%, occurring within 2½ hours. After an average of 2 hours, celiac flow returned to control. In 6 of 9 dogs, after returning to control, celiac flow then rose an average of 77%. SMA flow returned to control after an average of 1.7 hours, and in 7 of 9 dogs, after returning to control then rose an average of 35%. In a second group of dogs twice the concentration of norepinephrine was used. In this group there was a greater initial fall in blood flow, but a similar secondary rise above control. These experiments indicate that intraperitoneal norepinephrine is not an effective means of prolonged reduction of gastrointestinal blood flow and may indeed produce a marked rebound increase in arterial flow.

EFFECT OF AN ORAL CONTRACEPTIVE ON NACL APPETITE AND PREFERENCE THRESHOLD OF RATS. Melvin J. Fregly. Department of Physiology, University of Florida, College of Medicine, Gainesville.

Dietary administration of the oral contraceptive, Enovid^{R}, to male rats at 7.5 mg/kg food for 25 days was accompanied by a spontaneous appetite for salt solution when the rats were given choice between distilled water and 0.15M. NaCl solution to drink. Administration of the progestational component of Enovid^{R}, norethynodrel, at 7.5 and 15.0 mg/kg of food for 2 weeks induced a spontaneous NaCl appetite in other male rats. The estrogenic compound, ethynyl estradiol, administered in food at 1.0 and 2.0 mg/kg for 2 weeks also induced an appetite for NaCl solution in rats. Thus, the salt appetite induced by Enovid^{R} may be associated with both its estrogenic and progestational components. Other studies have been conducted to determine the effect of chronic administration of Enovid^{R} (7.5 mg/kg food) on preference (detection) threshold of female rats for NaCl solution. Drug treatment was accompanied by a significant reduction in preference threshold (0.015M.) compared to controls (0.030M.). The volume of NaCl solution ingested by treated rats was greater than that of control rats at all concentrations tested, including hypertonic concentrations. Thus, the experiments suggest that Enovid^{R} not only induces an appetite for NaCl but also reduces the preference threshold for this salt. (Supported by grant HL/HD14526-01 from National Institutes of Health)

EVIDENCE FOR THE ELECTRON-TRANSPORT-LINKED UPTAKE OF NEUTRAL AMINO ACIDS BY THE ENDOTHELIUM OF THE TOAD CORNEA.

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We have found that the endothelial (aqueous), but not the epithelial (tear), surface of the cornea of the toad, Bufo marinus, accumulates neutral amino acids. This uptake occurs via three saturable transport mechanisms, none of which is sensitive to anaerobiosis or cyanide. All three systems transport alpha-aminoisobutyric acid (AIB). One transport system preferentially transports alanine, requires sodium, and has a Km for AIB of 3.7mM. This system is inhibited by iodoacetate (41%) and by arsenite (36%). A second system transports proline and has a Km for AIB of 0.34mM. The third system, which does not depend upon sodium, transports leucine, and has a Km of 0.6mM for AIB. This system is not inhibited by iodoacetate and is markedly stimulated (56%) by 2mM arsenite. Arsenite, which is known to inhibit pyruvate dehydrogenase, leads to the accumulation of lactate in the tissue. The leucine system is also markedly enhanced (81%) by the addition of lactate (2mM) to the bathing medium. The effects of lactate and arsenite upon leucine uptake are not cumulative. Exogenous ascorbate, in the same concentration as found in the in vivo aqueous humor (20mM), caused a significant increase (34%) in the uptake of leucine, but had no effect upon the accumulation of alanine by the cornea. Our data suggest that arsenite, exogenous lactate, and ascorbate stimulate leucine uptake via an electron-transport-system linked to lactic dehydrogenase.

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Effect of pCO_2 on the vascular resistance of the pregnant sheep uterus.

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Four pregnant sheep uteri were perfused in situ with blood drained from the ewe's carotid artery through an extracorporeal circuit containing 2 occlusive double roller pumps arranged in parallel to permit the flow to each uterine horn to be controlled independently. The pCO_2 of the blood entering the uterine arteries was controlled by flowing CO_2 through a membrane lung distal to the roller pump(s). Hematocrit, oxygen saturation and temperature of the perfusing blood were kept constant during each experiment. Calculations of peripheral resistance were based on flows recorded from in-line electromagnetic flow probes and on differences between pressures measured at the tip of the perfusion cannulae and pressures recorded from a branch of the uterine vein. In 6 of 8 experiments, vascular resistance varied inversely with the input pCO_2. In the other 2, there was either minimal change in pCO_2 or insufficient data on the pCO_2 of the perfusing blood. The uterine horns of the 2 animals with near-term single lambs were about equally responsive to pCO_2 changes (slopes of regression lines of log pCO_2 vs. peripheral resistance ranged from -0.11 to -0.16 mmHg min/ml). No responses to changes in pO_2 were observed. The ewes had been primed with 100 mg of progesterone intramuscularly for 3 days prior to experiment to suppress uterine contractions. Data suggest that perfusion with hypocapnic blood brings about vasoconstriction of uterine arterial vessels; perfusion with hypercapnic blood, a vasodilation.

ENDOCRINE RESPONSES TO CHRONIC COLD EXPOSURE IN BABOON. C. C. Gale, M. Carino*, W. L. Green*, B. R. Webster*, W. Ruch*, and K. Muramoto*. Reg. Prim. Res. Ctr. and Depts. of Physiol. & Biophys. and Med., Univ. of Washington, Seattle, Wash., and Toronto General Hospital, Toronto.

Two male adolescent baboons (10-12 kg) were adapted to primate chairs and then subjected to 6° C ambient temperature (T_a) for 9 weeks in a climatic chamber. Both animals tolerated cold stress well, maintaining rectal temperature within 1-2° C of normal, increasing resting metabolism 20-30%, and elevating food intake 100%. Of interest, although cutaneous vessels were persistently constricted, neither baboon was observed to shiver in the cold. To evaluate the response of the sympathicoadrenomedullary (SAM) system to cold, daily measurements were made of 24-hr excretion rates of norepinephrine (NE) and epinephrine (E). From control rates of 3.9 and 4.5 ng/min, NE and E rose promptly to 13.5 and 6.6 ng/min respectively in the cold. Both catecholamines remained elevated until T_a was returned to neutral (25° C); NE and E then fell below control to 2.9 and 2.6 ng/min. To assess adrenal glucocorticoid production in cold exposure, urinary excretion rate of 17-ketogenic steroids (17-KG) was measured, and was found to follow SAM activity. From control rate of 5.7 mg/ 24-hr, 17-KG rose to 8.2 mg/24-hr in the cold and remained elevated until adjustment of T_a to neutral. Then urinary 17-KG fell below control to 5.2 mg/24-hr. To evaluate the participation of the pituitary-thyroid axis in chronic cold exposure, thyroxine I^{125} was infused i.v. before, after, and on 3 occasions during cold exposure. Fractional disappearance rate (FDR) for thyroxine I^{125} rose 15-25% in the cold, suggesting increased thyroxine production. However, concomitant alterations in serum thyroxine or TSH were not discerned. These data show increased SAM and adrenocortical activity in chronic cold exposure in the baboon, and at least suggest a rise in thyroidal activity. (NIH grants NS 06622, RR 00166; Med. Res. Counc. Can. MA 3596)

EFFECT OF INTERVAL TRAINING ON SYSTOLIC TIME INTERVALS. R. N. Gandee*, J. R. Anthony*, R. L. Bartels*, R. R. Lanese* and E. L. Fox. Depts. of Physical Educ. and Preventive Med., The Ohio State Univ., Columbus, Ohio 43210

Performance of the heart during and after exercise has traditionally functioned as a guide in assessing physical and cardiovascular fitness. Interest has recently been directed toward evaluating cardiac function by means of the systolic time intervals as derived from simultaneous recordings of the electrocardiogram, phonocardiogram and the indirect carotid artery pulse wave. This study attempts to elucidate the influence of exercise and a controlled interval training program upon the cardiac systolic electromechanical time intervals and, in turn cardiovascular function. Ten normal, non-athlete males, ages 18 to 24, participated in a controlled 7-week interval training program. The systolic electromechanical time intervals were measured before and after the training program in each subject while at rest, at heart rates of 120, 140, and 160 beats/min during supine leg exercise, and at 2-mins post exercise. The left ventricular ejection time (LVET), the total electromechanical systole (QS2), isovolumetric contraction time (IVCT), the pre-ejection period (PEP), and the rapid rise of the carotid pulse (RRCP) were significantly shortened ($p's<.001$) during exercise as compared to rest before and after training. Following training, the IVCT and RRCP were not changed during exercise, whereas the QS2 ($p<.01$) and the LVET ($p<.001$) were significantly increased. While the PEP was not significantly changed during exercise or recovery following training, the resting PEP was significantly increased ($p<.05$). (Supported in part by Office of Naval Research Contract N00014-67-A-0232-0008).

HEMODYNAMICS OF UNRESTRAINED FISHES. Walter Garey. Scripps Institution of Oceanography, La Jolla, Ca.

Studies of blood pressures and blood flows were conducted on two ecologically and behaviorally contrasting species of fishes, carp (Cyprinus carpio) and pink salmon (Oncorhynchus gorbuscha). Recordings were made from the indwelling catheters of carp maintained in laboratory facilities and from salmon confined to holding boxes set in a spawning stream. Relatively high blood pressures pertained in the salmon; however, the drop in hydrostatic pressure across the gills represented a similar fraction of the driving pressure in both species. Carp exhibited no alteration in blood pressure as the ambient water was warmed or cooled 10–15°C over a 2 hour period, but heart rate increased 2.5 fold upon warming and decreased upon cooling. The onset of exercise caused little or no change in blood pressure or heart rate in salmon. A sensitive compensatory regulation of vascular resistance to variations in cardiac output is indicated in these fishes. Changes in stroke volume are implicated as well in exercise.

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HEPATOCYTE RESPONSE TO PREGNENOLONE-16α-CARBONITRILE (PCN) IN THYRO-PARATHYROIDECTOMIZED AND L-THYROXINE-TREATED RATS. B.D. Garg*, S. Szabo* and B. Tuchweber. Institut de médecine et de chirurgie expérimentales, Université de Montréal, Montreal, Quebec, Canada.

PCN, a typical catatoxic steroid, raises the resistance of rats against many intoxications, mainly through the induction of hepatic drug-metabolizing enzymes. The hepatocytes respond to the steroid with a characteristic increase of smooth-surfaced endoplasmic reticulum (SER). L-thyroxine counteracts the prophylactic effect of some steroids (e.g., PCN, ethylestrenol); hence, we studied the reaction of the hepatocytes to PCN (1 mg in 1 ml water twice daily po. for 3 days) in female ARS/Sprague-Dawley rats (100 g), which were thyro-parathyroidectomized or treated with L-thyroxine (200 µg in 0.2 ml water once daily sc. for 3 days). In both groups, the rough-surfaced endoplasmic reticulum (RER) was slightly disorganized and fragmented, forming vesicular structures. These alterations were enhanced by PCN, which also caused an increase of hepatic weight and SER proliferation. Presumably, the thyroid and parathyroid glands are not significantly involved in the hepatocellular changes induced by PCN. (Supported in part by the Ministère des Affaires Sociales, Quebec, and the Medical Research Council of Canada.)

GLUCONEOGENIC ENZYME ACTIVITIES AND METABOLITE LEVELS IN LIVER FROM RATS FED BD-CONTAINING DIETS IN ABSENCE OF DIETARY FAT

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Excessive caloric intake is one of the primary causes of obesity in humans. This condition is commonly associated with a variety of metabolic diseases such as arteriosclerosis and diabetes. Since these health problems are affected by diet, dietary modifications may help to control obesity and its related diseases. Chemically synthesized compounds such as 1,3-butanediol, when utilized as food additives, can provide an excellent source of calories and control excessive fat deposition. In this study we have added BD in the absence of dietary fat and measured gluconeogenic enzyme activities and liver metabolite levels in order to substantiate our findings and show that carbohydrate replaced by BD or BD in the absence of fat leads to essentially the same results. Animals were fed synthetic diets for four to five weeks. Livers were quick frozen and metabolite levels determined. BD caused a significant decrease in lactate, pyruvate, glucose, α-ketoglutarate, cytoplasmic NAD^+/NADH(LDH), $NADP^+$/NADPH (ICDH) and mitochondrial NAD^+/NADH (B-OH). A significant increase in ketone bodies was found in rats fed BD. The adenine nucleotide levels were unchanged. BD caused increases in FDPase, G6Ptase, PC, and PEPck activities from liver. Body weight and adipose tissue weights were significantly decreased by BD. These changes in enzyme and metabolite levels representing the physiological state, parallel that of mildly starved conditions. Supported by a grant from G. D. Searle and Co. WOO-3511-49A

REINNERVATION OF THE CANINE HEART. W. Peter Geis, Departments of Physiology and Surgery, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Chronotropic reinnervation of the denervated heart has been variably demonstrated to occur from one month to 12 months post-denervation. Each study has utilized heart rate (HR) as a criterion for reinnervation although the sinus node represents only a small portion of the heart. The temporal occurrence of atrial and ventricular myocardial reinnervation has not been demonstrated. Accordingly, the presence of nodal and myocardial reinnervation was determined in anesthetized dogs 3 to 26 months following chronic cardiac denervation. Denervation was carried out by transection and re-implantation of the atria along with transection of nerves subjacent to the adventitia of the intrapericardial great arteries. Reinnervation was determined by electrical stimulation of stellate ganglia and vagus nerves during recording of HR and myocardial contractile force (strain gauge arches) from each atria and 3 sites on each ventricular chamber. Both sympathetic and parasympathetic reinnervation of the sinus node occurred 3 to 6 months after total cardiac denervation while sympathetic and parasympathetic reinnervation of the AV node was not demonstrated until 12 months after denervation. Sympathetic and parasympathetic reinnervation of the atria occurred by 12 months and was invariably complete at 16 months. Functional evidence of sympathetic reinnervation of ventricular myocardium first occurred at 12 months and was reasonably complete at 24 months. Qualitative myocardial responses suggest supersensitivity during early reinnervation. There appears to be no direct correlation between maximum HR responses to stellate ganglia stimulation and time since denervation. (Supported by Grant HE 08682 from the NHLI).

REACTIVE HYPEREMIA IN ARTERIOLES AND CAPILLARIES FOLLOWING MICRO-OCCLUSION. Robert M. Gentry* and Paul C. Johnson, Dept. of Physiology, University of Arizona, College of Medicine, Tucson, Arizona 85724.

We examined the question of whether blood flow is regulated at the level of individual capillaries by comparing the flow increase after brief (30-60 sec) micro-occlusions of single arterioles with that seen after occlusion of single capillaries and groups of capillaries. Studies were performed on the pectoralis muscle of the anesthetized frog (Rana pipiens) which was surgically exposed to permit transillumination and measurement of red cell velocity in the microvessels. Innervation and blood supply were kept intact. About one-third of the arterioles showed post-occlusive hyperemia. In some muscles every arteriole showed reactive hyperemia while in others none responded, presumably because of preparatory trauma. We also compared the flow increase in a capillary after occlusion of that capillary alone and after occlusion of its supply arteriole. In some instances the capillary was occluded along with several adjoining capillaries also. Post-occlusive capillary flow after arteriolar occlusion averaged 229% above control and flow debt repayment was 278%. After occlusion of several capillaries simultaneously these values fell to 63% and 74%. Occlusion of the capillary alone produced a barely perceptible response, flow increased 11% and flow debt repayment was only 12%. The results do not favor the concept that tissue metabolism regulates flow by an action at the capillary or precapillary sphincter level. (Supported by NIH grants AM 12065, HE 05884 and a grant-in-aid from the American Heart Association).

SLOW RECOVERY OF THE SODIUM SYSTEM FROM INACTIVATION IN CARDIAC FIBERS. Leonard S. Gettes and Harald Reuter*. Dept. of Medicine, Univ. of Ky., Lexington, Ky. and Pharmacology Institute, Univ. of Bern, Switzerland.

The Na inward current (I_{Na}) is responsible for rapid depolarization in cardiac tissues. The maximum rate of depolarization (dV/dt) of the action potential (AP) is proportional to this current. In the steady state, I_{Na} is inactivated and dV/dt decreases along a sigmoid curve as the membrane potential (MP) falls from -90 to -50 mV. I_{Na} is completely inactivated during the AP spike. We have studied the kinetics of the recovery of I_{Na} from inactivation in ventricular and Purkinje fibers by analysing dV/dt of the AP as the interval between two APs was progressively decreased. MP was varied between -90 and -60 mV by adding KCl to the perfusate. In both types of fibers, dV/dt in the second AP decreased as the interval was shortened. The time constant whereby dV/dt regained the steady state value (τr) was 5-20 msec when the MP ranged between -90 and -80 mV and increased to 35-70 msec when MP was -75 to -70 mV and to 100-200 msec when MP was -65 to -60 mV. A fourfold increase in external Ca shifted the steady state curve relating dV/dt to MP and the τr-MP curve by 5-10 mV in the depolarizing direction but did not alter the relationship between the degree of steady state inactivation and τr. These results suggest that the recovery from inactivation is a slower process than the inactivation of the Na system and must be considered when assessing the effects of changes in membrane potential or drugs on rapid depolarization, conduction velocity or refractory period.

TIME RELATIONSHIPS OF K+-INDUCED ALTERATIONS IN ELECTROPHYSIOLOGICAL PROPERTIES OF CANINE PURKINJE FIBERS. John A. Giddings*, Kalman Greenspan, and Alan R. Freeman. Departments of Medicine and Psychiatry Indiana University School of Medicine, Indianapolis, Indiana 46202.

Potassium (K+) enhances then depresses conduction, and it has been suggested that the cation-induced loss of transmembrane resting potential (TRP), rendering a cell membrane more excitable, is the electro physiologic mechanism involved. We noted, however, that conduction changes may occur without a change in TRP. This investigation was iniatiated to study the effects of K+ on membrane resistance of canine purkinje cells. Viable fibers were isolated and transferred to a super fusion chamber containing oxygenated Tyrodes' solution (K+=2.7mEq/L) maintained at 34°C. Individual cells were impaled with two ultra-microelectrodes, in close approximation, for recording voltage and passing current intracellulary. In normal Tyrodes', the purkinje TRP's varied between 80 and 90 mV with a spike overshoot of 20 - 30 mV. The effective input resistance ranged from 5×10^4 to 2×10^5 ohms. With each preparation serving as its own control, the K+ level was raised to 5.4 mEq/L resulting in resistance falling to values as much as 30% of the initial levels. This decrease in effective resistance occasionally occurred with no change in TRP, but was more often associated with an average hyperpolarization of 5 mV. This hyperpolarization was, however, transient (over a 5 minute period), resulting in a steady depolarization consistent with the Em vs K_o^+ relationship. These data indicate that K+, in a concentration of 5.4 mEq/L, hyperpolarized canine purkinje cells while, at the same time, membrane resistance decreased. The involvement of K+ induced electrogenic pumping is suggested by these findings. Hence, conduction alterations in purkinje tissue may be associated with changes in membrane resistance.

THE ROLE OF THE CAT'S CAROTID BODIES IN THE REGULATION OF ERYTHROCYTE PRODUCTION. D.B. Gillis* and R. A. Mitchell, Depts. of Anesthesia and Physiology and Cardiovascular Res. Inst. Univ. of Calif. San Francisco, 94122.

The role of the carotid body in the regulation of respiration is well established. It has been reported recently that the carotid body is a neuroendocrine organ and its removal in cats produces a profound anemia after a brief, intense reticulocytosis. In the present study we reexamine these findings in eight male cats. Five cats underwent bilateral carotid body removal, one was a sham-operated control and two were unoperated controls. At regular intervals we obtained blood by venepuncture from the anterior forelimb vein of unanesthetized cats. Baseline hematocrits were 42.5% for the unoperated controls and were reduced to 38.5% at conclusion of the study. Operated cat baseline hematocrit was 42 ± 1 (S.E.) and was reduced to 38.6% ± 1.8 (S.E.) at conclusion of the study 25 to 75 days after the operation. Bone marrow aspirations in both groups had a normal morphology throughout the study. In addition we determined $T_{1/2}$ for plasma iron removal, red cell iron incorporation, reticulocyte counts, and blood volume at various intervals up to 8 weeks post-operatively in the glomectomized group. The values obtained from these studies did not differ significantly from the control cats indicating normal bone marrow function. We conclude that the carotid body does not directly regulate erythropoiesis and that the anemia reported in a prior study was probably secondary to infection resulting from an indwelling femoral vein catheter.

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INTERRELATIONSHIPS BETWEEN PHYSICAL TRAINING AND HEAT-ACCLIMATION. C. V. Gisolfi and D. D. Lund (intr. by C. M. Tipton). Stress Physiology Laboratory, University of Iowa, Iowa City, Iowa 52240.

The purpose of this study was to determine (1) the maximal work-heat tolerance young men can achieve through physical training in a cool environment and (2) how long they must train to achieve such tolerance. Six healthy college students wearing shorts, shoes, and socks attempted a 100-min walk on a treadmill (MR 4 mets) in dry heat (48.9/26.7°C db/wb). After this initial heat-tolerance test (HTT) the men performed 11 weeks (10 January-24 March) of intensive interval training 30 min/day 5 days/week wearing shorts, shoes, and socks in a cool (21°C) temperature controlled environment. The workouts raised the men's rectal temperatures markedly (37.8-39.4°C) and illicited pronounced sweating (.21-.56 kg). After 4, 8, and 11 weeks of training another HTT was performed and subsequently each man was acclimated to work in the heat (48.9/26.7°C db/wb). Exposure time, rectal temperature (T_{re}), mean skin temperature, heart rate (HR), and sweat rate during the first HTT averaged 74 min, 39.2°C, 38.2°C, 186 beats/min, and 320 g/m^2·hr per °C rise in T_{re} above 37°C respectively. Corresponding mean values for the second HTT were 92, 39.3, 37.4, 165, and 338; for the third 95, 38.9, 37.0, 148, and 402; for the fourth 95, 38.8, 37.3, 142, and 429; and following heat-acclimation 100, 38.0, 36.2, 124, and 835 respectively. If heat-acclimation represents baseline and the terminal T_{re}'s and HR's observed during the first HTT represent maximal deviations from baseline, 11 weeks of training produced 30 and 71% reductions in T_{re} and HR respectively and increased exposure time 28%. Corresponding values after 8 weeks of training were 23, 61, and 28% respectively, and after 4 weeks of training 0, 34, and 24% respectively. (Supported in part by the Iowa Heart Assoc. 70-G-3, NIH Biomedical Sciences Support Grant FR-07035, and NIH General Research Support Grant FR-05372.)

MAXIMAL OXYGEN UPTAKE OF MICE DURING SWIMMING AND COLD STRESS. Roger M. Glaser* and Harold S. Weiss. Dept. of Physiology, The Ohio State University College of Medicine, Columbus, Ohio, 43210.

To determine cardio-respiratory fitness in mice, we constructed tests of $\dot{V}O_{2max}$ utilizing both swimming and cold stress. Male albino mice, 9-10 weeks old (av = 35g) were used. $\dot{V}O_{2max}$ (ml/kg/min) was monitored by open circuit spirometry. Swimming was performed in 36 C water with a 5% body load weight attached to the animal's tail, whereas for cold stress the restrained mouse was immersed to his neck in either 28 or 20 C water. Tests were limited to 5 min, and each mouse was used only once. $\dot{V}O_{2max}$ of swimming mice was 131.2 ± 3.17 (S.E.). During cold stress in 28 C water $\dot{V}O_{2max}$ plateaued at a high level with a max of 124.7 ± 6.28 as rectal temperature dropped 1 C over the 5 min. In 20 C water, $\dot{V}O_{2max}$ was 121.5 ± 3.52, but metabolism declined sharply as rectal temperature decreased 6 C. To establish test sensitivity, aerobic deficiency was simulated by having mice breathe 12% O_2 during the exposure. $\dot{V}O_{2max}$ at this PO_2 decreased 30.3% for swimming, 26.4% for cold stress in 28 C water and 22.3% in 20 C water. These data suggest that the swim (36 C) and cold stress (28 C) tests elicit similar $\dot{V}O_{2max}$'s and may be used interchangeably; 20 C water overwhelms mice and depresses metabolism; test sensitivity is directly related to aerobic stress; both tests are of short duration and training is unnecessary. (Supported in part by NASA NGR 36-008-004).

ARTERIAL LEVELS AND MYOCARDIAL EXTRACTION OF METABOLIC SUBSTRATES IN ACUTE BURN TRAUMA. V.V. Glaviano, A. Okamoto*, M. Kaye and D. Deets*. Univ. of Health Sci./The Chicago Med. Sch., Chicago, Ill. 60612.

The metabolism of the heart was investigated in anesthetized, closed-chest dogs subjected to a cutaneous burn covering 35% of the body surface area. Free Fatty Acids (FFA), glucose, lactate, pyruvate, lactate dehydrogenase (LDH), pH, pCO_2, and pO_2 were measured in arterial and coronary venous blood. With fluoroscopic aid, a catheter was placed in the coronary sinus via the left external jugular vein. After control blood samples were taken, the lower ventral surface was subjected to a full thickness skin burn with infra-red heat for 3 min. Four hours after the burn, samples of arterial blood showed a significant rise in FFA (72%), glucose (77%) and lactate (60%). During this time the myocardial extraction ratio for FFA declined while glucose increased from 13 to 20%. Within 30 min. following the burn, a marked increase in LDH activity was accompanied by a efflux of pyruvate from the heart. Although blood pH remained close to control, arterial pO_2 (86 to 76 mmHg) and pCO_2 (39 to 29 mmHg) decreased. In another group of experiments, hemodynamic parameters compared between control dogs and dogs subjected to burn trauma showed that the above metabolic changes were accompanied by a significant decrease in cardiac output (2.74 to 1.28 L/min), a slight decline in mean blood pressure and a marked increase in both hematocrit and total peripheral vascular resistance. The decline in cardiac output, followed by the rise in myocardial LDH activity and the inability of the heart to extract pyruvate, indicates that the burned animal undergoes serious alterations in myocardial metabolism. (Work supported by ONR Contract 3502(01) and NIH Grant HL 14673).

POSSIBLE CORRELATION BETWEEN PRIMARY AFFERENT DEPOLARIZATION (PAD) AND ULTRASTRUCTURE IN THE FROG SPINAL CORD. S.Glusman*, H.Vazquez*and P.Rudomin.Centro de Investigación y Estudios Avanzados,IPN & Instituto Nacional de Cardiología.México DF.

Orthodromic stimulation depresses the pre- and postsynaptic components of the cord potential fields produced by dorsal root stimulation with a time course resembling the dorsal root potential (DRP).Also, afferent terminals within the lateral neuropile show excitability increases coincident with the DRP.However,the pre- and postsynaptic fields, as well as the monosynaptic ventral root discharges produced by ventrolateral tract (VLT) stimulation are not changed during PAD. Serial reconstruction with EM in frog cords with chronic section of dorsal roots showed degenerating boutons synapsing with motoneuron distal dendrites.These boutons,as well as other non-degenerating boutons were frequently found in close apposition with S type boutons,some times with clear "active" axo-axonic synapses.In cords with chronic hemisections degenerating fibers,presumably from VLT,have been found to terminate also on motoneurons,mostly at the soma and proximal dendrites.Those degenerated boutons were rarely seen to be closely apposed to other boutons,and in those cases,no axo-axonic active synapses were found.Apparently, the density distribution of axo-axonic arrangements correlates well with the demonstration of PAD on afferent terminals and the lack of it on VLT descending fibers.

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AN IMPROVED MEASUREMENT OF THE MECHANICAL WORK OF BREATHING. M. Goldman,* G. Grimby*, and J. Mead. Harvard School of Public Health, Boston, Mass.

We measured the separate contribution to lung volume change of the rib cage and abdomen -- diaphragm (Konno & Mead, J. Appl. Physiol. 22 (3):1967.), and the associated changes in transthoracic and transabdominal pressures in 7 normal subjects breathing at rest and with ventilation stimulated by exercise and by rebreathing expired air. In agreement with earlier workers, (Agostoni & Mognoni, J.Appl. Physiol. 21(6):1966; and Grimby, Bunn, and Mead, J. Appl. Physiol 24(2):1968) we found that the chest wall is distorted from its relaxed configuration during increased ventilation. To assess the work associated with this distortion, we develop an estimate of the work of breathing which includes distortional work, along the lines suggested by Konno and Mead (J.Appl.Physiol.24(4):1968) and we compare this estimate, based on analysis of separate rib cage and abdominal volume-pressure tracings with the conventional approach based only on analysis of changes in intrathoracic pressure and lung volume (Campbell diagram), which does not reflect distortional work. We show that the work of distortion increases with increasing ventilation and accounts for 15-25% of the total work of breathing at ventilations between 50-100 liters/min. Thus, the conventional approach systematically underestimates the total mechanical work of breathing by an increasing amount as ventilation increases. The analysis developed here allows us to partition the work associated with rib cage and abdominal volume displacements between the diaphragm on the one hand, and the rib cage or abdominal musculature on the other. Supported in part by USPHS grants ES00044 and HL14580.

WIND CHILL - MAN IN THE COLD. *R.F. Goldman*, US Army Research Institute of Environmental Medicine, Natick, MA 01760

This 16 mm sound, color film (running time 31.22 min) draws on the facilities at the US Army Research Institute of Environmental Medicine to present the avenues of human heat loss and some of the physiological responses of man in the cold. Developed for the senior high school and college undergraduate student, it is designed to introduce concepts and elicit questions which the student will resolve in subsequent classwork with the references, laboratory exercise (and apparatus) and instructional guides to be prepared to accompany this film. The film demonstrates convective and evaporative heat loss, first with a kata thermometer and then with a copper manikin, after demonstrating conductive heat loss by immersing the manikin in a pool. It then introduces cold induced vasodilatation (CIVD) in a blackboard chalk talk and presents the concepts of wind chill and equivalent temperature. It concludes with a demonstration of an experiment on frostnip of a finger, in an attempt to correlate the concepts of heat loss, wind chill, CIVD and cold injury. This film was prepared under the auspices of the American Meteorological Society by EDC Corporation as a pilot film for a proposal to the National Science Foundation for support of an instructional series on Man and his Environment.

SURVIVAL TIME OF ANEMIC, NORMOTHERMIC RABBITS WITH AND WITHOUT FLUOROCARBON EMULSIONS. Frank Gollan, Joanne McDermott*, Albia Dugger* and George Musil*. VA Hosp. and Univ. of Miami School of Med., Miami, Fla.

Fluorocarbon fluids have the highest gas solubility known and therefore they can serve as respiratory media in intact animals. In the form of fine emulsions they can substitute for the gas exchange function of red cells in isolated, perfused organs. In this series of experiments we subjected 6 nembutalized, air-breathing rabbits to a slow blood exchange with an isotonic, iso-osmotic, buffered plasma expander and in 9 rabbits fluorocarbon (FC-43, 3M Co.) in a concentration of 10% or 20% was emulsified into the plasma expander. About 90% of the fluorocarbon microspheres were in the range of 1.5 to 5 microns in diameter. In both groups the hematocrit was lowered to less than 5%. Throughout the procedure measurements were made of arterial and venous pO_2, pCO_2, pH, oxygen content, oxygen extraction, standard bicarbonate, left ventricular pressure, central venous pressure, heart rate and temperature. None of these parameters, as well as the survival time of about 30 minutes, showed a statistically significant difference between the two groups of severely anemic animals. The cause of death was myocardial depression. The reason for the inefficiency of fluorocarbon emulsions to deliver oxygen to the tissues of intact animals is probably due to the presence of protein molecules in concentrations as low as a few microgram percent, which can change tension of the aqueous-fluorocarbon interface. In perfused small organs or organisms the protein content is probably too low to block oxygen diffusion from the fluorocarbon particles.

(Supported by Naval Research Contract NR 105-560)

PERIPHERAL AND CENTRAL THERMAL RESPONSES IN RABBITS TO ABRUPT CHANGES IN ENVIRONMENTAL TEMPERATURE. R.R.Gonzalez*, M.J.Kluger* and J.A.J. Stolwijk. John B.Pierce Foundation, Dept. of Epid., Yale School of Medicine, New Haven, Conn. 06519.

In a recent series of experiments it was found that steady-state thermoregulatory responses of the rabbit at ambient temperatures between 5-30°C are primarily affected by peripheral thermal receptors. In the present work we used transient response analysis to clarify the interplay of peripheral and central inputs during rapid alterations in ambient temperature. Six, unanesthetized, lightly restrained rabbits (2-4 kg) were exposed a minimum of 2 times each (after an initial steady-state period) to experiments in which T_a was changed rapidly (1°C/min) from 30-5-30°C, 5-30-5°C, 40-20-40°C, and 20-40-20°C. Measurements were made of metabolic heat production (M), respiratory rate (RR) and skin temperatures of the back, right ear, fore and hindlimbs, rectal (T_{re}) and preoptic/anterior hypothalamic (T_{hy}) temperatures. Average skin temperature ($\bar{T}_s$) was determined from skin surface area weighting. In steady-state the stimulus for increased M was primarily peripheral in origin. However, analysis of the appropriate transient each two minutes showed: (1) that at any given T_{hy} below 39.5°C M is inversely proportional to $\bar{T}_s$, (2) at any given constant $\bar{T}_s$ a lowering of T_{hy} causes an increase in M, which is negligible at $\bar{T}_s$=36°, and substantial at $\bar{T}_s$=28°C. $\bar{T}_s$ and internal body temperatures also interact in influencing panting thresholds (>200 breaths/min) such that for a low $\bar{T}_s \leq 28°$, panting does not occur at $T_{hy} \leq 39.2°$; panting rates approach a maximum at $T_{hy} \geq 40°$ and $\bar{T}_s \geq 34°$C. It is concluded that in rapidly and continuously changing environments both peripheral and central inputs are important in modifying thermoregulatory responses. (Aided in part by NIH ES00123)

SKELETAL MUSCLE HEMODYNAMICS AND LUMBAR SYMPATHETIC ELECTRICAL ACTIVITY DURING HYPO- AND NORMOVOLEMIC HEMORRHAGIC SHOCK. Ramon R. Gonzalez,Jr.* and Robert F. Bond. Bowman Gray Sch. of Med. of Wake Forest Univ., Winston-Salem, N.C. 27103

Mongrel dogs were anesthetized with α chloralose and urethane. Hind limb skeletal muscle outflow was functionally isolated by ligating medial and lateral saphenous veins, and was measured electromagnetically. Hind limb skeletal muscle vascular resistance (R_s) was calculated by dividing the arterial-venous pressure difference by the flow. Sympathetic nervous activity (A_n) was recorded from an isolated section of the paravertebral chain between L_4 and L_5. All parameters were measured during stepwise hemorrhage into an open reservoir, set to equal 35 mmHg hydrostatic pressure. Decompensation was initiated when the dog began to take up blood from the reservoir. After the dog had taken up 30% of the shed blood, the remaining blood in the reservoir was rapidly returned via the external jugular vein. Results: R_s and A_n both rose with bleeding. When the dogs started to spontaneously take up blood, the R_s fell, but the A_n was either maintained or increased further. During reinfusion A_n fell, but not all the way to control; R_s resembled reactive hyperemia. A_n remained high through out normovolemic decompensation. Just before death, R_s started to fall markedly, while A_n was maintained or increased. At death A_n increased in a burst of activity, then slowly declined to zero. Conclusion: These results suggest that the decrease seen in R_s during decompensation resulting from hemorrhage is not neurogenic in origin.
(Supported by NIH grants HE-05392 and -00487 and grants from the North Carolina Heart Association).

Mixed venous oxygen tension in dogs: Effect of changes in P_{CO_2}. David Gorenberg,* Yoshihiro Kakiuchi,* and Arthur B. DuBois. Department of Physiology, University of Pennsylvania, Philadelphia, Pa.

The influence of elevated and decreased CO_2 levels on the oxyhemoglobin dissociation curve has been well studied " in vitro". However, there is little experimental evidence concerning the "in vivo" effects on oxygen binding. We have studied the effects of varying levels of P_{CO_2} on mixed venous P_{O_2}. Ten dogs were anesthetized with chloralose and ventilated so as to alternate 20 - 30 minute periods of high and low P_{CO_2} with control periods of normocapnia. Hypercapnia was achieved by using 5% CO_2 in air as the inspired gas. Hypocapnia was produced by hyperventilation. Arterial oxygen saturation remained high throughout the experiment. Each dog demonstrated a rise in mixed venous P_{O_2} (range 4-14 mm Hg, mean 11 mm Hg) during CO_2 breathing. Conversely, each dog showed a sharp fall in mixed venous P_{O_2} (range 5-11 mm Hg, mean 9 mm Hg) during hyperventilation despite a significant rise in arterial PO_2. Though cardiac output usually increased during CO_2 inhalation and decreased during hyperventilation these changes can only account for 30% and 21% respectively of the observed increases and decreases in mixed venous P_{O_2}. Oxygen consumption does not change significantly throughout the experiment. Mixed venous P_{O_2} reflects venous capillary P_{O_2}. Thus, our data suggest that uncompensated respiratory acidosis facilitates the unloading of oxygen at the capillary level. Conversely, respiratory alkalosis, a common clinical state, would have deleterious effects on the unloading of oxygen to the tissues.

MINERALOCORTICOID ACTIVITY OF 18-HYDROXY-DEOXYCORTICOSTERONE. R.W. Gotshall*, and J.O. Davis. Dept. of Physiology, University of Missouri, Columbia, Missouri 65201.

To evaluate the relative mineralocorticoid activity of 18-hydroxy-deoxycorticosterone (18-OH-DOC), the assay technique of Liddle, et al. (J. Clin. Investigation 34:1410, 1955) was used. Seven female, adrenalectomized dogs were maintained daily on a high salt diet (200 mEq sodium, 24 mEq potassium) plus 5 mg. cortisone. The assay procedure consisted of measuring electrolyte excretion for five consecutive hours in the conscious dog. At the end of the first hour, which served as a control period, either 50, 300, or 650 μg of deoxycorticosterone acetate (DOCA) or 18-OH-DOC was diluted with 30 ml. saline and injected intravenously. The effects of the steroids on sodium and potassium excretion are expressed as a function of their sodium-retaining response, potassium response, and Liddle's aldosteroid index which combines the additive effect of a fall in urinary sodium excretion with an increase in urinary potassium output. The sodium-retaining response indicated that 300 and 650 μg of 18-OH-DOC were equivalent to 48 and 280 μg of DOCA respectively. For the potassium response, 300 and 650 μg of 18-OH-DOC equalled 48 and 60 μg of DOCA. The calculated aldosteroid index indicated that 300 and 650 μg of 18-OH-DOC were equivalent to 63 and 132 μg DOCA. As shown by the aldosteroid index, 18-OH-DOC has approximately 20% of the mineralocorticoid activity of DOCA. However, in terms of sodium-retaining activity alone 18-OH-DOC is approximately 30% as potent as DOCA. This finding is pertinent to reports that patients with benign essential hypertension frequently have elevated plasma levels of 18-OH-DOC. (Supported by USPHS grant HL10612).

PREDICTION OF EXERCISE CARDIAC OUTPUT. D. V. Goulding* and E. L. Fox, Exercise Physiology Laboratory, Ohio State Univ., Columbus, Ohio, 43210.

The purpose of this study was to investigate prediction (pred) of exercise (ex) cardiac output ($\dot{Q}$) from resting supine (sup) stroke volume (SV) and exercise heart rate (HR). Examination of changes of SV from resting conditions (sitting & supine) through a wide range of exercise intensities was also made to determine relative contributions of HR and SV. Using a treadmill, maximal aerobic power (VO_2max) was determined (open circuit spirometry) on 8 normal male subjects. $\dot{Q}$ (CO_2 rebreathing technique) was then measured at 5 predetermined exercise intensities (26,38,54,68 & 96% VO_2max) and at rest (sitting & supine). All $\dot{Q}$ measurements were made in duplicate to assess the reliability of the system. Results showed $\dot{Q}$ measurements to be reliable under both resting and exercise conditions ($r=0.80 - 0.96$ $p<.01$). Both $\dot{Q}$ and HR increased linearly with work, whereas SV exhibited a marked tendency to plateau at 54% VO_2max. SV showed no significant increase beyond 54% VO_2max. No significant differences occurred among SV at work loads $\geq$38% VO_2max (HR = 110 beats/min) and resting supine SV. Predicted $\dot{Q}$ ($\dot{Q}$pred = SV rest sup x HRex) and measured exercise $\dot{Q}$ values were compared ($r = 0.83$; $p<.01$); no significant differences were found at any exercise intensity. However, predicted values were most accurate at intermediate work loads (38 - 68% VO_2max). Predicted $\dot{Q}$ values were greater than measured values at low work loads (26% VO_2max) and lower at high work loads (96% VO_2max). The variance at the extremes resulted in identical means (12.0 l/min) for all predicted and measured $\dot{Q}$ values. (Supported in part by Office of Naval Research, Contract N00014-67-A-0232-0008).

MATERNAL-NEONATAL COLOSTRAL TRANSFER OF HUMORAL FACTORS IN THE PHYSIOLOGIC DEVELOPMENT OF HOST-DEFENSE IN THE NEWBORN. Charles W. Graham* and Thomas M. Saba. Dept. Physiology, Univ. of Ill. Col. of Med., Chicago, Ill. 60612.

Humoral recognition factors or opsonins are a major physiologic factor regulating the systemic host defense clearance capacity of the reticuloendothelial system (RES). In the present study, circulating serum opsonin levels and gastric aspirate opsonic activity in the newborn following feeding were evaluated at 7, 14, and 21 days after birth with an opsonin bioassay technique in order to evaluate the possible existence of a maternal-neonatal transfer of opsonins or phagocytosis stimulatory factors via the colostrum. At 7 days, serum opsonin levels in the newborn were comparable to adult serum opsonin levels. This serum level was 14% greater than adult levels by 14 days, and significantly ($p<0.01$) decreased 86% below adult levels by 21 days. Comparable to the temporal change in circulating serum opsonic activity, supernatant fluid from the gastric aspirate of the newborn obtained following feeding was identical to adult serum levels by 7 days, increased to 110% of control levels by 14 days, and significantly ($p<.05$) decreased 30% below adult serum levels by 21 days. Both gastric fluid and serum opsonic activity relative to stimulation of hepatic Kupffer cell phagocytosis of labeled foreign test colloids was heparin dependent. These findings coupled with the fact that the maternal serum opsonin level falls significantly ($p<0.01$) during the 21 day post-parturition nursing period suggest the presence of a maternal-newborn transfer of humoral RE regulating factors in the physiologic development of non-specific host defense in the newborn. (USPHS-AM 14382).

THE VARIABILITY OF OXYGEN DEBT IN MAN. T. Graham and G. M. Andrew (intr. by C. K. Chapler). School of Physical and Health Education and Department of Physiology, Queen's University, Kingston, Ontario.

Values for oxygen debt (O_2 debt) ranging from 57-248 ml/Kg have been reported for human subjects following exercise which required maximal oxygen uptake ($\dot{V}O_2$ max.). This study was designed to assess the contribution of the intraindividual variability (repeated measurements of O_2 debt in a single subject) to this wide range of values reported. Six fasted physical education students were tested on 5-7 occasions. The exercise consisted of walking on a treadmill for 15-19 minutes at 3 progressive, consecutive workloads; the final workload elicited a $\dot{V}O_2$ max., a heart rate > 180 beats/min., and a plasma lactate > 70 mg/100 ml. Expired O_2 and CO_2 concentrations and V_I were monitored during exercise and the first 30 minutes of recovery. $\dot{V}O_2$ values were derived and the O_2 debt was calculated by the trapezoid method. No progressive change in the $\dot{V}O_2$ max. of subjects occurred during the study indicating that a training effect was not present. The mean $\dot{V}O_2$ max. and O_2 debts ranged from 51.9-66.0 ml/Kg/min and 81.7-178.3 ml/Kg respectively; the smallest O_2 debt recorded was 43 ml/Kg and the largest was 228.9 ml/Kg. No difference in recovery time could be shown between subjects although 2 subjects had larger O_2 debts than the other 4 subjects ($p < 0.05$). The mean coefficient of variation for O_2 debt (21.3%) was significantly greater than that for $\dot{V}O_2$ max. (9.0%) ($p < 0.05$). The range of O_2 debts observed in different subjects was similar to that previously reported. The large coefficient of variation for O_2 debt indicates that the intraindividual variation can account for a major portion of the range reported in the literature.

(Supported by the Ontario Heart Foundation and Provincial Public Health).

BLOOD ELECTROLYTES AND TEMPERATURE REGULATION DURING EXERCISE IN MAN. J. E. Greenleaf and B. L. Castle.* Laboratory of Human Environmental Physiology, NASA-Ames Research Center, Moffett Field, CA. 94035.

In eight men blood electrolyte and osmotic concentrations were increased by dehydration (Δ body wt = -5.2%) and decreased by excessive water intake (Δ body wt = + 1.2%); an ad libitum control experiment was also performed (Δ body wt = - 1.6%). Under each of these three hydration regimes the men exercised on a bicycle ergometer at 49% of their max $\dot{V}O_2$ ($\bar{X}$ max $\dot{V}O_2$ = 4.6 L/min) for 70 min at T_{db} of 23.6°C and rh of 50%. Equilibrium levels of T_{re} were linearly related to the level of hydration; T_{re} changed 0.1°C for each 1% change in body wt. Equilibrium levels of $\bar{T}_{sk}$ and $\Delta\bar{T}_{sk}$ were constant and independent of body wt (hydration) changes between +1% and -5%. At rest there were low correlations between T_{re} and plasma total proteins, as an estimate of plasma volume (r = 0.15, N.S.); T_{re} and serum sodium (r = 0.05, N.S.) and T_{re} and serum osmolarity (r = 0.12, N.S.). At equilibrium during exercise the correlation of T_{re} with total proteins was (r = 0.34, N.S.); with serum Na (r = 0.71, $P<.05$) and with serum osmolarity (r = 0.71, $P<.05$). Equilibrium T_{re} was also correlated significantly with serum chloride, pH, respiratory rate and heart rate while equilibrium levels of $\bar{T}_{sk}$ were correlated only with sweat rate (r = -0.57, $P<.05$). These results suggest T_{re} is not set by a volume mechanism, but is more directly related to the serum osmotic and Na concentrations. Whether the osmols and/or Na ions act directly on the hypothalamic centers, on the sweat glands themselves, or on both remains to be answered.

REGIONAL DISTRIBUTION OF BLOOD FLOW IN THE LUNGS OF DOGS IN LEFT DECUBITUS POSITION. J. F. Greenleaf*, H. C. Smith*, D. J. Sass*, E. L. Ritman*, and E. H. Wood, Department of Physiology, Mayo Graduate School of Medicine, Rochester, Minnesota 55901.

Regional distributions of pulmonary blood flow (RDPBF) were measured in 6 dogs using radioactive microspheres 15μ in diameter injected into the right ventricle. High resolution measurements of RDPBF were obtained by computer controlled scintiscanning of the surfaces of each cross-section obtained by sectioning the entire excised fixed lungs into 1-cm thick slices. Regional pulmonary distortion caused by the excision and fixation process was determined by roentgenographically tracking the spatial positions of 30-40 1-mm diameter metallic markers distributed without thoracotomy throughout the pulmonary parenchyma of 6 additional normal dogs (Physiologist 14:155,232,1971). The relationship between the spatial geometries of the distribution of the parenchymal tags in the fixed and in-vivo lungs was characterized mathematically by fitting a three-dimensional polynomial to the vector field represented by changes in position of the markers between the two geometries. This function was used to contract the spatial geometry of the parenchyma of the inflated, fixed microembolized lungs to the parenchymal geometry of these lungs at the instants of the microsphere injections. Therefore, from the direct measurements in the fixed lungs, RDPBF, corrected for the geometry in the in-vivo lungs, could be determined at all spatial sites in units of ml/min/alveolus and ml/min/ml of lung tissue for each condition studied in the living animal. Relative alveolar volume gave a 4:1 decrease versus distance down the living lung. RDPBF was decreased in the most dependent regions of the lobes of the superior (right) as well as those of the dependent (left) lung. (Supported by research grants NIH HE4664, HE3532, FR-7; USAF 44620-71-C 0069; and AHA CI 10.)

SMALL VEIN RESPONSE TO HEMORRHAGIC HYPOTENSION. E.K. Greenwald,* D.E. Longnecker,* P.D. Harris and F.N. Miller.* Microcirculatory Systems Research Group, Depts. of Physical Medicine, Anesthesia and Physiology., University of Missouri School of Medicine, Columbia, Missouri 65201

A microscope eyepiece micrometer was used quantitate the small vessel response in the cremaster muscle to hemorrhagic hypotension in 6 Wistar rats (weight, 119±4.9 grams). After anesthesia with sodium pentobarbital (50 mg/kg, i.p.), the femoral artery was cannulated for pressure measurement and controlled hemorrhage. The experimental protocol consisted of a control period, a 30 minute hemorrhage period during which the arterial pressure was held at 30 mmHg, and a 30 minute recovery period which followed reinfusion of the hemorrhaged volume. Data (mean ± S.E.) for heart rate (HR), small vein diameter (VD), small artery diameter (AD), mean arterial pressure (MAP) and hemorrhage volume (HV) are presented below. Mean control values for these variables were: HR=400±29.4 bpm, VD=115±8.9 micra, AD=80±8.8 micra and MAP=112±4.0 mmHg.

VARIABLE	HEMORRHAGE		RECOVERY
	5 mins.	30 mins.	25 mins.
AD (% of Control)	84±1.5	81±2.6	100±1.5
VD (% of Control)	93±1.1	89±3.0	95±4.4
HR (% of Control)	76±8.0	81±6.7	109±7.4
MAP (mmHg)	30	30	109±4.9
HV (% of body wt)	1.4±0.1	2.5±0.3	---

Principal responses in the rat are small artery and vein constriction and bradycardia. In the subcutaneous tissue of the bat wing, the small veins dilated significantly during a similar experimental protocol (AJP 218: 560, 1970). (Supported by PHS HL12614, HL13207, and HL14647).

THE EFFECTS OF INTRAVENOUS ALCOHOL AND SALINE LOADING ON HISTAMINE-STIMULATED GASTRIC SECRETION. N.J. Grego*, M.H.F. Friedman and A. Janson*. Department of Physiology, Thomas Jefferson University, Philadelphia, Pa.

Forty experiments were conducted on thirteen cats equipped with chronic cannulated fistulas of the whole stomach. Continuous intravenous infusion for two hours of alcohol (7 ml of 7% ethanol per kilogram body weight per hour) had no excitatory effect on acid gastric secretion. This is in marked contrast to the biphasic secretory effect of intragastric administration of alcohol. Intravenous alcohol administration, however, increased the total acid output in response to intravenous infusion of histamine (0.1 mg per kilogram body weight per hour) by 206% ± 36%. A corresponding intravenous load of saline increased the acid output response to histamine by only 130% ± 10%.

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HISTOMORPHOLOGY OF THE PINEAL COMPLEX IN RODENTS. Joseph C. Gregorek and Hugo R. Seibel (intr. by Leslie E. Edwards). Med. Col. of Va., Va. Commonwealth Univ., Richmond, Virginia 23219.

The mode of secretion of the pineal gland has been questioned recently. Some authors indicate the pineal may secrete its antigonadic substance into the cerebrospinal fluid rather than the vascular system. These opinions have prompted further investigations into the gross morphology, anatomical relationships, and histomorphology of the pineal complex. Our studies show that in the six species of rodents under investigation, the dorsal pineal sac is not always contiguous with pineal parenchyma, the pineal itself often lacks physical continuity with the ventricles of the brain, and there is no vascular portal system between the pineal and other brain areas. The anatomical relationships in the pineal complex indicate a variability which appears inconsistant with major function via the ventricular system of the brain. Furthermore, the histomorphology of the pineal gland and the dorsal pineal sac indicates the possibility of the more conventual endocrine mode of secretion. The presence of the vena magna cerebri in all species studied suggests that the cerebrospinal fluid does not appear to be the prime physiological medium of transport of pineal substances.

OUTER AND INNER VENTRICULAR WALL METABOLISM FOLLOWING INTERRUPTION OF CORONARY FLOW. D.M. Griggs, Jr. and C.C. Chen*. Univ. of Missouri Medical School, Columbia, Missouri 65201.

Metabolic differences have been demonstrated between the outer and inner wall regions of the underperfused canine left ventricle (Am. J. Physiol. 222:705, 1972). The purpose of this study was to assess the possible importance of factors other than relative subendocardial underperfusion in the production of these regional metabolic differences. In open chest dogs the heart was allowed to function for 30 seconds after complete ligation of both the main left and right coronary arteries and then a transmural tissue specimen of the left ventricle was obtained for analysis of lactate (L), pyruvate (P), creatine phosphate (CP), and adenosine triphosphate (ATP) in the outer (O) and inner (I) halves. Results in 6 animals were compared to those in 8 control animals. Increases in L,P and L/P, were noted in both O and I without the development of regional differences. (Data for L/P were: 29.2±4.0 (SE) and 31.1±2.4 for O and I respectively, compared to 7.8±0.9 and 8.6±1.8 in the controls). Decreases in CP and ATP were noted in both O and I. Although the inner wall developed a slightly lower CP level than the outer wall, no regional differences were noted for the combined CP+ATP values. These findings are consistent with the view that transmural metabolic gradients in the underperfused left ventricle are flow mediated. No evidence of a nonuniform oxygen debt due to nonuniform wall stress was found. (Supported by NIH Grant HL11876).

SOME EVIDENCE CONSISTENT WITH PARTIALLY CARRIER MEDIATED PULMONARY O_2 AND CO TRANSPORT. G.H. Gurtner, P. Caldini, A.M. Sciuto*and B. Burns* The Johns Hopkins University, Baltimore, Maryland 21205.

We have previously reported that O_2 crosses the sheep placenta more easily than inert gases and that compounds which bind to a microsomal cytochrome (P-450) present in the placenta decreases placental O_2 transfer while not affecting inert gas transfer (Fed. Proc. 3/#2:348,1972). Prior to our work Longmuir has published evidence that cytochrome P-450 is involved in O_2 transport in the liver (C.f. above reference). Cytochrome P-450 is also present in the lung and it seems possible that it may act to facilitate pulmonary O_2 transport. Using a mass spectrometer we measured gas exchange in an isolated left lower lobe of dog lung during perfusion with blood. This preparation, in which the lobe is suspended with vessels dependant, allows relatively high flow rates (300-700 ml/min) without abnormally high pulmonary artery pressures. Experiments were performed with constant blood flow rates of 300-500 ml/min at room temperature. The lung was ventilated with a 7% O_2, CO_2, N_2 mixture, the blood was equilibrated with 100% argon in a disc oxygenator. Administration of the drugs (metapyrone 150-1000 mg, SKF-525A 1000 mg, and morphine 30 mg) all of which bind to cytochrome P-450, caused increases in (A-a) pO_2 gradients of from 10 to 20 mmHg. (A-a) gradients for CO_2, Argon and N_2 did not change systematically, indicating that the increased (A-a) PO_2 gradients are not due to alteration of $\dot{V}/Q$ ratios. In intact sheep, lambs and dogs SKF-525A caused decreases in pulmonary diffusing capacity for carbon monoxide measured by a rebreathing technique. The decrease was most striking at high inspired O_2 tensions. These experiments indicate that pulmonary CO and O_2 transfer may be partially facilitated by cytochrome P-450. (Supported by PHS Grant HL13721)

EARLY EVENTS IN ADAPTATION OF A POLYCHAETE AND A CRAB TO DILUTED SEA WATER. L. W. Haas*, Eve C. Haberfield*, C. S. Hammen. Univ. of Rhode Island, Kingston, R. I.

Marine invertebrates acclimate to reduced salinity by loss of salts and by reduction in the free amino acids (FAA) of the tissues and body fluids. The polychaete Nereis virens and the shore crab Carcinus maenas were transferred abruptly from sea water of 31.5-31.9 °/oo (SW) to sea water diluted by adding an equal volume of distilled water (SW/2). Samples of blood or coelomic fluid, the medium, and in some cases tissues were taken at various intervals from 1 to 12 hours, and analyzed for FAA and ammonia. The animals differ markedly in that Nereis takes in a large amount of water within the first few hours, while Carcinus displays very little weight gain. In Nereis the release of ammonia was greater in SW/2 in the first half-hour, and remained high, while the release in SW diminished to one-third the initial rate in 5 hours. FAA content of coelomic fluid was reduced only in proportion to its dilution, while FAA of the tissues was reduced in 3 hours somewhat more than expected from dilution alone. No FAA were found in the medium in any interval. In Carcinus, the release of ammonia was greater in SW/2 after 4 hours, and remained high, while the release in SW diminished to one-half the initial rate in 6 hours. Blood ammonia increased after 6 hours and blood FAA after 12 hours in SW/2. Release of FAA was 13-15% of ammonia release, and did not increase in SW/2.

EFFECT OF DIPHENYLHYDANTOIN ADMINISTERED IN VIVO ON NOREPINEPHRINE UPTAKE AND BINDING IN RAT SYNAPTOSOMES. M.Gary Hadfield and Michael E. Boykin (Intr. by: W.I. Rosenblum). Medical College of Virginia.

Widespread interest in the clinical anticonvulsant, diphenylhydantoin (Dilantin, DPH), has been generated by the ability of this agent to control seizure activity without causing neuronal depression. Therefore numerous investigations into the mechanisms by which DPH exerts its unusual pharmacological properties have been carried out. Heretofore these studies have frequently centered upon the effects of DPH on ionic transport across cell membranes or upon bioelectrical activity. However, work from this laboratory concerns the effect of DPH on putative neurotransmitters within nerve endings. In the present study synaptosomes were isolated from rats who received DPH orally and intraperitoneally. Incubations with H^3-l-norepinephrine(^{3}HNE) were then carried out in either isotonic sucrose or oxygenated Krebs-Henseleit media. When compared with controls, DPH stimulated the uptake and binding of ^{3}HNE in sucrose while in the physiologic medium this effect was reversed and inhibition of uptake of catecholamine occurred. These findings parallel previously published experiments employing in vitro DPH (Arch. Neurol. 26:78-84, 1972) and greatly strengthen our hypothesis that DPH may exert its pharmacologic action through an effect on neurotransmitter kinetics at the synapse. (Supported by Dreyfus Medical Foundation).

NEURALLY INDUCED CARDIAC TACHYARRHYTHMIAS. G.R. Hageman*, J.M. Goldberg, W.C. Randall, and J.A. Armour. Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Cardiac tachyarrhythmias were induced in adult anesthetized mongrel dogs by electrical stimulation of the ventral lateral cardiac nerve (VLCN) at the level of the inferior pulmonary vein. Electrical activity from seven myocardial bipolar silver electrodes (1 mm separation) was recorded on FM magnetic tape, replayed, and photographed for time expansion. The electrodes were in the regions of the sino-atrial node, anterior (AIN), middle (MIN), and posterior (PIN) internodal pathways, the atrioventricular nodal region, the right bundle branch, and the left atrium. Electrical stimulation of the VLCN resulted in a variety of supraventricular and ventricular tachyarrhythmias. Various degrees of heart block were observed, including junctional beats, fusion beats, second degree block rostral to the bundle of His, and total A-V dissociation. Atrial rates during the tachyarrhythmias were as fast as 500/minute, while the ventricular rates approached 350/minute. The nature of the tachyarrhythmias as determined by the seven electrical recordings are interpreted predominately as an ectopic focus. The ectopic foci were isolated by surgical incisions and found to originate in the area of the coronary sinus, PIN, or nodal-His region. Standard pharmacologic blocking agents, such as intravenous atropine, propranolol, hexamethonium, and phentolamine did not abolish the induced tachyarrhythmias. However, lidocaine or procaine were effective in termination and preventing the tachyarrhythmias. (Supported by NIH Grants HE 08682 and GM 999).

MECHANISM OF LARGE VESSEL CONSTRICTION AND FLUID MOBILIZATION DURING HEMORRHAGE. J. Hall*, B. LaLone*, M. Buck* and J. Schwinghamer* (SPON: W.D. Collings), Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

The contributions of passive vascular collapse and active smooth muscle contraction to large vessel constriction and fluid mobilization in skin (S) and muscle (M) during hemorrhage were examined in forelegs of anesthetized dogs with a combined gravimetric and segmental vascular resistance (R) technique. Forelimb perfusion pressure (P) was reduced in 25 mmHg decrements by compression of the brachial artery (BA) with a screw clamp. Large vessel R did not change significantly until BAP fell below 50 mmHg. At BAP 35 mmHg large artery R increased (↑) from control values of 0.33±0.01 (S) and 0.34±0.03 (M) to 0.50±0.04 (S) and 1.31±0.13 (M) while large vein R ↑ from 0.07±0.01 (S) and 0.05±0.01 (M) to 0.36±0.04 (S) and 0.38±0.03 (M). Clamping elicited a steady state weight loss which reached a maximum value of 0.02 g per 100 g forelimb per min at BAP 35 mmHg. After removing the clamp BAP was again reduced in 25 mmHg decrements by bleeding from a carotid artery into a pressurized container. All large vessel R_S were significantly elevated at BAP 100 mmHg and below. Maximum elevations occurred at BAP 35 mmHg where large artery R ↑ from control values of 0.43±0.02 (S) and 0.41±0.04 (M) to 5.57±1.04 (S) and 7.42±0.97 (M) while large vein R ↑ from 0.07±0.01 (S) and 0.07±0.01 (M) to 2.49±0.32 (S) and 3.49±0.66 (M). Bleeding to BAP 100 mmHg and below elicited a steady state weight loss which averaged 0.07 g per 100 g forelimb per min. These data indicate that hemorrhage-induced constriction of large arteries and veins in S and M results primarily from active smooth muscle contraction rather than from passive vascular collapse. The results also suggest that active constriction, by ↓ing vascular capacity and ↑ing the pre/post capillary resistance ratio, accounts for most of the intra and extravascular fluid mobilization from S and M during hemorrhage.

THE RELATIONSHIP OF THE VERTEBRAL VENOUS SYSTEM TO SPINAL CORD DECOMPRESSION SICKNESS. J.M. Hallenbeck,* A.A. Bove, and D.H. Elliott.* Naval Medical Research Institute, Bethesda, Md. 20014

Spinal cord lesions were produced in dogs anesthetized with morphine and chloralose by using a compression and partial recompression profile in a hyperbaric chamber. The cord lesions were revealed by extensor rigidity, loss of tendon reflexes, loss of panniculus reflex and, occasionally, paralysis of the diaphragm requiring respiratory assistance. Azygos and interosseous venography performed before the dive and again after the appearance of spinal cord dysfunction demonstrated obstruction of regions of the vertebral venous system. Cisternal spinal fluid pressure rose shortly before the onset of the cord lesion and returned to preparetic levels during the subsequent 30-45 minutes. Predive cisternal manometric responses to abdominal compression and lung inflation were normal. After signs of spinal cord damage appeared, the manometric response suggested obstruction of the vertebral venous system.

The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

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THE EFFECTS OF CATECHOLAMINE DEPLETION AND POTENTIATION ON HYPERBARIC OXYGEN TOXICITY IN THE RAT. Ronald E. Hammond* and Thomas K. Akers. Department of Physiology and Pharmacology, University of North Dakota, Grand Forks, North Dakota 58201.

It is well documented that the pulmonary system is affected by high (3-6 ATA) oxygen levels resulting in pulmonary hemorrhage and edema (Aerosp. Med. 41:1388). The adrenergic system is thought to cause the pulmonary damage (J. A. P. 3:394). Therefore, this study was designed to test the relative roles of depletion and potentiation of norepinephrine on the development of lung edema. Male Sprague-Dawley rats (150 ± 10 gms) were divided into 3 groups. The untreated control group was divided into hyperbaric (5 ATA O_2, 13 ATA He) and normobaric (1 ATA 80/20 He-O_2) groups and held at their respective pressures for 30 minutes. The second group (10 mg/kg reserpine/day for 3 days) was also divided and exposed to the same pressure as the controls. The third group (10 mg/kg cocaine/day for 3 days) was treated the same way. Hyperoxic-hyperbaric conditions produced significant increases in lung water in untreated animals. However, in the reserpine-treated high pressure animals, the lung water was decreased significantly below hyperbaric and normobaric controls, indicating that the presence of catecholamines is necessary for the pulmonary edema development. The hyperbaric cocaine-treated animals had significantly less lung water than the hyperbaric controls, but the same as normobaric controls. These animals convulsed earlier than any of the other animals. Even though cocaine supposedly potentiates catecholamine activity, the CNS effects of O_2 toxicity were overriding the pulmonary effects. ONR Contract No. N00014-68-A-0499.

BEHAVIOR OF HALF-MICRON AEROSOLS IN THE NORMAL HUMAN LUNG, J.L. Hankinson,* N.L. Lapp,* H. Amandus,* and E.D. Palmes, Appalach. Lab. for Occup. Resp. Dis., Morgantown, W. Va., and Inst. of Environ. Med., New York Univ. Med. Cntr., New York, N.Y.

Previous work (Palmes et al, Physiologist 9:261, 1966) has shown that persistence, expressed as half-life ($t_{1/2}$), of aerosol in the respiratory tract during breath holding can be used as an indirect method of estimating size of the airspaces containing the aerosol. The purpose of this study was to establish reproducibility of the aerosol results in individual subjects tested at various times and to determine the range of $t_{1/2}$ in a normal population. Values for standard error of the mean for repeated measurements of $t_{1/2}$ in 9 subjects ranged from 1 to 5 percent of the means. The mean $t_{1/2}$ and variance for 22 non-smoking males were 18.8 and 3.9 seconds respectively; for 8 non-smoking females comparable results were 18.5 and 2.9 seconds. These differences were not significant ($t = 0.180$, $p > .80$; $F = 1.768$, $p > .10$). Aerosol $t_{1/2}$ correlated poorly with age, height, weight, total lung capacity, forced vital capacity, and single breath CO diffusing capacity. These results are consistent with the findings of Matsuba and Thurlbeck (Amer. Rev. Resp. Dis. 104:516-524, 1971) who measured diameters of small airways in excised human lungs. (N.Y.U. participation supported by USPHS grants OH00317 and ES00260).

CONTRACTILITY OF VASCULAR SMOOTH MUSCLE IN DOCA-SALT AND SPONTANEOUS HYPERTENSION IN RATS: EFFECT OF TRANSMURAL PRESSURE. Timothy R. Hansen* and David F. Bohr. Dept. of Physiology, University of Michigan, Ann Arbor, Michigan.

Helical strips from femoral arteries of DOCA and spontaneously hypertensive rats show a decreased response to maximal stimulation with epinephrine or KCl when compared with normal rat strips. This difference may be secondary to the increased stress (transmural pressure) on the hypertensive artery wall. By occluding the iliac artery of a rat and then producing hypertension via DOCA and salt diet, or by iliac occlusion in a spontaneously hypertensive rat, a single animal will have one femoral artery with elevated transmural pressure and one with decreased or normal transmural pressures. Helical strips cut from the high and low pressure arteries of a hypertensive rat and from a normal rat were cut and hung in a suitably heated, oxygenated, and perfused muscle bath. Injections of epinephrine and KCl were made into the bath and tension recorded. However, there was no evidence that protecting a vessel from increased transmural pressure will also protect it from the changes in contractility in DOCA-hypertension or reverse the process in spontaneously hypertensive rats.

EFFECT OF DISTENSION ON DOG ILEUM. K. M. Hanson, Dept. of Physiology, Ohio State Univ., Col. of Med., Columbus, Ohio

Segments of dog ileum (mean wt. 147 gm), having a single artery and vein, were surgically isolated and autoperfused by the donor animal. Blood flow (electromagnetic flowmeter) and arterial and venous pressures were recorded. Stoppers were tied into cut ends of segment. They were inflated and deflated in a stepwise fashion with mineral oil. Intraluminal pressure was also recorded. Initial response to inflation step was increased lumen pressure, decreased flow and increased resistance; parameters showing return toward original values after several min. equilibration. In some cases flow actually increased with initial inflation steps. Inflation was carried to an equilibrium lumen pressure of about 50 mm Hg resulting at equilibrium in a mean 37% reduction (from 38 down to 24 ml/min/100 gm) in flow and 80% increase (from 3.2 to 5.8 mm Hg/ml/min/100 gm) in resistance. Distensibility was 8.3 ml/mm Hg/100 gm. Reduction in arterial pressure (120-80 mm Hg) resulted in 10% resistance decrease (autoregulation) but after inflation this resulted in 74% increase. Observations were repeated in 13 of 29 experiments following treatment of gut with papaverine. Distensibility increased to 15.1 and flow to 55; however, changes in flow and resistance during inflation were greater. It appears that ileum may be less distensible when compared with the colon. However, ileal blood flow and resistance may be affected less by lumen pressure. (Supported by grants from Central Ohio Heart Chapter and N. I. H. L. D., 5R01HE11411-05).

RESPONSES OF DE-EFFERENTED MUSCLE SPINDLE RECEPTORS TO SINUSOIDAL STRETCH AT LOW FREQUENCIES. Ziaul Hasan (intr. by J.Houk). M.I.T.,Cambridge Mass. and Harvard Medical School, Boston Mass.

In their linear ranges of stretch, primary and secondary endings of the mammalian muscle spindle are known to have similar frequency response characteristics for sinusoidal stretch frequencies greater than 0.03 Hz, except that they have different absolute gains. This contrasts with the known differences between the two types of endings in their dynamic responses to large ramp stretches. By extending the measurements of the frequency response characteristics of endings in the cat soleus down to 0.001 Hz, we have been able to observe differences in the dynamics of de-efferented primary and secondary endings in their linear ranges. Using stretch amplitudes between 16 and 70 μm peak to peak, the phase lead observed in the responses of primary endings is generally 15 to 30° more at 0.001 Hz than at 0.1 Hz; the corresponding difference for secondary endings is less than 10°. For both types of endings the gain at 0.001 Hz was found to be smaller by a factor of 2 to 4 compared to the gain at 0.1 Hz. Transfer functions with two poles and two zeroes provide fair fits in both cases, though with different parameters, over the 100-fold range of frequencies. Responses to slow ramp stretches (durations from 2 to 20 secs.) of intermediate amplitudes (40 to 1000 μm) are currently being studied in an attempt to understand the remarkable alteration in the properties of primary endings when stretch of the muscle exceeds the linear range.

CHANGES IN HEART MITOCHONDRIAL TRANSHYDROGENASE DURING COLD ACCLIMATION IN THE RAT. Philip L. Hawley (intr. by S. R. Rosenthal). College of Medicine, University of Illinois, Chicago.

Alterations in energy associated enzymes in response to stress are known and presumably such alterations participate in acclimatization. In myocardium one of the adaptive changes may be closely associated with the control of fatty acid metabolism. Central to fatty acid metabolism is the redox state of pyridine nucleotides which may regulate the catabolic-anabolic balance of fatty acids. The mitochondrial enzyme transhydrogenase which transfers hydrogen from NADPH to NAD independently of ATP may be of importance in accomplishing rapid adjustments of PN redox states in stress. Mitochondrial preparations of warm room control and cold acclimatized rat hearts were digitonized and transhydrogenase-active fractions separated by 20/40% sucrose gradient by ultracentrifugation. Activity was assayed by observing NAD reduction spectrophotometrically (390 mm) according to the method of Kaplan. The profile of active fractions from the cold acclimatized animals was different from the profile from control hearts indicating an alteration in sedimentation properties and a loss of total activity during cold acclimation. Reaction rates of comparable fractions of high activity did not, however, show significant differences. Upon dilution of enzyme from cold acclimated rat heart, a two-stage reaction became apparent which was not present in control hearts. The two-stage character of enzyme activity in cold acclimated hearts was lost upon heating (40°C, 5 min) while there was no change in activity in control hearts so treated. The data suggest two alternative conclusions: 1) with cold acclimation the native enzyme undergoes configurational changes which lead to multimolecular forms or, 2) several moieties are normally present only one of which is altered by acclimatization.

DEPRESSION OF POLYAMINE SYNTHESIS IN L1210 LEUKEMIC MICE DURING TREATMENT WITH A POTENT ANTILEUKEMIC AGENT, 5-AZACYTIDINE. Olle Heby* and Diane H. Russell, NCI, Baltimore Cancer Research Center, Baltimore, Md.

Polyamine metabolism was studied in spleens of BDF_1 male mice after i.p. inoculations of 10^6 L1210 ascites tumor cells. The stock tumor of lymphoid leukemia L1210 was carried in DBA/2 male mice. In BDF_1 mice, the spleen is rapidly invaded by the tumor cells and it accurately reflects the tumor activity throughout its time course. All the enzymes in the polyamine biosynthetic pathway, ornithine decarboxylase, putrescine dependent- and spermidine dependent-S-adenosyl methionine decarboxylases, were markedly elevated in the spleens of the tumor-bearing mice. Concomitantly, the concentrations of putrescine and spermidine increased, while that of spermine remained unchanged. 5-Azacytidine is an agent most toxic to cells in the S phase. This toxicity is likely to be the result of its incorporation into DNA and RNA and prevention of their further synthesis. When 5-azacytidine was injected i.p. on days 1 through 9 (3.0 mg/kg) into mice inoculated on day 0 with tumor cells, survival time was 300% that of untreated leukemic mice. During drug treatment all enzymes in the polyamine biosynthetic pathway were markedly depressed and, further, the accumulations of putrescine and spermidine normally observed in tumor-bearing mice were inhibited. The weight of the spleens, which more than doubled in leukemic mice by day 7, declined to near normal in the drug-treated leukemic mice. However, when 5-azacytidine injections were stopped, there was both a rapid increase in the synthesis of polyamines and their accumulation, accompanied by an increase in the weight of the spleens. In the L1210 system, 5-azacytidine is one of the most effective antileukemic agents so far tested. No detectable toxicity was apparent in control mice that received the 5-azacytidine regime. These results indicate that 5-azacytidine should be considered carefully for possible clinical use.

THE MOVEMENT OF THE AORTIC VALVE. J. L. Heckman*, P. R. Lynch, and G. H. Stewart*. Departments of Physiology and Medical Physics, Temple University Med. Sch., Philadelphia, Pa. 19140.

Canine aortic valve leaflets were coated with a non-toxic contrast material prepared from gelatin and a proprietary contrast agent. This mixture allowed the motion of the right aortic leaflet to be viewed radiographically for as long as 20 heart cycles. It has been postulated by others using models that the aortic leaflets begin to approximate long before either flow reversal or the pressure incisura. In this study the motion of the aortic valve was filmed at 540 frames per second, and then the angle through which the right aortic cusp moved was plotted. It was found that after reaching its widest excursion, there was a phase in which the leaflet began to move slowly toward a closed position. This phase began long before the pressure incisura. Following this slow closing phase, a rapid closing phase occurred which was associated temporally with the aortic pressure incisura. These observations are consistent with the hypothesis that the initial closing movements of the aortic valve leaflets are due to the vortices trapped in the sinuses of Valsalva. (Supported in part by NIH, NHLI Grant HL 08886 and NIH, NHLI Training Grant HL-05362.)

EFFECTS OF ACUTE COLD ON TOTAL, NUTRITIONAL & ARTERIOVENOUS ANASTOMOSES BLOOD FLOW IN THE EARS OF COLD- AND WARM-ACCLIMATED RABBITS.
W.L. Hedglin and L.D. Carlson, Univ. of Calif., Davis.

Cold-acclimation of rabbits is known to result in an increase in ear blood flow and heat conductance. Hands of cold-acclimated humans have higher blood flows and respond to acute cold with a more rapid onset of cold-induced vasodilation (CIVD). This CIVD response has been attributed to an increased arteriovenous shunt blood flow (SBF). Total blood flow (TBF) and capillary or nutritional blood flow (NBF) were measured in the ears of cold-acclimated (CA,5°C) rabbits (n=6) and warm-acclimated (WA,28°C) rabbits (n=6) at ear bath temperatures randomly shifted between 28,18 and 5°C. The SBF was estimated by the subtraction of NBF from TBF. The TBF was measured by an isotope-dilution technique using ^{51}Cr-labeled erythrocytes and the NBF by ^{133}Xe clearance. The CA group had a significantly higher TBF and SBF at 28 and 18°C but no difference was seen at 5°C. Both groups significantly decreased the TBF between 28-18°C but only the WA group significantly increased the TBF and SBF between 18-5°C. There were no differences in NBF between groups at any temperature. The only significant change in NBF was within the CA group between 28-18°C. Since there was no change in NBF between groups or between 18-5°C, the increased TBF with CIVD and the higher TBF of CA rabbits at 28°C and 18°C can be attributed to an increase in SBF.

ml/100g·min	CA 5°C	WA	CA 18°C	WA	CA 28°C	WA
TBF	34±2.7	32±1.3	28±2.4	23±1.3	38±2.6	28±1.8
SBF	24±3.3	21±2.2	20±2.1	11±1.3	27±2.3	17±2.2
NBF	10±1.2	11±1.4	8±0.9	11±1.7	11±0.7	12±1.0

STEADY-STATE NA FLUXES DURING AMINO ACID TRANSPORT IN THE MOUSE ASCITES TUMOR CELL. H. G. Hempling, Medical University of South Carolina, Charleston, S. C.

The mouse ascites tumor cell has been used as an example of how the Na gradient provides energy for the transport of amino acids. However, the kinetics of Na transport or the existence of several Na compartments has not been emphasized. An analysis of the kinetics of Na^{22} influx in the steady-state at 25 C by analog computer reiterates the presence of two cellular Na compartments which exchange at different rates. These compartments exhibit considerable exchange diffusion because in response to a metabolic inhibitor or to a cardiac glycoside, the tumor cell gained Na in each compartment and in the new steady-state, Na fluxes were higher than in the controls. When Na fluxes were measured during the uptake of the amino acid, glycine, no stimulation of Na fluxes was measured; only a reduction of the fluxes across the slowly exchanging compartment was measured. Although external Na is known to enhance the influx of amino acids, no reciprocal effect of the amino acid on Na fluxes was observed in these experiments.

SOME MECHANICAL PROPERTIES OF A VASCULAR SMOOTH MUSCLE PREPARATION OBTAINED FROM HOG CAROTID ARTERIES. J. T. Herlihy* and R. A. Murphy. Dept. of Physiology, Univ. of Va. Sch. of Med., Charlottesville, Va.

Small muscle strips (0.4 - 0.8 mm^2 cross-sectional area) were teased from the media of hog carotid arteries which had been slit longitudinally. Histological studies showed the strips consisted predominantly of smooth muscle cells with little or no advential connective tissue. The individual cells were oriented parallel to the long axis of the strip. A maximum isometric tension of 2.27 ± 0.17 SEM kg-wt/cm^2 was obtained by replacing Na^+ with K^+ in the bathing medium which contained 5 mM $CaCl_2$. The dose-response curve for norepinephrine lay in the range of 10^{-7} to 10^{-5} M, and the maximum tension was somewhat lower than that produced by K^+-depolarization. Acetylcholine was effective over the same range of concentrations. However, the maximal tension produced was lower than that elicited by norepinephrine. Isometric responses varying from 30 to 80% of maximum (ie. K^+-depolarization) were obtained by transverse electrical stimulation at optimal frequencies between 50 and 100 Hz. It is likely that functional nerve endings were present since both 10^{-4} M guanethedine and 10^{-4} M bretylium halved the response to electrical stimulation. The length-tension characteristics were similar to those of trachealis smooth muscle (Stephens, *et al.*, J. Appl. Physiol., 26, 685, 1964). This preparation has important advantages for studies of the mechanical properties of arterial smooth muscle. [Supported by NIH grants AM 13475 and HL 14547]

EFFECTS OF NORADRENERGIC BLOCKADE ON CEREBRAL BLOOD FLOW AUTOREGULATION. Milton J. Hernández-Pérez* and Howard H. Erickson. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Fourteen macaque monkeys were chronically instrumented with a Doppler ultrasonic flow transducer around the left internal carotid artery. Following a two week recovery period, arterial blood pressure and carotid flow were measured while the monkeys were lightly sedated with phencyclidine. Cerebral blood flow autoregulation (CBFA) was monitored during exsanguination and metaraminol infusion through a femoral vein catheter while the animal breathed ambient air. Phenoxybenzamine (1 mg/kg) was administered intravenously or by cisternal puncture in order to compare the effects of an alpha-adrenergic blocking agent on the noradrenergic nerve fibers innervating the cerebral arteries. While mean arterial blood pressure (MABP) dropped 34%, CBFA was present in all cases (a near constancy of flow was maintained in the MABP range of 70-180 mm Hg). However, in 10 of the 14 monkeys flow was 18% higher at the MABP of 100 mm Hg after the administration of phenoxybenzamine. There were no differences in the effects of phenoxybenzamine by either route of administration. These results suggest that the maintenance of CBFA is not a function of the cerebral arteries' sympathetic innervation but that these nerves do maintain cerebral vascular tone.

CURVE STRIPPING USING A SMALL LAB ORIENTED COMPUTER. D.G. Hess*, D.J. Duffy*, and K.C. Weber. ALFORD, NIOSH, USPHS, DHEW, And Department of Physiology and Biophysics, WVU Med. Ctr., Morgantown, W.V. 26506.

A Digital Equipment Corp. PDP12/30 system++ was used for stripping up to 235 points of multiexponential, evenly spaced decay data using a FORTRAN program. The stripping process is the same as manual curve stripping, with the computer doing the calculations and displaying the curves. The program allows user interaction by displaying the log of the data on a point plotter scope with a potentiometer controlled vertical line marking the beginning of the tail (linear end region of the curve). The vertical line may be set by the user to any point on the curve. After the tail is fitted, with a least squares fit, this exponential component is subtracted from the displayed curve, and the resultant values are displayed for fitting additional exponentials. This process is repeated until all exponentials are fitted. The data and the resulting fitted curve are then simultaneously displayed for visual judgement of fit. The average percent deviation of the data from the fitted curve is printed out along with the A_i, K_i, and half times for data of the form $X = \sum A_i \exp(K_i t_i)$. Provisions are available for the user to adjust any of the exponentials to any desired value instead of fitting its respective tail region by fitting an exponential to the diagonal of a rectangle formed by 4 potentiometer positioned lines. The rectangle is displayed along with the data curve. The program was run under the PS/8 system in 8K of core. Minimum requirements are a data display routine, point plotter scope and analog to digital converters for user interaction. Possible applications for the program are computing blood flow, blood volume and half times for kidney, skin, lung or any other organ in the body from washout data. Supported in part by NASA Grant 47-001-048. ++Use of brand names is for information only and does not constitute endorsement by the USPHS.

Calcium Uptake in Subcellular Fractions of Vascular Smooth Muscle. Michael L. Hess*, George D. Ford*, and F. Norman Briggs, Department of Physiology, Medical College of Virginia, Richmond, Virginia 23219.

Thoracic aorta was obtained from freshly slaughtered beef and placed in ice cold 0.3 M sucrose + 10 mM imidazole, pH 7.0 (Extraction solution). The medial, muscular layer was carefully dissected free of adventitia and intima, diced and homogenized in 5 vols. extraction solution. This homogenate was then subjected to differential centrifugation. Three separate pellets were studied: the first isolated at 1500 g-max x 10 min. (homogenate-H), the second isolated at 27,000 g-max x 30 min. (mitochondria-M), and the third isolated at 105,000 g-max x 60 min. (sarcoplasmic reticulum-SR). The final reaction mixture contained KCl 104 mM, imidazole pH 7.0 18 mM, ATP 5 mM, $MgCl_2$ 5 mM, $CaCl_2$ 0.045 mM, and 45 Ca 0.05 μc/ml. The H fraction accumulates 13 μmoles Ca^{++}/g protein at 3 minutes which is ATP dependent, K-oxalate (10 mM) independent, and Na azide (10 mM) inhibited. The SR fraction accumulates 18 μmoles Ca^{++}/g protein at 3 minutes which is ATP and K-oxalate dependent and virtually Na azide independent. The M fraction accumulates 50 μmoles Ca^{++}/g protein at three minutes which is ATP dependent, K-oxalate independent and largely Na azide inhibited. Due to the relative magnitudes of the calcium accumulation in the mitochondrial and sarcoplasmic reticulum fractions, it is postulated that mitochondria make a larger contribution to calcium sequestration in vascular smooth muscle. (Supported in part by PHS grant #06782 and a Grant from the Richmond Area Heart Association).

Anomalous position of fluoride in the halide conductance sequence of frog sartorius muscle membrane. J.D. Hestenes* and J.W. Woodbury, Dept. Physiol. & Biophys., Univ. Wash. Sch. Med., Seattle, Wash. 98195.

The position of fluoride in the halide conductance sequence of the anion channel is unknown. In Eisenman's equilibrium binding theory, weak electric field membrane cationic sites bind halides in the order $I^- > Br^- > Cl^- > F^-$, strong membrane sites bind halides in the reverse order and intermediate strength sites give five other possible sequences. In frog muscle, conductance is inversely related to binding energy. To determine the position of fluoride, we measured membrane conductance with various anions in the bath. A sinusoidal current flowed through one of two K_2SO_4-filled micropipettes inserted into a cell and the other measured voltage. Glutamate was the "impermeant" ion. All solutions contained 10^{-7} M tetrodotoxin. Two types of experiments tested for effects of Ca^{++} lack (CaF_2 is insoluble): Cl^-, Br^-, I^- conductances were measured with and without Ca^{++} and F^-, Cl^-, Br^-, I^- conductances measured in Ca^{++} free. The relative conductances are insensitive to $[Ca^{++}]$. (a) At pH = 9 the halide conductance sequence is $Cl^- > Br^- > I^- > F^-$ and the presumed binding sequence is the reverse. This is not an Eisenman sequence. (b) The sequence is not changed by lowering pH to 5.0. (C) Interference between an anion species and Cl^- was detected by measuring conductance as the anion is replaced stepwise by Cl^-. In contrast to Br^- and I^-, F^- does not interfere with Cl^- movements at pH = 8.3. The conductance sequence may be understood in terms of a one site version of Eisenman's theory: If ions pass only one rate limiting site, it is either a potential energy hill or valley. The site is regarded as nearly flat for Cl^-, as valleys for Br^- and I^- (they interfere) and as a high hill for F^- (no interference, lower conductance than I^-). The "binding" energy sequence is thus $I^- > Br^- > Cl^- > F^-$ as predicted for a weak site. Supported in part by USPHS grants GM00739 and NS01752.

BLOOD GAS AND ACID-BASE CHANGES IN MARATHON RUNNING AT ALTITUDE. Albert E. Heurich*, Maria Sousa-Poza*, Harold A. Lyons and Stephen N. Steen*. Dept. of Anesth., Harbor General Hosp. Campus, UCLA, Torrance, Calif. and Pul. Dis. Div., Downstate Med. Ctr., Bklyn., N.Y. Supported by U.S. P.H.S. Grants HE 05862-03 and HE 11932-03.

Serial determinations of arterial blood gas were made in 5 nonacclimatized, endurance trained, sea level residents immediately following participation in the August 1971 Pike's Peak Marathon. The race combined a 26.3 mile distance run with an 8200 foot ascent and descent. Inspired oxygen tension ranged between 93 and 116 mm Hg. Control arterial blood lactate values were low with an average of 4.8±1.2 mg per 100 ml. The maximal postmarathon recovery value averaged 18.7±3.6 mg per 100 ml. The lactic velocity constant averaged 0.028±.007. A final sprint resulted in little increase in lactate concentration (<5.0 mg per 100 ml). Recovery values showed a lack of acidemia, pH being 7.510±.078. Marked hypocarbia (initial mean paC02 - 18.2±4.7 mm Hg) with resultant alkalemia virtually masked metabolic changes related to increased arterial blood lactate, the observed pH values were between 7.564 and 7.631 in 3 of the 5 subjects. Subjects with the highest lactacidemia were also the most alkalotic. The mean maximal arterial blood lactate increase was 1.6 mEq/L and this was accompanied by a 2.8 mM/L decrease in [H⁺].

ERYTHROCYTE CALCIUM ACCUMULATION DURING ACUTE AND CHRONIC HYPERCAPNIA. Elly Heyder* and Karl E. Schaefer. Sub. Med. Resch. Lab., Groton, Conn.

Erythrocyte calcium accumulation has been reported in human subjects exposed to 1.5% CO_2 for 42 days (Schaefer et al, J. App. Physiol. 19: 48; 1964). A systematic follow-up was made in guinea pigs exposed to 1%, 3%, and 15% CO_2 for various periods up to 7 days. Plasma and erythrocyte calcium and inorganic phosphorus, and serum ionized calcium were determined. During the acute phase of respiratory acidosis induced by exposure to 15% CO_2, erythrocyte calcium became elevated for a period of 3 days. On the other hand, inorganic phosphorus showed a transient increase at 1 hour with a subsequent fall below control values by 3 days. These changes have been explained as resulting from inhibition of active transport due to depression of red cell glycolysis (Jacey and Schaefer, SMRL Rept. 652,1971). During exposure to 3% CO_2, erythrocyte calcium also increased significantly during the first 3 days, whereas red cell inorganic phosphorus tended to rise slightly. Since 3% CO_2 does not affect red cell metabolism, it was concluded that the elevation in erythrocyte calcium resulted from CO_2 induced changes in membrane permeability without involving metabolic inhibition. Exposure of guinea pigs to 1% CO_2 for 7 days resulted in a tendency towards increased erythrocyte calcium levels and a transient rise in inorganic phosphorus at 1 day. Exposure of human subjects to 1% CO_2 for 21 days caused a steady rise of red cell calcium which reached statistically significant levels at 3 weeks. Erythrocyte calcium levels returned to control values within 1 week following return to air.

SECRETION AND METABOLISM OF CORTICOSTEROIDS IN THE GOLDEN HAMSTER DURING COLD EXPOSURE AND HIBERNATION. L. G. Hiles* and S. F. Marotta. Department of Physiology, University of Illinois College of Medicine, Chicago, Illinois 60680.

Adrenocortical function has been shown to play an important role in many animals exposed to cold stress. The golden hamster (Mesocricetus auratus) responds to a chronically cold environment by either hibernating or not hibernating. Studies were undertaken to ascertain the interrelationships of cortisol concentrations in plasma and the adrenal cortex, as well as the Δ^4-reductase activity of the liver (degradation of cortisol). Adult male hamsters were housed at 5°C (cold-exposed and hibernators) and at 22°C (control). Plasma, obtained from the abdominal aortic blood, and adrenals were analyzed fluorometrically for cortisol. Liver homogenates, with added cofactors, were incubated at 37°C and 5°C. Plasma cortisol levels for hibernating and cold-exposed hamsters were 47% ($P < .01$) and 34% ($P < .01$), respectively, higher than for the control animals. On the other hand, the adrenal steroid levels for hibernators were 30% ($P < .01$) less, while the levels for cold-exposed were 68% ($P < .01$) more than those observed in the control animals. Hepatic reductase activity, when determined at 37°C and 5°C, was markedly more depressed ($P < .01$) in hibernators than in cold-exposed and control hamsters. The decreased activities in both the adrenal cortex and liver, concomitant with increased plasma levels in the anuric hibernator, suggest a general suppressed metabolism of steroids. In addition, the above data support the evidence that an increased plasma level observed during cold exposure is due mainly to increased adrenocortical activity. (Supported by USPHS PGM 738 and NR 101-580)

MATHEMATICAL SIMULATION OF PULMONARY OXYGEN AND CARBON DIOXIDE EXCHANGE, Esther P. Hill*, Gordon G. Power and L.D. Longo. Depts. Physiol. and Ob-Gyn., Loma Linda Univ., Loma Linda, CA 92354

We have developed a mathematical model simulating O_2 and CO_2 diffusion and blood reactions in the lung. Equations expressing diffusion and chemical reaction rates were solved by computer using a forward integration technique. The model considers the $HCO_3^- - Cl^-$ shift, interactions of O_2 and CO_2, and pH effects and predicts concentration changes in RBC's and plasma for O_2, CO_2, O_2Hb, carbamino, HCO_3^- and H^+ during a single pulmonary capillary transit. Experimental values were chosen for diffusing capacities, blood flow rates, mixed venous blood gas values and various chemical reaction rates. The model predicts CO_2 exchange enhances O_2 transfer by only 2% (Bohr effect), but the dependence of CO_2 exchange on O_2 (Haldane effect) accounts for 46% of total CO_2 exchange. Both P_{O_2} and P_{CO_2} in gas and blood reach almost complete equilibrium during a capillary transit. Chemical equilibrium is not achieved for CO_2, however, and pH, P_{CO_2} and $[HCO_3^-]$ continue to change slightly after blood leaves the exchange area. Eight seconds later, arterial P_{CO_2} has increased 0.5 mm Hg while pH increased 0.01 units. The importance of various factors on transfer rates was studied. Exchange is determined mainly by blood flow and mixed venous gas tensions rather than diffusion or reaction rates. The model calculates O_2 uptake to be 295 ml/min and CO_2 elimination rate to be 240 ml/min, RQ = 0.81. During respiration RQ varies from a peak of 1.0 near the end of inspiration to 0.58 near the end of expiration.

ACETYLCHOLINE CONTRACTURE OF THE RADULA PROTRACTOR OF BUSYCON CANALICULATUM: SODIUM DEPENDENCE. Robert B. Hill and Patricia McDonald*. Dept. of Zoology, University of Rhode Island, Kingston, Rhode Island.

The ionic mechanism of the oscillation in membrane potential difference and consequent mechanical rhythmicity, set up in the radula protractor by simultaneous action of acetylcholine and 5-hydroxytryptamine, is still in question. We have begun an investigation of that question by determining the dependence of the action of acetylcholine (ACh) on external cation concentration. Membrane potential was recorded with a single sucrose gap apparatus, using rubber membranes, while tension was recorded with isometric transducers at each end of the muscle. Electrode potential difference varied from 2 to 10 mv, but was usually around 6 mv. One end of the muscle was kept depolarized with isotonic KCl throughout each experiment. The other end of the muscle was perfused with ACh (10^{-5}M) in artificial sea water. Resting potential varied through a range from 20 to 88 mv, but was usually around 72 mv in "good" experiments. Acetylcholine depolarization ranged from 10 to 42 mv, but was consistent for each preparation. In sodium-free artificial sea water, acetylcholine depolarization and acetylcholine contracture were gradually abolished. In calcium-free artificial sea water, ACh contracture was more rapidly abolished while ACh depolarization persisted. Neither potassium-free nor magnesium-free artificial sea water affected ACh depolarization or ACh contracture. It seems probable that ACh depolarization is effected by inward sodium current, while excitation-contraction coupling is effected by calcium as activator.

PREVENTION AND REVERSAL OF MYOCARDIAL FAILURE IN ENDOTOXIN SHOCK. L. B. Hinshaw, L. T. Archer*, M. R. Black*, L. J. Greenfield, and C. A. Guenter. Veterans Administration Hospital and University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

The role of the heart in septic shock is under serious question. An experimental canine model developed in this laboratory regularly fails during the intermediate phase of endotoxin shock. The purpose of the present study was to explore possible beneficial actions of digoxin and atropine on the myocardium, utilized prior to the development of heart failure and during the later phase of shock. Early and late treatments of digoxin and atropine were explored in 49 heart experiments by comparing performance curves of the isolated working heart exchanging blood with a support animal. Heart failure was observed 5-7 hr after endotoxin, which was revealed by a markedly elevated left ventricular end diastolic pressure (LVEDP) and decreased myocardial contractility with depressed dP/dt and lowered cardiac power. Hearts treated early (+15 min post-endotoxin) with atropine alone performed similarly to the non-treated shock group. In contrast, atropine (0.1 mg/kg) and digoxin (50 μg/kg), or digoxin only, prevented the precipitation of heart failure when administered early after endotoxin (less than 1 hr) and when administered 5-7 hr post-endotoxin reversed the failure, as shown by better performance and longer survival of the heart preparation. Improvement of hearts was evidenced by increased dP/dt and cardiac power, decreased LVEDP and increased cardiac efficiency. The present study demonstrated that atropine did not appear to improve myocardial performance, but in each instance early injection of digoxin prevented heart failure and when given late after transfer partially improved or completely reversed the heart failure. (Supported by Veterans Administration Hospital and U. S. Navy Project N00014-68-A-0496.)

SITE OF ACTION OF A HORMONE ANTAGONIST FROM ADIPOCYTES R. J. Ho, J. D. Bomboy* and E. W. Sutherland, from Dept. of Physiology, Vanderbilt Univ. School of Med., Nashville, Tenn. 37232

Isolated fat cells (FC) of rat epididymal fat pad release a hormone antagonist (HA) after stimulation by epinephrine (E). The HA in turn inhibits hormone (H) stimulated cAMP elevation. It was postulated that the HA may be involved in a negative feedback control in the target cells. It has now been found that FC not only from rat but also from dog, rabbit, hamster and human all produce HA upon stimulation with H: E (0.6 μM), NE (0.6 μM), ACTH (2 mU/ml), glucagon (0.2 μM) for rat epididymal FC; ACTH for hamster epididymal FC and rabbit omental FC; E for dog omental FC; and isoproterenol (2 μM) for human FC. The HA formed by FC of one species not only inhibited the action of hormones on FC of the same species but also on FC of other species irrespective of the hormone used. Furthermore, the hormone stimulated rise and subsequent fall in adipocyte cAMP and the formation of the HA was correlated with a decrease in the homogenate adenylate cyclase activity. Epinephrine stimulated adenylate cyclase activity (homogenate) was decreased by 30% after incubation of FC with E for 20 min. The partially purified HA inhibited adenylate cyclase activity in washed FC particles. The degree of inhibition was increased when more HA was used and the inhibitory activity was overcome by more H added. Therefore, the HA appears to act on adenylate cyclase and the negative feedback control takes place at the level of cAMP synthesis. (Grant from USPHS HE-08332 and GM-16811).

SEROTONIN DISTRIBUTION IN THE STOMACH MUCOSA OF THE DOG. F.J. Hohenleitner* and M.F. Tansy. Department of Physiology and Biophysics, Temple University School of Dentistry Philadelphia, Pa.

A study was conducted to determine whether any correlation exists between the chemically measured and histochemically-indicated concentrations of serotonin in the fasted dog stomach. Spectrophotofluorometric determinations indicate that the mean serotonin content of the oxyntic gland mucosa is consistently greater than the serotonin concentration in the antral mucosa. This was also found to hold true for the microscopic observations of the size, degree of granularity, and distribution of argentaffin cells present in the two areas. In the oxyntic area there was a gradient of serotonin with the highest concentration near the cardia, but no difference between the greater and lesser curvature. Although low concentrations of serotonin may be found throughout a pH range of 1.0-7.5, highest concentrations were associated with an elevated pH in both antrum and the oxyntic mucosa. The information provided by this study should be carefully considered before expending further effort at determining the factors which influence the concentration of serotonin in the stomach.

AN EVALUATION OF THE INTERRELATION BETWEEN VENTRICULAR MURAL FORCE AND RESIDUAL FRACTION. J.E. Holl*, W.H. Newman*, E.F. Woods, and R.C. Duncan*. Department of Pharmacology, Medical University of South Carolina, Charleston, S.C. 29401.

Changes in the shape of left ventricular mural force (MF) recordings from a strain gage arch designed for continuous monitoring of such forces have been previously noted to occur with apparent alterations in cardiac pumping activity. To determine if these configurational changes actually reflected alterations in cardiac volumes, left ventricular MF and intraventricular pressure (P) were measured in open chest dogs at aortic valve opening and closing and applied to the formula for the Laplace Law ($MF=P\pi R^2$) to calculate estimates of internal radii of the left ventricle. These radii were substituted into the equation for the volume of a sphere ($V=4/3\pi R^3$) and volumes at aortic valve opening, end diastole (EDV), and aortic valve closing, end systole (ESV), were calculated and applied to the ratio ESV/EDV to determine left ventricular residual fraction (RF). RF and MF were varied by altering heart rate, aortic blood pressure and cardiac contractile force. The MF tracings were then examined to determine if changes in MF attendent to alterations of the above parameters were a reflection of RF changes. The accuracy of the changes in RF calculated from MF were verified by comparison with simultaneous RF determinations by thermodilution. The RF obtained from MF was regressed on RF determined by thermodilution and a significant correlation between the two RFs was obtained in 12 of 14 dogs. Also, a highly significant correlation coefficient was obtained when all data were pooled. These findings therefore indicate that MF changes during a cardiac cycle are a reflection of ventricular pump action, and can be used to estimate RF. Supported by NIH HL-12574 and HE 5972.

HEART RATE RESPONSE TO APNEIC FACE IMMERSION IN HYPERBARIC HELIOX ENVIRONMENT. Suk Ki Hong, T.O. Moore*, D.A. Lally* and J.F. Morlock*. Dept. of Physiology, Univ. of Hawaii School of Med., Honolulu, Hawaii.

The heart rate response to simple breath holding (BH) and to apneic face immersion (FI) in water of 30°C was studied in 5 male subjects at 12.5, 6.6, and 4.0 Ata during the decompression phase of a 9-day dry Heliox saturation dive. The control experiment was carried out at 1 Ata air. The dive profile involved 17 hrs at 8.6 Ata and 43 hrs at 16.1 Ata before decompression. The rate of decompression was approximately 100 ft per 24 hrs. Average environmental data were: P_{O_2} = 220 mmHg, P_{CO_2} < 2 mmHg, temperature = 28-29°C, relative humidity = 77.5%. During BH the heart rate tended to increase slightly at 1 Ata but decreased by 15% at 6.6 and 12.5 Ata ($p \leq 0.05$). During FI the heart rate decreased by 13% at 1 Ata, in contrast to 20, 27 and 36% at 4.0, 6.6 and 12.5 Ata, respectively. There was a linear relationship during FI between the magnitude of bradycardia and the ambient pressure. Such a potentiation of bradycardia during FI was also noted in 1 Ata air as the temperature of water decreased. The bradycardial response to FI in 30°C water at 12.5, 6.6 and 4.0 Ata Heliox was equivalent to that seen during FI in 6, 10 and 14°C water, respectively, in 1 Ata air. These results suggest that the facial thermal receptors behave paradoxically in Hyperbaric Heliox environment. However, other alternative explanations are not ruled out. (Supported in part by NOAA Sea Grant GB 8393 and a fund provided by the State of Hawaii Marine Affairs Coordinator's Office.)

INTRACELLULAR LOCALIZATION OF THE LUMINESCENT SYSTEM OF THE FIREFLY Thomas A. Hopkins and Charles H. Hanna, National Institutes of Health, Bethesda, Md. (intr. by Paul D. Altland)

Sucrose density gradient centrifugation of homogenized light organs of Photuris sp. enable the isolation of a class of nearly spherical particles of mean diameter 1 μ and density 1.25. Mixing these particulates with excess ATP, Mg^{++} and synthetic firefly luciferin results in light production proportional to the concentration of particulates. Measurements were made using a calibrated photometer. Little or no luminescence is obtained from any other fraction of the gradient. The particles are identical in size, E.M. structure, and in the DAB (diaminobenzidine) staining reaction (for catalase) to the "photocyte" or "photogenic" granules of the interior of the photocytes. The E.M. morphology, isopycnic density (in sucrose), and DAB staining (amino triazole and cyanide inhibited) of these particles identify them as microbodies. Measured with a Clark electrode, the catalase activity of the particulates in *in vitro* concentrates and in *in situ* preparations of tissue slices is entirely inhibited by cyanide and largely by amino triazole. These results support the identification of photocyte granules as microbodies. Further they identify "photocyte granules" as photogenic granules. The sequestering of the catalase and luciferase enzyme systems in particulates (microbodies) suggests that they play a vital role in the firefly flash-control mechanism.

EFFECTS OF HYPOKALEMIA AND HYPOMAGNESEMIA PRODUCED BY HEMODIALYSIS ON BLOOD PRESSURE IN THE DOG. W.J. Hoppe* and T.E. Emerson, Jr., Dept. of Physiol., Michigan State University, East Lansing, Michigan

We previously reported that hypokalemia or hypomagnesemia, produced within five minutes by a dilutional technique, raises arterial pressure (Emerson, et al., Am.J. Physiol., 218:234, 1970). We now report effects when the ionic changes are produced more slowly by a non-dilutional technique. Hypokalemia (n=10) or the combination hypokalemia and hypomagnesemia (n=10) were created by hemodialysis (Kiil Dialyzer) against a modified Ringer's solution lacking the cation(s) in question. The protocol involved 3 sequential steps: 1) dialysis against a normal modified Ringer's solution for 30 min (control); 2) dialysis against a solution lacking the experimental cation(s) for 30 min (experimental); 3) dialysis against a solution containing an excess of the experimental ion(s) to reestablish a normal plasma concentration (post-control). In a control series (n=9), dialysis was against a normal Ringer's solution for 1½ hrs. Decreasing plasma $[K^+]$ by 1.0 mEq/l or $[K^+]$ and $[Mg^{++}]$ simultaneously by 1.1 and 0.5 mEq/l, respectively, did not significantly alter systolic, diastolic, or mean arterial blood pressures or heart rate relative to control dogs in which no plasma cation abnormalities occurred. In another group of dogs, the neurologic barostatic system was rendered inoperable by spinal anesthesia. Decreasing plasma $[K^+]$ (n=10) or $[K^+]$ and $[Mg^{++}]$ (n=10) simultaneously still did not alter blood pressure significantly when compared to control spinally blocked dogs (n=9). These data suggest that hypokalemia or the combination hypokalemia and hypomagnesemia does not alter blood pressure significantly. Since the magnitude of the ionic changes were similar to those produced in the earlier study, the difference in the blood pressure response must result from some other factor, perhaps related to time or dilution. (Supp. by grants from NIH, HE 10899 and the Michigan Heart Assoc.)

EFFECT OF TEMPERATURE ON PRESSURE-VOLUME CHARACTERISTICS OF EXCISED CAT LUNG. T. Horie*, R. Ardila* and J. Hildebrandt. Virginia Mason Research Center, Seattle, Washington 98101.

PV curves, stress adaptation, and dynamic compliance (Cdyn) were obtained from excised cat lungs at 22C and 37C. Air PV curves at the two temperatures were similar, except on the deflation curve between 85-95% TLC where recoil was slightly reduced at 37C. Saline PV curves were unchanged throughout the entire cycle. Similarly, γA loops estimated from PV curves demonstrated only small temperature dependence.

In static adaptation experiments, lung volume was held fixed for 20 min at 55% and 70% TLC on the inflation limb from zero Ptp (third cycle) and also on the deflation limb from TLC. On the inflation limb, pressure always fell with time, and rate of fall was similar at both temperatures. However, on the deflation limb, pressure always rose and the small changes (0.7 cm H_2O) were slightly increased (to 1.0 cm H_2O) at 37C. Saline filled lungs contributed 1/4-1/5 of the total stress adaptation. Complete convergence of γ toward a single equilibrium value was never observed. Thus, equilibrium γ was found to be a function of volume and volume history.

In dynamic experiments, 20 min ventilation with tidal volume of 15% TLC was performed at the same end-expiratory volumes and following the same volume history as for static experiments. On the inflation limb changes in Cdyn were independent of temperature, whereas on the deflation limb reductions of Cdyn were slightly accelerated at 37C. Saline filled lung contributed only about 1/10 of the total changes of Cdyn. Since the effect of temperature on PV curves, and on rate of pressure change, both during static adaptation and during prolonged cycling was small, it would appear that the role of temperature in PV studies is much less significant than has been reported for extract studies.

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RESPIRATORY AND CARDIOVASCULAR RESPONSES TO FLUID ASPIRATION. A.D. Horres and M.C. Conrad. Department of Physiology, Medical University of South Carolina, Charleston, South Carolina 29401

In lightly anesthetized dogs, 2 ml/kg fresh water was rapidly injected into the lungs via an intratracheal catheter while recording tidal volume of breathing, cardiac output, pulmonary arterial and venous pressures, systemic arterial pressure and arterial P_{O_2} and PCO_2. Change in arterio-venous shunting within the lungs was evaluated from the response in arterial P_{O_2} to breathing 100% O_2. Injection of water produced apnea of 20-40 seconds duration followed by rapid shallow breathing, an immediate pulmonary hypertension, rise in pulmonary vascular resistance, decrease in arterial P_{O_2}, and evidence of marked A-V shunting within the lung. The apnea, rapid shallow breathing, reduced arterial P_{O_2}, pulmonary hypertension, increased pulmonary vascular resistance, and evidence of A-V shunting were abolished by vagotomy. Overinflation of the lungs for 3-4 respiratory cycles with positive pressure also returned arterial P_{O_2}, pulmonary hypertension and resistance, evidence of A-V shunting, and the rapid shallow breathing to normal. The results suggest that: (1) apnea following fluid aspiration is the result of a vagal reflex; (2) shunting of blood within the lung is probably associated with fluid obstructing the finer airways and not necessarily reflex closure of these airways, since increased inspiratory volume by either positive pressure overinflation or that associated with vagotomy abolishes the shunt following aspiration; and (3) the pulmonary hypertension and increased pulmonary vascular resistance could be related to the arterial oxygen level rather than to a vagal reflex vasoconstriction since either vagotomy or overinflation abolishes the decreased arterial P_{O_2} as well as the hypertension and increased pulmonary vascular resistance.

HYPOXIA-INDUCED CHANGES IN CORE TEMPERATURE AND METABOLISM IN THE SQUIRREL MONKEY. D. H. Horstman and L. E. Banderet (intr. by S. M. Robinson). U. S. Army Research Institute of Environmental Medicine, Natick, Mass. 01760.

Exposure to a hypoxic environment reduces rectal temperature in most species of animals, and we have observed such changes in both cage-roving and chair-restrained squirrel monkeys. To identify components of this reduced rectal temperature (T_{re}) during hypoxia, oxygen consumption ($\dot{V}O_2$), T_{re} and skin temperatures (abdomen, leg, tail) were measured in chair-restrained squirrel monkeys during 3 experimental conditions: (a) 21% O_2 - 420'; (b) 21% O_2 - 90', 11% O_2 - 240', 21% O_2 - 90'; and (c) 21% O_2 - 60', 11% O_2 - 120', 8% O_2 - 30', 8% O_2 + 5% CO_2 - 60', 11% O_2 + 5% CO_2 - 60', 21% O_2 - 60'. Results: Exposure to 11% O_2 resulted in a 20% decrease in $\dot{V}O_2$ and a 1.5°C reduction in T_{re}, and 8% O_2 resulted in an additional 10% reduction in $\dot{V}O_2$ and a further decrease in T_{re} of 0.5°C. The addition of 5% CO_2 to the 8 and 11% O_2 gas mixtures resulted in partial recovery of both $\dot{V}O_2$ and T_{re}. When 21% O_2 was restored, an initial $\dot{V}O_2$ overshoot of about 20% above normal was observed accompanied by the rapid recovery of T_{re} to slightly above normal levels. Skin temperature responses to hypoxia were varied and individualized and do not appear to be a major contributory factor to the observed decreases in core temperature. Thus, when squirrel monkeys are exposed to hypoxia, changes in body heat content can be accounted for by reduced heat production ($\dot{V}O_2$) since changes in T_{re} paralleled $\dot{V}O_2$ alterations.

EFFECTS OF GRADED EXERCISE ON LEFT VENTRICULAR DYNAMICS.
L.D. Horwitz, J.M. Atkins* and S.A. Dunbar*. U. Tex. Southwestern Med. Sch. at Dallas, Dallas, Texas.

Left ventricular (LV) dynamics during graded exercise were studied in 9 dogs running on a level treadmill. The animals ran for 3-minute periods at 3-4 mph (mild exercise), 6-8 mph (moderate exercise), and 10-14 mph (severe exercise). Measurements were made of LV internal diameter with a sonocardiometer, LV pressure with a solid state gauge, and aortic flow with an electromagnetic flowmeter. Oxygen consumptions, calculated from the flow and AV O_2 difference, increased from 6.1 ml/min-mg resting to 24.8, 32.7, and 45.0 with mild, moderate, and severe exercise, respectively. Heart rate increased from 107 ± 6 b/min (mean ± SEM) at rest to 190 ± 9 in mild, 221 ± 8 in moderate, and 263 ± 9 in severe exercise. Stroke volume increased by 14%, 19%, and 15% during mild, moderate, and severe exercise, respectively. Left ventricular end-systolic diameter decreased during mild exercise; end-diastolic diameter rose in moderate and severe exercise. Left ventricular end-diastolic and systolic pressures and mean aortic pressure rose progressively as the exercise load increased. It is concluded that augmentation in cardiac output with exercise occurs through increases in both heart rate and stroke volume, and that the changes in left ventricular dimensions vary according to the level of exercise stress.

Parotid Gland Response Following Exposure to Oxygen at High Pressure.
R.T. Houlihan and John R. Downs*, Dept. of Osteopathic Medicine, Michigan State University, East Lansing, Michigan

During recent years, evidence has accumulated substantiating an increased epinephrine oxidase activity as one factor in acute oxygen toxicity. The earlier controversy regarding this enzyme led to questions of its in vivo activity and to indications that it was in highest concentration in the parotid gland. It was, therefore, considered necessary to examine the parotid gland, both in terms of its histology and possible changes in epinephrine oxidase following exposure to oxygen at high pressure (OHP). For this study, 200 gm. male Sprague-Dawly rats were used. These animals were adapted to the laboratory regimen of a 12 hour photoperiod with food and water ad libitum for 2 weeks. The animals were exposed to OHP at 60 PSIG for 45 minutes, by which time all of the animals had exhibited severe convulsions. The animals were slowly decompressed, the parotid glands removed and fixed in formalin or homogenized in normal saline giving a 10% homogenate. The fixed glands were sectioned and stained with hematoxalin and eosin for examination. One ml alequates of the homogenate were incubated with and without 5 mg L-epinephrine for 30 minutes. One hundred µl of the incubate was chromatographed to separate the formed indoles which were then quantitated with GLC. The results of this study indicate the parotid gland is maximally stimulated by exposure to OHP. The tubule cells show significant lysis of the zymogen granules. The acinar cells are swollen. The nucleus is displaced and exhibits considerable hyperchromia. Measurements of epinephrine oxidase activity differ from the plasma enzyme. It is more reactive and produces less products of epinephrine with a preponderous of adrenochrome. This research is supported in part by a contract (N00014-70-A0159-0001) between the Office of Naval Research and the Michigan College of Osteopathic Medicine.

ACID BASE BALANCE IN SELECTED INVERTEBRATES AS A FUNCTION OF BODY TEMPERATURE. B. J. Howell, Dale Goodfellow*, H. Rahn and Clyde Herreid* Departments of Physiology and Biology, State University of New York at Buffalo, Buffalo, New York 14214.

Measurements of the pH and P_{CO_2} of the extracellular fluid of selected invertebrates acclimated to different temperatures suggest that a constant relationship between the pH of the blood and the pH of neutral water ($\Delta pH/\Delta t$) is maintained as previously described for cold blooded vertebrates (Howell, et al. A.J.P. 218, 1970). Furthermore, P_{CO_2} increases as the temperature increases while HCO_3^- tends to remain stable. In vertebrate transition from aquatic to aerial breathing the P_{CO_2} rises (Rahn, Resp. Physiol. 1, 1966). A similar rise is seen in decapods from the aquatic forms (King Crab, Carcinus) to terrestrial species (Gecarcinus).

		$\Delta pH/\Delta t$	PCO_2 (15°C)
	Water	.018	--
Aquatic	Limulus	.016	4.2
"	King Crab	.015	1.0
"	Carcinus	.016	4.7
Semi-aquatic	Uca	.018	6
Terrestrial	Gecarcinus	.016	8

(Supported in part by O.N.R. Contract No. N00014-68-A0216 and Alpha Helix, Bering Sea Program 1968.)

INHIBITORY EFFECT OF GEROVITAL H3 ON MONOAMINE OXIDASE OF RAT BRAIN, LIVER AND HEART. Josef P. Hrachovec, Dept. of Biological Sciences, University of Southern California, Los Angeles, California 90007

A number of studies indicate that Gerovital H3 (GH3), containing as active ingredient procaine hydrochloride (P) whose half-life in the organism was prolonged through a manufacturing process, has beneficial effects in various chronic diseases and complaints of old age, including arthritis, depression and hypertension. The claims made by clinical investigators using GH3 resemble closely the effect of drugs known as monoamine oxidase (MAO) inhibitors. The present studies were done to investigate this resemblance. Brain, liver and heart of adult male rats were homogenized and MAO activity was determined in the mitochondrial fractions. By in vitro experiments it was observed that both GH3 and P inhibit the MAO activity and that this effect is more pronounced with GH3. In another series of experiments GH3 or P were injected intraperitoneally to adult male rats and the inhibition of MAO activity was determined in mitochondrial fractions of the brain, liver and heart for various amounts of injected GH3 or P. It has again been observed that a given amount of GH3 has a stronger inhibitory effect on MAO activity than the same amount of P alone. Our observations gain a particular importance in view of recent observations by Robinson et al. (Lancet, i, p.290, Feb.5, 1972), which have linked the processes of aging and depression with higher levels of monoamine oxidase in the brain, platelets and serum of older persons. These, together with our observations, indicate that some of the claims in the field of aging made by Gerovital H3 are gaining a new significance and that further research on aging should focus on various facets of monoamine oxidase in connection with aging. The present investigations were supported in part by a grant from Rom-Amer Pharmaceuticals, Ltd.

THE O_2 DIFFUSING CAPACITY OF BLOOD AT TWO O_2 LEVELS. P. N. S. Huang*, F. G. Heineken* and G. F. Filley. Webb-Waring Lung Institute, University of Colorado Medical Center, Denver, Colorado.

A study of blood oxygenation in a membrane oxygenator of known geometry was undertaken at various controlled conditions. Analysis of the dependence of oxygen uptake on geometry, blood flow rate $\dot{Q}$, and ambient gas compositions permitted prediction of the O_2 saturation leaving the oxygenator as a function of the dimensionless length $\xi = \frac{\pi DZ}{2\dot{Q}}$ at a fixed ambient P_{O_2}. Testing with human blood was done under the conditions: (A) Ambient P_{O_2} = 116 mm Hg, initial venous saturation range from 40% to 74% and blood flow rate, $\dot{Q}$, from 0.103 to 4.12 cc/min. (B) Ambient P_{O_2} = 57 mm Hg with the other parameters as in (A). The data were found to fit the prediction when the overall diffusivity D was 5.5 x 10^{-4} cm^2/min. and 6.0 x 10^{-4} cm^2/min. respectively. The average P_{O_2} in each tube was calculated by utilizing the mathematical relationship between this average and the measured P_{O_2} at the exit of the oxygenator during the experiment. The diffusing capacity, D_C, of the blood oxygenator based on the average P_{O_2} in each tube increased with $\dot{Q}$ but at a smaller rate than in the human lung. At equivalent blood flow rates between man at rest and during exercise, the diffusing capacity ratio, $D_{C\ exercise}/D_{C\ rest}$ of the membrane oxygenator was approximately 1/2 that of the human lung. Diffusing capacity of the blood oxygenator was also calculated by use of an average oxygen tension $\bar{P}_{C_{O_2}}$ as determined by Bohr integration. The diffusion of O_2 in blood whose Hb was converted to Met. Hb was also studied and a substantial decrease of O_2 uptake was observed as compared to Part (A).

TRIGLYCERIDE CHANGES IN TISSUES FROM TORPID AND AROUSED PIGMY MICE, (Baiomys taylori). M.S.Hudecki* and C.A.Privitera. State University of New York, Buffalo, New York.

We have described changes in the morphology and composition in interscapular brown adipose tissue for the adult pigmy mouse, Baiomys taylori, during its short-term, cold torpor cycle. (J.Exp.Zool., in press). These changes prompted an in depth analysis of the lipid/triglyceride content of tissues of the mouse during this cycle. The tissues examined were: brown fat, liver, heart, and skeletal muscle. Tissues were extracted for total lipid by a modified method of Folch et al. Triglyceride analysis was estimated indirectly by an enzymatic assay. Extracts were also analyzed using T.L.C. Triglycerides appear to be the main tissue energy store for use by this organism throughout the cycle. Brown fat is depleted of its triglyceride, from 3.48mg/mg protein under control conditions to a low level of 0.39mg during torpor. There is a significant increase during arousal, 24 hrs. post-torpor. Data from liver suggest a reverse trend. The triglycerides range from a control level of 0.08mg/mg protein, to 0.24mg during extended torpor, and decreases significantly with arousal. Skeletal muscle represents 24% of the mass of the mouse. The muscle triglycerides decrease to half that of the control (0.10mg/mg protein) and remain at that level until 24 hours post-torpor. No similarly significant trends are found in heart tissue. The lipid levels of the tissues mirror the types of data already expressed for triglycerides. The decrease in muscle triglycerides may represent either endogenous utilization and/or the mobilization of these "stores" to other organs such as the liver and brown fat. It further appears that the skeletal muscle mass is most significant in the total bioenergetic economy of the pigmy mouse throughout cold exposure and arousal.

ISOMETRIC TENSION, HEART RATE AND ^{42}K EFFLUX FROM ISOLATED HEARTS OF SPERMOPHILUS RICHARDSONI AND S. TOWNSENDI DURING COOLING.[1] J. W. Hudson and N. J. Willems*. Section of Ecology and Systematics, Cornell University, Ithaca, New York.

Hearts of Spermophilus richardsoni acclimated to 15°C were perfused with a modified Krebs-Henseleit medium. T_H (heart temperature) was lowered at rates of 5 and 10 min/°C while ECG and isometric tension were recorded and perfusate was collected for radiopotassium counting. Animals were injected with 90 mg ^{42}K Cl (specific activity $\geq$ 1.35 μc/mgm) 2 or more hours prior to aortic cannulation. The hearts of S. richardsoni and S. townsendi continued beating below 0°C. In most hearts, the ^{42}K washout curve, when plotted semilogarithmically as a function of time and T_H, consisted of straight segments intersecting at heart temperatures characterizing these species. This abrupt decrease in slope is interpreted as reflecting an increased loss of intracellular potassium. In 4 out of 5 S. townsendi and 5 S. richardsoni a decrease in slope occurred at 7.9°C (range of 7.5 to 9.0°C) and 7.8°C (range of 6.5 to 8.5°C), respectively, which correlates with a marked increase in tension. In 3 of the 5 S. townsendi and 1 of the 5 S. richardsoni there were additional slope changes at 10.5 - 12.5°C and 2.5 - 5.0°C. Comparison of the T_H of S. richardsoni and S. townsendi with our previous studies of Peromyscus leucopus, indicate the heart performance of these two different genera differ in the temperature at which heart function is compromised, and is correlated with the lowest T_A at which the respective species spontaneously arouse from torpor.

[1]This investigation was supported by PHS Research Grant No. GM15889-05 from the National Institute of General Medicine.

Effect of Temperature Acclimation on Succinic Dehydrogenase Activity in Rainbow Trout. James B. Hughes* and Irving Gray, Dept. of Biology, Georgetown University, Washington, D.C. 20007.

Rainbow trout (Salmo gairdneri) maintain relatively constant activity over a wide range of environmental temperatures. This study was undertaken to determine if temperature acclimation affected succinic dehydrogenase (SDH) activity, and the role of this enzyme in this process. Experimental fish were maintained at 5°C, controls at 15±1°C. After the period of acclimation, intact mitochondria were isolated from the pooled lateral muscle of several fish. SDH activity was determined spectrophotometrically at three different temperatures following four different periods of acclimation. Potassium ferricyanide was the electron acceptor. Cyanide was used to inhibit the activity of the remaining components of the electron transport chain. The SDH from 15°C acclimated fish has two peaks of activity, 15°C and 5°C. There was a general increase in the level of succinic oxidation following exposure to 5°C environmental temperature. Significantly, when the enzyme was isolated from fish which had lived at 5°C for one week, it did not show the peak of activity at 15° but did show high activity at 10°C. Enzyme assays conducted after a two week period of acclimation to 5°C also showed one high peak of activity at 10°C. A third week of acclimation caused the pattern to revert to that of the control enzyme even though the levels of activity remain elevated above control values. Michaelis constants (K_m) and maximum velocities showed good correlation with the changes in specific activity. Determinations of the energy of activation of the SDH catalyzed reaction likewise indicated that temperature had indeed influenced the level of enzyme activity.

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THE EFFECT OF SUBLINGUAL ISOSORBIDE DINITRATE ON EXERCISE CAPACITY. L. Hurwitz, A. Miller, P. Gorman, and J. Naughton. The George Washington University Medical Center, Washington, D.C.

This study was performed to evaluate the effect of a vasodilator, isosorbide dinitrate, on the exercise capacity of patients with ischemic heart disease manifested by either angina pectoris and/or electrocardiographic abnormality. Eighteen men were assigned randomly either to a placebo or a drug treated group. After an overnight fast, each subject had a standard ECG, and a phonocardiogram (PCG), single lead ECG and carotid pulse contour (CPC) recorded simultaneously at supine rest. Thereafter, each subject performed a graded, multistage treadmill test during which blood pressure, heart rate and ECG were recorded during the last half of each minute. Walking was terminated either when the subject attained a predetermined age-adjusted peak heart rate level, developed chest pain or significant ECG changes. The PCG, ECG and CPC were recorded immediately after exercise with the subject at supine rest. The phases of systole including left ventricular ejection time corrected for heart rate ($LVET_c$) were measured. Following recovery, half of the subjects received placebo and half vasodilator. Each subject was restudied in the same manner thirty minutes later. The results indicated that the vasodilator produced significant reductions in systolic blood pressure (SBP)(123 vs. 107 mm Hg; $p < .02$), and $LVET_c$ (410 vs. 309 min; $p < .02$) with a concomitantly significant increase in heart rate (73 vs. 86 min; $p < .02$) in the resting state whereas the placebo did not. The peak values for SBP, HR, $LVET_c$ triple product and work capacity were not affected significantly by either placebo or vasodilator. These results indicated that while the sublingual vasodilator exerted a pharmacologically active effect in the resting state, the physiological working capacity in these subjects was not enhanced significantly.

GROWTH HORMONE (GH) CONTENT OF SOMATOTROPHS SEPARATED FROM THE RAT ADENOHYPOPHYSIS. W. C. Hymer and J. Kraicer. Dept. of Physiology, Queen's Univ., Kingston, Ontario, Canada.

Highly purified somatotrophs (90%) can be separated from the other adenohypophysial cell types by velocity and density gradient centrifugation. Morphology of the isolated cells, as judged by both light and electron microscopy, is virtually unaltered. Their viability is demonstrated by the finding that they incorporate ^{14}C-amino acids into protein in linear fashion for 3 hrs. As determined by radioimmunoassay, GH content of cells in the suspension prior to separation is 30-50 nanograms/1000 cells. After separation by velocity and density gradient centrifugation, cells in the somatotroph region contain 130-220 nanograms GH/1000 cells; in other regions cells contain only 5-25 nanograms GH/1000 cells. These data show that the isolation procedures used for cell purification produce a functional fraction of somatotrophs which retain their content of GH. Such cell preparations appear to provide an ideal model for study of the mechanism(s) by which secretogogues act on the pituitary somatotroph to effect secretion of growth hormone.

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A CIRCADIAN RHYTHM IN NEURONAL ACTIVITY DEPENDS ON CHLORIDE IONS. Jon W. Jacklet. SUNYA, Albany, N.Y. 12222

The isolated eye and optic nerve of Aplysia, the sea hare, maintained in a culture medium at constant temperature and darkness for up to 2 weeks while continuous recordings are made of the optic nerve activity expresses a circadian rhythm in the frequency of that activity. Eyes run in a culture medium composed of artificial sea water (ASW), blood and other constituents have a period of 26-28 hours. Eyes run in culture medium in which 115 mM of the 500 mM of chloride have been substituted with proprionate do not express the circadian rhythm but are still tonically active at normal frequencies. Acetate is less effective and nitrate not effective in suppressing the rhythm. Eyes run in less than 1 mM calcium ASW or 2.6 mM calcium medium (normal 10 mM) still express the circadian rhythm. In both the low calcium and substituted chloride solutions the light response is intact but the compound action potentials initially evoked are desynchronized but tonic evoked and spontaneous activity still occurs. The low calcium experiments indicate that chemical synapses are not necessary for the expression of the circadian rhythm or for the light evoked and tonic activity of the eye. The chloride experiments indicate that electrotonic synapses in the neuronal population are necessary for the expression of the rhythm since proprionate and acetate but not nitrate substitution of the chloride uncouples other electrotonic synapses (Asada and Bennett, 1971). Apparently partial uncoupling abolishes the interactions that produce the circadian rhythm but is not enough to completely uncouple the neurons and desynchronize the CAP. Support NIH 08443.

COMPARISON OF AIRWAY RESISTANCE MEASURED BY INTERRUPTER AND PLETHYSMOGRAPH TECHNIQUES. A. C. Jackson*, H. T. Milhorn, Jr., and J. R. Norman*. Univ. of Miss. Med. Ctr., Jackson, Miss. 39216

The purpose of this study was to compare airway resistance values determined by a modified interrupter technique to those determined by the plethysmograph method. Earlier studies by other investigators have indicated that the interrupter technique overestimates airway resistance of normal subjects. In these studies it was assumed that mouth pressure and alveolar pressure equilibrate early in the interruption period at approximately the second oscillatory peak in the mouth pressure curve. Evidence indicates that airway opening pressure upon interruption oscillates in a underdamped manner with a natural frequency in the order of 100 Hz. This oscillation lasts well into the interruption period. To correctly apply the interrupter technique the pressure recording must be of high enough resolution so that the curve can be accurately extrapolated back to the time of interruption, which was not adequately done in earlier studies. This modified technique was used to measure mean airway resistance at flow rates less than 0.5 liters/second of ten normal subjects. Upon comparing these values to the resistances at end inspiration and end expiration determined by the whole body plethysmographic method it was found that this technique still overestimates airway resistance. A regression analysis was then performed to calculate resistances at zero flow from the resistance-flow data of the interrupter method. If a wide range of flow rates is used for the extrapolation the results compare more favorably to the plethysmograph values. The resistances determined by this method showed a higher degree of variability than the plethysmographic method. This is thought to be due to variations in the diameter of the upper airways which is more pronounced during quiet breathing (used in the interrupter method) than during panting (used in the plethysmograph method).

CENTRAL PROJECTION OF CHEMOSENSORY PATHWAYS OF APLYSIA. Behrus Jahan-Parwar. Depart. Biol., Clark Univ., Worcester, Mass.

Behavioral and electrophysiological threshold studies show that chemoreceptors of the anterior tentacular cups are the most sensitive receptors of Aplysia to natural stimuli such as food attractants (seaweed effluents, glutamic acid, aspartic acid) and compounds from sexual glands of Aplysia. Intracellular study of over 200 neurons in various regions of cerebral and other central ganglia suggest that chemosensory pathways from each anterior tentacular cup area project into two identifiable symmetrical dark cell clusters in caudal quadrants of the cerebral ganglion. Neurons in these clusters are usually silent in absence of stimulation. Chemosensory stimulation of a given anterior tentacle drives neurons in both clusters but the effect is stronger and has shorter latency on homolateral neurons. These cluster cells also receive similar but slightly weaker chemosensory input from posterior tentacles. There are other cerebral ganglion units outside the dark cell clusters and in other ganglia, including the left pleural giant cell and the abdominal giant cell (R_2), that receive chemosensory input from the tentacles. However, the response of these cells to stimuli of the same quality and intensity is less intense and has longer latency than that obtained from neurons of the caudal dark cell clusters. These data suggest that these identifiable clusters of neurons are important centers for integrating chemosensory information. Supported by PHS Grant No. NSO8868 and Career Development Award No. K4-HD-5178.

ADRENERGIC MECHANISMS IN THE FEMORAL CIRCULATION OF BABOONS. D.P. Jaques*, D.G. Reynolds*, and K.G. Swan. Walter Reed Army Institute of Research, Washington, D. C.

The role of adrenergic mechanisms in the regulation of blood flow through the lower extremity of the anesthetized baboon was studied with an electromagnetic flowmeter to measure femoral arterial blood flow (FBF) as well as appropriately placed pressure recording catheters for measurements of arterial pressure (AP) and venous pressure (VP). During the control period FBF measured 150 $\pm$ 10 (S.E.) ml/min. AP and VP were 110 $\pm$ 5 and 5.0 $\pm$ 1.0 mm Hg respectively. Intraarterial injection of norepinephrine (NE) in doses, ranging from 10^{-3} to 10^{0} $\mu g\ kg^{-1}$ caused vasodilation at low concentrations and vasoconstriction at the higher concentrations. At all doses studied epinephrine (E) caused a vasodilator response. Isoproterenol (I) under the same circumstances evoked only a vasodilator response. Phenylephrine (PE) caused a vasodilator response at low doses and this response was replaced with vasoconstriction at higher doses. Following alpha adrenergic blockade with phenoxybenzamine (1.5 mg kg^{-1}, I.V.), NE, E, I and PE produced only vasodilator responses. This dose of phenoxybenzamine caused epinephrine reversal of arterial pressure. These findings suggest that hindlimb vasculature of the subhuman primate probably responds to the endogenous catecholamines, norepinephrine and epinephrine, with a predominant vasodilator effect. The beta adrenergic receptor potential of these drugs is evidenced by the fact that vasodilation is potentiated following appropriate alpha adrenergic blockade.

TEMPORAL RELATIONSHIP OF LH SURGE AND OVARIAN CHANGES ASSOCIATED WITH OVULATION IN THE CRAB-EATING MACAQUE (M. FASCICULARIS)*. S. Jaszczak,* J. Mori* and E.S.E. Hafez. Wayne State University School of Medicine, Detroit, Michigan.

The temporal relationship between midcycle LH surge and ovulation was studied in eight adult, cyclic female crab-eating macaques (M. fascicularis). Blood was collected at 12, 24, or 48 hr intervals, and LH was measured by radioimmunoassay technique. Ovulation was detected by laparotomy and/or laparoscopy. Ovarian histology was examined before, at, and after ovulation. At midcycle, before LH surge, the unruptured follicles were 5-7 mm in diameter. On the day of LH surge, freshly ruptured follicles of 3-5 mm in diameter showed minimal folding of granulosa tissue with shrinkage of follicular walls. One day after the LH surge, the freshly ruptured follicles decreased in diameter and showed extensive folding of granulosa tissue. Four days after LH surge there was luteinization of granulosa in the corpus luteum, and plasma progesterone was 5.1 mug/1 ml. In this study ovulation was estimated to have occurred 12-24 hr after the midcycle LH peak. Similar time relationships between LH surge and ovulation were previously found in man and some nonhuman primates.
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THE RESPIRATORY PATTERN AND METABOLISM IN CONSCIOUS RESTING DOGS. D. B. Jennings, H. H. Phillips* and C. C. Chen*, Department of Physiology, Queen's University, Kingston, Ontario.

In a previous communication we have described a sigmoidal relationship between respiratory rate (f) and minute ventilation ($\dot{V}_E$) in resting dogs breathing air. Despite the fact that the dogs lived and were studied in an ambient temperature of 20°C at rest, $\dot{V}_E$ ranged up to 30 L/min and f ranged up to 300 breaths/min. Respiratory rate increased out of proportion with increases in $\dot{V}_E$ so that tidal volume (V_T) reached a minimum; subsequent increases in $\dot{V}_E$ were associated with relatively small increases in V_T and f tended to plateau. Over several years, f, $\dot{V}_E$ and oxygen consumption ($\dot{V}_{O_2}$) have been measured simultaneously on many occasions in 11 dogs. We have found that there is also a sigmoidal relationship between $\dot{V}_{O_2}$ and $\dot{V}_E$. However, the relationships between f, $\dot{V}_E$ and $\dot{V}_{O_2}$ are best depicted by analyzing $\dot{V}_{O_2}$ and f at different ranges of V_T. At any given f, $\dot{V}_{O_2}$ is minimal with the lowest V_T (range 50 to 99 ml). At all ranges of V_T (up to 500-599 ml) there is a highly significant positive correlation between $\dot{V}_{O_2}$ and f up to an f of 140 breaths per minute. The slope and intercept of this relationship increase with increasing V_T. At frequencies greater than 140 per minute, only tidal volumes up to 200 ml are utilized, and $\dot{V}_{O_2}$ becomes fixed for any given V_T. A nomogram of these relationships will be presented and the average pattern of f, V_T and $\dot{V}_{O_2}$ found in conscious dogs will be described.

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ACTIVITY OF IDENTIFIED NEUROENDOCRINE CELLS IN THE HYPOTHALAMUS OF THE WAKING RHESUS MONKEY. David P. Jennings* and James N. Hayward. Dept. Anatomy & Neurology, Brain Res. Inst. & Reed Neurol. Res. Ctr., UCLA School of Medicine, Los Angeles, Calif. 90024.

Activity of antidromically identified supraoptic neurons in response to osmotic and non-osmotic stimulation was examined in the unanesthetized monkey (Macaca mulatta). Animals were prepared under barbiturate anesthesia with a cranial platform-cylinder arrangement, head-fixing bolts, pituitary stimulating electrodes and cannulae in the common carotid and right atrium. Isonel insulated tungsten recording electrodes were hydraulically driven into the supraoptic nucleus, units were identified by antidromic and collision techniques and tested for osmotic and behavioral responsiveness. The spontaneous firing patterns of these cells ranged from silence, through periodic discharges to sustained activity. Many cells with periodic firing patterns showed a 4-6 sec. period of accelerated discharge alternating with a 8-10 sec. period of silence. There was no clear influence of sleep-waking behavior or non-noxious sensory stimuli on these spontaneously firing cells. Neuroendocrine cells in the supraoptic nucleus were driven at constant latencies (5-12 msec.), showed collision with spontaneous orthodromic spikes and followed at high frequencies. These cells showed specific biphasic responses to intracarotid osmotic stimuli (0.45M NaCl) with an initial acceleration followed by a 5-10 sec.silence prior to return to baseline firing rate. These results confirm, in part, the earlier results on non-identified supraoptic neurons in the monkey (Hayward & Vincent, 1970) and further support the basic excitatory-inhibitory nature of firing pattern in these neuroendocrine cells.
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Respiratory Chain in Sea Urchin Eggs and Embryos. F. F. Jöbsis[1] and E. L. Chambers, Pigeon Key Field Station, University of Miami, Fla.

Cytochromes *a*, a_3, *b* and *c*, flavoproteins and NADH, i.e., all the usual components of the classic respiratory chain, have been identified spectrophotometrically in living eggs and embryos of Lytechinus variegatus and Tripneustes esculentus. A cyanide-insensitive, *b* type cytochrome, here referred to as "b_5", was also found. Cytochrome *b* and *c* occur in low concentrations compared to *a*, a_3 and "b_5". The "b_5" peak tends to obscure those of *b* and *c* when the system is completely reduced. Two fractions of a_3 are present: the extra one is reduced only very slowly during anoxia and does not react with NaCN. The concentration of the respiratory chain components do not show clear-cut variations during development through the gastrula stage. The appearance of echinochrome interfered with later studies. The cytochrome "b_5" level decreases during development; most rapidly in the early cleavage stages. Cytochrome P_{450} could not be demonstrated. The data on the steady-state reduction levels are consistent with the view that in the unfertilized egg a metabolic control step curtails the supply of oxidizable substrates. In the embryo the ADP level appears to exert control as usual.

[1] Fellow of the John Simon Guggenheim Foundation and Established Investigator of the American Heart Association.

EVIDENCE FOR ACTIVE Na-K TRANSPORT IN THE RAT CHOROID PLEXUS. C. E. Johanson and D. M. Woodbury (intr. by D. J. Reed). Dept. of Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

To test for Na-K transport activity in the choroid plexus (ch. pl.) of the rat, the sodium and potassium concentrations in plexus tissue have been analyzed under conditions which are known to stimulate this transport system in other tissues, e.g. 24 hr nephrectomy. Twenty-four hrs after nephrectomy (Nx), the following % changes in electrolyte concentrations (in mEq/Kg wet tissue or L fluid) from control were found: plasma Na and K, ↓3% and ↑145% ($P<.001$), respectively; ch. pl. Na and K, ↑5% and ↑30% ($P<.001$); CSF Na and K, ↑9% ($P<.001$) and ↑6%; brain Na and K, ↑2% and ↑5% ($P<.02$); and muscle Na and K, ↓35% ($P<.001$) and ↑11% ($P<.001$). Qualitatively similar changes were observed in the 1 hr Nx rats. Thus, changes in the Na and K content of ch. pl. tissue and CSF are in directions consistent with stimulation of Na-K transport. Measurements of ch. pl. water (directly by dehydration and indirectly by analysis of C^{14}-antipyrine distribution), extracellular space (with C^{14}-inulin), and red blood cell volume (with Cr^{51}), along with tissue electrolyte data, have allowed delineation of the cation contents of the cellular and extracellular compartments. Complementary studies of the distribution kinetics of tritiated water and C^{14}-antipyrine in the central nervous system suggest that the apical membrane of the ch. pl. cell is less permeable than the basal membrane. This supports the hypothesis that the Na-K pump is at the CSF-facing membrane of the choroidal epithelium. The directional nature of the proposed pump has been deduced from CSF- (and plasma-) electrolyte data and CSF-dynamics data. (Supported by USPHS Grants 5T1-GM-153 and 5-PO1-NS-04553.)

URATE REABSORPTION IN THE MONGREL DOG KIDNEY. D.R. Johnson and E.C. Foulkes, Depts. of Environ. Health & Physiol., Univ. of Cincinnati Col. of Med., Cincinnati, Ohio 45219.

Inhibition of urate secretion by probenecid and p-aminohippuric acid (PAH) has been previously documented (JPET 179:429, 1971). Therefore, if the administration of these drugs increases the fractional excretion of urate they must also have inhibited urate reabsorption. In our study we have used simultaneous double isotope injections into the renal artery to localize in the intact kidney the drug sensitive carrier systems mediating urate reabsorption. In two dogs treated with 30 mg/kg probenecid intravenously (IV) and two others given 2 mg probenecid directly into the renal artery (IA), the fractional reabsorption of urate decreased by 51 ± 8% (SD). In one dog given 200 mg/kg PAH IV and two dogs given 60 mg IA, the fractional reabsorption of urate decreased by 65 ± 26%. The urinary volumes of distribution (V) of ^{3}H-inulin and ^{14}C-urate were calculated from the mean artery-to-ureter transit times ($\bar{t}$) (PSEBM 139:1032, 1972). The ratio $\bar{t}_{Ur}/\bar{t}_{In}$ did not differ significantly from 1.0 before or after administration of either drug. The fact that $\bar{t}_{Ur} = \bar{t}_{In}$ implies that $V_{Ur} = V_{In}$; it follows that the inhibition of urate reabsorption by these drugs occurs at the luminal membrane. This view is consistent with the conclusion of others based on micropuncture studies in rats (JCI 50:35, 1971). (Supported by NIH grants HE10346 and 5P10 ES00159).

EFFECTS OF AN ANGIOTENSIN II ANALOG ON BLOOD PRESSURE AND ADRENAL STEROID SECRETION IN DOGS WITH THORACIC CAVAL CONSTRICTION. J.A.Johnson and J.O.Davis. Dept. of Physiology, Univ. of Missouri, Columbia, Mo.

An analog of angiotensin II (1-Sar-8-Ala-angiotensin II) was reported by Pals et al.(Circ.Res.29:673,1971) to be a specific competitive inhibitor of angiotensin II (AII) when evaluated by the rabbit aortic strip and by pressor action in the pithed rat. The present study was undertaken to determine if this analog could block the effect of AII on blood pressure and on aldosterone secretion in the dog. Five dogs with chronic caval constriction and ascites were studied. An adrenal catheter was placed surgically and 2 days later the experiment was performed under pentobarbital anesthesia. Each dog received 6 mg of dexamethasone 2 hrs before the experiment. Measurements of arterial blood pressure (ABP), plasma renin activity (PRA), aldosterone secretion (AS), and cortisol secretion (FS) were performed during 2 control periods of 15 min each. At this time the AII inhibitor was infused IV at a rate of 6 μg/kg min for 45 min; measurements were made at 15, 30, and 45 min. Infusion of the inhibitor was stopped and recovery measurements were made 45 and 60 min later. The data are summarized below: (means ±SEM; * = P<0.05)

	CONTROL		EXPERIMENTAL			RECOVERY	
ABP (mm Hg)	138±6	140±7	112±10*	109±10*	107±10*	134±8	138±9
PRA (ng/ml)	62±17	60±16	146±32*	141±28*	138±8*	102±11	89±13
AS (ng/min)	23±7	28±6	11±4*	6±4*	6±3*	30±10	18±6
FS (ng/min)	295±41	301±58	242±96	133±42	89±17	191±98	204±66

Infusion of the AII analog resulted in a decrease in ABP and AS despite a marked increase in PRA. These data indicate that this AII analog blocks the effect of AII on both the vascular system and the adrenal gland in the dog. (Supported by USPHS grant HL10612)

CONVECTIVE AND DIFFUSIVE MIXING IN PULMONARY OXYGEN EXCHANGE. Larry R. Johnson* and Hugh D. Van Liew, Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, New York 14214.

Continuous measurement of arterial oxygen tension (PaO_2) has been used to assess the importance of diffusive and convective mixing in the transport of oxygen from the ambient air to the alveolocapillary barrier. Anesthetized, paralyzed dogs were ventilated with three gas mixtures, each containing approximately 40% O_2 to eliminate complications due to the O_2 dissociation curve. The balance was either helium, nitrogen, or sulfur hexafluoride to provide a wide range of molecular weight. A Clark-type O_2 electrode covered with a six-micron teflon membrane and exposed to a constant flow of carotid arterial blood from the dog provided the continuous record of PaO_2. Diffusive mixing was examined by noting the rate of fall of PaO_2 during a breath-hold. The rate of fall was larger with N_2 and SF_6 than with He. Paired comparisons for each dog are summarized by least squares ratios: He/N_2=.85±.02 and SF_6/N_2=1.00±.07. When convective mixing was included, the efficiency of O_2 exchange was estimated by two additional measurements. First, during normal ventilation, the PO_2 difference between inspired gas and arterial blood was consistently smaller with N_2, the ratios being He/N_2=1.06±.01 and SF_6/N_2=1.12±.02. Second, after a breath-hold, the rate constant for the approximately exponential return of PaO_2 to its equilibrium value was larger with N_2(He/N_2=.87±.02 and SF_6/N_2=.97±.05). These three results suggest that although He allows faster O_2 diffusion and SF_6 provides a greater tendency for convective mixing, N_2, occupying the middle ground, is the most efficient carrier gas. (Supported in part by the U.S. Air Force, the U.S. Navy (ONR), and NIH Training Grant No.5 T01 GM00341.)

REGIONAL BLOOD FLOW DURING HYPOXIA. E.F. Jones*, A.W. Nelson*, H.H. Erickson, and H.L. Stone. USAF School of Aerospace Medicine, Brooks AFB, Texas, and Colorado State University, Fort Collins, Colorado.

This study was undertaken to document regional vascular changes that occur in the superior mesenteric, renal, and terminal aortic circulations during hypoxia in the intact, awake, and unmedicated dog. The role of alpha adrenergic receptor activity in effecting the circulatory changes was also investigated. Nine dogs were previously surgically prepared under anesthesia by implanting Doppler ultrasonic flow transducers around the superior mesenteric artery, left renal artery, and terminal aorta. Gas mixtures were inhaled through an endotracheal tube inserted in a chronic tracheostomy. Arterial measurements were made with a catheter extending into the aorta through a carotid loop. Changes in heart rate, regional blood flow, and arterial blood PO_2, PCO_2, and pH were measured in the spontaneously breathing dogs during hyperoxia and graded systemic hypoxia. Severe hypoxia (5% O_2, balance N_2) caused tachycardia (73%), systemic hypertension (14%), and increased renal (22%) and terminal aortic (34%) blood flow, with no significant change in the superior mesenteric circulation. Alpha-adrenergic blockade with phenoxybenzamine resulted in a relative systemic hypotension (11%). It also decreased packed cell volume (9%) and hemoglobin (9%) levels, indicating probable sequestration of erythrocytes in the spleen and/or plasma volume augmentation by extravascular fluid. The renal circulation exhibited both alpha receptor activity and a local autoregulatory mechanism. This mechanism apparently operates in opposition to, and in conjunction with, the renal alpha receptors. Although blood flow to each of the regional vascular beds increased during hypoxia, it was not determined whether the increase was due to an increase in cardiac output or to a redistribution of blood flow within the body as a whole.

CANINE INTESTINAL BLOOD FLOW IN THE TERMINAL PHASE OF THE GASTROINTESTINAL RADIATION SYNDROME. J. Kabal, L. J. Parkhurst* and D. E. Wyant*

In different shock states when the decreased cardiac output is compensated by increased peripheral resistance, the vasoconstriction of the small intestine is disproportionally increased (ischemia). Similar major hemodynamic deterioration is observed in the Gastrointestinal Radiation Syndrome which terminates in cardiovascular collapse. The initiating and one of the persisting factors present during the 4-day survival is the structural breakdown of the small intestine. However, in this clinical picture, the small intestinal hemodynamic participation is obscure. The objective of this study was to obtain information about the distribution of the small intestinal blood flow and its correlation to the cardiac output in the terminal phase of this radiation injury. One year old, male beagles (11.0 $\pm$ 1.0 kg BW) were subjected to 1500 rads of whole-body pulsed gamma-neutron radiation. Seventy-two hours postirradiation (after 16 hours starvation) they were anesthetized with 30 mg/kg Nembutal and through a catheter which was inserted into the left ventricle, tagged microspheres (^{169}Yb, 15 μC) in the size of 15 $\pm$ 5 μ were injected. Data were compared with a similarly treated, but nonirradiated group. The percent distribution of the cardiac output in the small intestine was 6.94 $\pm$ 2.01 for the irradiated, and 4.18 $\pm$ 1.00 for the control, nonirradiated group. The total mucosal weight of the small intestine 72 hours postirradiation was 26.73 $\pm$ 9.65 grams, compared to 96.33 $\pm$ 10.68g of the nonirradiated group. However, its percentage mucosal blood flow remained at the same level as the control. Therefore, we conclude that in the terminal phase of the GI Radiation Syndrome, instead of ischemia, a relative hyperemia is existing in the mucosal part of the small intestine.

BLOOD URIC ACID LEVELS AS AN INDICATOR OF SMALL BOWEL ISCHEMIA IN THE DOG. John E. Kaiser*, Peter M. Scholz*, Weldon B. Jolley, and Louis L. Smith*. Loma Linda University School of Medicine, Surgical Research Laboratory, Loma Linda, California.

Prior observations from our laboratory have demonstrated that temporary decrease in perfusion of the small bowel of the dog is associated with a marked increase in the level of uric acid in superior mesenteric blood. The present experiments report our findings of systemic blood uric acid levels following segmental as well as total superior mesenteric artery and vein ligations. Eighteen lightly anesthetized dogs had femoral artery vein and superior caval cannulation for sampling and measurement of arterial pressure, central venous pressure, heart rate, hematocrit and blood uric acid. Laparotomy was performed for ligation of the appropriate mesenteric vessel. Uric acid values were measured using a Varian high pressure liquid chromatograph. Ligation of the arterial supply to 75 cm segments of small bowel caused significantly higher femoral venous blood uric acid levels ($p<0.05$) at 7 hours post ligation when compared with sham-operated controls. Total superior mesenteric venous occlusion was followed by significantly higher uric acid levels than those observed in arterial occlusions ($p<0.02$). In general, venous occlusions caused higher blood uric acid levels ($p<0.007$). Low arterial pressure was associated with high blood uric acid levels ($p<0.02$). These findings indicate a major loss of high energy purines to uric acid as a result of intestinal hypoxia.

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CORRELATION BETWEEN PROTEIN CONFORMATIONAL CHANGE AND ATPASE ACTIVITY IN SUPERPRECIPITATING (SUPT.) ACTOMYOSIN SUSPENSIONS. George Kaldor and Quei-Shiow Hsu*, Dept. of Physiology and Biophysics, The Medical College of Pennsylvania, Philadelphia, Pennsylvania 19129.

ATP and actomyosin were mixed at $8^{o}C$ temperature which inhibited the onset of supt. During a 100-300 millisecond period after the stopped flow the oscillation of the actomyosin particles subsided. In order to initiate supt. a heating pulse raised the temperature of the still, well-mixed suspension to $23^{o}C$ within a few microseconds. These experiments showed that the supt. of skeletal and cardiac actomyosins started within one millisecond after the heating pulse. Thus the onset of the protein conformational change and the presteady state of the ATPase activity coincided while the steady state of the ATPase activity followed the onset of the turbidity increase by 250-500 milliseconds. A good correlation was reported between the extent of the initial phosphate burst and the velocity of the supt. (Federation Proc. 31, 338 Abs. (1972). It is suggested that a charge fluctuation on the actomyosin molecule during the presteady state (initial phosphate burst) due to the absorption of ATP + ADP + P_i above the "stochiometric" ratio is in causal correlation with the protein conformational change in supt. of actomyosins. It is stipulated that the increase of the initial phosphate burst above the "stochiometric" ratio is characteristic to the interaction of actomyosin and ATP at low ionic strength. Supported by NIH Grants NB06517 and HD06267.

SUPPRESSION OF OVULATION AND THE PROESTRUS SURGE OF LH AND FSH BY ATROPINE OR MELATONIN. I. A. Kamberi. UCLA School of Medicine, Harbor General Hospital Campus, Torrance, California.

Atropine sulfate (A) in .15 M NaCl was injected subcutaneously (600-700 mg/kg) or intraventricularly (200-300 µg/rat) in female rats by way of chronic cannulae. The administration of A was performed between 12:00-13:30 hrs on the day of proestrus. The blood samples were taken at various time intervals during the afternoon of the day of proestrus, via the carotid artery, previously cannulated and attached through tygon tubing to a peristaltic pump. Injection of A by either route suppressed the proestrus surge of LH and FSH, whereas, no effect was observed in saline treated rats. Furthermore, some of these rats examined for ova on the day of estrus (8-9 am) showed no evidence of ovulation (O). The inhibition of O can be overcome by intravenous injection of 10 µg LH or crude hypothalamic extract. This excludes the possibility that A acts directly at the ovarian or pituitary level. In addition, multiple injections of melatonin (M) intracardiac (1-5 mg/rat) or intraventricular (1-5 µg/rat) between 13:00-14:00 hrs on day of proestrus, also suppressed LH and FSH release and inhibited O. Intracardiac or intraventricular injection of M into adult male rats, or castrated animals of both sexes, also resulted in a decrease of plasma levels of LH and FSH. Contrary to the inhibitory effect of A or M, intra-arterial administration of 10-20 mg/rat of ℓ-3,4-dyhydroxyphenylalanine (DOPA) to ovariectomized estrogen-progesterone primed rats stimulated the release of LH or FSH and induced an early decrease in prolactin during the first 30 min. with an increase thereafter. These data show that cholinergic synapses and catecholaminergic or serotoninergic neurons all play a role in preovulatory discharge of LH, FSH and O. These data also suggest that biogenic amines are involved in regulation of gonadotropin and prolactin secretion. (Supported by Attending Staff Association GRS Grant 1389 from NIH).

PRESETTING THE WORK LOAD AND AIR TEMPERATURE TO ACHIEVE DESIRED PHYSIOLOGICAL RESPONSES. Eliezer Kamon and Kent Pandolf (intr. by Harwood S. Belding). Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania.

During work in temperate environments heart rate (HR) and rectal temperature (T_{re}) equilibrate at levels above resting depending on the relative oxygen uptake (V_{O_2} as percentage of max) but from our experience these two parameters will equilibrate at new levels under heat stress provided that the body can cope with the environment by dissipating the accumulating heat. This experiment was designed to preset either the metabolic level at air temperature (T_a) of 24°C or the T_a for a basic work load (W) such that the HR would equilibrate at a rate 20 or 30 beats/min above that apparent for the basic W. The coefficient for predicting W, V_{O_2} and the respective HR levels were based on past experience in our laboratory and reports by others. Ten young adults cycled for 30 minutes daily. The basic W was set at 40% of each individual's maximal value. Presetting of W and T_a was as follows: the increase of W at T_a 24°C was based on a regression of V_{O_2} on HR of 20 ml/beat and a regression of V_{O_2} on W of 2 ml/kgm; setting higher T_a at the basic W was based on a regression of HR on T_a of 1 beat/min per 1°C above 24°C (RH less than 20%). In all four combinations of changes in W or T_a the targetted HR was achieved within S.D. of 6 beats/min. Toward the end of the 30 minutes of exercise T_{re} equilibrated at three levels which were correlated with the three V_{O_2} levels but independent of the T_a levels. A unit of metabolic heat load caused three times more rise in HR than a unit of environmental load.

REFLEX BRADYCARDIA DUE TO AORTIC NERVE STIMULATION IN THE RABBIT. Merrill B. Kardon*, D. Fred Peterson* and Vernon S. Bishop. The University of Texas Medical School at San Antonio, San Antonio, Texas 78229.

A total of 24 anesthetized albino rabbits were used to quantitate the reflex heart rate reduction resulting from central stimulation of either cut aortic nerve. Systemic arterial blood pressure fell during aortic nerve stimulation with the onset of bradycardia always preceding the onset of the fall in blood pressure. No qualitative differences were seen between the right and left aortic nerves, although responses were found to be greater after the contralateral nerve was cut. Compound evoked potentials recorded during electrical stimulation indicated that both A and C fibers contributed to the bradycardia while the maximum response at a given frequency of stimulation required total fiber recruitment. The magnitude of the response was frequency dependent at any established stimulus intensity (stimulus voltage and duration held constant) increasing with frequency to reach a maximum at between 50 and 100/sec. The average response to maximal stimulation of either aortic nerve with the contralateral nerve intact was 47.1 beats/minute, a 15.1 ± 2.7% fall from the resting level. Selective denervation indicated that the efferent pathways of the reflex were partly in the vagi and partly in the cardiac sympathetic nerves. Bilateral vagotomy reduced the peak response by an average of 39%. Bilateral stellectomy reduced the peak response by 50% in unvagotomized rabbits and eliminated the response in previously vagotomized animals. A recovery in heart rate averaging 31% from the peak bradycardia was seen in 8 animals during maximal stimulation within a 25 second period while systemic blood pressure did not recover. Bilateral carotid sinus denervation elimnated this heart rate recovery while the reduction in blood pressure remained unchanged. (Supported by NIH #2 RO1-HL12415-04, San Antonio Heart Association, and AFOSR-71-2074).

DUODENAL AND ILEAL RATES OF INSORPTION OF HEXANOIC ACID AND SODIUM HEXANOATE IN DOGS. Darlene G. Kelly,* Charles F. Code and Jerry F. Schlegel.* Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55901

We set about to contrast rates of disappearance of hexanoic acid (HA) and sodium hexanoate (NaH) from loops of duodenum and ileum in 6 healthy, conscious dogs. Three had fistulae of duodenum and three of ileum. Test solutions containing 40mM HA or NaH were made to 150mM with NaCl, and tracer amounts of ^{14}C-HA and ^{24}Na added. A measured quantity of test solution was thoroughly mixed with residual loop contents, a sample taken and others then withdrawn at intervals. Initial and final residual volumes were determined by dilution of ^{24}Na and the quantities of acid or salt insorbed calculated from the concentration and volume changes. Insorption rate constants were determined from a plot of % of the ^{14}C-HA or NaH remaining against time. Results follow:

		Mean ±SEM insorption rate constants			
		Hexanoic acid		Sodium hexanoate	
Loop of	Dog	n	%/minute	n	%/minute
Duodenum	A	7	6.7±0.7	7	3.4±0.4
	B	7	6.3±0.5	7	3.3±0.7
	C	5	5.4±0.7	5	2.0±0.4
Mean of Means			6.1±0.4		2.9±0.5
Ileum	D	5	4.7±0.3	5	1.2±0.04
	E	10	6.4±0.4	10	4.6±0.3
	F	5	2.9±0.1	8	2.0±0.3
Mean of Means			4.7±1.0		2.6±1.0

Duodenal and ileal rates of insorption of both the acid and the salt were similar. However, HA was insorbed more quickly than NaH for loops of both the duodenum and ileum. (Supported in part by NIH Grant AM-2827.)

DIFFERENTIAL RESPONSES OF THE CANINE GASTRIC CORPUS AND ANTRUM TO ELECTRIC STIMULATION. Keith A. Kelly. Mayo Clinic and Mayo Foundation, Rochester, Minn.

How does the orad corporal gastric pacemaker entrain the distal stomach? Silver wire electrodes, bipolar for stimulation (interelectrode distance, 5 mm) and monopolar for recording electric activity concurrent with stimulation, were implanted on the anterior wall of the gastric corpus and antrum of four dogs. After recovery, electric stimuli were given intermittently to the fasted, conscious animals for 3 to 4 months. Pacesetter potentials (PP) were generated at both corporal and antral sites of stimulation. As the duration of a stimulus was decreased, its strength had to be increased to reach threshold; strength versus duration curves in both the corpus and antrum were equilateral hyperbolas. However, the antrum was more excitable than the corpus, had a shorter refractory period to a second identical pulse, and could be driven to faster frequencies by stimulation (Table). These characteristics of the antrum, coupled with its slower intrinsic PP frequency (Weber and Kohatsu, Gastroenterology 59:717, 1970), would facilitate entrainment of the distal portion of the stomach by the corporal pacemaker. (Supported by NIH Grant AM-2015.)

Gastric region	Rheobase (ma)	Chronaxie (msec)	Refractory period (sec)	Fastest driven PP frequency* (cpm)
Corpus	0.45	35	7.5	6.4
Antrum	0.25	24	5.2	7.4

*At least 10 consecutive PPs generated.

INCREASED SECRETORY LAG CAUSED BY INHIBITORS AND STIMULATORS OF GASTRIC ACID SECRETION. George W. Kidder III and Robert G. Kyrka* Biology Department, Wesleyan University, Middletown, Connecticut.

In bullfrog gastric mucosa, acid secretion resumes following anoxia with a pronounced lag as compared to cytochrome reoxidation or chloride transport. Previous work (AJP 221:421) has demonstrated that ATP, ADP and ITP will increase this lag by as much as 15 min (10 mM ATP, serosal) while not producing more than 50% inhibition of steady state (aerobic) secretory rate, which was explained by interactions of these compounds with the metabolic machinery. We now find that the "conventional" inhibitors SCN^-, OCN^-, NO_2^- and NH_4^+ likewise produce lag increases if low concentrations which give partial secretory inhibition are used. The inorganic ions are more effective than ATP (for SCN^-, 1.33 mM gives a 5 min lag increase). Surprisingly, 10 mM histamine also causes a lag increase as compared to the normal histamine stimulated (0.1 mM) control, with the high histamine producing a further steady state rate increase. L-histidine likewise produces similar effects. All compounds increase steady state PD and cause changes in cytochrome c redox steady state consistant with their secretory effect. Both the organic and inorganic compounds possess a nitrogen with an unshared pair of electrons, a feature postulated by LeFevre et. al. (AJP 207:613) as a requirement for secretory inhibitors. However, since neither adenosine nor inosine are effective either as inhibitors or in producing lag increases, other characteristics of the molecules must be important. The identification of the common features of the lag-increasing molecules should help resolve the question of the site of action of secretory inhibitors, a matter of long-standing debate. (Supported by NSF grant GB-8540.)

Contractile repriming and inactivation in denervated frog muscle. Albert C. Kirby*, Sherry C. Stuesse*, John R. Picken*, and Barry D. Lindley. Department of Physiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106.

Contractile responses of denervated muscle to depolarization by potassium are weaker than those of control muscle. We have investigated repriming and inactivation (Frankenhaeuser and Lännergren, Acta Physiol. Scand. 69:242) and the roles that they might play in this weakness. Solutions contained methanesulfonate as the anion and tris as the Na^+-replacing cation; pH was 7.0. Toe muscles (ELD IV) were removed from frogs in which the sciatic nerve had been severed 31-62 days previously. Muscles were kept in 1.5 mM Ca^{++} Ringer for 10 minutes prior to test (in some experiments, an additional 4 minute exposure to 0.4 mM Ca^{++} preceded the contractures). Peak tension in response to 100 mM K^+ one minute following a 10 second conditioning exposure to 100 mM K^+ is dependent on $[K^+]$ and $[Ca^{++}]$ in the intervening recovery solution. The ratio of peak tension in the testing contracture to that in the conditioning contracture was less in denervated than in control muscle; for recovery $[K^+]$ was 0.5 to 30.0 mM. In inactivation experiments $[K^+]$ was 5.0 to 30.0 mM for 1 min. Repriming is slower in denervated muscle and inactivation is complete at lower $[K^+]$ than in normal muscle. Both of these conditions are exaggerated in denervated muscle by exposure to 0.4 mM Ca^{++}. These results are consistent with our previously reported calcium dependence of tension (Fed. Proc. 31:323) and with our unpublished data which indicate that some superficial site involved in excitation-contraction coupling develops Ca^{++} sensitivity following nerve section and that this site is intimately involved in an alteration of the kinetics of relaxation.

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LACK OF CYCLIC AMP-DEPENDENT PROTEIN KINASE STIMULATION OF CALCIUM UPTAKE BY RABBIT SKELETAL MUSCLE SARCOPLASMIC RETICULUM. Madeleine A. Kirchberger*, Michihiko Tada*, Doris I. Repke*, and Arnold M. Katz. Mount Sinai Medical and Graduate Schools of the City University of New York, New York, N.Y.

A role for cyclic AMP-dependent protein kinase in the regulation of Ca-uptake by rabbit skeletal muscle sarcoplasmic reticulum (SR) was investigated. Ca-uptake was measured at 25 C in 5 mM ATP, 2.5 mM Tris-oxalate, 0.12 M KCl, 40 mM histidine buffer, pH 6.8, and 5 µg/ml SR protein. After 10 minutes preincubation with 0.1 mg/ml protein kinase and/or 10^{-6} M cyclic AMP (cAMP), reactions were started by addition of 45 Ca-EGTA buffer ($[Ca^{++}]$ = 0.75 µM). Neither the protein kinase nor cAMP stimulated Ca-uptake, and Ca-uptake was not enhanced after SR was preincubated with both. These results are in contrast to those we have obtained with canine cardiac microsomes in which oxalate-dependent Ca-uptake was approximately doubled following preincubation with cAMP and protein kinase under identical conditions. The latter studies suggest that epinephrine, which is known to stimulate adenylate cyclase, may in cardiac muscle act via a cAMP-dependent protein kinase to increase Ca transport into intracellular stores and thereby shorten systole and enhance contractility. The lack of cAMP-dependent protein kinase stimulation of Ca-uptake in skeletal muscle may explain the failure of epinephrine to increase active state intensity and shorten contraction time in intact skeletal muscle.

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SLEEP BEHAVIOR IN A PRIMITIVE MAMMAL, THE ARMADILLO. W. R. Klemm and A. E. Prudom*. Dept. Biol., Texas A&M U., College Station, Texas 77843.

Sleep behavior in 5 armadillos (Dasypus novemcinctus) was studied over continuous 24-hour periods in order to evaluate certain hypotheses concerning the relation of phylogenetic rank and life style to sleep. Wakefulness periods were short and scattered throughout the day. Armadillos fell asleep with unusual suddenness. Their polyphasic sleep behavior ranged from 11 to 19 episodes per day, with an average total sleep time of over 77% of the day. Rectal temperatures varied erratically over a wide range of 87-97°F and did not correlate with behavioral state, even though the immediate environment was maintained at 80°F.

During behavioral sleep, the typical mammalian slow-wave sleep EEG pattern was observed about 50% of the total sleep time, with the duration of a given period ranging from 0.75 to 375 minutes. The other portion of the sleep time was characterized by activated EEGs that were associated with 4 different combinations of REM and neck muscle activity patterns. These activated EEG episodes never lasted longer than 1.6 minutes and were interspersed randomly among slow-wave periods, with abrupt transitions between periods.

Analysis of paradoxical sleep (PS) was confounded by the extremely short durations of activated EEG periods and the incomplete signs of PS. Rapid eye movements (REM), with or without increased neck muscle activity, occurred 10% of the sleep time. The level of neck muscle activity was not decreased from that during deactivated EEG periods; a constant level of muscle activity occurred in conjunction with REM for 7.5% of the sleep time, and without REM for 24.5% of the sleep time. At least some of the periods of activated EEG during behavioral sleep could have reflected shivering or transient arousal from slow-wave sleep, rather than PS.

ELECTROPHYSIOLOGICAL STUDY OF NEUROSECRETORY CELLS OF BULL FROG IN VITRO. Kiyomi Koizumi. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Electrophysiological study of neurons of the mammalian supraoptic and paraventricular nuclei revealed some interesting behavioral characteristics of these neurosecretory cells (J. Physiol. 221:683,1972). In order to gain more insight concerning humoral influence on neurosecretory cells, a study has been made of the isolated hypothalamo- hypophysial system in bull frogs. After the frog was pithed, the diencephalon was isolated with the pituitary gland attached and placed in a tissue chamber and perfused by circulating frog Ringer's solution saturated with 95% O_2 - 5% CO_2. The temperature of the bath was maintained at 17-18°C. Recordings were made from preoptic nuclei cells with conventional glass capillary microelectrodes filled with 3M-KCl. Neurosecretory cells were identified by antidromic excitation following stimulation of the neurohypophysis by a single pulse. With few exceptions neurosecretory cells in vitro did not show "spontaneous" discharges. The antidromic potentials occurred with latencies of 20-40 msec and showed a notch on their rising phase. Two successive stimuli applied to the neurohypophysis at varied intervals revealed two separate components of the antidromic potential, as seen in most other neurons. The refractory period of the early A-spike was 20-30 msec, but the recovery process of excitability for the late B-spike was quite slow and varied; in certain cells ability to produce a B-spike was not fully recovered by 300-500 msec after the preceding discharge. A two-fold increase in NaCl concentration of bathing fluid reduced the size of antidromic potentials. The presence of pitressin in a bath (5-10 mu) caused a brief augmentation and later depression of antidromic potentials. (Supported by U.S. Public Health Grant NS-06537)

ESTIMATION OF EXERCISE DIFFUSING CAPACITY OF THE LUNG. J. Kollias, H. L. Barlett*, and J. L. Hodgson*. The Pennsylvania State University, University Park, Pennsylvania.

Measurement of steady state diffusing capacity of the lung for carbon monoxide (D_{CO}) in ten healthy young men was obtained at rest and during exercise. Measured D_{CO}s at rest, 1.37, 2.06, and 2.52 liters/O_2/min were, respectively: 27.0, 38.7, 50.1, and 57.0 ml/min·mmHg. Exercise D_{CO} was estimated from resting measurements of D_{CO}, functional residual capacity (FRC) "alveolar" volume (V_A) and change in "alveolar" volume with exercise. FRC and V_A at rest and during exercise were used to estimate the change in lung surface area (SA_L) and membrane thickness (T_h) with exercise. It was assumed that: a) the number of functional alveoli were constant, spherical in configuration with a resting membrane thickness of 0.7μ, and b) FRC did not change with exercise intensity. V_A was also measured at each exercise level. Estimated exercise D_{CO} values at measured $\dot{V}_{O_2}$ levels of 1.37, 2.06, and 2.52 liters/min were, respectively: 39.3, 49.5, and 58.7 ml/min·mmHg. The high correlation obtained between measured and estimated D_{CO} values during exercise could be explained on the basis of an increase in lung volume which produced a corresponding proportionate increase in SA_L and decrease in T_h.

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SINOAORTIC CONTRIBUTION TO THE ADJUSTMENT OF SYSTEMIC RESISTANCE IN EXERCISE. J. A. Krasney, R. C. Koehler* and M. G. Levitzky*. Dept. of Physiol., Albany Med. Coll., Albany, N. Y., 12208.

Dogs, instrumented with flow transducers and miniature solid state pressure gauges, were trained to run for 3 min at 4.8 Km/hr (5% grade). The data was recorded on magnetic tape and analyzed at consecutive 4 sec intervals by a PDP-12 computer in 75 experiments on 5 dogs. In a representative dog increases in mean aortic flow (1301 ml/min ± 72.4 SE to 2560.6 ± 90.8), heart rate (126.8 b/min ± 12.6 to 210.6 ±10.1) and mean arterial pressure (164.8 mm Hg ± 10.2 to 190.7 ± 12.5) were observed during exercise. Calculated peripheral resistance fell smoothly from 12.7 mm Hg/100 ml/min(± 1.0) to plateau at 7.5 (± 0.74). Subsequently, denervation of the sinoaortic reflexogenic zones was performed. After recovery from the denervation, exercise again increased aortic flow (949 ml/min ± 94.8 to 1745.7 ±96.2) and heart rate (147 b/min ±7.8 to 203 ± 4.2). During the first 30 sec an initial decline in arterial pressure now occurred (171.4 mm Hg ± 24.5 to 139.2 ± 19.7) with a later rise to 185.9 mm Hg (± 7.7). This was accompanied by an initial drop in peripheral resistance from 18.2 mm Hg/100 ml/min(± 2.4) to 7.6 (± 0.9). Resistance then rose later to plateau at 10.8 mm Hg/100 ml/min (± 0.75). A similar pattern was observed in the other dogs. These observations indicate that the sinoaortic zones, probably the baroreflexes, contribute to a smooth, sustained adjustment of peripheral resistance during exercise. Baroreceptor discharge would normally be augmented by increased arterial pulse pressure in the intact animal. It is therefore likely that the secondary tendency for resistance to rise as exercise continues in the denervated dog is a consequence of the absence of opposing baroreflex influences. (Supported by NHLI grant HL-11982 and The Heart Association of Eastern New York.)

CARDIOVASCULAR RESPONSES TO COMBINED STATIC AND RHYTHMIC WORK. K.V. Kuhlemeier*, Henry L. Taylor and Ernst Simonson. Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis, Minnesota 55455.

Eight healthy male college students performed 16 treatments of static and/or rhythmic work and 18 healthy middle-aged men performed four treatments. Static work consisted of holding a weight equal to 0 to 38.1% of the subjects' maximal voluntary contraction suspended from a suitcase handle so that isometric tension was developed in the flexor muscles of the middle phalanges. Rhythmic work consisted of walking on a motor-driven treadmill at work levels eliciting 8 to 65% of the subjects' maximal oxygen uptake. Blood pressures were taken by auscultation and heart rates (HR) from ECG recordings every minute. Estimated mean blood pressure (EMBP) increased 30% after three minutes of the highest static work level and the heart rate rose 11%. EMBP decreased 7% and the HR increased 54% at the highest level of rhythmic work. Lesser loads resulted in proportionately smaller changes. During the treatment which included the highest levels of both static and rhythmic work the EMBP increased 36% and the HR rose 98%. In the treatments involving only rhythmic work, HR and EMBP were nearly stabilized after the second minute of work; steady states were not reached in the treatments which included static work. The EMBP and heart rate increases above control levels were a function of both the level of static work and the level of rhythmic work. There was a significant interaction effect between the two types of work on HR but not EMBP. The responses of the younger men were the same as the responses of the older men for static work alone and in combination with rhythmic work. Norepinephrine excretion was greater during static work alone than during a control period and during rhythmic work both alone and with a static component. There were no significant differences between treatments in vanilmandelic acid excretion.

FIELD POTENTIALS EVOKED IN THE RABBIT'S BRAIN STEM BY STIMULATION OF THE AORTIC NERVE. M. Kumada and H. Nakajima (intr. by K. Sagawa). Dept. of Physiology, Univ. of Tokyo, School of Med., Tokyo, Japan.

By electrical stimulation of the aortic nerve, field potentials were evoked in the following structures of the lower medulla of the rabbit; nucleus tractus solitarii, tractus solitarius, nucleus alaris, nucleus ambiguus, and lateral reticular formation. Several components were distinguished from these potentials, and were classified into two groups; short-latency response (SLR, peak latency < 40 msec), and long-latency response (LLR, peak latency > 40 msec). SLR was associated with aortic A fibers, while LLR with aortic C fibers. The amplitude of LLR was sometimes much greater than that of SLR. There was no apparent difference in the topographical distribution of SLR and LLR within the nucleus tractus solitarii. However, LLR was more frequently encountered than SLR in the juxta-alar region of the nucleus tractus solitarii. Both SLR and LLR were seen in the nucleus alaris, but only SLR was observed in the nucleus ambiguus. In most cases the evoked potential in lateral reticular formation was recorded medial or dorsomedial to the nucleus ambiguus, and consisted of SLR only. (Supported by research grants from the Ministry of Education of Japan, and Tanabe Pharmaceutical Company).

RENAL-URETERAL COUPLING MECHANISM TO REGULATE URINE TRANSPORT
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St. Louis, Missouri

Ureteral peristaltic contraction during and after intermittent renal compression and renal vessel occlusion in 10 dogs was measured. At laparotomy under sodium pentobarbital anaesthesia and controlled urine flow rate, 32 studies of ureteral contraction pattern in 10 pairs of kidney-ureter combination were carried out before, during, and after: (1) 3 to 5 minutes intermittent manual compression of the kidney (2) occlusion of the renal artery and renal vein simultaneously. Renal compression increased peristaltic contraction rate 2-9 times the control rate in 90% of the studies, decrease in 8%, no change in 2%. Three to five minutes of venous occlusion increased the peristaltic rate 1-6 times the control rate in all studies and increased the bolus size, while renal artery occlusion decreased the contraction rate in 90%, with no change in 10% of the studies. Release of renal occlusion gradually slowed the rate of contraction in all studies; there was complete cessation for 2-5 minutes in some. Renal artery release gradually restored contractile frequency within 3-5 minutes, with an overshoot of control rate in 60% of the studies. In the recovery from manual renal compression peristaltic activity was depressed in 99% of the studies. A peristalsis for 4-8 minutes was observed in 2 dogs. Urine flow has long been known to be regulatory factor in ureteral peristalsis. These data suggest a wider context in which this factor may be operative, a renal ureteral coupling mechanism.

COMPONENTS OF EXERCISE HYPERPNEA IN DIVERS AND NON-DIVERS. D.A. Lally* and F.W. Zechman. Dept. of Physiology, Univ. of Hawaii Sch. of Med., Honolulu, Hawaii 96822, and Dept. of Physiology and Biophysics, Univ. of Kentucky Medical Center, Lexington, Kentucky 40506.

The initial (8-15 sec) and steady state (5-7 min) ventilatory responses to treadmill exercise were studied in 9 sedentary control subjects and 8 divers. Exercise was walking a 10% grade at 1, 2 and 3 mph. Heart rate, inspired tidal volume and end-tidal CO_2 were monitored continuously. It was found that at all levels of exercise the steady state ventilatory response was lower in divers than in controls, significantly so at 2 and 3 mph. The fast (neural) component of the hyperpnea was also less in divers, but this difference was less than half of the difference in steady state response and was not significant statistically. The R values were not different at rest or 1 mph, but were significantly lower in divers at 2 and 3 mph, suggesting retention of CO_2 during exercise in divers. At these levels of exercise, end tidal CO_2 was 5 to 9 mmHg higher in divers, suggesting that the relative hypoventilation seen in divers is primarily due to reduced sensitivity to CO_2, possibly secondary to physical conditioning. (This investigation is in part supported by NOAA Sea Grant GB 8393.)

KINETICS OF GASTRIN RELEASE IN RESPONSE TO ELECTRICAL VAGAL STIMULATION IN THE DOG. George Lanciault*, Carol Bonoma* and Frank P. Brooks. Univ. of Pennsylvania School of Medicine, Philadelphia, Penna. 19104.

The rate of rise and fall of circulating serum gastrin concentrations in response to electrical vagal stimulation was studied. Female mongrel dogs, anesthetized with morphine-chloralose, were subjected to continuous electrical stimulation of the distal cut ends of the cervical vagi for 30 min. During this time portal blood was sampled frequently to estimate the rate of rise of circulating serum gastrin levels. Gastric secretions were also collected during this time to determine gastric acid output. After the 30 min interval of stimulation, portal blood was again sampled to follow the rate at which serum gastrin levels returned to control values. The results obtained in 3 dogs showed that serum gastrin concentrations rose significantly within 5 min after initial electrical stimulation. Mean peak serum gastrin concentration of 333 pg/ml was noted 25 min after initial vagal stimulation. Serum gastrin levels fell and returned to control levels within 20 min after cessation of stimulation. Gastric acid output did not increase during the period of stimulation due, perhaps, to the insensitivity of the method used for recovery. We conclude that the rise of serum gastrin levels is prompt in response to electrical vagal stimulation and that the $t_{1/2}$ for the descending limb of the response curve is approximately 9 min and is similar to the gastrin half-life values obtained by other methods. (Supported by USPHS NB-IR01-AM 14563-02.)

EFFECTS OF CHRONIC EXERCISE ON HEART, ADRENAL, AND BRAIN CATECHOLAMINE LEVELS. **Arthur S. Leon, W. Dale Horst*, and Mary Ann Saviano*, Hoffmann-La Roche Inc., Nutley, New Jersey.**

Catecholamine (CA) release from adrenergic nerve endings and the adrenal glands occurs during physical and emotional stress. We studied the effects of chronic exercise stress (swimming under standardized conditions 1 hour daily, 5 days per week for 12 weeks) in 20 adult male rats. Animals were decapitated 24 hours after their last swim along with unexercised controls. Hearts, adrenals and brains were excised, weighed, frozen and extracted for CA. CA were separated by column chromatography. Norepinephrine (NE), epinephrine (E), and dopamine (DA) were determined flourimetrically by the method of Laverte and Sharman. Mean body weights of the exercised and unexercised group showed significantly heavier hearts, adrenals, and brains ($P < 0.001$). Organ CA levels ($\mu g/g \pm SE$) were as follows:

	Unexercised	Exercised	P
Heart NE	0.444 ± 0.028	0.555 ± 0.083	0.25
Adrenal NE and E	962 ± 36	764 ± 22	0.001
Brain NE	0.841 ± 0.116	0.676 ± 0.062	0.25
Brain DA	1.172 ± 0.066	1.256 ± 0.077	0.05

Thus chronic swimming resulted in a decrease in adrenal CA concentration and an increase in brain DA but did not significantly alter brain and heart NE.

CIRCULATORY EFFECTS OF PROLONGED HYPOXIA BEFORE AND AFTER ANTIHISTAMINE. J. E. Levasseur*, H. A. Kontos, D. W. Richardson, and J. L. Patterson, Jr. Dept. of Medicine, Medical College of Virginia, Richmond, Virginia.

Five dogs chronically instrumented with an electromagnetic aortic flowmeter probe and with intravascular cannulas in the pulmonary artery, left atrium and in a systemic artery were subjected to two periods of breathing 10% O_2 for five days in a plastic chamber. Each animal was studied before and during intravenous administration of the antihistamine promethazine (2 mg/kg every five hours). Hypoxia produced increases in heart rate, cardiac output, pulmonary and systemic arterial blood pressures and in pulmonary and systemic vascular resistances. Left atrial pressure decreased significantly. All changes were sustained for the entire five-day period except for the increase in cardiac output which lasted for only the first day of hypoxia. These responses were not significantly different during the administration of promethazine. These results do not support the view that histamine is a mediator for the circulatory responses to hypoxia. The return of cardiac output to normal levels after the first day of hypoxia is reminiscent of what is seen in man at high altitude.

AN ELECTROPHYSIOLOGICAL STUDY OF DENERVATED SARTORIUS MUSCLE OF FROGS MAINTAINED AT ELEVATED TEMPERATURES. Leonard Levine. Pacific Univ., Forest Grove, Or.

To explore the possibility that electrophysiological differences in the reaction to denervation of mammalian and frog twitch muscle might be temperature related, experiments were made on sartorius muscles dissected from "southern" frogs (Rana pipiens), which had been maintained in an incubator at 34 $\pm$ 1°C before and after motor nerve section. Conventional microelectrode techniques for intracellular recording were used. Miniature endplate potentials (mepps) disappeared in less than two days after denervation, most commonly between 20 and 30 hours. Resumed spontaneous miniature discharges have not been detected from 2 - 14 days. No early reduction in resting membrane potential occurred at the time the mepps disappeared, nor was the resting potential significantly different between operated and contralateral innervated sartorii, at any time during a three week period of denervation. Compared to contralateral innervated fibers of the same frog, denervated fibers produced action potentials which had statistically significant reductions in spike amplitude, maximum rate of rise, and maximum rate of fall of the action potential. There was no evidence of development of a positive afterpotential; the characteristic negative afterpotential persisted. The spike generating mechanism remained fully susceptible to tetrodotoxin in denervated fibers, being progressively inhibited by increasing concentrations to the same extent as in innervated fibers. Thus maintaining frog muscle at temperatures comparable to mammalian body temperature reduces some of the differences observed following denervation, but several differences remain. (Supported in part by USPHS Grant NS 09073)

ADRENERGIC HYPOSENSITIZATION IN THE GUINEA PIG *IN VITRO* AND *IN VIVO*. A.J.Lewis*, J.S.Douglas* and A.Bouhuys. Yale Univ. Lung Research Ctr. & J. B. Pierce Foundation, New Haven, Conn.

Increased mortality in patients using bronchodilator aerosols over extended periods may be the result of hyposensitization to both endogenous and exogenous sympathetic stimulation as a consequence of excess usage of these sprays. We produced an analogous situation in the guinea pig. Immediately after incubation of the spirally cut tracheal strip with isoproterenol (I, 50 ng/ml for 20 min) the contractile response to histamine (H) was abolished. This response to H returned to normal within 30-60 min after the incubation, but the ability of I to inhibit H contractions was still impaired and only returned 60-90 min later. Theophylline (100 µg/ml), dibutyryl cAMP (250 µg/ml) and norepinephrine (2 µg/ml) incubations for 20 min produced similar I hyposensitization and another phosphodiesterase inhibitor I.C.I 58, 301 (20 µg/ml) did likewise. Following i.m. administration of saline (S, 0.1 ml) or I (4 µg/kg) every 20 min for 5 h, paired S and I treated groups of animals (13/group) were challenged i.p. with different doses of H (1.5, 3.0 and 5 mg/kg). Mortality was significantly higher in I-treated groups for the two low doses used for H challenge. In the 5 mg/kg groups, S and I treated animals had equal mortalities but the I animals died later (approx. 15 min) than the S animals (<5 min). The actions of β-stimulants are believed to be mediated via cAMP and it is likely that the present findings can also be attributed to changes in cyclic nucleotide content. The *in vivo* data further emphasize the problems of chronic administration of bronchodilators. We conclude that airway smooth muscle of guinea pigs can be partially desensitized against the relaxant effect of I *in vivo* as well as *in vitro*.
This work was supported in part by US PHS Grants HE 14534 and HE 14179.

ON TRANSIENTS OF GOLDBLATT HYPERTENSION IN UNANESTHETIZED SINO-AORTIC DENERVATED DOGS. J. F. Liard*, A. W. Cowley, Jr., and A. C. Guyton. Dept. Physiol. & Biophysics, Univ. Miss. Schl. Med. Jackson, Miss.39216.

The role of the baroreceptors in the initial phase of various types of experimental hypertension is not fully understood. Using Goldblatt hypertension as a model, the extent to which the baroreceptors delay the appearance of blood pressure elevation was investigated in three unanesthetized sino-aortic denervated dogs. The arterial pressure was continuously monitored throughout the course of the experiment and the records analyzed with the aid of a Barlow curve scanning device coupled to a digital computer. An externally adjustable renal artery occluder with a chronic indwelling catheter implanted distally in the renal artery permitted atraumatic occlusions of known amounts to be made. A step decrease in renal perfusion pressure to 50-60 mm Hg resulted in a systemic rise in pressure of 20, 40 and 45 mm Hg after 15, 30 and 60 min respectively. Slow pressure oscillations were then observed with a cycle length of 6 to 8 hours before an elevated steady state level of 50 mm Hg above control was reached after 24 to 48 hrs. Heart rate showed little change during the course of the experiment in contrast to the decrease seen in intact dogs. Control plasma renin activity, as measured by radioimmunoassay of angiotensin I, was 0.6 $\pm$ 0.4 (S.E.M.) ng angio/ml/hr and following constriction rose to 4.1 $\pm$ 1.7 at 15 min, 6.6 $\pm$ 1.7 at 30 min, 7.0 $\pm$ 2.0 at 60 min, 5.4 $\pm$ 1.2 at 6 hrs. A decrease in renin activity to 2.1 $\pm$ 0.6 ng/ml/hr was evident by the 24th hour following constriction. These results indicate that the slow rise in pressure observed in intact dogs after renal artery constriction is dependent on baroreceptor activity which gradually adapts over a period of several days. Supported by Grants HE-11678 and HE-14306.

PERFORMANCE AND HISTOCHEMICAL COMPOSITION OF GUINEA PIG AND HUMAN DIAPHRAGM. D.A. Lieberman*, J.A. Faulkner, A.B. Craig and L.C. Maxwell*. Univ. of Michigan Med. School, Ann Arbor, Michigan 48104

Our purpose was to relate muscle fiber composition of the human diaphragm to an observed decrement in maximum voluntary ventilation (MVV) over time. The MVV after 30 seconds was 85% of the MVV after 15 seconds. A small decrement to 82% occurred after 5 min. The rapid decline of MVV in 30 seconds may be related to fatigue of some fibers in the diaphragm. In guinea pig diaphragm, a close relationship was demonstrated between histochemical composition and muscle fatigue. Fast and slow-twitch fibers were determined by myofibrillar ATPase and low and high oxidative fibers by succinate dehydrogenase activity. Sections of diaphragm, isolated in a muscle bath, were stimulated maximally at 2 pulses/sec. The tension declined with time, but reached a constant tension at 35% of maximum tension after 10 min of stimulation. The percentage of slow-twitch fibers in the guinea pig diaphragm was 34%. When the decrease in tension was plotted against time on semi-log paper, an initial rapid decline was observed during the first 5 min of stimulation, followed by a slower decline to the steady state. The proportion of fibers which showed a slow decline corresponds to the area composed of fast-twitch high oxidative fibers. In human diaphragm, 23% of the muscle fibers are low oxidative, and 77% are high oxidative. The rapid decrease in MVV to 82% of maximum may be the consequence of fatigue of low oxidative fibers. These data suggest that high oxidative fibers are not fatigued during the 5 minute MVV, and do contribute to the high MVV levels throughout the test. Of clinical significance is the possibility that MVV tests for 15 and 30 sec may reflect the histochemical characteristics of the diaphragm.

PLASMA TESTOSTERONE AND SEX HORMONE BINDING GLOBULIN (SBG) IN ALCOHOLIC SUBJECTS. J. Liegel*, L. F. Fabre, Jr.*, P. Y. Howard* and R. W. Farmer. Texas Research Institute of Mental Sciences, Houston, Texas.

Previously, this laboratory reported increased urinary testosterone glucuronide excretion, and decreased individual 17-ketosteroid excretion in alcoholic male subjects with normal liver function. This report concerns plasma testosterone and SBG measurements in this population. Plasma testosterone was within normal limits (557±49.6 ng%, $\bar{x}$±SE) in abstaining alcoholics (508±43.8 ng%), decreased during drinking, blood ETOH 100-200 mg% (387±68.0 ng%), and increased during withdrawal (802±111.5 ng%) compared with age paired controls. SBG was significantly ($P<.01$) elevated in male alcoholics (1/p=.404±.071) as compared to normal males (1/p=.219±.028), but not ($P<.01$) to normal female values (1/p=.624±.071). During ETOH consumption no changes were noted. *In vitro*, ETOH (100-200 mg%) decreased protein binding in normal male and female sera. This factor may be related to the decrease in plasma testosterone during drinking. The phenomena observed here may be related to the decreased "maleness" clinically observed in male alcoholics.

CARDIAC OUTPUT AND ITS DISTRIBUTION IN THE UNANESTHETIZED RAT DURING DIVING. Y.C. Lin and D.G. Baker*. Dept. of Physiology, Univ. of Hawaii Sch. of Medicine, Honolulu, Hawaii 96822.

The diving response was elicited by submerging the head of an unanesthetized rat in water of 26°C. The cardiac output obtained by the radioisotope dilution method was reduced by 77% from the average of 194 ± 29 ml/min-kg as determined in 6 rats. The heart rate decreased by 64% from the predive value of 399 ± 12 bt/min. The calculated stroke volume decreased by 35%. The mean arterial blood pressure increased by 15% from the predive value of 118 ± 2 mm Hg while the calculated total peripheral resistance increased 4 fold from the predive values. The fractional distribution of the cardiac output was determined on a separate group of rats using the technique described by Sapirstein (Am. J. Physiol. 193:161, 1958). Cs^{137} was used as the radioactive indicator. The fractional distribution of Cs^{137} increased 3-4 times from the predive values in the ventricle, the lung and the brain hence the blood flow to these tissues was maintained at the predive level. The blood flow to other organs (e.g. the skeletal muscle, the liver, the kidney, the spleen, the adrenals, the intestine, the diaphragm, skin and the tail) was reduced. More than 95% reductions were observed in the skin, the tail, the spleen, the kidney, and the intestine. These findings indicate that the rat exhibits a diving response similar to that of the diving mammal. (This investigation is supported in part by the Hawaii Heart Association and Office of Naval Research Contract No. N00014-67-A-0387-0014.)

THE RELATIONSHIP BETWEEN CATECHOLAMINES AND ACTH: THE EFFECTS OF 6-HYDROXYDOPAMINE. Arnold S. Lippa*, Seymour M. Antelman*, E. Edwin Fahringer*, and Edward S. Redgate. Depts. of Psychology and Physiology, University of Pittsburgh, Pittsburgh, Pa.

The importance of brain catecholamines (CA) in the regulation of ACTH secretion in the male rat was investigated with the use of 6-hydroxydopamine (6OHDA) hydrobromide, a drug reported to cause a selective destruction of CA containing neurons. Resting levels of plasma corticosteroids were fluorometrically determined from external jugular blood samples four days before an intraventricular injection of either 200 µg of 6OHDA (n = 8) or an isovolumetric vehicle solution (n = 5). Plasma corticosteroid levels were again sampled at 3 and 11 days after injection. While plasma corticosteroids were significantly reduced in 6OHDA treated animals at 3 days ($p < .01$), they were completely recovered at 11 days. Ketamine HCl (K) was administered at 28 days to investigate the corticosteroid response to drug stimulation. Forty-five minutes after an intraperitoneal injection of K (120 mg./kg), the 6OHDA treated animals showed a decreased corticosteroid response: 6OHDA 21.9 ± 3.0 (n = 8); vehicle 34.3 ± 3.8 (n = 4); normals 31.9 ± .6 (n = 6). Biochemical determinations of norepinephrine and dopamine revealed a 74% and 43% depletion, respectively, in the 6OHDA-treated animals. The data imply the possibility of an excitatory catecholaminergic input for ACTH release.

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AUTONOMIC INNERVATION OF THE LEFT VENTRICULAR FREE WALL. D.B. Lippincott* and W.C. Randall. Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Stimulation of individual thoracic cardiac nerves causes changes in contractile force on epicardial and endocardial surfaces. Innervation of the canine left ventricular (LV) free wall was studied by suturing Walton-Brodie strain gauge arches to the endocardium. One gauge was positioned near the apex and another at the base near the valve ring. Gauges were also placed on the epicardium directly over both of the endocardial locations. The thoracic cardiac nerves were electrically stimulated before and after atropine. Left (LSS) and right (RSS) stellate stimulation each caused a significant percent increase in contractile force in all muscle segments. The endocardial base showed a larger force increase (341% ± 35 SE) than the endocardial apex (291% ± 22 SE) during LSS. Both changes were larger than the respective force increases (238% ± 26 SE and 238% ± 17 SE) of overlying epicardial segments. Of the individual thoracic cardiac nerves the ventral lateral cervical cardiac nerve (VLCN) elicited the greatest response. The endocardial basal and apical gauges (283% ± 29 SE and 275% ± 24 SE respectively) revealed a larger response than the epicardial gauges (193% ± 23 SE and 226% ± 34 SE respectively). The recurrent cardiac nerve also provided significant innervation to the LV free wall with endocardial and epicardial gauges showing equivalent force increases. Endocardial responses of the basal LV free wall were generally greater than the apical free wall. The epicardial segments were never more responsive than the underlying endocardial segments. During stimulation of several of the small nerves the epicardial response was equal that of the endocardium. All muscle segments showed positive inotropic responses during isoproterenol injection at the conclusion of each experiment. (Supported by NIH Grants HE 08682 and GM 999).

EFFECT OF ALBUMIN ON FUNCTION OF ISOLATED PERFUSED RAT KIDNEY, John R. Little* and Julius J. Cohen, Department of Physiology, University of Rochester, School of Medicine and Dentistry, Rochester, New York, 14642.

The effect of perfusate albumin concentration on function of the isolated rat kidney has been studied with an apparatus which recirculated the medium at 38°C. The perfusate consisted of a bicarbonate buffered physiological salt solution containing 0 to 8 g bovine serum albumin per 100 ml; renal arterial pressure was 100 mm Hg. Fractional reabsorbtion of water and Na^+ was studied in 20 kidneys by clearance techniques using inulin as a measure of glomerular filtration rate (GFR).

Increasing the perfusate albumin concentration from 0 to 8 g/100 ml: 1) increased perfusate flow rate from 5 to 21 ml/min·g wet weight; 2) increased fractional reabsorbtion of water and Na^+ from 0.55 to 0.95; 3) decreased water content of the kidney to almost normal. The GFR values were considerably lower than normal and were unaffected by changes in albumin concentration. The occurrence of significant reabsorbtion of water and Na^+ when albumin was absent from the perfusate is in agreement with results of peritubular capillary microperfusion experiments described by Windhager et al. (Nephron 6: 247, 1969). As extrarenal hormonal influences can be excluded, this effect of increasing albumin concentration on fractional reabsorbtion of water and Na^+ supports the view that the peritubular capillary colloid osmotic pressure facilitates reabsorbtion of tubular fluid. Supported by NIH 5-FO3-AM42886, AM03602 and the Genesee Valley Heart Association.

STUDIES OF THE EFFECTS OF A RADIOPAQUE PERFLUOROCARBON ON THE BLOOD CHEMISTRY AND CELL COUNTS. Mai-Shian Liu, Ph.D.* and David M. Long, M.D., Ph.D. Division of Cardiovascular and Thoracic Surgery, University of Illinois Hospital, Chicago, Illinois.

The radiopaque perfluoroctylbromide ($C_8F_{17}BR$) as a contrast medium in gastroenterography and bronchography has been extensively studied in our laboratories. It is superior to the currently available contrast media. This paper presents the studies on blood chemistry and cell counts after oral administration of 16 ml/kg of $C_8F_{17}BR$ in rats and dogs and after tracheal administration of 2-4 ml/kg of $C_8F_{17}BR$ emulsion in dogs. It was found that serum levels of ICD, GOT, and AP were not significantly altered either after oral or tracheal administration of $C_8F_{17}BR$. No elevation of BUN or creatinine was seen after tracheal administration. Blood coagulation remained normal by either route. The fragidity of RBC was not affected by $C_8F_{17}BR$ when given orally or brought in direct contact with the blood. The values of RBC count, hemoglobin, hematocrit and WBC counts (total and differential) in dogs did not change after oral or tracheal administration of $C_8F_{17}BR$. The results further substantiate the safety of $C_8F_{17}BR$ as a contrast medium for gastroenterograms and bronchograms.

FETAL MYOGLOBIN: QUANTITATIVE DETERMINATION AND IMPORTANCE FOR OXYGENATION. Lawrence D. Longo, Brian J. Koos*, and Gordon G. Power. Depts. of Physiol. and Ob-Gyn., Loma Linda Univ., Loma Linda, CA 92354

In an effort to understand the factors affecting fetal tissue oxygenation we measured myoglobin concentrations [Mb] in cardiac, skeletal and diaphragmatic muscle of sheep and human fetuses and compared them with adult values. [Mb] was measured spectrophotometrically as carboxymyoglobin in the supernatant of muscle homogenates after correcting for carboxyhemoglobin. [Mb] averaged 0.082 (± .018 SD) mM/kg in 14 near-term lamb hearts, a value to be compared with 0.17 mM/kg in adult sheep hearts. [Mb] averaged 0.046 mM/kg in lamb diaphragm compared with 0.24 mM/kg in the adult. More strikingly, skeletal muscle [Mb] was less than 0.0004 mM/kg in the fetus, a barely detectable quantity, and far less than adult level of 0.26 mM/kg. Heart muscle [Mb] was 0.036 mM/kg in 3 human fetuses at about 24 weeks gestation, but by 4 months after birth had increased to 0.11 mM/kg in two infants. We conclude: 1) Mb levels of about 50% of adult values in fetal heart, 20% in diaphragm, but less than 1% in skeletal muscles probably reflects the activity of these muscles in utero; 2) [Mb] is not an important factor in oxygenation of fetal skeletal muscle in spite of a relatively low fetal arterial P_{O_2} ; 3) [Mb] gradually increases during gestation and following birth, but the time course of this change has not been defined. This is the first quantitative study of fetal myoglobin concentrations. (Supported in part by USPHS grant HD-03807).

ROLE OF MACROPHAGES IN MALARIA INDUCED IMMUNOSUPPRESSION. L. D. Loose*
J. A. Cook*, and N. R. Di Luzio. Dept. Physiology, Tulane University School of Medicine, New Orleans, Louisiana.

A state of immunosuppression has been demonstrated to occur in a malaria infection. Since antigen uptake and processing by macrophages is an initial event in antibody response, studies were undertaken to define possible macrophage dysfunction as a contributory factor in malaria immunosuppression. The intravascular clearance and tissue distribution of ^{51}Cr-sheep red blood cells (SRBC) in malaria infected mice were comparable to that manifested in control groups. The normal fate of the particulate antigen was associated with a profound reduction in splenic plaque forming cells in malaria infected mice. Studies on macrophage antigen processing revealed that peritoneal macrophages obtained from normal mice upon exposure to SRBC's were capable of evoking an immune response when transferred to either normal or malaria infected mice. The immune response in the latter group was, however, significantly reduced. A further reduction in the immune response was observed when antigen exposed peritoneal macrophages from malaria infected mice were transferred to either normal or malaria infected mice. These results indicate a malaria induced impairment in macrophage antigen processing as a contributing factor in malaria induced immunosuppression. (Supported by U.S. Army Medical Research and Development Command).

CARDIOVASCULAR EFFECTS OF ACUTE ENDOTOXEMIA IN CONSCIOUS DOGS: ANTAGONISM BY A NEW ANTI-INFLAMMATORY AGENT. M. Losada*, J.P.Buyniski, J.S.Fleming* and M.E.Bierwagen*. Cardiovascular Section, Bristol Laboratories, Syracuse, New York 13201.

Conscious mongrel dogs with previously implanted aortic pressure catheters and isometric strain gauge arches sutured to the right ventricular myocardium were used to study the effects of 3 and 10 mg/kg of S.typhosa endotoxin i.v. Responses measured were aortic pressure, contractile force, cardiac rate, ECG, aortic blood pH and blood gases, hematocrit, body temperature, and the degree of platelet aggregation as determined by the screen filtration pressure technique. I.V. administration of 3 mg/kg of endotoxin to 9 conscious dogs reduced aortic pressure (115±3 to 47±6 mmHg), elevated cardiac rate (115±5 to 178±11 beats/min), elevated screen filtration pressure (55±2 to 117±13 mmHg), increased hematocrit and evoked little or no change in myocardial contractile force in the acute phase of endotoxemia. In contrast, 30 minute pretreatment of conscious dogs i.v. with 30 mg/kg of (-) 5-cyclohexylindan-1-carboxylic acid, a new non-steroidal anti-inflammatory agent, markedly altered the responses to endotoxin. The reduction in aortic pressure was reversed to a small pressor effect, the increase in cardiac rate was antagonized, and the rise in screen filtration pressure was partially antagonized over a 3 hour observation period. However, the rise in hematocrit was not markedly changed. Antagonism of the acute cardiovascular responses to endotoxin may reflect stabilization to vascular smooth muscle effects of endotoxin in key organ circulations (Buyniski et al., Int.Cerebral Blood Flow Symp., 1971, In Press) as well as an anti-aggregating effect for blood platelets (Fleming et al., Arch.Int.Pharmacodyn., 1972, In Press).

RIGHT CORONARY ARTERY BLOOD FLOW IN CONSCIOUS NORMAL DOGS AND DOGS WITH CONGENITAL PULMONIC AND/OR SUBPULMONIC STENOSIS. H. S. Lowensohn, D.E. Gregg, E. M. Khouri, R. L. Pyle*, and D. F. Patterson*. Walter Reed Army Institute of Research, Wash., D. C. 20012, and University of Pennsylvania, Philadelphia, Pa. 19104.

Right coronary artery blood flow (RCABF), central aortic blood pressure (CABP), and right ventricular pressure were recorded from resting dogs with implanted electromagnetic flow transducers and pressure tubes. Normal RCABF pulse contour was positive with respect to zero and resembled a CABP pattern; systolic pulse amplitude was nearly that of early diastole. Normal RCABF diastolic pattern was similar to previously published left coronary artery diastolic flow patterns. Peak flow pulse response to 10 second right coronary artery occlusion yields an augmented normotensive hyperemic flow contour resembling control. In congenital dogs with right ventricular hypertension (RVH), systolic RCABF was attenuated, particularly in the latter half of this phase. The degree of flow restriction was inversely related to the RVH level. At marked hypertensive levels (peak right ventricular systole > 140 mm Hg), late systolic flow was retrograde; diastolic flow pattern remained essentially unaltered. In RVH, systolic hyperemic augmentation contour was similar to control but elevated. Systolic hyperemic flow was attenuated inversely to the degree of RVH; diastolic flow increased as in the normotensive state. In the severely hypertensive animal, systolic flow was positive but greatly impeded. Mean peak right hyperemic flow response in the normal and RVH dog was comparable to that of the left coronary artery. Mean RCABF/100g/tissue in congenital dogs (29.9 $\pm$ 1.8 ml/min) was less than for normal dogs (40.5 $\pm$ 5.7 ml/min) with comparable CABP. These studies show that restriction of RCABF in RVH occurred in systole with flow per unit tissue being less in RVH.

IODOANTIPYRINE: A SPURIOUS DIFFUSIBLE INDICATOR? E. Lowenstein, J. Cooper, H. Yoshikawa (intr. by M.B. Laver) Mass. Gen. Hosp., Boston, Mass.

Gamma radiation tagged iodoantipyrine (IAP) has previously been suggested as a convenient substitute for tritiated water (THO) in determination of pulmonary extravascular water (PEVW) in vivo. The pulmonary extravascular distribution space (PEVD) of IAP and THO were simultaneously compared 65 times in anesthetized dogs and 33 times in awake human beings. The ratio of PEVD of IAP to THO in dogs was 1.17 $\pm$ .16 (S.D.); in humans .92 $\pm$ .13 ($t = 8.27$; $p < .001$). Six additional dogs were studied after anesthesia; after acute normovolemic hemodilution with balanced electrolyte solution to hct 7.4 $\pm$ 2.9% and total serum protein 0.30 $\pm$ .15 g/100 ml; and after reconstitution of osmotic pressure with human albumin to a total protein of 3.6 $\pm$ 0.3 g/100 ml. The ratio of the distribution space first increased from 1.15 $\pm$ 0.7 to 1.42 $\pm$ .13 ($p < .01$) with protein depletion, then decreased ($p < .01$) to 90 $\pm$ .10 (a value identical to that of humans) after reconstitution with human albumin. In vitro dialysis confirms plasma protein binding of IAP in dog and man. Binding of IAP to human and dog erythrocytes is also suggested by in vitro studies. We conclude that protein binding importantly affects the pulmonary extravascular distribution space of IAP, and that in vivo protein binding of IAP is greater in man than in the dog. The use of IAP as a diffusible indicator may be misleading.

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EFFECT OF L-DOPA ON RAT PINEAL MELATONIN CONTENT IN VIVO. H. J. Lynch*, P. Wang*, and R. J. Wurtman. M.I.T., Cambridge, Mass.

Melatonin content of the rat pineal is rapidly and markedly elevated in vivo following the subcutaneous injection of L-dopa in saline suspension. Injection of the vehicle alone results in a modest increase in pineal melatonin content as compared with that of untreated control animals. In view of Deguchi and Axelrod's observations that administration of L-dopa induces rat pineal N-acetyltransferase and that this effect is potentiated by prior pineal sympathetic denervation, we examined the effect of L-dopa on pineal melatonin content in rats pretreated with intravenous 6-hydroxydopamine (a drug that destroys sympathetic nerve terminals). Pineal sympathetic denervation alone was associated with higher pineal melatonin levels following vehicle injection than those found in intact animals receiving vehicle. L-Dopa also increased melatonin content in the pineals of rats treated with 6-OH-DA; however, this increase did not appear to be of a significantly greater magnitude than the increase observed in intact rats. The increase in pineal melatonin content that follows L-dopa treatment may reflect increased synthesis of melatonin; the increase that follows vehicle injection may reflect decreased release of melatonin from the pineal.

THE NON-RELATIONSHIP OF PINEAL MELATONIN AND CERTAIN PHOTIC INPUTS. Steven E. MacBride* and C. L. Ralph. University of Pittsburgh, Pittsburgh, Pa.

We sought to determine if retino-pineal connections are essential for continuance of the diurnal rhythm in chicken pineal melatonin content and whether reduction of light passing through the skull could affect this rhythm in any way. Forty chickens, housed under a diurnal photoperiod (lights on 0600-1800 EST), were divided into four groups of ten birds each (normal, normal/opaqued, blinded, blinded/opaqued). Bilateral enucleation was performed under ether anesthesia on 2-week-old White Leghorn cockerels and opaquing was accomplished by subcutaneous injection of India ink (0.5 cc) over the dorsum of the skull 1½ weeks prior to sacrifice. When 37 days old, 5 birds from each group were sacrificed at midnight and at noon and the melatonin content of individual pineals was quantitatively determined by bioassay. The results are summarized below; mean values are in nanograms melatonin/pineal.

	Normal	Normal/Opaqued	Blind	Blind/Opaqued
Noon	2.2±0.1	2.6±0.2	2.2±0.1	2.3±0.1
Midnight	16.2±0.7	16.2±1.2	16.2±0.7	15.0±0.9

Melatonin content was not significantly different among the groups either at noon or at midnight. Within each group, however, melatonin content was about 7 times greater in chickens killed at midnight than in those killed at noon and these differences were significant ($P < 0.001$). Therefore, the eyes are not essential for the apparent continuance of the diurnal rhythm in melatonin content of the chicken pineal and, similarly, reduction of light transmitted to the brain does not affect pineal melatonin levels. (Supported by N.I.H. grant NS08554.)

THE ROLE OF THE CAROTID BODY IN THE HEART RATE RESPONSE TO NaCN IN THE CHICKEN. Michael Magno, Dept. of Physiology, Albany Medical College, Albany, N.Y. 12208.

Although many animals show a fall in heart rate during arterial hypoxia when the ventilatory response is prevented, the chicken shows an increase in heart rate under these conditions. In those species showing a bradycardia, it has been established that this response is initiated by the carotid body chemoreceptors. In the present study, 0.01 mg/kg of NaCN was injected into the arterial supply of the carotid bodies in five adult White Leghorn hens anesthetized with sodium pentobarbital. This dose of NaCN had only minimal effects on the cardiovascular and respiratory systems when injected intravenously, but caused marked increases in the rate and depth of respiration when injected intra-arterially. After nine injections in three animals heart rate was increased by 5 to 26 beats/min. In two animals, heart rate was increased by less than 4 beats/min. Because these increases in heart rate were associated with pronounced respiratory responses, they could have been initiated by the lung inflation reflex as has been shown in the dog. In order to test this possibility, close arterial injections of NaCN were made before and after curare was given in another group of anesthetized hens. After curare, close arterial injections of NaCN still failed to produce a bradycardia and in some animals was again associated with a cardiac acceleration. These data indicate that stimulation of the carotid body in the chicken does not produce a bradycardia as it does in other species. (Supported by the Heart Association of Eastern New York and by USPHS Grant No. FR 5394).

RADIOGRAPHIC CHANGES IN CARDIAC DIMENSIONS DURING EXHAUSTIVE EXERCISE IN MAN. J. T. Maher,* G. A. Beller,* J. M. Foster,* and L. H. Hartley. US Army Research Institute of Environmental Medicine, Natick, MA. 01760

Recent reports have suggested that an alteration in cardiac function occurs in normal man at the onset of exhaustion which may be a limiting factor in the performance of endurance exercise. To test this hypothesis noninvasively, a roentgenographic method of evaluating serial changes in myocardial function was employed. Forty-inch ECG-synchronized anteroposterior X-rays of the chest were taken of 9 healthy young males at rest, during the course of supine bicycle exercise, and at exhaustion. Exposures were triggered in end-diastole during end-expiration. The workload was on the average 789 kg-m/min (range 700-900) with a mean endurance time of 63 ± 7 (SE) min. Heart rates (HR) at rest and exhaustion were 61 ± 3 and 156 ± 3 beats/min, respectively. There was a significant ($P < 0.001$) reduction (9%) in the mean transverse cardiac diameter (TCD), corrected for magnification, from rest (137 ± 2 mm) to exhaustion (125 ± 2 mm). The end-diastolic TCD decreased linearly with respect to the increase in HR ($r = -0.77$) throughout the course of exercise ($P < 0.001$). Thus, under the conditions of this study, the normal physiologic response of decrease in heart size with increase in heart rate was not altered. The data are interpreted to suggest that the capacity of healthy young men for prolonged leg exercise is not bound by the limits of myocardial performance.

VENTILATION, BLOOD pH and P_{CO_2} IN HIBERNATING MARMOTS. A. Malan, Lab. Physiol. Resp., C.N.R.S., Strasbourg, France (pres. add. State Univ. New York at Buffalo). (Intr. by H. Rahn.)

Ventilation has been measured in hibernating marmots, *Marmota marmota*, with a total body plethysmograph specially designed for recording low-frequency breathing with a small body-to-ambience temperature difference. Depth of hibernation was controlled by measurement of oxygen consumption. Respiratory periods ranged from 0.5 to 6 min (average 1.1 min); mean ventilatory flow rate was about 31 $ml_{BTPS} \cdot min^{-1}$. Arterial blood samples from hibernating marmots (body temperature 8°C) with indwelling aortic catheters gave the following values (mean ± 2 S.E.): pH = 7.57 ± 0.01; P_{CO_2} = 33.3 ± 1.4 torr; $[HCO_3^-]$ = 52.8 ± 1.9 mEq · L^{-1}; β = 22.6 ± 2.5 mEq HCO_3^- · L^{-1} per pH unit. During a respiratory cycle maximal variation of pHa did not exceed 0.03 pH unit. These data corroborate those obtained in European hamsters and confirm the existence of a relative acidosis in hibernating rodents.

ALTERATIONS IN ADRENOCORTICAL SECRETORY RATES TO CHANGES IN CEREBRAL VENTRICULAR pH OF THE ANESTHETIZED DOG. L. J. Malasanos* and S. F. Marotta. Department of Physiology, University of Illinois College of Medicine, Chicago, Illinois 60680.

Prior work from this laboratory has established the necessity for intact carotid and aortic bodies in obtaining augmented 17-OHCS output following exposure to acute hypoxia. The role of the peripheral chemoreceptors is well established for respiratory changes accompanying hypoxia. Since cerebrospinal fluid acid-base changes have been implicated in the respiratory response to hypoxia, this study was undertaken to determine the role of cerebrospinal fluid $[H^+]$ in hypothalamo-hypophyseal-adrenocortical activation. Perfusion of the cerebral ventricles was accomplished via cannulae placed in the lateral ventricle and the cisterna magna thereby assuring contact with the median eminence. Lateral ventriculocisternal perfusion with mock cerebrospinal fluid at pH 7.40 for one hour evoked no change in 17-OHCS secretory rates measured from specimens collected per left lumboadrenal vein cannulation. However, basic solutions (pH 7.60) depressed (-6.5 ± 1.4 µg/min/gm) while acidic solutions (pH 7.20) facilitated (+4.9 ± 1.9 µg/min/gm) the 17-OHCS secretory rates from control levels. Secretory changes were evident within 5 minutes and were maintained throughout the testing period. Essentially no alterations were manifested in peripheral arterial P_{CO_2}, P_{O_2} and pH, as well as respiratory rate, pulse rate, blood pressure, fectal temperature or adrenal blood flow. Assuming similar pH modifications occur as a phenomenon of hypoxia, it is amenable to postulate their participation in the regulatory role for 17-OHCS output.

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CORONARY FLOW IN NORMAL AND HYPERTROPHIED LEFT VENTRICLES. A.B. Malik, T. Abe, H. O'Kane and A.S. Geha (intr. by A.E. Baue). Washington University School of Medicine and The Jewish Hospital of St. Louis, Missouri.

We have compared flow to normal and hypertrophied left ventricles (LVH) in 13 normal and 7 hypertrophied dogs anesthetized with 30 mg/kg sodium pentobarbital. LVH was produced by banding the ascending aorta in puppies 6-12 months prior to study; there were no signs of failure at the time of study. Flow to the left ventricle (Q_{LV}) was measured electromagnetically; left ventricular O_2 consumption ($V_{LV}O_2$) was calculated as the product of Q_{LV} and arterio-venous difference in O_2 content across left ventricle $[(A\text{-}V)O_2]$. Left ventricular venous pyruvate (P) and lactate (L) concentrations were determined enzymatically. Q_{LV} in normal dogs was 104±9 ml/min/100 gm and 85±15 ml/min/100 gm in LVH. $(A\text{-}V)O_2$ in LVH of 11.5±0.6 vol% was greater ($p < 0.05$) than the 8.9±0.7 vol% in normals. $V_{LV}O_2$ in normals and LVH (9.4±1.6 vs 9.8±2.4 ml/min/100 gm) were not significantly different. L/P ratio of 24.0±1.7 in LVH was significantly greater ($p < 0.05$) than the value of 19.1±2.3 in normals. These findings indicate that blood flow to the hypertrophied left ventricle is impaired and that increased flow requirements are not met even though factors that increase coronary blood flow such as tissue hypoxia, increased perfusion pressure and increased cardiac work are present. The O_2 demand of the hypertrophied left ventricle is met by an increase in O_2 extraction rather than by increase in Q_{LV}. (Supported by USPH, NIH Grant 5RO1 HL 13088.)

RELATIONSHIP BETWEEN ELASTIC RECOIL AND "CLOSING VOLUME". Anthony Mansell*, Chagai Dubrawsky*, Charles Bryan and Henry Levison*. Dept. of Paediatrics and Anaesthesia, Univ. of Toronto, Research Inst. Hosp. for Sick Children, Toronto, Canada.

We have measured "closing volume" by the single breath nitrogen technique and static elastic recoil in 46 normal subjects (age 6 to 69 years) and in 30 patients with lung disease (asthma and cystic fibrosis). There was a highly significant relationship between closure and lung recoil, where closing volume as % VC = 39.15 - 3.39 x $Pst_{(L)}$ cm H_2O at 60% TLC, r = 0.85. As a result, despite a wide range in "closing volumes" (0 to 50% VC), closure occurred at about the same transpulmonary pressure (2-4 cm H_2O) in all subjects. These results suggest that elastic recoil is the most important determinant of closing volume and that a high closing volume is not necessarily a reflection of intrinsic small airways disease.

UNIT RESPONSES IN ANTEROLATERAL HYPOTHALAMUS TO LOCAL STIMULATION. L. A. Marco, A. M. Edelson* & S. Gilman. Dept. of Neurology, College of Physicians & Surgeons, New York.

311 units were recorded in the hypothalamus (A15-17, L3-5, V0 to -2.5) in nembutalized paralyzed cats. Single stimuli of 0.2 msec were delivered to one of three electrodes in semicircular array (caudal, medial, lateral) 1.5 mm from the micropipette. 51% of the units fired spontaneously (1-50/sec) but could not be driven by any of the three stimuli. 31% were driven at lat. 8-9 msec but did not fire spontaneously. 18% fired spontaneously and were driven by stimuli. 5% followed pulses at 50/sec. Most responses (81%) consisted of a single spike, less of a doublet (10%) or a burst of spikes (6%). 3% responded to single shocks repetively at 150-400/sec. The effectiveness of the 3 stimulating electrodes was: in 86% of driven cells responses were evoked by only one of the 3 electrodes while only 14% were driven by all 3. This indicates that spread of current from one electrode to another was negligible; that direct depolarization of cells was not obtained; and that some neurons received input from multiple directions. Relatively long latencies plus poor following to high frequency stimulation suggest that responses were transynaptic through a network involving several links. 45% of units firing spontaneously were arrested for 70-500 msec by stimulation. Some of these units were also driven at av. lat. 6.8 msec. Inhibition occurred 10-15 msec following the stimulus, suggesting that it is postsynaptic in nature. Intracellular records showed that the period of spike inhibition corresponded to membrane hyperpolarization. In 55% of units firing spontaneously, spikes could not be arrested by stimulation, which may correlate with absence of IPSPs in some units. This again provides evidence that, despite close apposition, intranuclear stimulation is sufficiently discrete to permit analysis of neuronal response patterns. (Supported by Clinical Research Center for Parkinson's & Allied Diseases NS 05184).

VAGAL CONTROL OF THE INTERDIGESTIVE MYOELECTRIC COMPLEX. Francis Marik* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Szurszewski (Am J Physiol 217:1757, 1969) described a caudad-moving band of large-amplitude action potentials sweeping in recurring cycles every 90-180 minutes over the entire small bowel of fasted dogs. Marlett and Code showed that this activity front is part of a complex which starts simultaneously in the stomach and duodenum and recurs without interruption for many days in fasted dogs (Fed Proc 30:609, 1971). Since neither continuity of the bowel wall nor movement of its contents is essential for coordinated propagation of the complex (Carlson et al, Am J Physiol 222:1027, 1972), we undertook to determine the role of vagal innervation of stomach and small bowel in control of the complex. Eight healthy mongrel dogs were used. Monopolar silver-silver-chloride electrodes were implanted on the serosal surface of stomach and duodenum in 4 and on stomach, duodenum, jejunum and ileum in the others. Recordings of the pacesetter and action potentials were made with an 8-channel Brush rectilinear pen writer (Mark 200) while the dogs were conscious and resting comfortably in a supporting sling. After 3-5 cycles of the interdigestive myoelectric complex had been observed in control sessions, 2-3 cm of both vagal trunks were resected just orad to the diaphragm. Vagotomy produced: (1) longer periods of absence of the complex; (2) greater irregularity in duration of its different phases; (3) greater variability in intensity of the active phase; (4) increased variability in periodicity of the complex; and (5) failure in 6 of the 8 dogs of feeding of 50 gm of meat to interrupt the complex whereas, before vagotomy, this had always done so. Each animal repeatedly displayed one or more of these abnormalities. Results indicate that vagal innervation is an important factor in neural regulation of the interdigestive myoelectric complex of dogs. Supported in part by NIH Research Grant AM-2015.

NASAL AIRWAY RESISTANCE AND BLOOD FLOW. J. Martin* and M.H.F.Friedman. Department of Physiology, Thomas Jefferson University, Philadelphia, Pa.

Continuous recordings of nasal airflow and bloodflow were obtained in 14 young adults. Nasal airway flow rates were monitored by pitot tube, intraluminal nasal airflow pressure by a differential pressure transducer, nasal airflow sounds by dynamic microphone and thoracic respiratory movements by pneumograph. Simultaneously, nasal septal pulsatile bloodflow and finger pulsatile bloodflow were recorded by photocell plethysmography. Nasal airway resistance was calculated from the values for peak expiratory intraluminal nasal airflow pressure divided by the respective nasal airflow rate. The analysis of variance technique was used to determine the statistical significance of the results. Application of ice to the face or immersion of the hand in ice water resulted in a significant increase in airway resistance with a concurrent significant decrease in nasal bloodflow. On the other hand, use of warm water resulted in an increase in both airway resistance and nasal bloodflow. Water at ambient temperature was without effect. Airflow sounds were related to the rate of airflow and only in conditions of nasal congestion to the airway resistance. Decrease in airway resistance by sympathomimetic drugs administered by nebulized spray occurred to a significant degree for brief periods only in the presence of nasal mucosal congestion. Finger bloodflow was reduced whenever sympathomimetic agents affected nasal bloodflow.

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RESPONSE OF RESISTANCE VESSELS TO CHRONIC LOCAL HYPOTENSION. J.B. Martin* and M.C. Conrad, Med. Univ. of S.C., Charleston, S.C. 29401

In mongrel dogs, the vascular bed of the left hind limb was made hypotensive by ligation of the superficial and deep femoral arteries. Following six weeks of exposure to decreased transmural pressure, flow resistance of the portion of the bed distal to the re-entry of collaterals was compared to that of the contralateral extremity following a similar acute reduction in pressure by a femoral screw clamp. Flows were measured in both popliteal arteries and pressures were measured and drugs infused via a branch of the popliteal. Blood gases were measured in popliteal vein samples. At equal pressures, the following values were obtained in the acute and chronically hypotensive beds:

	Acute	Chronic	Paired t-test (acute vs. chronic)
Resting resistance (PRU)	0.101	0.083	$p < 0.01$
Resting venous P_{O_2} (mm Hg)	41.9	46.3	$p < 0.01$
Resting venous P_{CO_2} (mm Hg)	37.1	35.2	$p < 0.01$
Response to Vasodilators: (% change in resistance)			
acetylcholine (% change)	-43.2	-59.7	$p < 0.01$
adenosine (% change)	-28.0	-43.9	$p < 0.001$
Resistance at max. dilation (PRU) (EGTA-buffer perfusion)	0.031	0.025	$p < 0.05$

The data indicate that an anatomic change occurs in the peripheral resistance vessels in response to chronic reduction in transmural pressure since (1) their resting resistance is decreased in spite of the absence of a metabolic stimulus, (2) they have an increased residual tone, as defined by their response to vasodilators, and (3) their resistance is lower after elimination of all vessel tone.

INFLUENCE OF ABDOMINAL PRESSURES ON REGIONAL DISTRIBUTION OF LUNG VOLUME IN SUPINE MEN. R.R. Martin*, B. Bake*, M. Desmeules*, W.R.D. Ross* and N.R. Anthonisen. Respiratory Division, Royal Victoria Hospital and McGill University, Montreal.

The distribution of regional lung volumes from lung apex to base was examined in 5 supine subjects using ^{133}Xe. At comparable overall lung volumes - about 1 L above supine FRC - regional volumes were measured: A) when the volume was achieved voluntarily by use of the inspiratory muscles, B) during relaxation with negative pressure applied to the abdomen, C) by active inspiration when positive pressure was applied to the abdomen. Under control conditions (A) apical regions were somewhat more expanded than basal suggesting either that there was a small apex to base pleural pressure gradient in these horizontal subjects or that the static elastic properties of upper lobes differed from lower lobes. When negative pressure was applied to the lower abdomen (B) apex to base difference in expansion increased sharply, and approached that seen in erect subjects at FRC - a similar lung volume. Thus in supine subjects, applying a negative pressure to the abdomen sufficient to increase FRC to a value similar to that seen in the erect position induced an apex-to-base pleural pressure gradient comparable to that seen in the erect position. These results are similar to those of Agostoni and D'Angelo (Resp. Physiol. 12: 102, 1971) in supine animals. No consistent change in regional lung volumes was seen when positive pressure was applied to the abdomen. Supported by grants from MRC of Canada and Francis S. North Foundation.

THE CHEMICAL CONTROL OF VENTILATION DURING MODERATE PHYSICAL EXERCISE. R.G. Masson* and S. Lahiri. Cardiovasc.-Pulm. Div., Depts. of Med. and Physiol., University of Pennsylvania, Philadelphia, Pa.

The physiologic mechanisms responsible for the augmentation of ventilation during hypoxic exercise are not understood. This phenomenon was studied in 8 adult human subjects by relating ventilation to arterial levels of P_{O_2}, P_{CO_2} and pH during steady states of rest and mild exercise ($\dot{V}_{CO_2} \simeq 1$ L/min), in normoxia ($Pa_{O_2} \simeq 90$ mm Hg) and hypoxia ($Pa_{O_2} \simeq 50$ mm Hg) with and without exogenous hypercapnia. Breath by breath ventilation, inspired and end-tidal P_{O_2}, P_{CO_2}, heart rate, ECG and systemic intra-arterial pressure were recorded continuously. At each steady state $\dot{V}_E$-Pa_{CO_2} point 4-6 ml of arterial blood were slowly sampled and analyzed for P_{O_2}, P_{CO_2}, pH, lactate and in vitro CO_2 dissociation. During exercise the augmentation of ventilation at $Pa_{O_2} \simeq 50$ mm Hg was such that the Pa_{CO_2} decreased from 36.7 ± 3.0 to 34.9 ± 3.0 mm Hg (mean ± 1 SD). pH values were 7.424 ± .014 and 7.445 ± .031 respectively. Also contributing to the alkalinity of hypoxic exercise was a small but consistent increase in plasma (HCO_3^-) (ca. 1 mEq/L). Small increases in Pa_{CO_2} during hypoxic exercise caused a prompt further increase in ventilation, unlike resting hypoxia. CO_2 sensitivity, as defined by the slope of the CO_2 response line, was not increased during hypoxic exercise. This extra effectiveness of arterial (H^+) in the hypocapnic range without an increase in sensitivity in the hypercapnic range offers some explanation for the augmented ventilation during hypoxic exercise. Since presumably the magnitude of neither the mean arterial chemoreceptor activity (Davies and Lahiri, The Physiologist 14:130, 1971) nor the peripheral neural input (Dejours et al, J. Physiol., Paris 52:63, 1960) changes during hypoxic exercise, it appears that the augmented ventilatory response may be due to the presence of a central "excitatory state." (Supported by NIH grants HE-08805 and HL-05239.)

THE INFLUENCE OF HYPOXIA ON CNS-INDUCED CARDIAC ARRHYTHMIAS. H. Page Mauck, Jr., * A. J. Szumski, Tsu-Ching Fu,* Martha Clendenin,* and James Forbes.* Medical College of Virginia, Division of Health Sciences, Virginia Commonwealth University, Richmond, Virginia 23219.

Stimulation of higher neural centers evokes a variety of supraventricular and ventricular cardiac arrhythmias. However, the influence of hypoxia on these effects is unclear. To assess the role of decreased arterial Po_2 on the frequency and severity of cardiac rhythm disturbances evoked by stimulation of the mesencephalon, the following experiments were performed. Twenty-five cats were anesthetized with α-chloralose and respiration paralyzed and controlled with a respirator. Bipolar steel electrodes were stereotaxically positioned in the mesencephalic reticular formation. Arterial Po_2 was decreased to average 37 mm Hg (30-42 mm Hg range) while Pco_2 was maintained at normal levels. Stimulation (0.4 ma - 1.0 ma) of identical regions of the mesencephalon at constant stimulus intensity in all experiments evoked more marked sympathetic and parasympathetic responses during hypoxia than at normal arterial Po_2. During hypoxia 23 cats showed significantly greater increases in arterial pressure and heart rate, and frequently exhibited severe ectopic ventricular rhythm disturbances. Two animals showed initial parasympathetic responses consisting of bradycardia and hypotension which increased with stimulation during hypoxia. A combination of bilateral vagal section and propranolol, 2 mgs/kg, abolished all autonomic effects on cardiac rhythm. The results demonstrate that CNS stimulation during moderate arterial hypoxia and eucapnea produces enhanced sympathetic and parasympathetic responses which may lead to serious cardiac arrhythmias.

THERMAL REFLEX REGULATION OF SWEATING. Thomas V. McCaffrey*, Robert D. McCook, and Robert D. Wurster. Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Previous experiments have tested the reflex influences of cutaneous thermoreceptors upon the control of sweating in man. To separate the influences of central from the peripheral thermoreceptors these experiments were performed by heating or cooling the lower extremities to which blood flow occluded, while the sweating response of the upper limbs was measured. Studies of the firing characteristics of the classical cutaneous thermoreceptors of the cat have shown that occlusion of the blood flow to these receptors markedly affected their temperature response characteristics. The present experiments were designed to test the reflex influences of the cutaneous thermoreceptors upon sweating in man without occlusion of the blood flow. Twin adjacent temperature chambers permitted a subject to be rapidly heated or cooled on the lower extremities independent of the rest of the body. Alteration of core temperature was prevented during these manipulations by the drinking of cold or warm fluids. Sweating was monitored simultaneously on six areas of the body using resistance hygrometers. Oral, tympanic, and twelve cutaneous temperatures were also recorded. The data was punched on digital paper tape at 30 sec intervals and later analyzed on a Digital PDP-12 computer. Experiments were performed to determine the sweating response to different rates of heating and cooling of the lower extremities from various initial cutaneous and core temperatures. The results indicate that cutaneous receptors can initiate reflex changes in sweating on the unchanged body segment. These changes in sweating are dependent on the skin temperature and the rate of cooling, but not consistently on the rate of heating of the skin. Sweating is also dependent on tympanic temperature but not on the rate of change of tympanic temperature. (Supported by NIH Grants HE 08682 and GM 999).

ACUTE EFFECTS ON THE TIMING OF OVULATION IN RATS INDUCED BY SUDDEN ALTERATIONS IN THE ONSET OF THE PHOTOPERIOD. Charles E. McCormack. Univ. Health Sci./Chicago Med. Sch., Chicago, Ill. 60612

Results of earlier experiments (Fed. Proc. 31:811Abs, 1972), showed that in rats the time of the onset of ovulation could be shifted more readily by subtracting morning light or adding evening light to the daily photoperiod than by adding morning light or subtracting evening light. If this generalization is valid, then delaying the onset of the photoperiod (length of photoperiod held constant) should produce a rapid delay in the onset of ovulation, because the rats are exposed each day to both of the stronger stimuli mentioned above. Moreover, advancing the onset of the photoperiod should advance ovulation, but rather slowly, because the rats are only exposed to the weaker stimuli. Groups of 22-day-old female Holtzman rats were exposed daily for 7 days to 14 hr. of light (0500 - 1900). On the 8th day (day 29) the onset of the photoperiod was advanced by 5 hr in one group, delayed by 5 hr in a second group, and held constant in a control group. The length of the photoperiod remained at 14 hr for all groups throughout the experiment. On the morning of day 30 all rats were injected with 8IU of pregnant mares serum gonadotrophin in order to induce puberty, and early on the morning of day 33, the oviducts were examined for ova. In the group in which the onset of the photoperiod had been advanced, the time of ovulation was unchanged from that of the control group (i.e. ovulation began at about 0200), but in the group in which the onset of the photoperiod had been delayed, the time of ovulation was delayed by 4 hours. Thus, these results confirm the aforementioned generalization on the relative effectiveness of lighting stimuli in shifting the time of ovulation. (Supported by NSF-GB5260).

EXPERIMENTAL CARDIAC NECROSIS IN ALTITUDE-EXPOSED RATS. J. J. McGrath, B. Ostadal*, V. Pelouch*, and J. Prochazka*. Dept. of Environmental Physiology, Rutgers University, New Brunswick, N. J. 08903 and Czechoslovak Academy of Sciences.

Male, white rats age 60 days were exposed to 23,000 feet in a barometric chamber for 4 hours/day for 24 days and then treated with necrotizing doses (80 mg/kg) of isoproterenol. Two groups of rats were maintained under sea level conditions and used as controls. One group of controls (SLA) was the same age as the altitude exposed rats (HA), but weighed more at the end of the experimental period. The second control group (SLW) was 45 days old and weighed approximately the same as the HA group. The severity of cardiac damage resulting from isoproterenol treatment was rated on a 0-4 basis. The hearts of the HA rats sustained a mean rating of 1.9 while the mean scores for the SLA and SLW groups were 3.1 and 3.0, respectively. The distribution of the ratings was such that 77% of the SLA and 75% of the SLW rats received scores of 3 or more, while only 25% of the hearts from the HA group were damaged this extensively. The evidence suggests that high altitude exposure exerts a protective effect against this type of cardiac necrosis and that the protective effect cannot be explained on the basis of body weight. (Supported in part by an agreement between the National Academy of Sciences of the U.S., and the Czechoslovak Academy of Sciences).

THE LATENCIES OF SEVERAL COMPONENT PARTS OF THE LABELLAR RESPONSE OF THE MOSQUITO. T. McKean. Department of Zoology and Physiology, University of Wyoming, Laramie, Wyoming.

The labellar response of the mosquito consists of initiation of spike activity in the labellar chemosensory hairs by the application of an adequate stimulus, conduction of these impulses to the CNS, integration by the CNS with initiation of efferent spike activity and finally development of muscle action potentials and muscle tension to open the labella. The overall time for the labellar response was 39 msec. Chemoreceptor latency was 5-10 msec, total combined afferent and efferent conduction time was 16 msec and finally, the time required for integration was 12-17 msec.

The labial nerve was examined histologically and contained primarily fibers with a diameter of 1 micron. These fibers conduct at a velocity of 0.4 mm/msec. A few larger fibers with a diameter of 2 microns were also seen in the nerve section. The data for conduction velocity, central delay and chemoreceptor latency may be used to predict the latency of the proboscis extension reflex of the blowfly. The predicted latency differs from the measured latency by only 6% suggesting labellar contact chemosensory induced feeding responses in diptera are very similar neurophysiologically.

In addition, the response characteristics of a mechanoreceptor activated by hair movement are described.

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ADRENERGIC MECHANISMS IN THE CANINE URETER. David G. McLeod*, David G. Reynolds* and Kenneth G. Swan. Walter Reed Army Institute of Research, Washington, D. C.

The role of adrenergic receptor mechanisms in the ureter has been incompletely described. The present report evaluates the effects of adrenergic stimulation and blockade on motility of the canine ureter. Under pentobarbital anesthesia a cystotomy and retrograde catheterization of a ureter was performed. The ureteral catheter was attached to a pressure transducer and ureteral motility recorded in terms of amplitude (A) and frequency (F) of contractions. Arterial pressure (AP) was also recorded. During the control period mean AP was 148 $\pm$ 9 (SE) mm Hg A was 13.7 $\pm$ 2.0 mm Hg and F was 16.7 $\pm$ 3.5 contractions/min. Intravenous injections of norepinephrine (NE) or epinephrine (E), ranging from 0.5 to 2.0 µg/kg, caused progressive, dose dependent, increases in both AP and F, along with a decrease in A. Alpha adrenergic blockade (phenoxybenzamine, 1.5 mg/kg, I.V.) reversed the AP response to E and attenuated the AP response to NE. Ureteral motility responses to both NE and E were attenuated following alpha adrenergic blockade ($p < .05$). These findings indicate that motility of the canine ureter is regulated in part by adrenergic receptor mechanisms since alpha adrenergic stimulation increased frequency and decreased amplitude of spontaneous motility and these effects were inhibited by appropriate adrenergic blockade.

EFFECTS OF HIGH DOSES OF SEROTONIN INFUSED LOCALLY ON CANINE FORELIMB WEIGHT, PRESSURES, BLOOD FLOWS, AND SEGMENTAL VASCULAR RESISTANCES.
G.F. Merrill, R.L. Kline, F.J. Haddy and G.J. Grega. Department of Physiology, Michigan State University, East Lansing, Michigan 48823

The collateral-free, innervated forelimb perfused either naturally or at constant inflow (pump perfusion) was used to study the effects of high doses of serotonin (150 ug base/min) on transvascular fluids fluxes and segmental vascular resistances. At natural inflow serotonin failed to alter forelimb weight relative to control. Skin blood flow decreased markedly whereas skeletal muscle blood flow increased, the net effect being a fall in total forelimb blood flow. Total forelimb vascular resistance increased owing to a marked rise in total skin resistance despite a fall in total skeletal muscle resistance. The huge rise in total skin resistance was largely due to large vessel constriction (large artery and large vein) and to a much lesser extent small vessel constriction. The fall in total skeletal muscle resistance was largely attributable to small vessel vasodilation. This same high dose of serotonin infused while inflow was held constant increased forelimb weight and shifted blood flow from skin to skeletal muscle. The resistance responses were similar to those seen at natural inflow. The weight gain at constant inflow (0-15 min; +8 g) may have been attributable to an increased extravascular fluid volume subsequent to a rise in microvascular pressure. Small vein pressure, which represents a minimum for capillary hydrostatic pressure, was markedly increased in both skin and skeletal muscle. At natural inflow extravascular fluid volume may have also increased slightly (2-15 min; +4 g). In contrast to histamine (Microvascular Res., In press), high doses of serotonin infused locally into the forelimb clearly do not produce significant edema formation, although marked hemodynamic alterations occurred.

The Morphometric Measurement of Pulmonary Edema.
E.C. Meyer and R. Ottaviano (intro. by M.H.F. Friedman) Mercy Catholic Medical Center, Darby, Pa. 19023

The distribution of edema fluid in the lung is anisotropic by being oriented not only in perivascular tissues but also in gravity dependent lung regions. Despite these characteristics, absolute edema volume can be measured morphologically using random stereologic probes. We demonstrated this in 10 dogs with Alloxan pulmonary edema varying between 5 and 32 ml/kgm. In each dog we homogenized the right lung to determine extravascular lung water. We inflated the left lung, fixed it with formalin steam, and cut it into dependent and non-dependent portions to decrease edema anisotropy. After measuring the volume of each portion, we measured edema by a combination of macro- and microscopic point counting using data from 4 control dogs to determine control interalveolar and perivascular tissue volume fractions. We compared edema volumes derived from morphometric and homogenate data. In no instance did the two volumes differ by more than 10%. The techniques used are valuable in the study of edema distribution in the lung. Within the limits of edema studied, tissue capacity for fluid was 1.4 ml/kgm maximally. Alveolar filling occurred in mild edema when tissue contained less than 0.5 ml/kgm fluid.

(Supported by NIH Grants HE 08601 and HE 13596)

A TEST OF COLD ACCLIMATION OF LABORATORY RATS EMPLOYING HYPOXIA. F. R. Meyer and the late R. W. Bullard. Anatomy-Physiology Dept., Indiana University, Bloomington.

An extensive literature describing various aspects of nonshivering thermogenesis (NST) of cold-acclimated laboratory mammals has developed, yet many questions remain. A major difficulty is that at present there exists no suitable test for the quantitation of NST. The two methods currently used are the assessment of the electro-myographic record of shivering and curarization. Both of these tests are difficult to administer and another test was sought. Donhoffer, as well as others, has shown that moderate hypoxia abolishes shivering thermogenesis in small mammals. This raises the question of whether or not hypoxia similarly effects NST. If not, then this in itself could be developed into a suitable quantitative test or a means of evaluating the relative contribution of NST and shivering thermogenesis to the maintenance of homeothermy in cold-exposed animals. In addition this study sought to describe some of the characteristics of NST and to answer some of the questions concerning the remission of shivering as a primary heat source during the period of cold acclimation, the nature of the control system, and the characteristics of the stimulus for NST. This hypoxic test revealed some distinct functional differences between the two groups. (Supported by NIH Grant PHS GM1233-01 and NSF Grant GB-11).

CARBON MONOXIDE AND CONTROL OF VENTILATION. John R. Meyer*, Robert F. Grover and John V. Weil.* Univ. Colorado Medical Center, Denver, Colo.

Breathing carbon monoxide (CO) reduces the amount of hemoglobin available for oxygen transport and thus reduces O_2 content without changing O_2 tension. Recent studies (J.Appl.Physiol.25:494-502, 1968) have raised the fundamental question of whether the carotid body (CB) responds primarily to decreased arterial O_2 tension or O_2 content. To resolve this problem and to evaluate possible direct influences of CO on peripheral chemoreceptors and central respiratory center, a new method was developed to assess carotid body neural output (CBNO) using the amplitude variance (σ^2) of the carotid nerve bundle signal. In 5 pentobarbital anesthetized cats spontaneous ventilation ($\dot{V}_E$), CBNO, P_AO_2 and P_ACO_2 were simultaneously measured during breathing of CO (.1% in air) which produced an increasing carboxyhemoglobin saturation (S_{COHb}) of about 1% per minute. Neither σ^2 nor $\dot{V}_E$ changed until S_{COHb} exceeded 50% (see chart). At very high S_{COHb} (50%) apnea occurred and P_AO_2 fell. It was only at this point that a large CBNO increase occurred. Progressive isocapnic hypoxia increased CBNO with a parallel increase in $\dot{V}_E$; these responses were unchanged by S_{COHb} below 50%. It is thus concluded that S_{COHb} below 50% exerts no direct effect on either CB sensitivity to hypoxia or the central respiratory center and that CB is monitoring O_2 tension rather than O_2 content.

%S_{COHb}	0	10	20	30	40	50	> 50
$\dot{V}_E/\dot{V}_{E_0}$ †	1.00	1.05 ±.02	1.00 ±.03	1.04 ±.02	.98 ±.05	.98 ±.08	0
σ^2/σ^2_0 †	1.00	.99 ±.02	1.05 ±.07	1.08 ±.09	1.11 ±.11	1.13 ±.13	6.35 ±1.57

(† refers to value at control. N=5)

DOUBLE OPPONENT-COLOR CELLS IN THE PRIMATE STRIATE CORTEX. Charles R. Michael. Yale Med. School, New Haven, Conn.

Extracellular recordings were made with tungsten microelectrodes from 137 color-sensitive cells in the striate cortex of 7 unanesthetized rhesus monkeys. These cells had center-surround or simple receptive fields. Most did not have rod inputs. Those units with concentric fields were driven only by one eye and were found primarily in layer IV. They had one red-green opponent mechanism in the field center and the reverse in the surround. They did not respond to white light. The spectral sensitivity curves for the center were the mirror image of those for the surround.

Simple cells also had a double opponent-color organization but were sometimes driven by both eyes. They had one red-green system in the rectangular central area of the field and the opposite opponent organization in the two flanks. Consequently they responded to red or green slits but not to white. They were insensitive to diffuse white or monochromatic stimuli. These cells were found mainly in layers III and IV.

Multiple-unit recordings made from one of these cell types and one of its afferents indicate that the center-surround cells receive inputs from color-coded geniculate axons while the simple cells are innervated by the center-surround cells.

Supported by Grant EY 00568 from the National Eye Institute.

Long-term effect of diethylstilbestrol on the uptake of uridine by the mouse uterus. John C. Mickus* and George H. Gass. Southern Illinois University, Carbondale, Illinois.

C_3H/FeJ and C_3HeB/FeJ female mice were maintained on low (25 ppb) and high (250 ppb) diet levels of diethylstilbestrol for periods of up to 300 days. Low level treatment with DES caused an increase in uterine weight, reaching a maximum by the 15th day, after which no further gain in weight occurred. When compared to control animals, there was no significant difference in the uptake of radioactive uridine by the uterus when equated on a CPM/mg uterine tissue basis. The high level treatment with DES caused an increase in uterine weight which plateaued by the 15th day of treatment. Equated on a CPM/mg uterine tissue basis, there was a significant decrease in the uptake of radioactive uridine when compared to control animals. Stimulation with a high level of DES caused maximal uptake of uridine by uterine tissue at an earlier period than did stimulation of uterine tissue with a low level of DES. A ten-fold increase in the level of DES in the diet resulted in only a two-fold increase in the total uptake of uridine by the uterus. Finally, the presence of the mammary tumor virus (MTV) in the C_3H/FeJ mice did not alter the sensitivity of the uterus to a high level of DES when administered over a 210 day period. The fact that increasing the level of hormone does not bring about a similar increase in the incorporation of RNA precursors reflects the situation in which continued uterine growth is not seen after a particular hormonal level is reached.

EVALUATION OF ADRENERGIC RECEPTORS IN THE BAT WING: TOPICAL APPLICATION OF NOREPINEPHRINE, EPINEPHRINE AND ISOPROTERENOL. F.N. Miller*, P.D. Harris, D.E. Longnecker*, and E.K. Greenwald*. Microcirculatory Systems Research Group; Depts. of Physiology, Anesthesia, and Physical Medicine, Univ. of Missouri School of Medicine, Columbia, Mo. 65201.

Closed-circuit television microscopy was used to quantitate the effect of catecholamines on the small arteries (37-77 micra) and the small veins (57-136 micra) in the wing of unanesthetized bats, Myotis lucifugus and sodalis. Concentration-response curves were obtained with topical norepinephrine (NE), epinephrine (E) and isoproterenol (I). Both NE (n=5) and E (n=6) produced constriction of the arteries and veins. I (n=3), even in high concentrations (10^{-5} g/ml), did not significantly change small vessel diameters. The effects of NE and E are summarized in the table as the concentrations ({MC}) which produced maximal constriction, the maximal constriction (MC) as a percent of control and the concentrations ({50% MC}) that produced 50% of the maximal constriction.

	EPINEPHRINE		NOREPINEPHRINE	
	ARTERY	VEIN	ARTERY	VEIN
{MC}	1×10^{-7}	1×10^{-7}	1×10^{-6}	1×10^{-7}
MC	59 ± 7.0	53 ± 6.5	53 ± 6.4	64 ± 1.8
{50% MC}	1.3×10^{-8}	0.7×10^{-8}	3.6×10^{-8}	1.8×10^{-8}

For subcutaneous tissue in the bat wing, our data indicate that 1) there are probably no beta adrenergic receptors in the small arteries and veins since isoproterenol did not produce vasodilation, 2) there are no significant differences among the maximal effects produced by NE and E, 3) E appears to be a more potent vasoconstrictor than NE, 4) both NE and E appear to be more potent vasoconstrictors for small veins than for small arteries. (Supported by HL12614, HL13207 and HL14607.)

EFFECTS OF PROLONGED ISCHEMIA ON CANINE FORELIMB WEIGHT, PRESSURES, BLOOD FLOWS, AND VASCULAR RESISTANCES FOLLOWING RELIEF OF ISCHEMIA. G.L. Miller, R.L. Kline, F.J. Haddy and G.J. Grega. Dept. of Physiol., Michigan State University, East Lansing, Michigan 48823

Collateral-free, innervated forelimbs perfused either naturally or at constant inflow (Sigmamotor pump) were used to study the effects of ischemia on transvascular fluid fluxes. The brachial artery (natural inflow) was clamp-occluded for a period of 2 hours. Forelimb weight decreased markedly initially (0-3 min) but then remained relatively steady throughout the remainder of the 2 hour occlusion. On release of the occlusion mean forelimb weight rapidly increased, exceeding the control weight by 8 g within 2 min, and then decreased and returned to control levels within 1 hour. The abrupt increase in weight was associated with markedly reduced skin and skeletal muscle vascular resistances and huge increases in blood flows. Large vein pressures were greatly increased at this time. Hence, the initial rapid weight gain was mainly attributed to an increased forelimb vascular volume subsequent to vasodilation. The secondary fall in forelimb weight paralleled the return of skin and skeletal muscle vascular resistances to control levels suggesting that it was attributable to a declining vascular volume. These conclusions are supported by data from the constant flow studies. The weight loss pattern after stopping the pump was similar to that described above. On starting the pump the forelimb weight gain failed to exceed control weight despite the fact that skin and skeletal muscle vascular resistances were markedly reduced. These data fail to provide evidence for an ischemia-induced rise in extravascular fluid volume or a pressure independent increase in microvascular permeability to plasma proteins sufficient to produce significant edema formation in the collateral-free, innervated canine forelimb.

SEASONAL VARIATION IN HEART RATE-CORE TEMPERATURE RELATIONSHIP IN RANA PIPIENS: THE ROLE OF THE AUTONOMIC NERVOUS SYSTEM. L. Craig Miller* and Sherwin Mizell. Indiana University, Bloomington, Ind.

The heart rate of normal and drug-treated, intact, unrestrained and unanesthetized adult male Rana pipiens was studied over a range of core temperatures (16-30° C.) during a 12-month period. We have previously reported that a typical summer response to increasing core temperatures was a linear increase in heart rate. However, during the winter a biphasic response of heart rate to core temperature was observed with a flattening out of response at core temperatures above 26° C. During the summer, treatment with reserpine and dichloroisoproterenol (DCI) significantly reduced the normal increase in heart rate due to increasing core temperature. Treatment with atropine during the summer did not change the basic physiological response of the heart rate to increasing core temperature. During the winter, treatment with reserpine and DCI did not alter the normal heart rate response to changing core temperature. Treatment with atropine during the winter caused the heart rate response to change in core temperature to assume a linear response over the full core temperature range (16-30°C.). With regard to the heart rate-core temperature relationship, sympathetic activity seems greatest in the summer and minimal in the winter, while parasympathetic influence appears greatest during the winter and nearly absent during the summer. Supported by Grant #GB 6937 from the Nat'l. Sci. Found., #C-0014 from the U.S. Air Force, and by the Indiana Heart Assoc.

ADRENAL SYSTEM FUNCTION IN THE POSTERIOR-HYPOPHYSECTOMIZED RAT. Ralph E. Miller, Univ. of Ky. School of Medicine, Lexington, Ky.

We determined how posterior-hypophysectomy affected adrenal system function during several different states of hypothalamic stimulation. Adult male Long-Evans rats had their posterior hypophyses exposed. The glands were aspirated - PH rats, or not touched - Sh rats (confirmed histologically). Several weeks later some rats from each group had chronic jugular vein cannulas implanted. Blood was sampled before and after stress of different types and intensities. Other rats had left-adrenalectomies 3 wks after hypophyseal surgery. Their right adrenals were examined for hypertrophy 2 wks later. Sh and PH rats had the same pre-stress (basal state) plasma corticosterone concentrations (determined flourometrically), and significant ($p < .01$) mean responses to all stresses. A comparison of the mean responses of the 2 groups showed then to be the same after Histamine (18 ug/100g b.w.-i.v.) and Cage Moving ("low-level" stresses) or Ether Plus Laporotomy ("maximal" stress), but after Histamine (36 ug/100g b.w.-i.v.) or Cage Moving Plus Bell ("moderate" stresses) the PH mean response was less than the Sh. ($p < .04$) An hypothesis: In basal and "low-level" stress states the posterior hypophysis plays no role in adrenal system function, at "moderate" and "maximal" stress levels it is recruited and secretes ACTH or a releaser of ACTH. A deficient mean stress response is seen in PH rats subjected to "moderate" stress. It is not seen after "maximal" stress because the capacity of the adrenals to secrete corticosterone is saturated by anterior hypophyseal ACTH and the presence or absence of posterior hypophyseal function is not revealed by peripheral corticosterone concentrations. N.I.H.-G.R.S.G.-RP 05374; Ky. Heart Assoc. T3827.

PURIFICATION OF MYOSIN A WITH POLYETHYLENE GLYCOL (PEG, M. W. 6000) FRACTIONATION. Byung K. Min* and George Kaldor, Dept. of Physiology and Biophysics, The Medical College of Pennsylvania, Phila., Pa. 19129.

Myosin A was extracted from the ground muscle by 0.6M KCl or KI. The supernatant of the crude extract was mixed with an equal volume of 0.05M pH 6.2 histidine buffer. Myosin was precipitated by the addition of PEG to a final concentration of 6% (weight:volume). The mixture was centrifuged after 15' incubation in the cold room. The ppt was washed free from PEG at low salt concentration. The Ca^{2+} activated ATPase activity of the myosin A prepared by PEG fractionation was about 50% higher than that of the control myosin A (precipitated by dilution). The PEG precipitated myosin A showed a sharp peak in the ultracentrifuge. The absolute viscosity, sedimentation constant molecular weight and total helical content the PEG precipitated myosin A were the same as those of the native myosin A prepared by the conventional dilution method. Gel chromatography showed one main band and two smaller bands with these proteins. The PEG precipitation is suitable to concentrate myosins from dilute solutions (0.5-1.0 mg/ml) and the ATPase activity of the myosin A remained stable after three consecutive precipitations with PEG. Supported by NIH Grants NB 06517 and HD 06267.

INTERACTION OF HUMORAL AGENTS ON AIRWAY SMOOTH MUSCLE RESPONSES (ASMR) IN MAN. C.A. Mitchell*, D. Piscitelli* and A. Bouhuys. Yale Univ. Lung Research Center, New Haven, Conn.

In animal experiments aerosolized histamine (H) and methacholine (M) have been shown to have a synergistic action on ASMR (Fed. Proc. 31: 336, 1972). This drug interaction has been demonstrated *in vitro* using isolated guinea pig superfused trachea. ASMR to the same drugs was assessed in man by measuring maximum expiratory flow rates at total lung capacity less 60% of the control vital capacity, on the partial expiratory flow-volume (PEFV) curve - an expiratory maneuver from mid-vital capacity. This measurement was found to be the most sensitive to flow change induced by airway constrictor drugs (J. Clin. Invest. 48:1159, 1969). Near threshold concentrations of these drugs, usually H-10 mg/ml and M-25 mg/ml, were administered, both separately and concurrently in random fashion, from a Dautrebande D-30 nebulizer which generated 0.12 ml of aerosol over 30 seconds. When administered concurrently, the mean reduction in flow rates (approx. 0.6 l/sec) was in excess of the sum of the effects of the separate drugs. We conclude that histamine and methacholine act synergistically in intact man as well as in the isolated guinea pig trachea. This implies that similar mechanisms of drug interaction may exist in human and in guinea pig airway smooth muscle. These mechanisms may involve modifications of cyclic nucleotide content in the smooth muscle cell. This work was supported in part by USPHS Grant HE 14179.

FAILURE OF EXERCISE TO ENHANCE CLEARANCE OF ^{85}KRYPTON FROM SKELETAL MUSCLE DURING CONSTANT TOTAL FLOW. D.E. Mohrman*, D.A. Schnaar*, and H.V. Sparks. University of Michigan, Ann Arbor, Michigan 48104.

Exercise increases the potential for blood-tissue exchange of ions such as K^+, Rb^+, and Na^+ even when total flow is held constant. To determine whether the same is true for lipid soluble gases such as O_2, we studied the clearance of ^{85}Krypton from dog calf muscles. The blood supply to the calf muscles was isolated, the calf skinned and the paw removed. Venous outflow was measured during rest and during exercise at 1 twitch/sec. Thereafter, muscles were pump perfused with a flow midway between the rest and exercise flows. The clearance of an intraarterial bolus of ^{85}Kr was monitored during each of alternate, 1 hr rest and exercise periods. Clearance curves could be described as the sum of 3 monoexponential components with half times of approximately 1, 4, and 30 min. Autoradiographs, made from cross sections of calves rapidly frozen at selected times after injection, demonstrated that the slowest component of the clearance curves was due to clearance from the marrow of the tibia and that the remaining two components resulted from an uneven distribution of flow within muscle. The average nutrient muscle flow, calculated from these two components, did not increase during exercise but rather decreased slightly (-4%, p=.14). Exercise decreased the rate of the fast muscle component (-15%, p=.04) and increased the rate of the slow muscle component (+9%, p=.04). These results indicate that exercise does not shift flow from non-exchanging to exchanging pathways for lipid soluble gases but that it does cause a slightly more uniform distribution of nutrient flow within muscle. Supported by USPHS Grant HL 14516 and the Michigan Heart Association.

INHIBITORY RESPONSES FROM CENTER AND SURROUND STIMULATION IN RABBIT RETINA. S. Molotchnikoff (intr. by W.K.Noell). Neurosensory Lab., Dept. of Physiology, SUNY at Buffalo, Buffalo, New York.

Localized light stimuli delivered to center and surround of phasic ganglion cells of rabbit retina produce inhibitory pauses in relation to "on" and "off". By recording from single optic tract axons, the excitatory "bursting" effect of brief transretinal electrical stimuli acting upon distal elements of the retina was used to analyze the inhibitory periods with respect to temporal parameters. Two spots of light in different parts of the receptive field were further used to characterize the inhibitory periods. Two different inhibitory periods were distinguished for both on- and off-center units, corresponding, with some qualification, to Granit's "pre" and "post" excitatory inhibition. Both center and surround have individual channels for inhibition, and a separate organization for both types of inhibitory action. Results can be expressed in the form of a simple network model characterized by interacting excitatory and inhibitory channels which feed into a common element.

RESPIRATORY ACID-BASE BALANCE IN THE UNANESTHETIZED CAT DURING ACUTE HEAT STRESS. Mary L. Morgan* and Thomas Adams. Dept. of Physiology, Michigan State University, East Lansing, Michigan. 48823

Furred homeotherms facing an acute heat stress protect against increases in body temperature by regulating respiratory evaporative heat loss (E). Increasing air movement across lingual, buccal, nasopharyngeal and respiratory surfaces requires increases in respiratory frequency (f) and/or depth (V_T), possibly affecting alveolar ventilation and whole body acid-base balance. The regulation of respiratory patterns to satisfy both metabolic and thermoregulatory requirements was evaluated in 5, adult, non-heat acclimatized, unanesthetized cats by measuring V_T, pH_a, P_{aCO_2}, P_{aO_2}, f, average skin ($\overline{T}_s$), hypothalamic (T_{hy}) and rectal (T_{re})[2]temperatures during multiple steady state exposures to controlled ambient temperatures (T_a) of 32-41°C with low (<40%) relative humidities. At T_a increments of 32-41°C, P_{aCO_2} decreased linearly from 43 to 28 mm Hg., f increased from 35 to 250 per min. and T_{re} rose from 39.0 to 41.0°C, but pH_a did not change from 7.380; f was equally well correlated with $\overline{T}_s$, T_{hy} and T_{re}, although T_{hy} was even further below T_{re} during polypnea-inducing heat stress than it was during thermoneutral exposures. So-called "second stage panting" (characterized in larger mammals by slowed f and increased V_T during profound hyperthermic distress) was not observed. The non-heat acclimatized domestic cat appears to combat hyperthermia by tolerating an elevated total body heat content and by increasing E, involving progressive hyperventilation but avoiding respiratory alkalosis by effective H^+ buffering. For the cat, the alteration of blood pH does not seem to be as limiting a factor in countering successfully a heat stress as does the direct caloric load of the animal.

SELF-PACED RESPIRATION IN RATS: THE EFFECT OF FEEDBACK DELAY. R. P. Morgan*and A. L. Kunz. Department of Physiology, The Ohio State University, Columbus, Ohio, 43210.

In anesthetized rats, a Ag-AgCl microelectrode (70-80 micron) was stereotaxically placed in the area of the medulla reported, by Davies and Yamamoto (1966), to permit pacing of respiration with low frequency (0.5-2.0 Hz) electrotonus-like, sinusoidal currents ($\pm$75 microamps about mean 30). An electronic spirometer recorded tidal volume and period, and produced the analog voltage signal used as feedback to produce the stimulating current to the medulla. Result, a self-paced rat; each breath stimulating the next. A time delay in the feedback loop increase the period of respiration an amount equal to the delay, until period of 2X normal when further increase reverts period to normal. Now additional delay increases period by only 1/2, until again 2X normal. Reverts to normal. Now added delay increases period only 1/3, etc... These findings are consistent with concept that pacemaker may involve the feedback interplay of inspiration and some consequence such as CO_2 lowering.

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The effect of gastrin on transport of valine in rat jejunum. J. MORISSET, J. DUNNIGAN* and G. CHOUINARD*. G.I. Research Unit, Sci. Fac., Sherbrooke Univ., Sherbrooke, P.Q. Canada.

The purpose of this study was to determine and compare effects of exogenously injected gastrin and in vitro gastrin on jejunal transport of L-valine as measured by the technique of OH and Beck. Rat jejunum (8 cm) was excised about 30 cm from the pancreatic duct and incubated in Krebs-Ringer Bicarbonate buffer pH 7.4 containing glucose (14 mM) and L-valine (5 mM) on both sides of the mucosa. On the mucosal side were added 1 µC of L-valine-^{14}C (0.004 mM) and the gastrin preparation (1.5, 3 and 6 µg) for the in vitro studies. In vivo gastrin was injected at doses of 1.5 and 3 µg/Kg, the animals were sacrificed 15 and 30 minutes later and amino acid transport was then measured in vitro. Jejunal transport of valine was linear for 90 minutes. In vivo administered gastrin (1.5 and 3.0 µg/Kg) 15 and 30 minutes before sacrifice did not modify jejunal transport of L-valine-^{14}C. In vitro gastrin added to the mucosal side (1.5, 3 and 6 µg) did not change rate of L-valine-^{14}C transport across the jejunum. In these experiments, free L-valine-^{14}C and L-valine-^{14}C incorporated into intestinal protein were not affected by gastrin. Our findings indicate that, under these conditions, in vivo injected gastrin and in vitro added gastrin have no effect on jejunal transport of L-valine. Supported by NRC Canada Grant A-6369.

EFFECT OF pH AND PCO_2 CHANGES ON THE VASCULAR RESISTANCE OF THE FETAL PLACENTA. E.K. Motoyama, T. Fuchigami*, C.J. Zigas*, and H. Cohen*. Depts. of Anesthesiology and Pediatrics, Yale School of Medicine, New Haven, Connecticut 06510.

Previous studies indicated that fetal hypoxemia associated with maternal hyperventilation and alkalemia was in part the result of hypoperfusion of the fetal side of the placenta (Fed. Proc. 28:439, 1969). The present study investigated the effect of changes in maternal and fetal P_{CO_2} and pH on the vascular bed of the fetal placenta in pregnant ewes. The fetal side of the placenta was perfused in utero through an extracorporeal circuit which was fed by maternal carotid artery blood. Blood returning to the umbilical veins was infused back into the maternal jugular vein. In 5 experiments a decrease in fetal P_{CO_2} from the control level (mean umbilical artery P_{CO_2} from 43.0 ± 2.4 to 25.2 ± 1.0 mmHg) was associated with a significant increase (36.5 ± 5.5%, $p < 0.01$) in the vascular resistance of the fetal placenta. Pressure-flow curves were shifted to the right (higher resistance) with hypocapnia and returned toward the control values when eucapnia was restored. Hypercapnia and acidemia of the fetal placental blood had the opposite effect. Maternal hypocapnia without changes in umbilical P_{CO_2} and pH had little effect on the vascular resistance of the fetal placenta. Thus fetal placental vessels constrict with hypocapnia and dilate with hypercapnia. This mechanism appears to play an important role in fetal hypoxemia during maternal hyperventilation. (Supported by NIH grants: HD03119, HL14179).

MYOSIN ATPase ACTIVITY AND MECHANICS OF SOLEUS MUSCLES IN INTACT AND CHRONICALLY ADRENALECTOMIZED CATS. R.A. Murphy[1] and A.C. Beardsley*. Dept. of Physiology, Univ. of Va. Sch. of Med., Charlottesville, Va.

The effects of chronic (9-13 days) bilateral adrenalectomy (adx) on the contractile system and function of a homogeneous slow-fibered muscle were studied in mature male cats. Mechanics measurements were performed *in situ* with a pneumatic isotonic lever system adapted from Fales, *et al.* (J. Appl. Physiol., 13, 307, 1958). Muscles were directly stimulated using needle electrodes with 20 μsec supramaximal pulses. Myosin was isolated from individual muscles and the ATPase activity measured at 0.1 or 0.3 mg myosin/ml, 25°C, pH 7.0, μ = 0.1, and 5 mM CaATP. Anatomical studies revealed a fairly constant fiber length in each muscle (95% were within ± 5% of the mean length), but the cells averaged only 37% of the total muscle length. The maximum isometric tension was 2.24 ± 0.13 SEM kg-wt/cm^2 in 9 control muscles and unchanged after adx (2.16 ± 0.12, N = 11). While the twitch/tetanus tension ratio showed no significant changes from a value near 0.2, the stimulation frequencies for fusion of mechanical responses and for maximum dP/dt decreased significantly after adrenalectomy. Maximum dP/dt fell from 18.4 ± 1.6 to 12.5 ± 0.6 kg-wt/sec after adx. Maximum shortening velocity was unaltered (5.62 ± 0.44 muscle lengths/sec and 4.94 ± 0.50), nor was the myosin ATPase activity (0.232 ± 0.011 and 0.226 ± 0.010 μMoles P_i/mg·min) in 9 control and 11 adx cats, respectively. When subjected to trains of 1 sec tetani at 0.8 Hz, muscles of adx cats showed a more rapid onset of fatigue and increased recovery time. Any impairment in soleus function after adx may be due to alterations in the active state or secondary to the lower blood pressure and inadequate metabolic provisions. [1Recipient of an NIH Career Development Award; supported by NIH grants HL 14547 and HL 09924]

IDENTIFICATION OF FACTORS PERTINENT TO INCREASED SURVIVAL IN HELIUM-COLD HYPOTHERMIC HAMSTERS. X.J. Musacchia, Wynn Volkert*, Garth Resch* and G.L. Anderson*. Physiol. Dept. and Space Sci. Res. Ctr., Univ. Mo., Columbia, Mo. 65201

Two features have been identified as relevant to survival in hypothermic (T_{re}7C) hamsters: A) shortened induction time and B) depletion of carbohydrate metabolites. Induction time is shortened in two ways: by prior heat acclimation, and by adding 2.5% halothane into the helium:oxygen (80:20) helox mixture at T_a0C. Induction times, from normothermia T_{re}37C to hypothermia T_{re}7C, were as follows: "routine" 80:20 helox, 80:20 helox + halothane, 2 wk heat acclimated (T_a34C) + "routine" 80:20 helox, and 2 wk heat acclimated (T_a34C) + 80:20 helox + halothane, respectively 5.8, 1.6, 3, and 1.5 hrs. In the same order, survival times in hours at T_{re}7C were 27, 106, 59, and 103. Reduced induction times are relatable to increased survival in hypothermia. In addition, a combination of helox and halothane is an improved method for inducing hypothermia. Both liver glycogen and blood glucose levels are affected by hypothermia and are relatable to survival. Liver glycogen falls from 69.2 to as low as 2.5 mg/g w.w. With induction of hypothermia, blood glucose falls from 100-110 to @10 mg% when death ensues at 24-27 hr. There is a sparing action with rapid induction (helox + halothane). With replenishment of blood glucose via a carotid cannula, 200 mgs/ml every 4 hrs, blood level is sustained at 30-45 mg% and survival increased to 2-3 days. (Supported by NASA, NGR 26-004-021.)

CALCIUM AND MAGNESIUM METABOLISM IN SPINAL MAN AND RAT. N.E. Naftchi, A. Viau*, M. Demeny*, G.H. Sell*, and E.W. Lowman*. Inst. of Rehab. Med., N.Y.U. Med. Cntr., New York, N.Y. 10016.

Urinary excretion of calcium and magnesium ions was measured by atomic absorption spectroscopy during acute, subacute, and chronic phases of spinal cord injury. The patients were fed ad libitum. In fourteen (ten quadriplegic and four paraplegic) subjects the mean and standard deviations for calcium and magnesium ions respectively were: 259 $\pm$ 124 and 213 $\pm$ 180 mg/24 hr. during the acute phase; 203 $\pm$ 70 and 76 $\pm$ 22 mg/24 hr. in the subacute phase; 144 $\pm$ 56 and 102 $\pm$ 24 mg/24 hr. in the chronic phase of the injury. In eight patients with incomplete lesions during the acute phase the mean and standard deviations were significantly lower than those with complete lesions; being 119 $\pm$ 39 and 59 $\pm$ 32, respectively ($P < 0.05$). Four of these eight subjects who were retaining both divalent cations developed myositis ossificans. In a group of six rats fed on a semi-synthetic diet the control excretion of urinary calcium was 204 $\pm$ 68 µg/day. This was changed to: 182 $\pm$ 50 in 1 to 5 days, 556 $\pm$ 167 µg/day in 5 to 10 days, and 206 $\pm$ 19 in 10 to 60 days after transection. The results of magnesium excretion for the same dates changed from a control value of 1.28 $\pm$ 0.095 mg/day to: 1.30 $\pm$ 0.113, 1.91 $\pm$ 0.132, and 1.39 $\pm$ 0.185 mg/day, respectively. The results indicate that the bone resorption during the acute phase evidenced by the high excretion of calcium and magnesium ions subsides during the subacute phase and normalizes during the chronic phase of the injury. The therapy, therefore, should be directed at the patients with lesions of the spinal cord immediately after onset of the injury.
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CHOLINERGIC CONTROL OF BILE FLOW AND COMPOSITION. D.L. Nahrwold, D. L. Kaminski* and R. C. Rose*. The Pennsylvania State Univ., College of Medicine, Hershey, Pa.

This experiment was designed to test the effect of cholinergic blockade on insulin choleresis. Four dogs were prepared with cholecystectomy, a gastric fistula and a duodenal cannula through which the common duct was intubated. All tests were done during continuous intravenous infusion of sodium taurocholate (NaT) in dosages ranging from 4.5 to 72 µEq/ min. Biliary and gastric responses were measured during continuous insulin infusion (1.5 U/kg IV followed by 0.15 U/kg/hr), continuous atropine infusion (0.8 mgm/kg IV followed by 0.08 mgm/kg/hr), and during continuous infusion of both insulin and atropine in the same dosages. Biliary Na^+, K^+, Cl^-, HCO_3^- and gastric H^+ concentrations were measured by standard methods and bile salt concentrations were calculated. Mean bile flow rate during insulin alone ranged from 205 µL/min at 4.5 µEq/min NaT to 612 µL/min at 72 µEq/min NaT. Flow rate with atropine alone ranged from 120 µL/min at 4.5 µEq/min NaT to 501 µL/min at 72 µEq/min NaT. Simultaneous administration of atropine and insulin gave responses identical to those with atropine alone at all NaT dosages. Bicarbonate output with insulin alone ranged from 5.2 µEq/min to 22.2µEq/min at the above NaT dosages, and with atropine alone it ranged from 2.9 µEq/min to 9.9 µEq/min. Bicarbonate output with insulin plus atropine was identical to that with atropine alone. Atropine also blocked the effect of insulin on the concentrations of HCO_3^-, K^+ and bile salts, and on the outputs of Na^+, Cl^- and bile salts. Atropine completely blocked insulin-induced gastric acid secretin. These studies show that insulin-induced changes in bile flow and composition are mediated by a cholinergic mechanism which is completely blocked by atropine.

ON THE MECHANISM OF EXCITATION OF VASCULAR SMOOTH MUSCLE. Akira Nakajima*, Minayori Kumamoto*, and Leif Horn. Kyoto University, Japan and N.J. Med. Sch., Newark, U.S.A..

We have shown earlier that excitation of vascular smooth muscle is: unaffected by tetrodotoxin, Ca^{++}-dependent, and inhibited by transition metals, i.e. Mn^{+++}. The current voltage relationships, obtained from experiments utilizing double sucrose gap voltage clamping techniques, show that tetraethylammonium (TEA) increases early inward current and shifts the reversal potential 20-30 mV beyond the calculated equilibrium potential of Na^{+} in longitudinal muscle of the superior mesenteric vein of the quinea pig. The above tends to support a mechanism different from the Na^{+}-hypothesis. Our present experiments with the same preparation, using microelectrode techniques show that spontaneous electrical activity is abolished in Na^{+}-free solutions and that TEA fails to restore the spontaneous activity at low Na^{+}-concentrations.. The data indicate that Na^{+}- is required for normal spontaneous activity. Attempts to evoke action potentials in Na^{+}-free solutions by electrical stimulation were also unsuccessful. With low Ca^{++}-concentrations the amplitude of the action potential (AP) is reduced as are the maximum rates of rise and fall. At low Ca^{++}-concentrations TEA increases AP-amplitude and dereases rate of fall further. High concentrations of Ca^{++} hyperpolarize the preparation and increase AP-amplitude. TEA at high Ca^{++}-concentrations causes no further hyperpolarization but increases AP-amplitude associated with a slight increase in rate of rise and a decrease in the rate of fall. Ionic mechanisms of excitation and the mode of TEA will be discussed. (Supported by the Japan Ministry of Education and the US-Japan Association for Promotion of Science).

EFFECTS OF VASODILATORS ON SEGMENTAL RENAL VASCULAR RESISTANCE AND GLOMERULAR PRESSURE. L. G. Navar and P. G. Baer.* Dept. of Physiology and Biophysics, Univ. of Miss. Sch. Med., Jackson, Miss.

To investigate the alterations in intrarenal hemodynamics that occur following vasodilator infusions, experiments were performed such that changes in glomerular pressure and segmental vascular resistances could be estimated by determining minimal pre-glomerular resistance as previously described (A.J.P. 219:1658, 1970). In 18 dogs, responses to graded reductions in renal arterial pressure were compared to those obtained during intra-arterial infusion of acetylcholine, dopamine, papaverine, and prostaglandin. At control blood pressures, vasodilator infusion increased renal blood flow (RBF) by 40 to 100%, and intrarenal venous pressure (IVP) by 45 to 120%. GFR was not altered with acetylcholine or dopamine, decreased by 34% with papaverine and increased by 25% with prostaglandin. Afferent vasodilation was predominant and estimated glomerular pressure increased by an average of 29% in all but the papaverine series. With the decrease in arterial pressure from 130 mm Hg to 70 mm Hg, average control responses without vasodilator included decreases of 8% in RBF, 24% in GFR, 16% in IVP and 9% in glomerular pressure. During vasodilator infusion, the same decrease in blood pressure resulted in average decreases of 19% in RBF, 27% in GFR, 38% in IVP and 35% in glomerular pressure. These experiments indicate that vasodilator infusion generally increases glomerular pressure but proximal tubular pressure, as estimated from IVP, also rises. Reductions in arterial pressure during vasodilation result in concomitant decreases in both glomerular pressure and IVP. These results help explain previous observations showing maintenance of GFR autoregulatory efficiency during vasodilator infusions.

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NEWER INDICES OF MYOCARDIAL CONTRACTILITY: Normalized first and second derivatives of ventricular pressure (dP/dt)/P and (d^2P/dt^2)/P. N. S. Nejad, M. D. Klein and B. Lown (introduced by L. B. Hinshaw). Harvard School of Public Health, Boston, Mass. and University of Oklahoma Health Sciences Center, Oklahoma City, Okla.

Maximum velocity of contractile element shortening (V max) obtained by extrapolation of the force-velocity curve to zero load, had been utilized as an index of myocardial contractility. In the failing heart with elevated end-diastolic pressure (EDP), extrapolation over a long interval may introduce large errors. To obviate this problem a study was made of the changes in peak (dP/dt)/P and (d^2P/dt^2)/P during various hemodynamic interventions in sixteen heart-lung preparation (HLP) and nine intact dogs. In HLP increase of EDP (4-20 mmHg) by varying either preload or afterload, resulted in little change in peak (dP/dt)/P or (d^2P/dt^2/P). In those hearts subjected to acute failure, with sustained elevation of EDP greater than 20 mmHg, peak (dP/dt)/P and (d^2P/dt^2)/P were depressed by an average of 35% and 41% respectively. Isoproterenol (0.1 µgm/min) restored them to control values. In the non failing HLP, isoproterenol increased peak (dP/dt)/P from 47 to 61 sec^{-1} and raised peak (d^2P/dt^2)/P from 2044 to 5048 sec^{-2}. In intact dogs isoproterenol infusion (2 µgm/min) increased the peak (dP/dt)/P and (d^2P/dt^2)/P by 20% and 35% respectively. Maximum value of the second derivative of LVP was shown to occur within 5 mesc of peak (dP/dt)/P and served as a guide to the time of occurrence of maximum intensity of the active state. These results suggest that peak (dP/dt)/P and (d^2P/dt^2)/P can be used to gauge myocardial contractility and that peak (d^2P/dt^2)/P may be a more sensitive tool for measuring myocardial contractility than peak (dP/dt)/P.

ALVEOLAR pCO_2 REGULATION OF THORACIC COMPLIANCE AND RESISTANCE. J.F. Neville, Jr., P. Kane, W. Webb, J. Askanazi, T. Stellato, B. Farrell, SUNY, Upstate Medical Center, Syracuse, N.Y.

During total cardiopulmonary by-pass in patients having cardiac surgery, alveolar pCO_2 has been regulated by altering inspired CO_2 concentration. Arterial pCO_2 was held constant by the oxygenator. The observed changes in compliance and resistance were therefore related to the local effects of hypocapnia. Below 2% end expired CO_2, resistance increased and compliance decreased. Hyperinflation temporarily modified both parameters. Restoration of pCO_2 reversed the changes. The response could be repeatedly elicited in the same individual. The observations indicate that alveolar hypocapnia will produce changes in local pulmonary mechanics tending to improve ventilation-perfusion abnormalities.

COMPARISON OF REFLEX AND MUSCLE RESPONSES TO RAMP STRETCHES AND RELEASES. T. Richard Nichols (intr. by J.Houk). Harvard Medical School, Boston, Mass.

The change in force in a muscle when it is stretched or released depends on the mechanical properties of the active muscle as well as on reflex recruitment and increments in discharge rate of motor units. In current experiments on the soleus muscle in decerebrate cats,ramp stretches and releases (0.4-2mm;0.2-2 sec.in duration) are applied to muscles stimulated through their ventral roots and to muscles with intact stretch reflexes. Responses of muscles whose ventral roots are stimulated asynchronously at 8/sec. are characterized by a peak in force during the ramp, a sharp dip at the end of the ramp and a creep toward a steady level at the longer length. The responses to release about the same operating length are larger and consist of a decrease in force during the ramp followed by a slow rise. The muscular stiffness (obtained by dividing the final change in force by the change in length) is not predicted by the slope of the length-tension curve at the operating length. The response of a muscle with an intact reflex consists simply of a peak at the end of the ramp followed by a decay to a steady level. The reflex response is typically several times the magnitude of the muscle response and is more symmetric in size and shape with respect to stretch and release. These data support the idea that one function of autogenetic reflexes, besides increasing the mechanical stiffness of the system, is to mask the irregular dynamic properties of the active muscle.

TRANSMEMBRANE AND ACTION POTENTIALS OF SPONTANEOUSLY CONTRACTING SMOOTH MUSCLE CELLS OF VENULES IN UNANESTHATIZED BAT WING MICROVESSELS. PAUL A. NICOLL AND ROSS SPEDEN. DEPTS. PHYSIOLOGY, INDIANA UNIVERSITY AND UNIVERSITY OF TASMANIA (HOBART): BLOOMINGTON & INDIANAPOLIS, IND.

Transmembrane and action potentials were recorded from single vascular smooth muscle cells along venules of 40 to 80 microns resting diameter in unanesthatized bats (Myotis leucifugus). Microelectrodes with 20 to 60 meg. ohms initial resistance suspended by 50 micron Ag. wire are inserted by gravity as the vessel is observed at magnification of 600 to 1000 times. Since these cells exhibit spontaneous contraction at regular rhythmical rates of 20 to 30 times per minute all potentials regardless of their apparent character were considered artifacts or tip potential changes unless an action potential immediately preceeding the vessels contraction occured. These vessels have only a single layer of circularly orientated smooth muscle cells. The magnitude of the resting potential appears to vary but technical problems associated with establishing the zero base make absolute measurements difficult. The values ranged from 25 to 40 m. v. and averaged about 31 m. v. In many instances action potentials were recorded when transmembrane potentials were very small. Here probably only the upper portions of the true action potentials were involved. No slow waves unassociated with action potentials can be identified. Action potentials arise from slowly rising resting values. Spike potentials may or may not be a prominent feature of the rising phase of the action potentials. Rise time is very slow and ranges from 140 to 350 m. sec. The depolarization phase averages around 600 m. sec. Recovery is usually slower than the rise time and averages 300 m. sec. Action potentials range from negligible values to 45 m. v. and rarely exhibit any overshoot. Negative after potential rarely occure. Supported in part by PHS grant #HL 08618

DIFFERENTIAL RESPONSES OF THE RIGHT AND LEFT VENTRICLES TO STIMULATION OF THORACIC VENTRAL ROOTS. Jeanne E. Norris* and Robert D. Wurster. Loyola University, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Myocardial contractile force was monitored with strain gauge arches in nine areas of the left and right ventricles during stimulation of the first five thoracic ventral roots. Twenty-seven anesthetized dogs were used in this study. Systemic arterial pressure and heart rate were also monitored during all stimulations. Significant increases in contractile force, heart rate, and systemic pressure resulted from stimulation of all five roots of both sides. In general, greater inotropic responses were seen in both ventricles during stimulation of the first two roots of the left side. In two areas of the left ventricle, however, greater inotropic effects resulted from stimulation of the first two right roots. The magnitude of the inotropic response was generally smaller below the level of the second root. Although significant increases in heart rate were seen during stimulation of all roots, significantly greater chronotropic responses were seen during stimulation of the first three roots of the right side. Highly significant increases in systemic blood pressure were seen during stimulation of all five roots of both sides but larger increases resulted during stimulation of the first four left roots. The findings indicate that the first five roots of the right and left sides participate in both inotropic and chronotropic responses. Stimulation of the right roots has a greater chronotropic influence than those of the left while the degree of inotropic influence of the right or left side is dependent upon the specific area of the ventricle being monitored. (Supported by NIH Grants HE 08682 and GM 999).

THE PRESSOR REFLEX TO STATIC (ISOMETRIC) SKELETAL MUSCLE CONTRACTION. D. O. Nutter, M. L. Fisher, and T. E. Ratts (intr. by N. S. Skinner, Jr.). Emory University School of Medicine, Atlanta, Georgia.

The cardiovascular (CV) pressor responses to static hindlimb muscular contraction and to stimulation of somatic afferent nerve fibers (SAF) were studied in chloralose anesthetized dogs. Thirty second static contractions (SC) were induced by direct electrical stimulation (0.2 msec pulses, 25 - 50 Hz, 2 - 5 x threshold) of spinal ventral roots L_{6-7} (VR). SAF stimulation (0.5 msec pulses, 100 Hz, 40 - 100 x threshold) of spinal dorsal roots L_6 - S_1 (DR) and of tibial nerve muscular branches was done during neuromuscular blockade (succinylcholine). Ventral root SC (n = 6) caused a prompt rise in mean aortic pressure (MAP), 122 - 138 mmHg; and increased heart rate (HR), 192 - 200 beats/minute; stroke volume (uncalibrated aortic electromagnetic flowprobe), 14%, and cardiac output (CO), 17%; but did not significantly alter calculated systemic resistance (SR). A significant CV response did not occur during rhythmic contractions of hindlimb muscle groups and no response occurred when VR stimulation was performed during neuromuscular blockade. Dorsal root SAF stimulation (n = 6) evoked a potent pressor response as MAP rose 122 - 164 mmHg; HR fell 189 - 172 beats/minute; stroke volume and CO rose by 27% and 12%; however, in contrast to SC, systemic resistance increased by 24%. A similar pressor response (MAP 112 - 136 mmHg, 21%; HR 192 - 182, -5%) resulted from tibial nerve muscular branch stimulation (n = 5). Baroreceptor denervation augmented this CV reflex (MAP 146 - 181 mmHg, 24%; HR 182 - 238, 31%). In summary: the CV pressor reflex to static contractions in a canine model appears to depend on increased HR and CO. The pressor reflex to somatic afferent fiber stimulation is modulated by baroreceptors and depends on both increased CO and SR.

CONTROL OF LEUCINE CATABOLISM IN TISSUES OF NORMAL AND FASTING RATS. Richard Odessey* and Alfred L. Goldberg. Dept. Physiology, Harvard Medical School, Boston, Mass.

A major fraction of leucine-1-^{14}C, valine-1-^{14}C and isoleucine-1-^{14}C entering rat muscle is oxidized to $^{14}CO_2$. Diaphragms from fasted rats are several fold more active in oxidation of these amino acids than tissues from fed controls. Kidney slices, but not brain or liver slices, also increased their rate of leucine oxidation on fasting. Within 24 hrs. of food deprivation, incorporation of leucine into protein decreased in all tissues studied. Increased oxidation of branched chain amino acids was not observed until 48 hrs. after food removal and subsequently increased further. Readministration of food reduced leucine oxidation to control levels. Increased oxidation did not result simply from increased tissue uptake of the amino acids but reflected greater capacity to degrade the branched chain amino acids. The control of oxidation was investigated in cell-free extracts. Homogenates of rat gastrocnemius from fed and fasted rats were incubated with leucine-1-^{14}C and cofactors. Transaminase was assayed by production of ^{14}C-α-ketoisocaproic acid and the decarboxylase by production of $^{14}CO_2$. The decarboxylase activity of the homogenates, localized exclusively in the mitochondrial fraction, was 2-3 fold more active in extracts from fasted rats. Upon dialysis, the activity of homogenates from muscles of fed rats increased to levels of extracts from fasted muscle. Thus normal skeletal muscle appears to contain a small molecular weight inhibitor of leucine oxidation, which is lost during prolonged fasting.

HEART RATE RESPONSES TO PHASIC OCCLUSION OF VENA CAVA, PULMONARY ARTERY AND OF ASCENDING AND DESCENDING AORTA. Winfried W. Ohm,* Allen M. Scher and Cyril S. Ito.* Dept. of Anesthesiology and Dept. of Physiology & Biophysics, University of Washington School of Medicine, Seattle, Wash.

Pressoreceptors are found in the carotid and aortic arteries, in the atria and in the pulmonary artery. The arterial receptors control the arterial pressure. The atrial receptors regulate the concentration and amount of extracellular fluid, and "low pressure" receptors may control heart rate and resistance in specific vascular beds. In our experiments, cuffs to alter arterial and atrial pressure were implanted around the inferior vena cava, pulmonary artery, ascending aorta and descending aorta of healthy dogs. A week or more after surgery, dogs were studied under chloralose anesthesia. Cuffs were inflated sinusoidally, and the time relationship between the sinusoidal components of the arterial pressure and of reflex heart rate change were examined. Results: (1) When the descending aortic cuff was inflated, a rapid heart rate change was seen; (2) when the ascending aortic cuff (or the pulmonary artery cuff) was inflated, the heart rate changes were slower; and (3) when the vena cava cuff was inflated, heart rate changes lagged arterial pressure even more. These differing results (2 and 3) seem to indicate that there may be heart rate responses from receptors in the low pressure side of the circulation (the possibility exists that a difference in the arterial pressure waveform caused the difference in results in 2 and 3). If the speed of response is considered, the results indicate that a fall in pressure in both the aorta and the low pressure system (3) brings on a more sympathetic response than a decrease in pressure in the aorta accompanied by a rise in pressure in one or both atria (2). Supported by National Institutes of Health grants HL 07746-10 and GMO 1160-09.

RESPONSE PATTERNS OF INTERPOSITUS NEURONES TO STIMULATION OF FORE- AND HINDLIMB AREAS OF SENSORIMOTOR CORTEX. Tadao Ohno*, Gary I. Allen and Gian Battista Azzena*. Lab. of Neurobiology, Dept. of Physiology, State Univ. of N. Y. at Buffalo, N. Y. 14226.

In forming the output of the pars intermedia, interpositus neurones collect the inhibitory Purkyně cell signals and the excitatory collaterals of mossy fiber (MF) and climbing fiber (CF) afferents. Single interpositus neurones were recorded in cats under light thiopental anesthesia in order to analyze the responses to stimulation of fore- and hindlimb regions of the sensorimotor cortex and to compare the projection patterns from cortex and nerves with those in Purkyně cells. The responses to cortical stimulation consisted of an early excitation mediated by collaterals of MFs from lateral reticular (LRN) and possibly pontine nuclei, followed by inhibition from Purkyne cells activated by these two groups of MFs. Subsequently, a later excitation appeared, mediated by collaterals of both CFs and late MFs of LRN origin, followed by an inhibition due to Purkyne cell activation by the CFs and late MFs. The presence and size of each component depended upon the cortical area stimulated and varied from one neurone to another. In addition, the responses for most neurones could be elicited over most of the sensorimotor cortex, including both fore- and hindlimb regions. There were relatively few interpositus neurones receiving cortical and peripheral inputs restricted to one limb, as has been observed in Purkyne cells of the pars intermedia. Even though there was less somatotopical sharpness than for Purkyně cells, the strongest cortical and peripheral inputs still represented the same limb in 50 of 69 units. Therefore, it may be possible for information specific to a certain limb to pass through the interpositus nucleus, even if a higher degree of integration exists.

NEUROHUMORAL-HORMONAL SECRETORY STIMULATION OF PULMONARY SURFACTANT IN THE RAT. D. B. Olsen (intr. by G. F. Filley), Univ. Colo. Sch. of Med. and The Webb-Waring Lung Institute, Denver, Colo. 80220

It is widely accepted that the lamellar bodies (lbs) of the pulmonary alveolar type II cells are the source of pulmonary surfactant and that they are secreted into the alveolar spaces. The influence of a parasympathomemetic and a β-agonist on the discharge of lbs from the type II cell was analyzed by using morphometric techniques at the ultrastructural level. The number of lbs in the lungs of control and treated animals was compared. Single injections of pilocarpine and isoproterenol were used alone and in combination with their respective blocking agents atropine and propranolol. The number of lbs per cell profile was reduced 45% ($P < .05$) after 1 hr. in lungs of pilocarpine-treated animals and returned to the value in the control animals (11.4) after 18 hr. Isoproterenol treatment lowered the number by 34% ($P < .01$) after 30 min. The influence of these drugs as demonstrated by counting the lbs was confirmed by unbiased volume density (V_V) calculations. The V_{Vlbs} was reduced by 58% ($P < .001$) at 1 hr. with pilocarpine treatment. Isoproterenol lowered the V_{Vlbs} by 50% ($P < .001$) at 1 hr. The secretion elicited by pilocarpine and isoproterenol was blocked by their respective antagonists. The amount of phospholipid (determined by phosphorus content) present in lung lavages of animals treated with pilocarpine or isoproterenol was 40% greater than in controls. This increase did not alter slow expiratory pressure volume curves measured on the excised lungs. I conclude that the secretory processes of the type II cell are influenced by neural and hormonal stimulation and infer that the surfactant content of the alveoli may be modified by physiological demands.

A NONDESTRUCTIVE TECHNIQUE TO MEASURE WALL DISPLACEMENT IN THE PULMONARY ARTERY. Robert M. Olson, David K. Shelton, Jr.* and Julian P. Cooke. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

A simple, precise, non-surgical technique is described for continuously monitoring the pulsatile changes in the diameter of the pulmonary artery with an accuracy of 40 micra. The technique utilizes an ultrasonic crystal mounted on the tip of an esophageal probe by means of a platform which can be tilted remotely so as to aim the crystal. Ultrasound is passed across the esophageal wall and reflects from the walls of the pulmonary artery. The reflected signals are processed, like radar, to track the position of the reflecting surface,--i.e., the pulmonary artery walls. Diameter tracings recorded in this manner are similar in shape to pressure tracings recorded by a cardiac catheter threaded into the pulmonary artery under fluoroscopy. Using this technique in a series of six dogs, it was found that the pulmonary artery expands 20 $\pm$ 7% of its diastolic diameter with each beat. Preliminary studies suggest that the technique can detect the acute onset of pulmonary hypertension, such as occurs with some cases of decompression sickness, since the rise in pressure is accompanied by a rise in diameter. For example, in dogs ascending from a depth of 100 feet of water, pulmonary artery diastolic diameter increased 10 $\pm$ 4%.

ACTION OF HIGH AND LOW PRESSURE MECHANORECEPTORS ON RENAL HEMODYNAMICS IN RABBITS. Norbert T. Ott*, Peter P. Frohnert*, David M. Wilson*, and John T. Shepherd. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Renal plasma flow (RPF, as C_{PAH}) and glomerular filtration rate (GFR, as C_{IN}) were investigated in the intact kidney (IK) and in the contralateral denervated kidney (DK) of 13 rabbits under pentobarbital anesthesia in a state of mild mannitol diuresis. Studies were made before and after denervation of the mechanoreceptors as shown in the table.

SERIES I n=6	CONTROL	SINO-AORTIC NERVES CUT	P	SINO-AORTIC NERVES & VAGI CUT	P
BP(mm Hg)	97±23	138±25	0.001	123±18	NS
IK:RPF	2.14±0.37	2.38±0.36	NS	1.74±0.65	0.025
GFR	0.70±0.12	0.87±0.13	0.01	0.62±0.20	0.01
DK:RPF	2.54±0.36	2.45±0.29	NS	2.19±0.83	NS
GFR	0.78±0.13	0.93±0.11	0.05	0.86±0.19	NS
SERIES II n=7	CONTROL	VAGI CUT	P	VAGI & SINO-AORTIC NERVES CUT	P
BP(mm Hg)	89±14	97±11	0.005	147±15	0.001
IK:RPF	1.74±0.71	1.90±0.70	NS	0.61±0.76	0.02
GFR	0.57±0.17	0.61±0.19	0.10	0.28±0.37	0.10
DK:RPF	1.98±0.54	2.19±0.43	NS	1.85±0.49	0.10
GFR	0.53±0.11	0.70±0.13	0.02	0.70±0.20	NS

($\bar{x}$ $\pm$ SD; P of paired data; RPF and GFR: ml/min/gm kidney)

With vagi intact, section of carotid and aortic nerves caused an increase in BP with little change in RPF of the IK; with vagi cut, the section caused a similar increase in BP, but there was a three-fold decrease in RPF. In the DK, autoregulation occurred. Thus, vagal afferents serve to inhibit the increased sympathetic activity to the kidney when the high pressure mechanoreceptors are denervated.

VASCULAR RESPONSES TO NOREPINEPHRINE (NE). Henry W. Overbeck. Departments of Physiology and Medicine, Michigan State Univ., E. Lansing, Mich.

We have previously reported evidence (Fed. Proc. 31:814, 1972) that the vascular response to NE is maximal at intermediate levels of vascular wall tension, in pump-perfused forelimb vascular beds of dogs. Some of the dogs studied had renal hypertension, in others we elevated forelimb resistance (and vascular wall tension) by intrabrachial arterial infusions of vasopressin, and then measured NE responses. We have now extended our study by measuring NE responses in forelimb vascular beds of 12 additional dogs in which initial limb resistance (IR) was reduced by neurectomy or by intrabrachial arterial infusions of acetylcholine or sodium nitroprusside. At each steady-state level of limb IR thus produced, response (ΔR) to NE (0.4 μg/min) was measured. Over these lower ranges of IR so produced, there was a positive relationship between IR and ΔR to NE. Furthermore, plotted against the levels of IR produced, these NE response data appeared homogenous with our previously reported data. Finally, response points for hypertensive dogs again fell within the 95% confidence belts established by response points in these normotensive dogs. These findings lend further support to our conclusions that 1) the vascular response to NE is maximal at intermediate levels of vascular wall tension, similar to the relationship reported for vascular smooth muscle *in vitro*, and 2) there is no true abnormality in the vascular response to NE in renal hypertensive dogs. In addition these data suggest that, over the lower ranges of IR, functional increases in IR are associated with increases in response to NE, as predicted by Redleaf and Tobian (Circ. Res. 6:185, 1958). Over the higher ranges of IR, functional increases in IR are associated with decreases in response to NE, as predicted by Folkow and Öberg (Acta Physiol. Scand. 47:131, 1959). (Supported by a Michigan Heart Association Research Grant).

NOREPINEPHRINE SENSITIVITY OF EAR ARTERY STRIPS FROM COLD- AND WARM-ACCLIMATED RABBITS. T.L. Owen* and L.D. Carlson, U. of Calif., Davis.

Cold-acclimation is known to result in a decreased response of the peripheral circulation to injected catecholamines. To determine if this is due to decreased sensitivity of the vascular smooth muscle, smooth muscle strips were prepared from ear arteries of cold-acclimated (CA,5°C) and warm-acclimated (WA,30°C) rabbits. Responses of each strip were recorded at temperatures of 13, 23 and 33°C using norepinephrine concentrations of (5 to 50) x 10^{-10} g/ml. Log dose-response curves were made by calculating the mean response of CA (n=5) and WA (n=5) arterial strips at each temperature. All curves were approximately linear and had equal slopes over the range of doses used. At 13°C the dose-response curves for CA and WA arterial strips were not different from each other. Strips from WA animals showed significant increases in sensitivity to norepinephrine at temperatures of 23 and 33°C, whereas strips from CA animals showed no significant change in sensitivity at the higher temperatures (see table). These results indicate that a lower vascular sensitivity to sympathetic catecholamines may be one explanation for the increased cutaneous blood flow noted in cold-adapted animals.

mg tension ± SEM

g NE	CA 13°C	WA	CA 23°C	WA	CA 33°C	WA
$5x10^{-9}$	127±20	158±11	161±26	264±25	180±19	326±19
$2x10^{-9}$	88±20	93± 9	113±23	206±20	124±17	267±17
$1x10^{-9}$	50±13	49± 9	55±13	132±14	63±10	223±21
$5x10^{-10}$	28±11	21± 4	27±11	76±17	23± 6	183± 9

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A MODIFICATION OF THE CARREL-LINDBERGH PERFUSION APPARATUS. J. A. Panuska and E. E. Morris*, Dept. Biology and Dept. Chemistry, Georgetown University, Washington, D. C. 20007.

The Carrel-Lindbergh pulsatile perfusion system (Carrel, A. and Lindbergh, C. A., Science 81:621, 1935) has continued to be useful for the *in vitro* maintenance of whole organs. Some modifications have been proposed which provide greater flexibility (e.g., Lindbergh, C. A., *et al.*, Cryobiology, 3:252, 1966). We have designed and tested a modification which retains the excellent stability of the original system, but has an organ perfusion component with separable parts. There are four units interconnected by standard taper joints and Teflon sleeves: (a) an organ chamber, (b) its top containing access ports and the organ attachment cannula and connecting tube to the fluid reservoir, (c) the fluid reservoir, (d) a unit containing floating glass valves which connects the organ chamber and the reservoir. The possibility of disassembly has the advantage of allowing easier cleaning, maintenance, replacement, and the substitution of organ chambers of varying sizes without altering units (c) and (d). There is good access to the perfused organ, allowing greater ease in the placement of electrodes and in the withdrawal or addition of fluids. Oxygenation is excellent, and only 250-300 ml of perfusion medium are required. The system proved to be very stable for systolic perfusion pressures of 20-140 mmHg, and diastolic pressures of 5-120 mmHg. (The technical assistance of Patricia Mahan is gratefully acknowledged. Supported in part by Contract N0014-69-A-0220 from the Office of Naval Research.)

ATTEMPTS TO CONDITION GASTRIC SECRETION AND THE MYOELECTRICAL POTENTIAL IN THE DOG. William P. Paré (intr. by W. H. Gantt). Pavlovian Lab., V.A. Hospital, Perry Point, MD. 21902.

Dogs, prepared with Pavlov pouches, were exposed to random tone-shock presentations. Heart rate (HR) tachycardia and an inhibition of gastric secretion occurred during the noxious stimulation periods. In a second experiment, Pavlov pouch dogs were conditioned to discriminate between a CS+ which signaled the presentation of food and a CS- which signaled the absence of food. On test trials, during which food was omitted, conditional HR tachycardia occurred in the presence of the CS+ as well as a significant increase in total gastric output and decrease in gastric pH. Attempts to condition (CS-tone followed by a US- foot shock) the myoelectrical potential of the stomach were conducted in another experiment. Recording electrodes were attached to the greater curvature of the dog's stomach. Conditional increases in HR occurred to the CS-tone and on occasional trials the pattern of the gastric electrical activity during the CS mimicked the pattern following the US-shock. This change, however, was infrequent and not significant. Similar results were observed in a fourth experiment in which positive reinforcers (food and milk) were used for the unconditional stimulus. These experiments suggest that the function of certain systems within the stomach (e.g., gastric secretion) can be conditioned, whereas other systems (e.g., myoelectrical potential) function independently and are not susceptible to externally-induced stimulus control. These findings extend Gantt's theory of organ-system responsibility to disparate functions within a single organ.

BIOCHEMICAL AND PHYSIOLOGICAL CHARACTERISTICS OF Na-K-ACTIVATED ADENOSINE TRIPHOSPHATASE OF THE TOAD SKIN. Yang S. Park* and Suk Ki Hong. Dept. of Physiology, Univ. of Hawaii School of Med., Honolulu, Hawaii.

The Na-K-activated adenosine triphosphatase (Na-K-ATPase) activity was determined in epidermal homogenates of Bufo marinus, which were prepared by the method of Kawada et al. (Comp. Biochem. Physiol. 30:965-975, 1969). The initial velocity of enzyme reaction was directly proportional to the enzyme concentration regardless of ATP or Na concentration in the medium. However, the rate of reaction was dependent on the concentration of ATP and Na. Km values for ATP and Na were 0.23 and 5 mM, respectively. ATP:Mg ratio for the maximal rate of reaction was 1:1 in the presence of 3 mM ATP in the medium and 1:2 in the presence of 1 and 2 mM ATP. The effects of various substances which are known to influence the transport of Na across the amphibian skin on this Na-K-ATPase were studied in vitro and the results are summarized as follows:

Substance	Ouabain	NEM	Ethacr. acid	Vasopressin, c-AMP, Amiloride	Insulin
Effect	inhibit	inhibit	inhibit	no effect	increase
Conc. for 50% inhib.	1.6×10^{-3} mole	1.6×10^{-2} mole	8×10^{-4} mole		

The ouabain-induced inhibition of Na-K-ATPase activity was reversed by high concentration of K. The activation of Na-K-ATPase by insulin amounts to approximately 40% of the basal level. These results indicate the presence of Na-K-ATPase in the toad skin epithelium and also suggest that the effects of vasopressin, cyclic-AMP and amiloride on Na transport across the amphibian skin are not directly linked to alterations in Na-K-ATPase; on the other hand the effect of insulin on Na transport seems to result from the activation of this enzyme. (This investigation was supported in part by a U.H. intramural research grant.)

VASCULAR EFFECTS EVOKED IN THE KIDNEY AND INTESTINE BY SELECTIVE STIMULATION OF THE CAROTID BODIES WITH HYPOXIA AND HYPERCAPNIA. P. Parker*, J. Dabney, J. Scott, and F. Haddy. Dept. of Physiol., Michigan State University, East Lansing, Michigan 48823

We previously reported (Physiologist, 14:207, 1971) that in anesthetized, vagotomized (V) dogs selective stimulation of carotid bodies by low O_2 and/or high CO_2 increased systemic blood pressure and forelimb vascular resistance (both skin and muscle). We now report the effects of the same stimuli on renal (P_R) or ileal segment perfusion pressure (P_I) and ileal motility at constant blood flow. Arterial blood was pumped through an isolated lung ventilated with various gas mixtures and then pumped at constant flow through the carotid sinuses at a pressure (P_{CS}) nearly equal to systemic pressure (P_S).

Ventilatory Mixture (Isolated Lung)	Kidney[1]			Ileum[2]			Sinus Blood	
	P_{CS}	P_S	P_R	P_{CS}	P_S	P_I	P_{O_2}	pH
20% O_2-2½% CO_2 (Control)	105	102	91	111	116	111	110	7.38
0% O_2-20% CO_2	105	134*	150*	112	158*	152*	19	6.95
20% O_2-2½% CO_2 (Control)	103	101	87	112	111	125	111	7.37
0% O_2- 5% CO_2	104	120*	130*	112	133*	140*	15	7.29
20% O_2-2½% CO_2 (Control)	101	99	86	103	101	118	115	7.37
20% O_2-20% CO_2	103	122*	124*	104	126*	138*	121	6.89

*$P<0.05$ relative to preceding control; $^1n=10$(V), $^2n=9$(V)

P_S and P_R rose during ventilation with low O_2 and high CO_2 before vagotomy but P_I did not. Intestinal motility was not regularly affected by chemoreceptor stimulation either before or after vagotomy. In four vagotomized animals superior mesenteric artery perfusion pressure at constant flow also rose during chemoreceptor stimulation. These studies support our suggestion that low O_2 and high CO_2 act on carotid chemoreceptors to elicit changes in autonomic outflow to heart and blood vessels similar to those induced by lowering pressure in the carotid sinus.

EFFECT OF L-FUCOSE ON SUGAR TRANSPORT IN RABBIT ILEUM. Terry W. Pearson*, Michael D. Swanson* and Andrew M. Goldner, Dept. of Human Physiology, Univ. of Calif. Med. Sch., Davis, Calif., 95616.

The structural requirements for net sugar transfer across the intestine and into the mucosal epithelial cells are a pyran ring, a methyl group at ring carbon 5, and a hydroxyl group at the 2 carbon in the D glucose configuration. The unidirectional transmural fluxes of 2 deoxy-L-galactose (L-Fucose) across the in vitro rabbit ileum indicate that this sugar is not transferred against a gradient. The mucosal to serosal flux ($J_{m\rightarrow s}$ 0.12±0.01 μmoles/hr·cm^2) and the serosal to mucosal flux ($J_{s\rightarrow m}$ 0.10±0.01 μmoles/hr·cm^2) are equal. However, the presence of L-Fucose reduces the net transport of 3-O-methyl-D-glucose (3MG) across the intestine. This net reduction is caused by a decrease in the $J_{m\rightarrow s}$ from 0.66 to 0.41 μmoles/hr·cm^2. The unidirectional influx of L-Fucose from the mucosal solution across the brush border into the epithelial cells is a linear function of L-Fucose concentration in the mucosal solution and is independent of the Na concentration in the mucosal solution. In the presence of L-Fucose, the influx of 3MG is competitively inhibited. The inhibitor constant (K_I) for L-Fucose inhibition of 3MG influx is a function of the Na concentration in the mucosal solution. Furthermore, the influx of L-Fucose is reduced 30% by phloridzin, a specific inhibitor of sugar transport. These results indicate that although L-Fucose does not fit the structural requirements for transport, it does interfer competitively with sugar transport. The postulated mechanism of sugar transfer involves two steps, a binding and a translocation step. These studies suggest that L-Fucose interacts with the binding step.

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INTESTINAL TRANSPORT OF NAPHTHYL GLUCURONIDE IN VITRO. Jerome C. Pekas. U. S. Department of Agriculture, ARS, Animal Science Research Division, Metabolism and Radiation Research Laboratory, Fargo, N. Dak.

These studies were conducted to investigate whether naphthyl glucuronide could be transferred from the site of synthesis to the mucosal and serosal fluids by diffusion. Everted sacs of small intestine (27 sacs; 9 rats) were incubated in Krebs-Ringer medium, pH 6.5, containing 1-naphthol-1-^{14}C (10^{-5}M) for 120 min. The ^{14}C-constituents in sac homogenates and serosal and mucosal fluids were partitioned. Benzene extracted 2-15% of the ^{14}C label (nonmetabolized naphthol-^{14}C) from homogenized sacs; 55-87% of the ^{14}C was recovered in the aqueous phase; and 2-38% was nonextractable. These values depended on the region of intestine analyzed. The concentration of water-soluble ^{14}C-labeled metabolites in serosal fluid (primarily naphthyl-^{14}C glucuronide) exceeded that in the tissue of the same sac (average, 1.54 times higher). Nearly all, 93%, of the ^{14}C-labeled metabolites in aqueous phases of serosal and mucosal fluids and tissue homogenates was dialyzable. These data indicate that considerable transfer of the aqueous ^{14}C-metabolites could occur by diffusion down a concentration gradient, particularly during the early phases of the incubation when the fluid metabolite concentration was low and the tissue content increasing. Also, S/M concentration ratios greater than one, as observed here and in previous studies, could result from more rapid equilibration of the tissue with the small serosal fluid volume (4 ml) than with the large volume of mucosal fluid (100 ml). However, some mechanism other than diffusion must be considered to explain the higher concentration in serosal fluid than in tissues.

DIURNAL RHYTHM OF SERUM MELATONIN IN CHICKEN: ABOLITION BY PINEALECTOMY. Russell W. Pelham* and Charles L. Ralph. University of Pittsburgh.

There is a large body of evidence suggesting that pineal secretory activity is enhanced in response to periods of darkness. We have recently reported the identification of melatonin in chicken serum (Pelham, et al., 1972, BBRC 46 (3):1236) and now report the results of experiments which further characterize its diurnal fluctuations in blood. Sixty White-Leghorn cockerels were pinealectomized (PX) or sham-operated (S) at 3-4 days of age and maintained under a diurnal photoperiod with lights on from 0700 to 1900 EST until 4 months of age when blood samples were collected by heart puncture. After extraction into chloroform and evaporation in vacuo, the samples were introducted into the Rana pipiens bioassay for melatonin. The results for S animals are expressed as ng of melatonin/ 10 ml of serum ± standard error:

TIME OF DAY					
2400	0400	0800	1200	1600	2000
2.2±0.3	0.45±0.1	0	0	0.29±0.1	1.9±0.2

Melatonin was not detected at any of these times in serum from PX animals, while serum extracts from PX animals did not inhibit the bioassay response from added standards. This indicates a possible diurnal rhythm in secretion (or destruction) of melatonin and a role for the pineal in this rhythm.

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RESPONSES OF RENAL AND HIND-LIMB VESSELS TO THE CAROTID BAROREFLEX AND TO STIMULATION OF MUSCLE RECEPTORS. Conrad L. Pelletier* and John T. Shepherd. Mayo Foundation, Rochester, Minnesota.

In 13 anesthetized dogs, artificially ventilated with oxygen, the vagi were cut and the carotid sinuses (CS) isolated. One hind limb and kidney were perfused at constant flow in 7 dogs and at constant pressure in 6. The effect of maximal changes in carotid baroreceptor input on the hind-limb and renal circulation was studied, as were the responses to stimulation of the muscle receptors by capsaicin injected into the opposite hind limb. During constant flow perfusion, decreasing CS pressure from 250 to 45 mm Hg caused the hind-limb and renal perfusion pressures to increase by 99 ± 10 and 34 ± 4 mm Hg (mean ± SE) respectively. Capsaicin, injected while CS pressure was kept at 45 mm Hg, caused a further increase of only 35 ± 9 mm Hg in the hind limb, as compared to 203 ± 17 mm Hg in the kidney. With constant pressure perfusion of the two beds, the same decrease in CS pressure resulted in blood flow decreases of 80 ± 4% in the hind limb and 19 ± 6% in the kidney. The capsaicin injection caused no further significant change in hind-limb blood flow (4 ± 2%), in contrast with renal blood flow which decreased by an additional 49 ± 9%. Ganglionic blockade abolished the reflex responses to the baroreceptors and to capsaicin, and resulted in hind-limb and renal blood flows averaging 57 and 31% greater than those obtained with maximal CS pressure respectively. Thus, the vasoconstrictor response to withdrawal of baroreceptor input is nearly maximal in the hind limb, whereas in the kidney the reflex constriction can be greatly increased by simultaneous stimulation of the muscle receptors. (Supported by NIH Grant #HL-5883 and the Medical Research Council of Canada).

INFLUENCE OF HYPERCAPNIA UPON ERYTHROPOIESIS. William E. Pepelko, USAF School of Aerospace Medicine, Brooks AFB, Tex.

In earlier studies it was reported that during chronic hypoxia (70 torr P_{IO2}), concomitant hypercapnia (60 torr P_{ICO2}) resulted in a considerable normalization of tissue P_{O2} levels. Despite the near normal tissue O_2 tension, red cell numbers were still considerably elevated. This experiment was designed to determine if red cell production differed in 3 groups of rats having the same tissue P_{O2}'s but different P_{CO2}'s. Subcutaneous gas pocket P_{O2} and P_{CO2} were used as an index of tissue hypoxia or hypercapnia. All rats were exposed for 40 days to an automatically maintained total barometric pressure of 380 torr. Inspired gases, pocket gases and hemopoietic parameters are shown as follows:

P_{IO2} torr	P_{ICO2} torr	Pocket P_{O2} torr Day 4	Pocket P_{CO2} torr Day 4	Reticulocyte % Day 4	HCT Day 40	Circulating Red Cells Day 40
93	0	21.7±3.9*	39.5±3.0	0.80±0.45	44.3±3.1	2.96±0.45
70	30	22.3±1.9	48.7±3.4	3.97±0.75**	56.9±3.4**	4.53±0.59**
60	60	21.7±3.0	73.3±8.1	2.84±0.40**	56.7±3.6**	4.69±0.59**

*Standard deviation. **Significantly different from normocapnic rats ($P < .01$)

Although pocket gas P_{O2} levels did not differ among the three groups, reticulocyte counts, hematocrit and circulating red cell volumes were significantly greater in rats inspiring increased CO_2 levels. If the pocket P_{O2} levels adequately reflect oxygen tensions in tissues controlling red cell production, then CO_2 is a factor of considerable importance in the control of erythropoiesis. In contrast to previously reported work this effect now appears to be stimulatory rather than inhibitory.

OPERANT CONDITIONING OF WENCKEBACH PERIODS IN THE RHESUS MONKEY. Jorge Pérez-Cruet. Dept. of Psychiat. and Behavioral Science, The Johns Hopkins Univ. School of Med., Baltimore, Md.

Previously it has been shown that disorders of conduction in the heart can be conditioned using Pavlovian techniques (J. Pérez-Cruet, Clin. Res., 11:395, 1963 and Clin. Res., 17:582, 1969). The present study was designed to study whether it is also possible to condition EKG changes operantly. A total of 22 rhesus monkeys were studied at different periods for six years (1961-1967). Operant performance was programed under a contingent reinforcement schedule (CRF) based on reinforcements of occasional Wenckebach periods spontaneously occurring in these monkeys. Later the CRF schedule was changed to a fixed ratio schedule (FR) where the Wenckebach periods were also used as the contingent variable. FR 2 and FR 3 were attempted. Reinforcement consisted of an artificial orange juice (Tang) dissolved in a 1:3 solution and delivered automatically by a EKG monitoring equipment immediately after the appearance of a Wenckebach period. Six rhesus monkeys showed operant conditioning of Wenckebach periods by the third day of training. Operant heart rate conditioning in the form of a mild bradycardia was also observed as reported previously (J. Pérez-Cruet and J.V. Brady, 1968). This study shows that disorders of conduction in the heart can be conditioned either operantly or by Pavlovian methods. These findings suggest that the underlying physiological and neurotransmitter mechanisms of these two types of cardiac conditioning may be similar. (This work was supported by NASA grant Nsg 520).

MECHANISM OF REFLEX TACHYCARDIA DURING ACUTE CORONARY OCCLUSION IN THE CONSCIOUS DOG. D. Fred Peterson*, Robert L. Kaspar*, George E. Barnes* and Vernon S. Bishop. The University of Texas Medical School at San Antonio, San Antonio, Texas 78229.

The origin and pathways of reflex tachycardia due to acute occlusion of the left circumflex coronary artery were studied in 7 conscious dogs. All animals had been instrumented under general anesthesia and sterile conditions 3-5 days prior to experimentation. Each dog contained a balloon occluder around the left circumflex artery, two left atrial catheters and a mammary or carotid artery pressure catheter. One minute occlusions produced increases in heart rate between 10 and 61 beats/min. Onset of left atrial pressure rise occurred within 7.5±0.9* sec tachycardia within 8.8±0.8 sec and systemic hypotension within 23.3±1.9 sec. In some animals pulse pressure fell simultaneously as heart rate increased. In these dogs saline or blood infusion into the left atrium maintained pulse pressure while heart rate increased thus eliminating reflex effects from arterial baroreceptors. Reflex pathways were studied using pharmacological blocking agents and by nerve section. Beta receptor blockade with propranolol (1 mg/kg) reduced the maximum heart rate response from 34.6±2.6 to 22.7±3.3 beats/min. The addition of atropine sulfate (0.1 mg/kg) further reduced the response to 6.0±0.6 beats/min. Section of the left ansa subclavia did not alter reflex tachycardia due to coronary occlusion. Section of the right ansa subclavia reduced the response from 33.6±4.0 to 14.6±3.3 beats/min. It was further reduced by atropine sulfate to 2.0±0.6 beats/min. Our results indicate that reflex tachycardia due to acute coronary occlusion occurs after increased pressure in the left atrium and prior to decreased pressure changes affecting arterial baroreceptors. The efferent limb of the reflex has been shown to be in the cardiac sympathetic nerves and the vagus. * Mean ± S.E.M. (Supported by NIH #2 R01-HL12415-04 and AFOSR-71-2074).

THE EFFECTS OF 5% CO_2 ON THE HYPOTHALAMIC SET-POINT FOR SHIVERING IN A CONSCIOUS DOG. J. L. Plewes* and D. B. Jennings, Department of Physiology, Queen's University, Kingston, Ontario.

Hypercapnia has been associated with body cooling and our experiments confirm a fall in hypothalamic temperature (T_H) and a tendency for rectal temperature (T_R) to fall in animals breathing 5% CO_2 over a 2 hour period in an ambient temperature of 20° ± 1°C. During hypercapnia, minute ventilation ($\dot{V}_E$) rose threefold, yet there was no change in oxygen consumption ($\dot{V}_{O_2}$) and therefore probably no change in heat production. Repeated experiments were carried out in a conscious resting dog breathing through a chronic tracheostomy and with thermodes implanted in the anterior hypothalamus by the method of Hammel and Hardy. To determine whether change in T_H might be playing a role in control during the acute exposure to hypercapnia, the fall in T_H previously seen was prevented by artificially keeping T_H constant. In the hypercapnic dog where a fall in T_H was prevented by clamping, rectal temperature decreased below that seen in the hypercapnic dog with falling T_H and significantly below that in a clamped dog breathing air. Additional experiments in which T_H was artificially lowered by perfusion of the thermodes with water revealed that at comparable rectal temperature ranges, the hypothalamic "set-point" for shivering as measured by increase in $\dot{V}_{O_2}$ was decreased by more than 2C° in the hypercapnic dog.

Supported by the Defence Research Board of Canada.

COCHLEAR POTENTIALS FROM FLYING BATS. G. Pollak*, O. W. Henson, Jr.* and A. Novick, Yale Univ., New Haven, Conn. Electrodes were implanted close to the cochlear aqueduct in three Chilonycteris p. parnellii (Gray) and cochlear microphonic (CM) potentials were monitored in bats actively engaged in echolocation. Particular attention was directed to the constant frequency (CF) component of the emitted pulses and echoes. Prior to each experiment the CM audiogram was determined and found to be sharply tuned to a frequency close to the 60 kHz CF component of the pulse. Precise measurement of the CF component of the pulses and echoes revealed the following: 1) in both flying and non-flying bats the CF component of the emitted pulses was, on the average, about 1500 Hz below the tuned peak of the CM audiogram; 2) during flight the CF component of all echoes was Doppler shifted upward into the more sensitive region of the bat's audiogram; 3) frequency variation of the CF component from pulse to pulse was very minor and compensatory changes of the type reported by Schnitzler (Z. vergl. Physiol. 68, 25 (1970)) were not observed; 4) most of the pulses elicited larger CM responses than did the echoes but during certain periods of most flights loud pulses evoked either very small or no CM responses; 5) when the pulse-evoked responses were small the echo-evoked potentials were usually large and were elicited while the pulses were being emitted. This demonstrates that the CF component of the echo can be more favorably received than the pulse even during periods of pulse-echo overlap. Furthermore these results suggest that Chilonycteris possesses a mechanism, in addition to its sharply tuned system, that can selectively attenuate pulse energy without attenuating the echo and this may possibly be of great importance for listening to echoes during periods of overlap. (Supported by AFOSR Grant 72-2201 and PHS Grant NB-7616-09).

EFFECT OF SYMPATHETIC STIMULATION ON REGIONAL BRAIN BLOOD FLOW. J. T. Ponessa,* P. Sandor,* A. G. B. Kovach,* M. P. King,* and E. T. Angelakos. Hahnemann Medical College, Philadelphia, Pennsylvania.

A thermal washout technique has been employed to measure regional brain blood flow. Cats were anesthetized with a chloralose-urethane mixture and bilateral probes were stereotaxically placed in the thalamus or in sites lateral to the hypothalamus. Electrical stimulation of the cervical sympathetic for two minutes caused a reduction in ipsilateral regional blood flow. There was a 15% reduction of flow at the end of stimulation, reaching a maximum fall of 30% three minutes thereafter with return to control flow 10 to 15 minutes following stimulation. These flow changes were substantially diminished following alpha adrenergic blockade with dibenzylene or phentolamine. Microscopic examination of probe placement sites, combined with fluorescence histochemistry for catecholamines indicated that the probes were in regions of the brain where the vasculature had an adrenergic innervation. It is concluded that stimulation of the cervical sympathetic in the cat can cause reductions in blood flow in certain regions of the brain.

ACTIVATION BY ANTIDIURETIC HORMONE OF AN ELECTROGENIC SODIUM PUMP IN THE TOAD BLADDER. H. Pour-Hassani* and S. Klahr. Washington University, St. Louis, Mo. 63110

Exposure of the serosal surface of the isolated and short-circuited toad bladder to a high K^+ (116 mEq/L), low Na^+ (2.5 mEq/L) Ringer's (KR) results in an immediate but transient fall in short-circuit current (SCC) and potential difference (PD). Thereafter, concomitant with a net gain of K^+ by the cells, a portion of which occurs by a ouabain-sensitive component, and a significant expansion of ICF, there is a rise in SCC and PD values to about 60 to 70% of the values observed when both surfaces of the bladder are exposed to conventional Ringer's solution. Under these experimental conditions the transfer of electric charge by the Na pump accounts for the SCC. Addition of ADH markedly alters the pattern described: 1. SCC and PD after an initial fall, rise rapidly to values considerably higher than those without ADH. 2. The stimulation of SCC by ADH is long lasting as compared to the transitory effect observed when both surfaces of the bladder are exposed to regular Ringer's. 3. The entry of K^+ from serosal medium to cell interior is markedly decreased. 4. There is no expansion of ICF throughout the period of observation. 5. Both Na^+ content and intracellular Na^+ concentration are reduced. All these effects of ADH are mimicked by 3',5' cyclic AMP, and all are abolished by ouabain. These results suggest that both ADH and cyclic AMP may activate an electrogenic Na^+ pump.

DIFFERENTIATION OF EPINEPHRINE STORAGE SITES IN CANINE SPECIALIZED CONDUCTION SYSTEM WITH BRETYLIUM. Donald V. Priola, Harold A. Spurgeon and Charles P. Montoya*. Dept. of Physiology, University of New Mexico School of Medicine, Albuquerque, N.M. 87106.

Previous work has suggested that chromaffin tissue may be intimately related anatomically to the specialized conduction system of the heart. It has been shown that bretylium tosylate (BT) has differential effects on neurally-stored catecholamines as opposed to that stored in chromaffin cells. Therefore, BT was administered to dogs in an attempt to localize chromaffin tissue in the heart. In order to eliminate the interference of the intramyocardial sympathetic nerves, the experiments were performed on 15 dogs whose hearts were denervated using the 2-stage technique of Geis et al. Denervation produced norepinephrine (NE) levels of 0.01 mcg/gm in all areas sampled except the SA node where the level was 0.10 mcg/gm. Epinephrine (E) levels decreased to between 0.04 and 0.06 mcg/gm. 9 animals were treated acutely with cumulative doses of BT of 100 mg/kg. In these hearts, NE levels were identical to the untreated animals in all areas. E levels in the muscle of the four chambers were also identical with the untreated groups. However, E levels in the nodes including immediately adjacent myocardium (SA=0.25 and AV=0.19 mcg/gm) and in the major bundle branches (Rt.=0.24 and Lt.=0.08 mcg/gm) were significantly higher than those in similar animals not treated with BT (SA=0.06 and AV=0.04 mcg/gm; Rt.=0.06 and Lt.=0.05 mcg/gm). The data are consistent with the hypothesis that chromaffin cells are intimately related anatomically to the specialized conduction system and remain intact following chronic extrinsic denervation. It is theorized that BT produces its effect on E levels in these areas either by decreasing release or by enhancing uptake.

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TRANSPORT INTERACTION OF GLYCINE AND CEPHALEXIN IN RAT JEJUNUM. John F. Quay. Lilly Research Laboratories, Indianapolis, Indiana

Comparison of the unidirectional permeabilities of excised rat jejunum to cephalexin under short circuit conditions provided evidence for active transport of the antibiotic in this tissue. Further experiments indicated that the path or process was shared with glycine. (The Physiologist 13:287, 1970). In isolated pieces of rat jejunum cephalexin partially inhibits the uptake of ^{14}C-glycine into the fraction of villous water inaccessible to inulin. Cephalexin fails to inhibit the uptake of 3-O-methyl glucose, cycloleucine and sarcosine under the same conditions, indicating that the effect on glycine uptake is not due to tissue toxicity nor to competition for the imino acid carrier nor to competition for the monoamino monocarboxylic acid carrier. The initial rate of uptake of glycine is maximally inhibited by cephalexin at pH 5.0 and is minimally inhibited at pH 8.0, paralleling the amount of cephalexin present in the zwitterionic form. With sarcosine and cycloleucine added to reduce glycine uptake via the carrier for these substances glycylglycine (I) and L-phenylalanylglycine (II) inhibit glycine uptake. Additional reduction of glycine uptake by cephalexin occurs in the presence of (I) but not (II). Thus cephalexin and (II) compete for a tissue site that mediates a portion of the total glycine uptake and the entrance step for the active transport of cephalexin.

PINEAL VASOCONSTRICTION AT DAILY ONSET OF LIGHT: ITS PHYSIOLOGICAL CORRELATES AND CONTROL. W. B. Quay. Department of Zoology, University of California, Berkeley, California.

Studies on 24-hour changes in carbonic anhydrase (CA, carbonate hydro-lyase, EC 4.2.1.1) activities of choroid plexuses, brain regions and pineal glands of adult rats revealed distinct cyclic changes only in the pineal gland. Parallel quantitative microscopic studies on pineal contents of erythrocytes (RBC) show the daily rhythm in CA activity to be accountable largely if not entirely on the basis of the pineal vascular RBC content. The daily cycle in pineal RBC content has as its most sharply timed event a 50% reduction centered about the time (05:00) of daily onset of light (RBC/mm^3 tissue/10^3: pineal cortex and capsule, at 03:00 - 536±34, at 06:00 - 269±36 [$P<0.001$]; pineal medulla at 03:00 - 520±47, at 06:00 - 225±27 [$P<0.001$]). Early experimental investigations on pineal blood content (Quay, W. B., Am. J. Physiol. 195:391, 1958) demonstrated that norepinephrine (NE) inhibits daytime vasodilation within the rat pineal, such as that resulting from ether anesthesia. NE content of rat pineal sympathetic nerves is maximum near the end of the daily dark period and falls thereafter (Wurtman, R. J. and J. Axelrod, Life Sci., 5:665, 1966). A current hypothesis that daily NE release drives the 24-hour biochemical rhythms of the pineal gland may derive support from these results. However, the probable metabolic consequences of the daily vasoconstriction complicate a simple characterization of the intermediate mechanism(s) of the pineal's circadian drive. (Supported in part by USPHS NIH research grant NS-06296 and The Miller Institute for Basic Research in Science, University of California, Berkeley.)

EFFECTS OF HIGH POTASSIUM MEDIA ON RADIOACTIVE LEUCINE INCORPORATION INTO APLYSIA NERVOUS TISSUE. Jeffrey Ram (Intr. by F. Strumwasser). California Institute of Technology, Pasadena, 91109.

To study possible coupling between membrane polarization and protein synthesis, elevated external K^+ levels (K_o^+) were used to depolarize the cell membranes in isolated Aplysia abdominal ganglia. The effect of this treatment on the incorporation of labeled leucine into proteins in the ganglia was analyzed on sodium dodecyl sulfate (SDS) polyacrylamide gels. Ganglia were preincubated 3 hours and incubated 4 hours in either control medium (^{14}C-leucine) or high K_o^+ medium (^{3}H-leucine). An ^{3}H- and a ^{14}C-labeled ganglion were homogenized together in 1 mM PO_4^{3-} buffer and centrifuged; the supernatant was run on SDS gels, which were then sliced and counted. There was a decrease in total leucine incorporation as K_o^+ was increased. At 90-110 mM K_o^+, a relative decrease in incorporation at higher molecular weights occurred, but a relative increase in incorporation appeared in a distinct peak at 50,000 Daltons (50 K). At 90 mM K_o^+, patterns for right connective nerve showed little relative increase at 50 K, suggesting that the 50 K peak might not have its origin in axons, glia, or connective tissue. The aqueous insoluble proteins of the ganglion did not show a significant relative increase at 50 K, showing that the effect did not occur with all 50 K proteins. To check whether the high K_o^+ effect was a post-synthesis effect, ganglia were pre-labeled in normal media and then exposed to high K_o^+. No relative increase occurred in previously labeled 50 K proteins. If further experiments show that the effect on protein synthesis is due to the K^+ induced depolarization, this may provide a model system for studying the coupling of membrane polarization to protein synthesis.

CIRCADIAN RHYTHM OF VENTRICULAR SUSCEPTIBILITY TO ISOPROTERENOL INDUCED HYPERTROPHY E.E. Rau* and D.K. Meyer. Dept. of Physiology, School of Medicine, University of Missouri, Columbia.

It is known that isoproterenol can cause myocardial hypertrophy (Rona, et al. AMA Arch. Path. 67:443, 1959). The objective of this study was to determine whether the time of day at which isoproterenol is administered can affect the degree of resulting hypertrophy. A total of 120 rats averaging 200g in weight were entrained on an alternating light (0600-1800 hrs.)-dark (1800-0600 hrs.) cycle. Experimental rats received isoproterenol (2mg/kg of 0.02% Isuprel) intraperitoneally. Control rats received equivalent volumes of isotonic saline. One group of 10 experimental and 10 control rats was injected at 0000 hrs. and 5 successive groups were treated at 4 hour intervals afterwards (0400,0800,1200,1600 and 2000 hrs.). Each group of 20 animals was treated once daily and for 4 consecutive days. All rats were sacrificed 24 hrs. after the final injection. The degree of ventricular hypertrophy was greatest in rats injected during night hours with an average increase over controls of 40.2mg ventricular weight/100g body weight. The corresponding value for light hours injected rats averaged only 24.3mg/100g body weight. The results support the hypothesis that rat ventricular susceptibility to isoproterenol as a stimulus to hypertrophy varies according to the time of day the isoproterenol is given. (Supported in part by HL05055 and HL05810).

ACID BASE RELATIONSHIPS BETWEEN CSF AND BLOOD DURING COMPENSATED METABOLIC ACIDOSIS. A.K. Razavi*, B. Burns*, D.G. Davies and G.H. Gurtner. The Johns Hopkins University, Baltimore, Maryland 21205.

We have previously shown using the Astrup equilibration technique that steady state differences in Pco_2 and HCO_3^- occur between CSF and venous blood from the brain (internal maxillary vein after ligation of superficial branches) during uncompensated metabolic acidosis (Fed. Proc. 30:1668, 1971; 1971 Aspen Conference, Chest 61:Suppl. 31S-39S, 1972). We have explained the Pco_2 differences by the mechanism proposed by Gurtner, Song and Farhi (Resp. Physiol. 6:173-187, 1969). During pure respiratory alkalosis the Pco_2 and HCO_3 differences do not occur. This can also be explained by the same hypothesis since relatively large blood flow rates are required to maintain the Pco_2 differences. Using standard electrodes we measured the Pco_2 and pH of CSF, internal maxillary (IM) blood and saggital sinus (SS) blood during compensated metabolic acidosis in anesthetized dogs. $PaCO_2$ was maintained at 10-15 mmHg and steady state arterial HCO_3^- values of 7-10 meq/L were achieved after infusion of dilute HCl, PHa was approximately normal. We found in 10 of 12 dogs that $Pco_2(CSF) > Pco_2(SS)$, $\Delta Pco_2(CSF\text{-}SS) = 8.1 \pm 2.5$. In the animals without CO_2 differences the Po_2 and O_2 saturation of saggital sinus blood was low indicating low cerebral blood flow. In 5 of 5 dogs $Pco_2(CSF) > Pco_2(IM)$, $\Delta Pco_2 = 9.1 \pm 1$. When Pco_2 differences occurred, HCO_3^- of CSF was higher than that of blood, similar to the results during uncompensated metabolic acidosis reported previously. It seems that the presence of CO_2 differences is related to arterial H^+ activity rather than arterial Pco_2. This may be mediated through brain blood flow rate. This mechanism may be important in the regulation of CSF H^+ activity (see article in Chest). (Supported in part by PHS Grant HL 13721.)

Changes in Ventilation During Exercise

A.S. Rebuck*, N.L. Jones, and E.J.M. Campbell, Department of Medicine, McMaster University.

Changes in ventilation during progressive exercise were measured in 11 normal usbjects, using stepwise increases in power on a cycle ergometer. Ventilatory response to CO_2 in the same subjects was also recorded at rest, using a rebreathing technique.

The range of ventilatory response to exercise was 16.6 to 32.0 litres/min./litre CO_2 output per minute (mean 22.7; S.D. 5.35). Ventilatory response to CO_2 (S_{CO_2}) ranged from 0.81 to 3.11 litres/min./mm.Hg. P_{CO_2} (mean 1.87; S_{CO_2} S.D. 0.62).

There was a significant ($p < 0.001$) correlation between the changes in response to increasing CO_2 output and S_{CO_2}.

The results are compatible with the suggestion that ventilation during exercise in normal subjects is directly related to their chemosensitivity to CO_2, those having the highest sensitivity showing the greatest exercise ventilation. However, the possibility cannot be excluded that these subjects would breathe more in response to other stimuli as well.

EFFECTS OF PROLONGED 70% O_2 UPON RAT LUNG LIPIDS. R.A. Redding*, T. Arai*, H. Tsurutani*, W.H.J. Douglas*, and M. Stein. Brown University and The Memorial Hospital, Pawtucket, R.I. 02860

Sixty-six respiratory disease free rats divided into four groups were exposed to 70% O_2 for 1, 4, 7 and 10 days and compared with 31 litter mates exposed to room air (R.A.) for equal times. Crude lung surfactant was separated from macrophages and potential serum protein contamination by differential centrifugation. Changes in whole lung and alveolar phospholipids, both qualitative and quantitative, were correlated with slow dynamic compliance and ultrastructural morphology. In the O_2 rats, developing lung oedema was demonstrated by increased fresh/dried lung weight ratio (dried weight remained constant) and an increased quantity of alveolar protein of which 5-10% was associated with lung surfactant. An increased macrophage count was observed on day 10. Concurrently compliance fell progressively (maximum day 7), and the hysteresis loop at half lung volume became wider. Ultrastructurally, the only abnormality seen was an irregular widening of the alveolar capillary basement membrane on day 10. Comparable body weight gains were noted in R.A. and O_2 exposed rats until day 4, thereafter O_2 rats rapidly lost weight. Expressed per gram dried lung tissue, total alveolar lecithin decreased only slightly during the 10 days O_2 exposure, whereas total lung lecithin moderately increased. In the lung tissue and alveoli, lecithin remained highly disaturated throughout the exposure period. These results suggest that the initial mechanical and morphological alterations in lungs of rats exposed to 70% O_2 are not dependent upon lung surfactant alterations. The rising lung tissue/alveolar lecithin ratio may be related to general body weight loss and fat mobilization. (Supported in part by NIH-71-2153 and a Hines Estate Grant)

ISCHEMIA-INDUCED CONTRACTILE DEFECT IN CANINE MYOCARDIUM. Yerradhoddi S. Reddy*, Leigh E. Wyborny*, Arnold Schwartz and Joseph M. Merrill. Div. of Myocardial Biol., Baylor College of Medicine and the Fondren-Brown Cardiovascular Research and Training Center, Methodist Hospital, Veterans Administration Hospital, Houston, Texas.

Superprecipitation (Spt) of control (C) and ischemic (I) native actomyosin (NAM) were studied both in the absence and presence of EGTA. In the absence of EGTA the extent of Spt was similar both in C-NAM and I-NAM. C-NAM was more sensitive to EGTA than I-NAM; inhibition of Spt (in minutes) were 5.08 ± 1.1 and 1.1 ± 0.27 respectively. Spt of reconstituted actomyosin (RAM) made by combining either C or I native tropomyosin (NT) (CNT or INT) with desensitized actomyosin (DAM) or aged NAM, in the presence of EGTA shows same results as their parent NAM from which CNT and INT were isolated. CNT inhibits Spt of NAM in the presence of EGTA. EGTA inhibition of ATPase of C-NAM and I-NAM (%) were 38.6 ± 1.1 and 8.5 ± 3.5 respectively. ATPase of RAM made by combining either CNT or INT with DAM = C-NAM and I-NAM. EGTA inhibited (%) 40 and 12 respectively (2 expts). NAM was isolated from co-homogenates of C and I myocardium; in the presence of EGTA time of onset and completion of Spt and ATPase were 1.5 x I-NAM. Conclusion: Ischemia induces significant changes in native tropomyosin (tropomyosin + troponin); involvement of H^+ ions is suggested.

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CAROTID SINUS - CARDIAC REFLEX IN HYPERTHERMIC DOGS. Emerson A. Reed, Dept. of Physiology & Biophysics, Hahnemann Med. Coll., Phila. Pa.

Mongrel dogs (7) were anesthetized with morphine and chloralose. Pentobarbital was used as a supplement when needed. The external carotid arteries were ligated between the sinuses and the occipital arteries. The internal carotid arteries were ligated distal from the sinuses. The common carotid arteries were cannulated. The two carotid cannulae were connected via a Y tube and a three-way valve to a pressure bottle which contained normal saline under 240 mmHg pressure. The heart rate was monitored by an ECG. The central body temperature was monitored by a thermistor in the esophagus at the level of the heart. Body temperature was raised by circulating warm water through blankets around the dog. Oxygen was insufflated into the trachea at 3 liters/min. The stimulus consisted of the endosinal pressure being raised suddenly by a turn of the valve from atmospheric pressure to 240 mmHg. Pressure was maintained for 15 to 20 heart beats. The response was measured by comparing the average of the first ten R-R intervals after the beginning of the stimulus with the last ten R-R intervals preceeding the stimulus.

Body Temperature Range °C	No. of Runs	Mean Prestim. Control R.R.	Mean Stimulated R.R.	Mean of the R.R. Diff.	Mean of the % Diff.
36.5 - 39.4	45	.48 ± .03	.77 ± .06	.28 ± .006	54 ± 6
39.5 - 43.0	35	.36 ± .02	.46 ± .04	.10 ± .003	23 ± 3
Diff. of Means		.12	.31	.18	31
P		.003	.0002	.0005	.0004

± = S.E. of mean.

EFFECT OF VAGOTOMY WITH PYLOROPLASTY OR ANTRECTOMY ON GASTRIN RELEASE IN DUODENAL ULCER PATIENTS. D.D. Reeder*, H.D. Becker*, C.S. Clark, Jr.* and J.C. Thompson. University of Texas Medical Branch, Galveston, Texas

Vagotomy with pyloroplasty (V+P) and vagotomy with antrectomy (V+A) are the most commonly used operations for the treatment of duodenal ulcer (DU). We have studied the effect of both operations on the serum gastrin response to a meal in 17 DU patients, and have compared this to the average postprandial gastrin response in 10 healthy volunteers. Method: Blood samples were taken for radioimmunoassay of gastrin before and at regular intervals after a high-protein meal. Results: The mean fasting gastrin concentration for the 17 DU patients was 129 ± 11 picograms (pg)/ml which differed significantly from that for 10 control subjects (84 ± 7 pg/ml). After the meal, gastrin rose to a maximum of 122 ± 11 pg/ml in healthy man and to 195 ± 25 pg/ml in DU patients. The 60 min. postprandial integrated gastrin output was 1.78 ± 0.33 nanograms (ng)/ml in the control group and 3.04 ± 0.98 ng/ml in DU patients. V+P (10 patients) resulted in a significant increase of basal gastrin concentration from 130 ± 9 pre-op to 167 ± 14 pg/ml. There was a 52% increase in gastrin in response to the meal pre-op and a 60% increase post-op. After V+A (7 patients) the basal fasting gastrin concentration fell slightly from 128 ± 21 to 109 ± 13 pg/ml. The gastrin response to food was not changed by V+A (49% ↑ pre-op, 52% ↑ post-op). Conclusions: Basal and postprandial gastrin levels in DU patients tend to be higher than controls. V+P caused an increase in basal and postprandial gastrin values; V+A caused no significant change in either, suggesting important extra-antral sources of gastrin.

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EFFECT OF PROSTAGLANDIN E_1 ON FOOD STIMULATED GASTRIN AND GASTRIC SECRETION IN DOGS. D.D. Reeder*, H.D. Becker* and J.C. Thompson. University of Texas Medical Branch, Galveston, Texas

Prostaglandin E_1 (PGE_1) is known to inhibit gastric acid secretion stimulated by food, gastrin, pentagastrin, histamine and 2-deoxyglucose in man and dogs, but the effect of PGE_1 on endogenous gastrin release is unknown. We have studied the effect of intravenous PGE_1 on the serum gastrin response to a meal in five Heidenhain pouch (HP) dogs. Method: Studies were performed on 2 days. In control studies, blood samples for radioimmunoassay of gastrin were taken before and at intervals for 3 hrs. after a meat meal. HP acid output was measured every 30 min. In test studies, the protocol was repeated and, in addition, 15 μg/kg/hr of PGE_1 was infused i.v. during the initial 90 min. after eating. Results: The average basal serum gastrin concentration on the day of the control study was 69 ± 4 picograms (pg)/ml; after the meal, gastrin rose to a peak of 116 ± 8 pg/ml (↑ 65%) at 30 min. On the test day when PGE_1 was given, serum gastrin rose from basal of 86 ± 10 pg/ml to 235 ± 75 at 15 min. (↑ 186%) and to a peak of 562 ± 165 pg/ml (↑ 585%) at 90 min. after the meal. On the control day the Heidenhain pouch output during the first 90 min. after eating was 4.23 mEq. PGE_1 caused a highly significant diminution in this response (1.13 mEq; $p < 0.01$). After the PGE_1 infusion was halted, acid output rose to above control levels. Conclusion: These studies provide direct evidence that PGE_1 potentiates the serum gastrin response to food. The inhibition of acid output after PGE_1 appears to be due to blockage of the action of gastrin on the parietal cell.

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INTRACELLULAR pH OF FROG SKELETAL MUSCLE: TEMPERATURE DEPENDENCE DETERMINED BY CARBON DIOXIDE CONTENT METHOD. Robert Blake Reeves, Dept. of Physiology, St. Univ. of New York at Buffalo, Buffalo, N.Y. 14214

Recognition of the unique role body temperature plays in poikilotherm animals in determining blood pH (pH_B) and pCO_2 has raised the question of how intracellular pH changes with body temperature (T_B). Reeves and Wilson (Fed. Proc. 28:782, 1969) have determined pH_i of frog muscle in vivo using the DMO method, $pH_i^{DMO} = 7.27 - 0.0152\ T_B$. The average $pH_B - pH_i = +0.68$ u. To check these findings by an independent method, the CO_2 content method has been used under similar conditions (Resp. Physiol. 14:219, 1972). CO_2 content of sartorius and gastrocnemius muscles from adapted bullfrogs (T_B 5-28°C) were made on KOH digests by macro Van Slyke determinations. Blood pH and Astrup pCO_2 analyses were also made. A muscle water content of 81.7% and an inulin space of 13.7% independent of T_B were used to calculate intracellular CO_2 content from total muscle C_{CO_2} mM $kg^{-1} = 11.37 + 0.087\ T_B$. Results were $pH_i^{CO_2} = 7.815 - 0.0165\ T_B$, a line nearly parallel to pH_B and pH_i^{DMO}. Although the two techniques yield different values for pH_i ($pH_i^{CO_2} - pH_i^{DMO}$ about 0.5 u), temperature dependence of the relationships are approximately equal. Thus pH_i change with T_B as determined by two techniques is consistent with a constant charge state of protein histidine imidazole groups in accord with the imidazole alphastat hypothesis of acid-base regulation. (Supported in part by ONR Contract N00014-68-A-0216.)

IMBALANCE OF A AND C FIBER ACTIVITY AS THE SOURCE OF PAIN INDUCED BY ICE WATER: A THERMAL ANALYSIS. Kenneth H. Reid, Department of Physiology and Biophysics, University of Louisville School of Medicine, Louisville, Kentucky.

In connection with a student laboratory study of the cold pressor response, 32 medical students reported pain levels every 5 seconds during a 60 second immersion of hand and forearm in a mixture of water and crushed ice. A continuous scale was used, with limits "no pain" and "my pain is as bad as it could possibly be." Variance analysis showed 10 distinguishable pain levels between these limits. Thermal analysis of a simple model of the hand-ice water situation indicated that the temperature in the depth range 0.2 to 2 mm under the skin, where the bulk of the cutaneous nerve ramifications and receptors lie, fell to between 5 and 10^{o} C during the 60 second immersion. Since A fibers are more sensitive to cold than C fibers (Douglas and Malcolm, 1955) it is postulated that the intense pain induced by ice water but not by water at 5^{o} C or above is due to differential blockade of myelinated cutaneous afferent fibers. On the basis of the Melzack-Wall "gate control" theory, such a differential blockade would strongly excite nociceptive pathways, accounting for the paradox of severe pain with minimal tissue damage produced by this stimulus. This experiment can be used to place some quantitative bounds on the signal transformations possible at the "gate".

SODIUM EXCRETION AND THE GLOMERULAR BLOOD FLOW DISTRIBUTION IN THE NEWBORN DOG. J.H. Reuter* and L.I. Kleinman, Dept. of Physiol., Univ. of Cincinnati Col. of Med., Cincinnati, Ohio 45219.

The ability of the newborn animal to respond to an IV saline load was studied in 28 mongrel puppies aged 1 to 30 days. Following a control clearance period, a priming dose of .9% saline was infused at a rate of 2.0 ml/min/kg for 15 min followed by a rate of .5 ml/min/kg until the termination of the experiment. Glomerular blood flow distribution was determined by radioactive microspheres (15 ± 5 μ). The mean C_{Na}/C_{In} during the control period, .002, was not significantly different from that for the adult ($p > .50$). Following the saline infusion, puppies demonstrated large variations in C_{Na}/C_{In} and Na excreted/Na infused (Na_e/Na_i) with means of .025 and .105 respectively, values substantially lower than that for adults, .063 and .322. There was no correlation between Δ C_{Na}/C_{In} (Δ = experimental-control) or Na_e/Na_i and age during the first month of life. Following saline infusion in the puppy, there was an increase in outer cortical glomerular blood flow (OC) relative to inner cortical flow (IC) i.e., the IC/OC ratio decreased ($p < .001$). However, the magnitude of the individual Δ C_{Na}/C_{In} did not correlate with the magnitude of the Δ IC/OC. Arterial blood pressure (BP) increased following the saline infusion ($p < .01$). There was a correlation between the magnitude of the individual $\Delta C_{Na}/C_{In}$ and Δ BP ($p < .01$). In conclusion, the newborn puppy is not able to increase C_{Na}/C_{In} following a saline infusion, to the same extent as the adult, resulting in a lower Na_e/Na_i. The decrease in IC/OC ratio, alone, does not appear to be a major physiological mechanism for increased sodium excretion in the puppy.

QUANTITATION OF HYPOCAPNIC INHIBITION IN ACUTE HYPOXIA. W.J. Reynolds* and H.T. Milhorn, Jr. Univ. of Miss. Med. Ctr., Jackson, Miss. 39216

The degree of inhibition of ventilation due to hypocapnia during acute hypoxia was quantitated by measuring the dynamic response of ten normal male subjects to step inputs of 9,8, and 7% oxygen, allowing the alveolar P_{CO_2} to fall during one series, and maintaining it at its basal level in another. In the isocapnic series the P_{CO_2} was controlled by a rapidly responding external control system (capnostat) which maintained isocapnia during both steady-state and transient conditions. Breath-by-breath calculations of tidal volume, respiratory frequency, minute ventilation, and alveolar P_{O_2} and P_{CO_2} were performed by using an off-line digital computer and the responses of each variable under both hypocapnic and isocapnic conditions compared. Small overshoots in the ventilation on-transient were observed in approximately half of the subjects during the hypocapnic experiments but were not present at all in the isocapnic series. Small undershoots in the ventilation off-transient were observed in both experimental series, in each case resulting from an undershoot in the frequency off-transient. The half-times for the ventilation and P_{O_2} on-transients were approximately equal in the hypocapnic series, but the ventilation increase lagged behind the decrease in P_{O_2} in the isocapnic series. The steady-state values for ventilation at the end of the ten-minute stimulus period were 9.5, 12.3, and 14.9 l/min. for the stimuli of 9,8, and 7% oxygen respectively and increased to 13.8, 19.9, and 27.9 l/min. respectively when the alveolar P_{CO_2} was held at its prestimulus resting level by the capnostat. (Supported in part by NIH Grant HE 11678.)

NET UPTAKE OF GLYCEROL BY ISOLATED PERFUSED RAT LUNG. R.A. Rhoades* and E. R. Buskirk. The Pennsylvania State University, University Park, Pa. 16802

Surfactant synthesis and energy transformation in the lung depend upon uptake of circulating substrates. Lung slices incubated with glycerol-^{14}C have shown oxidation of glycerol to CO_2 and incorporation into lipids. Such studies provide information about substrate flux but not about net uptake derived from a-v difference. The net uptake of glycerol by isolated perfused lungs from fed and fasted (72 hrs.) rats was examined. Isolated lungs were perfused with washed bovine red blood cells diluted with Krebs Ringer bicarbonate containing 4% bovine serum albumin, and 6 mM glucose, 2 mM palmitate, and 0.2 mM glycerol. The lungs were ventilated at 120 ml/min with a 95% O_2 - 5% CO_2 gas mixture. A correction was made for substrate uptake by the medium. Pulmonary blood flow was 7 ml/min and the perfusion pressure was 5 mmHg. Increase in lung weight following perfusion was less than 5%. The isolated perfused lung retained its capacity for glucose uptake (139 μ moles/hr/g dry wt.) with approximately 40% converted to lactic acid. There was no significant difference between initial and final concentrations of glycerol from perfused lungs of fed or fasted animals indicating no net uptake of glycerol. It was concluded that glycerol does not serve as a physiologic substrate in the lung and the relative contribution of glycerol to lung metabolism is of minor importance.

EFFECT OF MASS ON HUMAN TREMOR FREQUENCY WITH CONSTANT LIMB POSITION. R.R. Rietz and R.N. Stiles (intr. by J.M. Ginski). University of Tennessee, Medical Units, Memphis, Tennessee

The behavior of a muscle-load system, with certain restrictions, can be described by a linear, lumped-parameter, second-order model (Stiles and Randall, 1967, J. Appl. Physiol. 23:324; Stiles and Alexander, 1972, Math. Biosciences, In Press). A major assumption of this model is that active muscle force is generated either in part or entirely by an increase of the elastic coefficient, K_m, of muscle. Previous work indicates that the frequency of human limb tremor is partially determined by an equivalent elastic coefficient, K_e, which is in turn partially determined by K_m. The present study was performed to determine if an increased muscle force equal to an increased weight of an unsupported limb was accompanied by a proportional increase in the value of K_e. A second-order model predicts that an increase in K_e proportional to the added weight, mg, would result in a constant tremor frequency. With certain assumptions, such a proportional increase in K_e could be equated to a proportional increase in K_m. Tremor frequencies were determined for a constant mean limb position and variable limb weights for three different muscle-limb systems of human subjects. The results show a statistically significant decrease in tremor frequency with added weight for all three systems. It is proposed that the deviations from the predicted results can be accounted for in part by the geometry as well as the distribution of muscles of these systems. (Supported in part by USPHS Grant NB-08692).

SELECTED ENZYME ACTIVITIES IN RATS IN RELATION TO A FEEDING REGIMEN. John S. Rinehart and R.R. Nielson . Department of Zoology, Miami University, Oxford, Ohio 45056.

Organisms exhibit cycling for many experimental variables. One type of experimental variable which has demonstrated cycling is the enzymatic activity of certain enzymes from rats which have been maintained with a feeding regimen. The regimen allows for 5 hours of feeding in every 24-hour period with the 5 hours occuring at the same time each day. Using a homogenate technique and assaying manometrically, it was found that succinic dehydrogenase exhibits cycling for liver tissue and psoas muscle but not for cardiac muscle. Using a homogenate technique and assaying spectrophotometrically, it was found that phosphofructokinase did not exhibit cycling for any tissue assayed; whereas lactic dehydrogenase exhibited cycling for liver tissue and alpha-1,4-glucanphosphorylase exhibited cycling for all 3 tissues assayed(liver, psoas muscle, and cardiac muscle). For all cases of cycling in liver tissue, the lowest values were observed at 6 hours after feeding. For SDH the highest value was observed at 21 hours after feeding; however, for LDH and phosphorylase the highest value was observed at 18 hours after feeding. A second study extended the feeding cycle to 36 hours but still retained the 5-hour feeding period. Assaying for SDH activity in liver tissue, it was observed that the lowest activity occurred at 6 hours after feeding and the highest value occurred at 30 hours after feeding. From the above experiments it would seem that the cycling found for certain liver enzymes in rats is related to the feeding regimen.

DAILY FOOD INTAKE AND GROWTH OF INFANT RHESUS MONKEYS. A.J.Riopelle, Margaret L. Kelly*, Doris R. Salter* and James L. Faure*. Louisiana State Univ., Baton Rouge, and Delta Regional Primate Research Center, Covington, Louisiana.

The typical rhesus infant in our laboratory weighs about 476 gm at birth. Over the next few days it loses about 45 gm, regaining its birth weight two weeks later, after a period of stable weight. Daily intake of simulated human milk at recommended concentration rises from about 225 ml/kgm to about 400 ml/kgm by 10 days of age and to a plateau at about 440 ml/kgm between days 15 and 30, after which it declines to about 330 ml/kgm at day 100 if the infants are hand-fed 7 times per day between 8 AM and 10 PM and if body weights are taken just before the morning meal. Reductions in feeding to 4 per day after 30 days and to 3 per day after 50 days of age result in minor transient reductions in intake. The first meal after the overnight fast tends to be larger than the one following it, but there is no rise in intake preceding the night fast. Large day-to-day and within-day fluctuations occur in total intake. For example, a 70-day-old monkey weighing about 680 gm gains daily about 101 grams, or 15% of its morning weight. It also loses about 93 grams, or 12% of its nighttime weight. Since food consumption is frequently reported in relation to body weight, interlaboratory or interexperimental differences in both weighing and feeding schedules may make interexperiment comparisons and the establishment of "norms" difficult. Supported in part by grants HD05340 and RR0164 from the National Institutes of Health.

LEFT ATRIAL CONTRIBUTION TO LEFT VENTRICULAR END-DIASTOLIC AND EJECTION VOLUMES. E. L. Ritman*, R. E. Sturm*, and E. H. Wood, Department of Physiology, Mayo Graduate School of Medicine, Rochester, Minnesota 55901.

Left ventricular roentgen angiograms were performed in dogs (~ 12 kg) with chronic atrioventricular conduction block. Roentgen contrast medium (1 ml 69% renovist/kg body weight) was injected into the left atrium via transseptal catheter so as to reduce the direct mechanical effect of the injection on the ventricular volume. Right atrial and right ventricular bipolar electrode catheters and electronically coupled pacemakers were used to control the atrial and ventricular contraction frequency and atrioventricular stimulation interval. A gating circuit coupled to the volume displacement potentiometer of the injection syringe provided the capability of omitting a single atrial or ventricular stimulus during the period of maximum opacification of the ventricular cavity. The videotaped angiograms recorded with and without single dropped atrial or ventricular beats at heart rates ranging from 60 to 180 beats per minute were analyzed by an operator interactive real-time videometric system (Fed Proc 29:719, 1970) which provided simultaneous 60-per-second measurements of pressures, ECG, ventricular volume and shape. Comparison of the isolated heart cycles without an atrial systole with the immediately preceding normal cycles showed the expected decrease in end-diastolic filling of the ventricle and stroke volume. These effects increase relative to the stroke volume with increased heart rate. At 160 beats per minute, omission of an atrial stimulus resulted in the following end-diastolic volume being about 3 ml less than the predicted volume (30% of stroke volume) whereas the corresponding decrease was only about 2 ml at 70 beats per minute (10% of stroke volume). Since this effect occurs within a period of less than 0.3 second, it is believed to be a mechanical consequence of the omitted atrial beat. (Supported in part by grants NIH HE4664, HE3532, FR-7, AHA CI 10, NASA, and Minnesota Heart Assn.)

THE EFFECTS OF PRELOAD ALTERATIONS ON IN SITU CONTRACTILE FORCE MEASUREMENTS RECORDED BY THE WALTON-BRODIE STRAIN GAUGE ARCH.
Robie, N.W.*, Newman, W.H.* and Woods, E.F. Department of Pharmacology, Medical University of South Carolina, Charleston, S.C.

Strain gauge arches have been used in over 800 published investigations to determine myocardial contractility. Definitive studies of the influence of alterations in preload on these measurements have not been performed. Therefore, the following investigations were undertaken. In the open-chest dog preparation preload was increased incrementally by three infusions of a blood volume expander, each infusion equal to 1% of the animals body weight. Measurements of left ventricular contractile force (CF) were made with Walton-Brodie arches perpendicular ($\perp$CF) and parallel (//CF) to the anterior descending coronary artery. Changes in preload were determined by measurements of diastolic mural force (ΔDMF) recorded with a Hefner arch sutured to the ventricle. The $\perp$CF and //CF were corrolated with ΔDMF. Results indicated that $\perp$CF declined in a consistant and predictable manner that could be described by the equation $\% \perp CF = 99.9 - 1.13 (\Delta DMF)$. //CF declined in a similar manner, but appeared to be influenced by pressure also. It was determined that these findings could not be explained on the basis of a Frank-Starling effect, but probably were due to changes in ventricular size which were manifested in the form of force vectors in the wall of the ventricle tending to pull the feet of the arch apart, thereby reducing the total contractile tension sensed by the arch. Supported by NIH HL-12574 and HE 5972.

VISCOSITY OF PACKED RED CELLS. Arthur L. Rosen, Ph.D.*, LaVergne Malone, M.S.* and David M. Long, M.D., Ph.D. Division of Cardiovascular and Thoracic Surgery, University of Illinois Hospital, Chicago, Illinois.

We have studied flow properties of blood, particularly in terms of the changes that occur in injury or sickness. A valuable addition to measurements on whole blood, plasma, and serum is the packed cell preparation, both with and without the buffy coat. A rotational viscometer using cone-in-cone geometry was employed. It has a quartz fiber suspension, and generates a uniform rate-of-shear field within the fluid gap. Shear rates ranged from 0.03 to 158 inverse seconds. All measurements were performed at 37°C. Dextran polymers of mean molecular weights 40,000 (D-40), 70,000 (D-70), and 500,000 (D-500) were evaluated for their extra-vivum properties. These effects were analyzed via matched packed cell samples. Determinations were performed on a group of 19 control subjects, 34 patients with blunt trauma, and 43 patients with significant penetrating trauma. All flow curves for packed cells departed from the linear homogeneous model of a Newtonian fluid. The apparent viscosities markedly increased at the lower shear rates. No attempts were made to estimate stress at zero shear. For control subjects, D-40 and D-70 produced no significant alterations in viscosity. D-500 produced significant increases, particularly at lower shears. D-40 exhibited no significant effects on packed cell viscosities for the blunt trauma and penetrating trauma groups. Packed cell viscosities increased at high shear rates for both varieties of trauma with the addition of D-70. D-500 produced marked increases in packed cell viscosities at all shear rates for both trauma groups.

HEMODYNAMICS OF HYPERACUTE REJECTION. J. C. Rosenberg. Wayne State University, Detroit, Michigan.

Hyperacute rejection occurs when organs are transplanted to presensitized recipients. Preformed antibody causes immediate destruction of the transplants. This form of immunologic injury appears to be mediated by a vascular lesion which results in a striking reduction in blood flow. Since dogs harbor a naturally occuring antibody, against porcine tissues, the pig to dog transplant constitutes a convenient experimental preparation for the study of hyperacute rejection. The hemodynamic changes were studied in a series of 14 pig to dog kidney grafts in order to determine how antigen-antibody reactions produce immediate destruction of transplants. Mean arterial pressure remained stable at 143 $\pm$ 4 mm Hg. Renal blood flow fell at an exponential rate. One minute after revascularization the mean blood flow was 110 $\pm$ 7 ml/min. At four minutes it was 24 $\pm$ 3 ml/min. At four minutes it was 24 $\pm$ 3 ml/min and at eight minutes it was 5 $\pm$ 1 ml/min. Vascular resistance increased to drastic levels. At four minutes mean resistance was 563,200 $\pm$ 71,400 dyne-sec/cm^5. Interstitial pressure remained stable at a mean of 16 + 4 mm Hg. Organ weights before and after hyperacute rejection increased 3%. Arteriograms showed obstruction of the interlobular branches of the renal artery. These hemodynamic data indicate that the pathophysiologic basis of hyperacute rejection of pig-to-dog xenografts is a rapidly progressing occlusion of the arterial side of the capillary bed. Pathologic evaluation of the rejected organ and hematologic studies of the venous effluent suggest that platelet-leukocyte plugs are responsible for the increased resistance to flow.

RESPIRATION OF SKIN SLICES FROM ISCHEMIC HUMAN LIMBS. T. Rosett*, R. Penneys, J. S. Sierocki*, and D. J. Pappajohn*. Dept. of Biochem., Temple Univ. School of Dent.; P. V. Sects., Phila. Gen. (Div. of Cardiology), and Hahnemann Hosps. (Dept. of Med.), Philadelphia, Pa.

The purpose of this study is to determine if chronically ischemic skin, shown in previous experiments to have a very low oxygen tension in vivo, can respire actively, in vitro. Such skin was obtained from the distal portion of five amputated ischemic legs. Slices of skin containing all of the epidermis were removed with a safety razor (J. Invest. Derm. 39: 395, 1962), and placed in a standard Warburg respirometer; the oxygen uptake was measured for three hours. Control skin samples, for comparison, were taken from the most proximal portion of the severed limb, where the tissues are known to be less ischemic. Microscopic sections showed approximately equal amounts of epidermal cells to be present in the various skin slices. Oxygen uptake of all samples of distal skin was at least as great as that of the proximal skin, averaging 1.8 (1.5 to 2.0) microliters/gram of wet weight/minute. Chronically ischemic skin is thus still capable of active respiration. This finding warrants further investigation of the metabolic behavior of ischemic skin.

EARLY CHANGES IN KIDNEY FUNCTION AFTER THE INTRAVENOUS INFUSION OF ADH AND ANGIOTENSIN II IN SHEEP. Mario Ruiz* and Harold R. Parker. Dept. of Physiological Sciences, University of California, Davis, California.

Intravenous arginine vasopressin (ADH) at 0.5 milliunits/kg/min. in ewes mildly diuresed with constant infusion of 5% glucose induced a near threefold increase in C_{PAH}. A simultaneous decrease in C_{cr} as well as natriuresis and kaliuresis further characterized these infusions. This dose of ADH was sub-pressor in most sheep. Infusions of 0.06 γ/kg/min. angiotensin II reduced both C_{PAH} and C_{cr}, but usually did not change blood pressure. Natriuresis and kaliuresis was induced as with ADH. Increased C_{PAH} and decreased C_{cr} were again induced by simultaneous infusion of ADH and angiotensin II. Na^+ and K^+ excretion rates were no greater than when either of the hormones was acting separately. The two hormones had a slight additive effect on blood pressure. Pretreatment for 5 days with DOCA (0.2 mg/kg/day) lessened the extent to which C_{PAH} increased and C_{cr} decreased after infusion of ADH. The steroid had an effect on blood flow response to angiotensin causing a twofold increase in C_{PAH} while C_{cr} decreased slightly. DOCA augmented natriuretic and kaliuretic response to ADH and decreased excretion rate of these cations following angiotensin infusion. Excretion of Na^+ and K^+ in response to simultaneous infusion of the two hormones was no different than before DOCA administration, but their pressor effect was slightly ameliorated. Increased C_{PAH} and reduced C_{cr} suggested lessened efferent glomerular resistance following ADH. Lowered C_{PAH} and C_{cr} indicated afferent vasoconstriction following angiotensin. DOCA appeared to alter activity of these hormones, limiting vasodilation by ADH and lessening glomerular resistance after angiotensin. Natriuresis and kaliuresis suggested tubular effects by the hormones as well as alterations of blood flow through the vasa recta.

LOCALIZATION OF THORACIC RECEPTORS ESSENTIAL FOR THE ABDOMINAL EXPIRATORY REFLEX IN CAT. James A. Russell* and Beverly Bishop, Department of Physiology, State University of New York at Buffalo, Buffalo, New York 14214.

Maintained inflation of the lung evokes an abdominal expiratory reflex in anesthetized cats only if the vagal nerves are intact, indicating the importance of vagal receptors. To determine the location of these receptors the thoracic vagi were serially sectioned at three levels in 17 Dial-anesthetized cats. After chest closure and reinstatement of spontaneous respiration, the response patterns of the abdominal muscles, diaphragm and heart rate before, during, and after maintained lung inflation were compared to those before denervation. Vagotomy below the root of the lung did not alter these responses. Denervation at the root of the lung abolished the abdominal expiratory reflex and the Hering-Breuer inflation reflex of the diaphragm without altering heart rate responses. Denervation of the heart and great vessels did not interfere with the abdominal or diaphragm reflexes, but did abolish heart rate responses. It is concluded that pulmonary receptors are essential for the abdominal expiratory reflex, but those in the abdomen, esophagus, upper trachea, heart, and great vessels are not. (Supported in part by USPHS Training Grant No. 5 T01 GM00341.)

ENZYMATIC ADAPTATIONS FOR ENERGY PRODUCTION DURING SEPSIS
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Proteolysis, lactacidemia, and high cardiac output are commonly present during severe infection. In order to evaluate the status of energy production during this period we have measured the activity of pyruvate dehydrogenase (PDH) in liver and muscle of normal and cecally ligated rats. PDH catalyses an irreversible oxidative decarboxylation of pyruvate to yield acetyl-CoA. In diaphragm PDH activity is decreased from a fed value of 12.72± 1.55* (n=15) to 6.55± 1.04 (n=15) during fasting and to 3.97 ± 0.51 (n=14) in septic starved rats. Simultaneously, liver PDH increases from a fed value of 2.56 ± 0.31 (n=15) to 3.18± 0.38 (n=14) and 3.84± 0.47 (n=14) in starved and septic-starved groups, respectively. The gluconegenic enzyme, phosphoenolpyruvate carboxykinase, is also elevated in the livers of septic rats relative to both starved and fed controls (fed:57. 8± 8.2*; fasted:107. 9 ± 7.6; septic fasted: 147. 8± 9.1; n=10, 10, 16 resp.). Considered with the increased level of circulating lactate, these data suggest a decreased peripheral oxidation of pyruvate and a concurrently increased peripheral conversion of pyruvate to lactate, coupled with an accelerated hepatic pyruvate utilization. This enhanced Cori cycle activity could perhaps be necessary to sustain tissues hypoperfused as a consequence of vascular shunting such as is postulated in the literature to be responsible for the high cardiac output of sepsis.

*micromoles / min / gram protein

COMPARATIVE EVALUATION OF LIVER CIRCULATORY AND PLASMA OPSONIC ALTERATIONS AS THE BASIS FOR RETICULOENDOTHELIAL FAILURE FOLLOWING SURGICAL TRAUMA. Thomas M. Saba and William A. Scovill*. Depts. of Physiology and Surgery, Univ. of Ill. Col. of Med., Chicago, Ill. 60612.

The involvement of the reticuloendothelial system (RES) in systemic host defense has been clearly demonstrated. In the present investigation, the phagocytic activity of the RES was evaluated both during and following surgery (right hemicolectomy) relative to the circulating plasma opsonic activity and hepatic blood flow. Mongrel dogs (13-18 kg) anesthetized with pentobarbital intravenously (30 mg/kg) were used. R.E. function was evaluated by the clearance of the gelatinized ^{131}I "RE test lipid emulsion", and plasma opsonic activity was determined by in vitro bioassay. In contrast to normal RE function by 1 hr, a significant ($p<0.05$) depression in phagocytic activity was present at 2, 3 and 4 hr following the initial incision. In this regard, the phagocytic index K was 0.063 ± 0.004 prior to surgery and 0.033 ± 0.006 at the 3 hr point of maximum depression. Hepatic sinusoidal blood flow measured with a tracer technique prior to surgery was 539.2 ml/min., and 0.96 ml/min/g of liver. No alteration in liver blood flow occurred throughout the experimental period. In contrast to the circulatory stability, plasma opsonic activity was decreased significantly ($p<.01$) during the periods of RE depression. While RE failure was related to an opsonin deficit, the intravenous injection of opsonized test colloids during the period of maximal RE depression was reflected in a normal clearance. These findings demonstrate a significant host defense failure during and following surgical trauma mediated by a deficiency of circulating plasma opsonin activity, and not by hepatic circulatory alterations. (USPHS-AM-14382).

HISTOCHEMICAL AND NEUROPHYSIOLOGICAL CORRELATIONS OF PRIMATE LARYNGEAL MUSCLES. V. SAHGAL* AND M. H. HAST. NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO, ILLINOIS.

The intrinsic laryngeal muscles of adult anesthetized rhesus monkeys were removed by microsurgical technique. The muscle tissue obtained was quickly frozen in isopentane and liquid nitrogen. Serial but not contiguous 10-12 μ sections were cut in a cryostat and studied for the following histochemical reactions: ATPase with and without acid preincubation at pH 4.2, NADH, LDH, SDH, and PAS. Routine ATPase reaction studies showed that the abductor muscle, posterior cricoarytenoid, exhibited 68% by count Type II and 32% Type I fibers with a high content of oxidative enzymes. The tensor muscle of the vocal folds, cricothyroid, showed a predominance of Type II fibers (98%) which also gave a uniformly strong reaction for the oxidative enzymes. The thyroarytenoid muscle contained 80% Type II and 20% Type I fibers; this latter muscle showed a typical checkerboard pattern of oxidative enzymes. The lateral cricoarytenoid and interarytenoid muscles were almost exclusively composed of Type II fibers. In addition, some fibers were observed which showed both acid labile and acid stable ATPase characteristics. In mammalian muscles, the speed of contraction has been shown to correlate with the amount and the nature of myosin ATPase (Guth & Samaha: Expr. Neurol., 25:138, 1969). The pattern of multimotor end plate fibers, histochemical profile and characteristic mechanical properties of the laryngeal muscles indicate a system of singly or multiaxonally innervated muscle fibers. (Supported in part by S.R.S. Grant 16-P-56809-5-04 and N.I.H. Grant NS 08728-04.)

TIME COURSE OF HORMONE-INDUCED CHANGES IN INTRACELLULAR CYCLIC AMP IN THE TOAD URINARY BLADDER.

Victor S. Sapirstein and Walter N. Scott, Depts. of Physiology & Ophthalmology, Mt. Sinai School of Medicine of the CUNY, New York, N.Y.

Oxytocin stimulate both hydro-osmotic and sodium flux across the toad urinary bladder, presumably by increasing the intracellular levels of cyclic AMP (cAMP). We have found that oxytocin causes a brief, concentration-dependent, increase in intracellular cAMP, followed immediately by a constant rate of decay of cAMP towards basal levels. In response to 1×10^{-8}M oxytocin a peak cAMP level was attained after approximately 5.0 min. The onset of the physiological response (in these experiments sodium short circuit current was continuously monitored) corresponded to the doubling of the basal cAMP level, which for 1×10^{-8}M oxytocin was approximately 3.3 min. We found that regardless of hormonal concentration the cAMP levels increased for a constant time period after the basal level had been doubled. Higher hormone concentrations required less time to double the basal level and therefore peak levels were observed at a shorter time period. The higher levels of cAMP in the tissue resulting from increasing hormone concentrations is therefore a result of a greater rate of increase in cAMP over a fixed period of time rather than a greater time over which the hormone is effective. The doubling of a basal level of cAMP was further investigated and found to correspond to a threshold, in that concentrations of oxytocin that were insufficient to raise the cAMP to this level did not evoke a significant change in sodium flux.

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ORIGIN OF VASCULAR INTERFACE POTENTIALS: RELATIONSHIP TO THROMBOSIS,THE CHANGES PRODUCED BY INJURY AND PHARMACOLOGIC AGENTS; P.N.Sawyer,S.Srinivasan,T.Lucas,B.Stanczewski,Electrochemical & Biophysical Laboratories of Vascular Surgical Services of Department of Surgery & Surgical Research, Downstate Medical Center, Brooklyn, New York

The measurement of a negative surface charge on the vascular interface was first documented in 1951. Succeeding experiments revealed that the origin of this bioelectric potential possesses various components, the largest contribution being that of the electrokinetic phenomenon at the blood-blood vessel wall interface. Sawyer et al have indicated that the linear streaming potential produced by the hemostatic pressure difference during blood flow is of major importance in maintaining a negative vascular potential. The experiment was designed to detect alterations in the streaming potential following (1) injury(comparable to atherogenesis);(2) administration of heparin (following injury) & its antagonist protamine. The experiment has been carried out with various mammalian species; in arteries & veins, in vitro & in vivo. The results indicate that injury causes a reduction in the normal negative surface charge of the vascular wall, as indicated by a reduction in the streaming potential. In several cases the vascular wall became positive, which is conducive to platelet adhesion & thrombosis. The administration of heparin following injury returned the surface charge to normal & sometimes more negative. Protamine on the other hand, made the vascular interface positive. Scanning electron microscopy of the vascular intima, indicated that the normal vascular endothelium folds were destroyed exposing traumatized collagen leading to visible platelet adhesion & thrombosis. The need for a more comprehensive physical chemical understanding of the etiology of vascular thrombosis is evident. In addition, the role of intermediary enzymatic metabolism in generation of bioelectric potentials & their relationship to thrombosis is not yet clear.

EFFECT OF OUABAIN ON RESPIRATION OF LIVER SLICES IN HEMORRHAGIC SHOCK. M.M. Sayeed, A.E. Baue, G. Perry*, R. Schieber*, G.J. Planer*, I.H. Chaudry* and M.A. Wurth. Washington University School of Medicine and The Jewish Hospital of St. Louis, Missouri 63110.

In liver slices, the rate of respiration is reduced when active transport of Na and K is inhibited by the cardiac glycoside ouabain. The ouabain sensitive portion of respiration has been considered to represent the energy required for the transport processes. We have previously measured a decrease in Na-K transport in shock and have investigated now the ouabain sensitivity of respiration in late shock. Albino rats were bled through a femoral artery cannula to 40 mm Hg and hypotension maintained until 70% of the shed blood had to be returned to maintain this pressure. Livers from unbled control and shock animals were sliced at a thickness of 0.5 mm and their respiration measured polarographically in an oxygenated Krebs Ringer-bicarbonate medium with or without ouabain. Oxygen consumption [μliter O_2(mg dry tissue x 10 min)] in control and late shock animals, respectively, was: 1.01±.04 (Mean ± SEM) and .50±.07. The presence of 1 mM ouabain decreased the control value to 0.80±.09 but did not affect respiration in liver slices from the shock animals. These results indicate that the ouabain inhibitable portion of tissue respiration was absent in liver slices from the animals in shock. The decrease in respiration with shock was greater than the respiration found to be required for cation transport in control animals. It seems likely that part of the decrease in respiration in tissues in shock is due to the decrease in cation transport but the altered intracellular ionic milieu in late shock could also have affected cellular respiration. (Supported by USPH, NIH Grant HE-12278 and U.S. Army Contract DADA-17-69-C-9165.)

CARDIAC EFFECTS OF HYPOXIC HYPOXIA AND CARBON MONOXIDE INDUCED HYPOXIA. Steven M. Scharf* and Baruch Bromberger-Barnea. The Johns Hopkins University, Baltimore, Maryland 21205.

In isolated perfused dog hearts, arterial oxygen content (CaO_2) was reduced by either reducing inspired PO_2, or by administering carbon monoxide (CO) to the donor dog. The effects of these two types of hypoxia on coronary flow, coronary venous O_2 content, oxygen consumption, and contractility were compared at constant perfusion pressure. Coronary flow increased, and coronary venous O_2 content (CvO_2) decreased in both cases. At moderate reductions in CaO_2 (10-15 vol%), flow increased approximately 55% and CvO_2 decreased from 14.0 vol% to 10.5 vol% in both hypoxic hypoxia, and CO hypoxia (O_2 extraction ratio = CaO_2-CvO_2/CaO_2 = .29 to .31). At severe reductions in CaO_2 (5 vol%), coronary flow was approximately doubled with hypoxic hypoxia, and with CO was 15-40% more than that with hypoxia; CvO_2 decreased to 2.2 ± .4 vol% with hypoxic hypoxia (O_2 extraction = .60), but only decreased to 3.7 ± .2 vol% with CO (O_2 extraction = .35). Oxygen consumption ($\dot{V}O_2$) increased as CaO_2 was reduced down to 10 vol% (77% increase with hypoxia; 16.5% increase with CO) and then decreased to values still slightly higher than control at 5 vol% CaO_2. Contractility, as measured by per cent change in dp/dt of a strain gauge arch, increased 30-35% with CO at both moderate and severe CaO_2 reduction. With hypoxic hypoxia at moderate CaO_2 reductions the increase was 11-18%, and at severe CaO_2 reductions the increase was 91%. Factors explaining the results may include: flow related changes in contractility, greater sympatho-adrenal stimulation with hypoxic hypoxia than with CO at severe hypoxia, and decreased O_2 extraction due to possible interference by CO with myoglobin facilitated O_2 diffusion.

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SYNTHESIS OF CORONARY HEMODYNAMICS FOLLOWING CORONARY OCCLUSION. Konrad W. Scheel*, H. Granger*, and D. A. Brody. The University of Mississippi Medical Center, Jackson, Miss., and The University of Tennessee Medical Units, Memphis, Tenn.

The magnitude and time-course of coronary collateral development following a gradual occlusion of one of the left coronary arteries of dogs was investigated. Contributions of collaterals from the two unoccluded to the occluded vessels were quantitatively determined. It was also noted that the peripheral resistance distal to the occlusion increased with time (probably due to changes of the vascular resistance following myocardial ischemia), while the peripheral resistance of the unoccluded vessel decreased with time. Since the magnitudes and time-courses of a) the gradual occlusion, b) collateral development, c) changes in peripheral resistance were known, these parameters could be incorporated into a computer program for more detailed analysis. Thus, the changes in peripheral coronary pressure (PCP), collateral flow, peripheral resistance, and the relationship between collateral resistance and PCP could be investigated. Following conclusions were reached: 1) Ischemia lasts longer following occlusion of the anterior descending artery than after circumflex occlusion. 2) If the stimulus for collateral growth is of a mechanical nature rather than ischemic, recovery is hastened. 3) The relationship between peripheral coronary pressure and collateral resistance, as well as the relationship between PCP and collateral flow, is non-linear. (Supported in part by USPHS grants HL-11678, and HL-09495).

EXPERIMENTAL EVIDENCE FOR CROSS-CURRENT GAS EXCHANGE IN AVIAN LUNGS. Peter Scheid and Johannes Piiper (intr. by John C. Eccles). State Univ. of New York at Buffalo, N.Y. 14226 and Max-Planck-Inst. f. exp. Medizin, Göttingen, Germany.

Two basically different models have been proposed for analysis of gas exchange in the parabronchial lungs of birds, the counter-current model (Schmidt-Nielsen, Sci. Am. 225, No.6 (1972) 72-79) and the cross-current model (Scheid and Piiper, Respir. Physiol. 9 (1970) 246-262). Both models are suited to explain qualitatively the gas exchange data obtained in birds during normal respiration, in which the parabronchial air flow has been shown to be unidirectional during both inspiration and expiration. For reversed parabronchial air flow, however, each model leads to different predictions regarding gas exchange performance: the efficiency should be decreased considerably according to the counter-current model, but remain essentially unaffected according to the cross-current model. In ducks the mesobronchi of both sides were blocked between the origins of the ventrobronchi and dorsobronchi by balloon catheters introduced via a tracheal cannula, and the postthoracic air sacs were opened. By inflow of air into the trachea or into the postthoracic air sacs a continuous parabronchial air flow in either direction could be achieved. It was found that PCO_2 and PO_2 in arterial and mixed venous blood as well as in expired (end-parabronchial) gas were independent of the parabronchial air flow direction. Furthermore, with both flow directions PCO_2 in the expired (end-parabronchial) gas in most cases exceeded the arterial PCO_2. The results are not compatible with the counter-current gas exchange model, but are in agreement with the cross-current model which is also in accordance with anatomical data.

RELATIONSHIP BETWEEN URINARY SODIUM EXCRETION AND PROXIMAL REABSORPTION AS DETERMINED BY PHOSPHATE EXCRETION IN THE CONSCIOUS DOG. Edward G. Schneider, John A. Haas*, L.R.Willis*, Jack W. Strandhoy* and Franklyn G. Knox. Nephrology Research Laboratory, Department of Physiology, Mayo Clinic & Foundation, Rochester, Minnesota.

The objective of the present study was to determine if the postprandial rise in sodium excretion is accompanied by a decrease in proximal sodium reabsorption in the conscious dog. Changes in phosphate excretion were used as an index of changes in proximal sodium reabsorption. 24 mongrel dogs were fed an identical low sodium diet (2 mEq/day) with the exception that 14 dogs received a supplement of 100 mEq of sodium whereas 10 dogs received no sodium supplement. Urine collections were obtained for the first 8 hours following feeding and for the next 16 hours. In the high sodium dogs, the average sodium excretion for the 8 hour period was $5.6 \pm .3$ mEq/hr which was significantly greater than the average for the next 16 hour period of $2.3 \pm .2$ mEq/hr. In the same dogs phosphate excretion was $2.23 \pm .17$ and $2.25 \pm .24$ mg/hr for the 2 time periods, respectively. Thus, the significant change in sodium excretion was not accompanied by a significant change in phosphate excretion. In dogs on the low sodium diet, sodium excretion was $.17 \pm .02$ and $.14 \pm .02$ mEq/hr in the 2 time periods, respectively. Phosphate excretion was $1.98 \pm .12$ and $1.79 \pm .15$ mg/hr, respectively. These changes were not significant. The findings indicate that, to the extent that phosphate excretion is an index of proximal sodium reabsorption, the postprandial rise in sodium excretion is not accompanied by a significant change in proximal sodium reabsorption in the conscious dog.

THE EFFECT OF β-ADRENERGIC BLOCKADE ON CORONARY AND SYSTEMIC ADAPTATION TO PACED HEART RATE INCREASE IN THE UNANESTHETISED DOG. Francine V. Schrijen*, Walter Ehrlich, David T. Krausman*, Paolo Caldini, and Joseph V. Brady*. Johns Hopkins Univ., Sch. of Medicine and Sch. of Hygiene, Baltimore, Md. 21205

The changes of coronary and systemic circulation during the transition from heart rate at rest to electrically-paced increase of heart rate were investigated in 30 trials with 3 unanesthetised dogs, beginning 1h after i.v. administration of .5 mg of propranolol/kg weight. These changes were compared with changes of circulatory functions during 34 control trials with the same animals. In the animal at rest, β-blockade increased total peripheral resistance and coronary resistance. It had a negative inotropic and chronotropic effect on the heart, as we described previously. The cardiovascular changes caused by paced increase of heart rate after β-blockade are similar to those in control trials. The differences are essentially caused by the effect of β-blockade on the prepacing rest values. The pacing increased cardiac output by 1L./min from the relative prepacing level, both after β-blockade and in control trials. The β-blockade decreased, however, the enhancements of coronary flow with pacing. After β-blockade, the heart rate increase of 70 beats/min enhanced the flow in the circumflex branch of the left coronary by 13 ml/min, whereas, in the control trial, the heart rate increase of 60 beats/min enhanced the circumflex flow by 17 ml/min. This difference seems to show that adaptation of coronary flow to the needs of the increased myocardial work is impeded by the greater constriction of the coronary vessels after β-blockade.

EFFECTS OF BARBITURATES IN INHIBITION OF FROG ACID SECRETION. Manuel Schwartz and Mumtaz A. Dinno*. Department of Physics, University of Louisville, Louisville, Ky.

Previous work on the inhibition of acid secretion in frog gastric mucosa using anesthetics with no more than four carbon atoms indicated a correlation between anesthetic potency and the oil/gas partition coefficient. Mullins (Fed. Proc. 27, 898, 1968) pointed out the existence of a site size limitation for anesthetic compounds since by the time one reaches C_{10} or C_{12} there is no anesthetic activity. It was, therefore, of interest to compare the behavior of barbiturates with anesthetics under similar conditions. For this purpose, mucosae of Rana pipiens were mounted between cylindrical chambers with Cl^- Ringer on the nutrient side and Cl^- secretory solution on the secretory side. Both sides were gassed with 95% O_2 and 5% CO_2. The pH was maintained at 4.90. The PD, resistance ($\Delta PD/i$) and H^+ secretory rate were measured. With 1.0 mM barbiturate on the N side, the decrease in H^+ rate was determined in the 20-25 minute interval following the addition of barbiturate to the nutrient solution. The logarithm of the octanol-water partition coefficient, log P, was used as a measure of lipid solubility. The barbiturates studied had log P extending from 0.65 for barbital to 3.23 for thiamylal. A plot of the decrease in H^+ rate was essentially linearly related to log P with some deviation from linearity approaching 80% decrease in H^+ rate. As expected, thiopental which precipitates partially at 1 mM concentration in Ringer solution fell below the curve. These results indicated, as in the case of anesthetics, lipid solubility as a factor influencing the potency of barbiturates in acid secretion. Unlike anesthetics, however, barbiturates exhibited inhibitory activity up to C_{12}, in fact, showed increased potency for each series as the number of carbon atoms increased.

EFFECTS OF DIAMOX AND CHLOROTHIAZIDE ON TOAD BLADDER ADENYL CYCLASE-EVIDENCE FOR DIFFERENT RECEPTORS FOR HYDRO-OSMOTIC AND SODIUM FLUXES.
Walter N. Scott & Victor S. Sapirstein*, Depts. of Ophthalmology & Physiology, Mt. Sinai School of Medicine of the CUNY, New York, N.Y.

Preincubation of the toad urinary bladder with 0.1-1.0mM Diamox (D) or 0.1-1.0mM Chlorothiazide (CT) gave a dose-dependent inhibition of the oxytocin-induced hydro-osmotic flux. D and CT did not inhibit the hydro-osmotic flux induced by exogenous cAMP or caffeine. These inhibitors block the hormone stimulation of adenylate cyclase in the intact bladder and in membranes, with no effect on the enzyme basal rate. The kinetics of the inhibition indicate it is competitive in nature. The effects of D and CT are not related to their inhibiton of carbonic anhydrase because the acetyl derivative of CT, which has no effect upon carbonic anhydrase, is as effective an inhibitor of hormone as is CT. Also, dichlorophenamide, a carbonic anhydrase inhibitor whose potency is comparable to D though structurally different, is ineffective in blocking oxytocin. These inhibitors (D and CT) had no effect upon oxytocin stimulation of sodium flux. In that these inhibitors seem to be acting at the adenylate cyclase receptor level, their lack of effect on the hormone stimulation of sodium flux implies the existence of two receptor systems. This conclusion is supported by our results using the oxytocin analog, 2-(ala)-oxytocin, which stimulated hydro-osmotic flux but not sodium flux. At concentrations of the analog below that required to give a response, it was found to act as a competitive inhibitor oxytocin-induced hydro-osmotic flux. There was no inhibition by 2-(ala)-oxytocin of the oxytocin stimulation of sodium flux.
(Supported by NIH Grant # AM-15205 & American Heart Association)

EFFECT OF STATIC EXERCISE ON LIMB VENOMOTOR TONE IN MAN.
R.G. Seaman*, R.L. Wiley*, J. Goldey*, and F.W. Zechman, Jr. Miami U., Oxford, O. and U. of Kentucky, Lexington, Ky.

Normal adult male volunteers, in the supine position, were studied to asses the effect of forearm static exercise on limb venomotor tone. Two methods were employed to measure changes of venous tone. Volume changes of the calf were measured plethysmographically(Whitney strain gauge)at a constant occluding pressure. Using the Wallace "isolated" limb technique, venous pressure changes in several forearm superficial veins were recorded in the non-exercising forearm. Volume and pressure changes were compared in rest, exercise, and recovery. Venous filling decreased and venous pressure increased during static exercise, compared with rest, indicating venoconstriction. The results from both methods were in agreement and showed that there is a significant increase in limb venomotor tone during a static exercise. Tensions of 20, 30, and 40% of each individual's maximal voluntary contraction(MVC) were used to determine if the venomotor response was graded. The magnitude of change in venomotor tone during exercise appeared to be related to the relative tension produced, although the differences were not statistically significant. The results also indicate that there is a significant difference in the degree with which different individuals respond to the same relative tension. The importance of an increase in venous tone during a static exercise as we have shown occurs at least in the limbs, is in maintaining the increased cardiac output which occurs in static effort.

IMPROVED SEPARATION AND QUANTITATION OF PLASMA CHOLESTERYL ESTERS BY THIN-LAYER CHROMATOGRAPHY USING CONTINUOUS DEVELOPMENT AND "IN SITU" SPECTROPHOTOFLUOROMETRY. Ramon Segura* and David Cardus, Baylor College of Medicine, Houston, Texas 77025.

With routine procedures used until now a limited resolution of the plasma cholesteryl esters can be achieved. Usually four different fractions are obtained, with a variable degree of overlapping; either densitometry or colorimetry is used for quantitative purposes. By employing an original and simple device, which can be adapted to the regular TLC tanks, it is possible to perform a continuous development and substantially improve the separation of the cholesteryl esters. Using, with this system, a solvent of very low polarity, an increased number of fractions can be separated, with a higher degree of resolution than that obtained with current procedures; the plasma cholesteryl esters are resolved into six or seven different fractions. The esters are rendered fluorescent by placing the chromatoplate in a sealed jar containing ammonium bicarbonate and by keeping the system at 130° C for several hours. The reaction with the vapor phase produces a bright fluorescent derivative which is stable for many weeks. The flurochrome shows "in situ" a maximum excitation at 385 mμ and a maximum emission at 475 mμ. Scanning spectrophotoflurometry and integration of the peak area allows direct quantitation of the compound present in each fraction, the response being linear from 0.2 μg to at least 20 μg of cholesteryl ester. Applications of this original procedure to the analysis of plasma cholesteryl esters from normal individuals and from patients with different pathological conditions will be presented.
(We thank Farrand Optical Corporation for the use of their spectrofluorometer.)
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RELATIONSHIP OF INDOLES AND PEPTIDES TO THE PINEAL-HYPOPHYSEAL-GONADAL AXIS. H. R. Seibel* and F. M. Bush, Medical College of Virginia, Richmond, Virginia, U.S.A.

Our prior studies showed that blinding decreases testes and seminal vesicle weight, an effect abolished by simultaneous pinealectomy. A pineal-pituitary antagonism existed as hemicastration increased weight in the remaining testis, an effect decreased by blinding. Some antigonadotrophin passes between parabionts as testes weights of paired normal and blinded are smaller than normal but larger than those of both blinded parabionts. The effects of indoles and peptides on this axis were investigated. The results showed that neither serotonin nor melatonin injected separately or in combination increased the effects of blinding. Injected oxytocin, vasopressin, 5-methoxytryptophol, 5-methoxy-or 5-hydroxyindole acetic acid or PCPA feeding had no effect upon organ weights after blinding. Apresoline administration ruled out vasoconstriction as the cause of testicular atrophy in blinded hamsters. Inability to show an additive or antigonadotrophic effect upon blinding suggests that pineal effects may be secondary to a primary effect on cerebral metabolism in the hamster.

RENAL BLOOD FLOW DURING ENDOTOXIC SHOCK IN THE SUBHUMAN PRIMATE. J.P. Selmyer*, D.G. Reynolds* and K.G. Swan. Walter Reed Army Institute of Research, Washington, D. C.

The effects of E. coli endotoxin (LD_{80}) upon renal arterial blood flow (RBF) were studied in the anesthetized baboon. RBF was measured with an electromagnetic flowmeter. Arterial (AP) and venous (VP) pressures were recorded. Resistance (R) across the renal vascular bed was calculated and expressed in resistance units (PRU). Control RBF was 191 $\pm$ 24 (S.E.) ml/min; AP and VP were 118 $\pm$ 4 and 5 $\pm$ 1 mm Hg. R measured 0.64 $\pm$ 0.08 PRU. Following I.V. endotoxin there was a progressive and significant ($p < .01$) fall in AP to 55 $\pm$ 5.0 mm Hg within two hours. Hypotension was sustained for the duration of the four hour observation period. During the same time RBF fell to 143 $\pm$ 21 ml/min and at four hours the value (129 $\pm$ 11 ml/min) was significantly ($p < .02$) below control. VP was not significantly ($p > .05$) changed from the control value. R fell gradually to 0.36 $\pm$ 0.03 PRU at 2½ hours and this was significantly ($p < .01$) below control. R gradually recovered but never exceeded control. Histologic examination of the kidney at four hours revealed microthrombi within glomeruli, necrosis within proximal tubules and an eosinophilic transudate within distal tubules. Urinary output was negligible following endotoxin injection. The fall in resistance indicates that renal ischemia is secondary to inadequate perfusion pressure sufficient to cause microscopic evidence of damage to both glomeruli and collecting systems.

SITE OF CIRCADIAN RHYTHM PRODUCTION IN APLYSIA EYE.
Robert Sener (Introduced by Felix Strumwasser), Division of Biology, California Institute of Technology, Pasadena, California 91109.

The isolated eye discharges compound action potentials (CAPs) in response to light and spontaneously in darkness, where their frequency follows a circadian rhythm (Jacklet, 1969). A necessary step towards understanding the controlling mechanism is to locate the site of rhythm production within the eye. The basal region is selectively sensitive to localized passage of DC current at 1×10^{-7} to 1×10^{-6} amperes from an anodal extracellular micropipette. At the base such current blocks CAPs, while other parts of the eye and the optic nerve are less sensitive. Systematic reduction of tissue to the extreme base alters neither the occurrence of the circadian rhythm nor its period. Light responses are unaffected. To quantify the relative amounts of tissue removed, its aqueous-soluble protein is measured by the technique of Lowry et al. (1951) and compared with values for whole control eyes, corrected to exclude lens and clear jelly. EM examination of isolated basal tissue shows no fine-structural damage and reveals that some primary photoreceptors are still present, explaining the normal light responses of tissue-reduced eyes. These results diverge from the conclusions of Jacklet and Geronimo (1971) that (1) tissue reduction alters circadian periodicity and that (2) the circadian rhythm is produced by a large population of interacting non-circadian oscillators distributed throughout the retina. The present data require a model in which (1) sites of coupling among CAP-producing neurons are highly localized within the base of the eye, and (2) neuronal somata, processes and couplings in non-basal regions are not immediately essential for normal light responses, spontaneous dark discharge and the production of circadian rhythmicity.

FEEDING AND TEMPERATURE RESPONSES TO THIRD VENTRICULAR INJECTIONS OF Ca^{++} AND Mg^{++} IN SHEEP. J. R. Seoane* and C. A. Baile (spon. M. Kare), Univ. of Penn, Philadelphia, Pa. and Smith, Kline & French Research Center, 1600 Paoli Pike, West Chester, Pa 19380.

Intraventricular injections of Ca^{++} elicit feeding and hypothermia in cats, rats and monkeys. In these experiments we have injected Ca^{++} and Mg^{++} into sheep. Ten wethers were surgically implanted with guides directed toward the third cerebral ventricle for injections and an intraperitoneal (IP) tube to measure temperature. Solutions (0.5 ml) were injected at 0.19 ml/min 1 hour after the ad libitum fed sheep received their daily ration. There was a dose dependent feeding response elicited by both ions, with a latency of about 2 min post-injection. Ca^{++} injections (1.5, 4.0, 5.0 and 10.0 umoles/sheep), however, resulted in greater feed intakes than equimolar doses of Mg^{++} (54 g for synthetic CSF; 97 vs 58 g, 121 vs 71 g, 228 vs 112 g, 307 vs 208 g respectively for Ca^{++} vs Mg^{++} with increasing doses during 60 min post-injection). There was an increase in IP temperature (0.4°C, $P<0.01$) after injections of 10 umoles of Mg^{++} which was independent of feeding. 10 umoles of Ca^{++} elicited a 0.2°C increase in IP temperature ($P<0.02$); however, this appeared to be dependent on the feeding response. There was no evidence of ataxia as a result of injections of either ion. The feeding response was elicited by doses lower than those required to increase temperature and in no case was there hypothermia even when feed was withheld. The mechanism by which the hypothalamus controls feed intake is apparently sensitive to small increases in Ca^{++} and Mg^{++} concentrations. The elicited feeding may be related to the neurodepressant properties of both ions, which may decrease inhibition of the ventromedial area over the lateral hypothalamus (Supported in part by an NSF Grant #GB-28836).

EFFECTS OF RENAL ARTERIAL INFUSION OF ADH AND ANGIOTENSIN II ON RENIN SECRETION IN THE NONFILTERING KIDNEY. R.E. Shade*, J.O. Davis, J.A. Johnson, R.W. Gotshall*, and W.S. Spielman*. Dept. of Physiology, Univ. of Mo. School of Medicine, Columbia, Missouri 65201.

In a previous study (Amer. Soc. Nephrol. Absts., 1971), the renal arterial infusion of NaCl or KCl inhibited renin secretion in filtering kidneys of dogs with thoracic caval constriction (TCC) but failed to influence renin secretion in nonfiltering (NF) kidneys of dogs with TCC. To study the mechanism of action of ADH and angiotensin II (AII) on renin secretion, the present experiments were performed in sodium depleted dogs with NF kidneys. After control observations, AII was infused at 7 ng./100 ml. of renal blood flow for thirty minutes and renin secretion was measured at fifteen and thirty minutes. Thirty minutes after stopping the AII infusion recovery observations were made. This was followed by a thirty minute infusion of ADH at 5 μU/ml. of renal blood flow. In a second series the same protocol was followed except that the order of infusion of AII and ADH was reversed. Renin secretion in NF kidneys decreased from 496 to 253 and 246 ng. angiotensin/min. ($P<.03$) with AII as the first infusion and from 523 to 194 and 30 ng. angiotensin/min. ($P<.03$) when AII was infused second. Infusion of ADH decreased renin secretion in NF kidneys from 698 to 136 and 134 ng. angiotensin/min. ($P<.03$) with ADH given first and from 305 to 174 ($P<.05$) and 134 ng. angiotensin/min. ($P<.02$) when ADH was the second infusion. ADH had no effect on renal blood flow or arterial blood pressure. In some instances AII decreased renal blood flow and arterial blood pressure. The earlier data indicated that Na and K required the presence of an intact renal tubular system to inhibit renin secretion. ADH and AII, however, decreased renin secretion in the absence of a functional macula densa. (Supported by USPHS grant HL10612).

THE EFFECTS OF EDEMA ON THE DEFLATION PRESSURE-VOLUME CHARACTERISTICS OF ISOLATED CANINE LUNGS. Michael A. Shanoff* and Solbert Permutt, Johns Hopkins Univ. Sch. of Hygiene & Public Health, Baltimore, Md. 21205.

We studied the deflation pressure-volume curves of canine lung lobes following inflation to 40 cmH_2O from the degassed condition. Before inflating the degassed lobes we increased the fluid content by adding saline via the bronchus or blood vessels. Airway closing pressure (ACP) was considered as the sharp inflection where $\Delta V/\Delta P$ approached zero. It increased from a mean of -.65 cmH_2O without fluid to 4.1 cmH_2O in lungs 80% fluid filled. The ratios of the air volume at any given transpulmonary pressure to the air volume at 40 cmH_2O decreased significantly as fluid content increased. If the fluid had completely filled some alveoli and excluded air without affecting other alveoli the ratios would have stayed constant. At high pressures total air and fluid volumes (AFV) were close to air volumes in controls without added fluid. At low pressures (< 15 cmH_2O) increasing amounts of fluid caused sharp increases in AFV at any given pressure compared to the air volumes of the controls. All effects of the fluid reversed when the fluid was removed. The data suggest that at high lung volumes elastic forces predominate, and air and fluid act similarly. At low pressures, airway closure occurs trapping air and fluid and causing increased AFV compared to control air volume. This trapping parallels the rise in ACP, but must begin at pressures exceeding ACP to account for the data. Increased fluid may increase ACP and trapping because rising interstitial and vascular pressures near small airways cause airway closure. (Supported in part by PHS Grant HL 05453.)

INTESTINAL BLOOD FLOW AUTOREGULATION AND AUTOREGULATORY ESCAPE: A. P. Shepherd and H. J. Granger (Intr. by E. D. Jacobson). Program in Physiology, U.T.M.S.H., Houston, Texas and U.M.C., Jackson, Mississippi.

In order to determine whether a metabolic feedback mechanism could account for intestinal autoregulation and autoregulatory escape, we have developed a mathematical model of circulatory control in the gut. The model consists of equations describing hemodynamics, oxygen transport, and local and nervous effects on mesenteric arteriolar and precapillary sphincter tone. We assumed the local system controls intracellular pO_2 by 1) regulating arteriolar resistance to change blood flow; and 2) by opening or closing precapillary sphincters, thereby determining capillary density (the number of open capillaries) and the diffusion parameters (surface area and diffusion distance). Sympathetic activation increases arteriolar and precapillary sphincter tone. In computer simulations the model responded to step changes in arterial pressure by autoregulating blood flow to control O_2 delivery. The degree of autoregulation increased whenever the amount of extractable O_2 in the blood decreased. This has been observed experimentally in skeletal muscle but not yet in the intestine. In simulations of autoregulatory escape, sustained sympathetic activation caused a fall in mesenteric blood flow, capillary density and O_2 delivery. Capillary density remained depressed, but blood flow and O_2 delivery returned toward control. The end of sympathetic activation was followed by hyperemia and an overshoot in capillary density. These results agree with those obtained experimentally. However, our model predicts that as capillary density is depressed by the sympathetic input, the degree of autoregulatory escape and post-stimulation hyperemia will increase. The degree of autoregulation varied greatly with initial flow conditions, yet the escape index hardly changed. This finding could account for the failure of experimental attempts to correlate the degree of autoregulation with the degree of escape. We conclude that the metabolic feedback hypothesis can adequately explain autoregulation and autoregulatory escape; however, a description complete enough to account for intestinal hemodynamics in some experimental conditions (e.g. venous pressure elevation) must also include certain myogenic properties of the intestinal vasculature. (Supported by HE 11678, DADA 17-69-C9025, and a Miss. Heart Assoc. grant).

STUDIES ON THE ADENYL CYCLASE OF RAT RENAL CORTICAL AND MEDULLARY PLASMA MEMBRANES. L. J. Shlatz* and I. L. Schwartz, Dept. of Physiology, Mount Sinai School of Medicine, New York, N.Y.

Renal cortex and medulla were separated by dissection and each tissue was then minced, homogenized, and subjected to differential and zonal (sucrose gradient) centrifugation, according to the method of Kinne and Kinne-Saffran (Pflugers Arch. 308, 1, 1969). The band containing plasma membranes was harvested, washed by centrifugation and resuspended in Tris-HCl buffer (pH 7.5). For determination of the adenylate cyclase activity, 80 to 100 μg of membrane protein were incubated at 37°C for 20 minutes in a solution containing varying concentrations (range 10^{-9}M - 10^{-5}M) of synthetic arginine vasopressin (AVP) or highly purified parathyroid hormone (PTH), 0.1 mM [α-P^{32}]-ATP, 4 mM $MgCl_2$, 0.1% bovine serum albumin, 0.1 mM EDTA, 40 mM Tris-HCl buffer (pH 7.5), 0.5 mM unlabeled cyclic AMP (cAMP), 25 mM creatine phosphate and 0.1 mg/ml creatine kinase, total volume 50 λ. Reactions were terminated by the addition of 50 λ of a solution containing 4 mMATP, 4 mM cAMP and 4 mM 5'-AMP and heating at 100°C for 3 min. The adenylate cyclase of the cortical cell membrane fraction (basal cAMP production 0.92 pmoles cAMP/min/mg membrane protein) proved to be highly sensitive to PTH (maximal stimulation 34.0 pmoles cAMP/min/mg membrane protein) as compared to AVP (maximal stimulation 6.0 pmoles cAMP/min/mg membrane protein) whereas the adenylate cyclase of the medullary cell membrane fraction (basal cAMP production 9.4 pmoles cAMP/min/mg membrane protein) proved to be much more sensitive to AVP (maximal stimulation 76.7 pmoles cAMP/min/mg membrane protein) as compared to PTH (maximal stimulation, 29.4 pmoles cAMP/min/mg membrane protein). These findings extend the observations of Chase and Aurbach (Science 159,645,1968) on rat renal cortical and medullary whole tissue homogenates.

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MONOSACCHARIDE TRANSPORT RECEPTORS IN DOG KIDNEY. Melvin Silverman. Div. of Clin. Sci., Univ. of Toronto, Ont., Canada.

Radioactively labelled myoinositol, mannitol, glucosamine, and mannosamine have been used to further probe the specificity of monosaccharide interaction with transport receptors in dog kidney. By means of the single injection multiple indicator dilution technique in anesthetised mongrel dogs (plasma glucose 60-80%), a mixture of indicators including tracer test pyranosides, creatinine (extracellular reference) and T-1824-albumin (vascular reference) is injected into the renal artery and outflow curves are obtained simultaneously from renal vein and urine. The transit patterns for the amino-sugars and mannitol each superimpose on the creatinine curves in renal vein and urine. However myoinositol exhibits interaction with both the brush border and peritubular surfaces of the nephron. Based on molecular models of myoinositol and on previous studies (Amer. J. Physiol., 218, 743, 1970) it is predicted that myoinositol shares the glucose transport receptor on both membranes. These results suggest that in the interaction of monosaccharides with renal tubular surfaces; i) the ring oxygen in pyranosides probably plays a minor role, and ii) NH_2 and COOH substituents on Carbon #2 affect pyranoside interactions either because of their bulkiness compared to OH groups or by altering the reactivity of adjacent OH groups.

INHIBITION OF GLUCONEOGENESIS BY PHYSIOLOGICAL CONCENTRATIONS OF INSULIN. Celia D. Sladek (intr. by S.F.Marotta) Dept. of Physiology, Univ. of Illinois, College of Medicine, Chicago, Illinois.

Gluconeogenesis was measured in isolated, rat livers perfused with physiological concentrations (conc.) of insulin (I) in order to determine if the ability of I to inhibit gluconeogenesis is significant at I conc. which occur in vivo. The rate of incorporation of U1-C^{14}-alanine into glucose was measured in livers perfused at 7 ml/min with I conc. of 10,50,100,200,500 and 1,000 μUnits/ml. The rate of gluconeogenesis was found to be a linear function of the perfusate I conc. in the range of 10-500 μU I/ml. However, increasing the I conc. to 1,000 μU/ml had no further effect on the rate of gluconeogenesis. At an alanine (ala) conc. of 2.8 mM the linear portion of the relationship was described by the standard linear equation: Rate of Gluconeogenesis (μm/hr/gm liver) = 15.93 - 0.0084 (μU/ml I). The slope and the intercept were both significantly different from zero ($P < .001$). Increasing the perfusate I conc. from 10-500 μU/ml did not significantly alter the response of the liver to changes in the perfusate ala conc. A linear relationship existed between the rate of gluconeogenesis and the ala conc. over the range of 0.45 to 4.0 mM ala. At an I conc. of 10 μU/ml this relationship was described by the equation: Rate of Gluconeogenesis (μm/hr/gm liver) = 0.61 + 5.53 (mM Ala) (T_{sb}=6.93, $P < .001$). Increasing the I conc. lowered the mean rate of gluconeogenesis ($P < .01$), but did not change the slope significantly. The conc.-dependent effect of I on gluconeogenesis also was seen at an ala conc. (10 mM) which was sufficient to saturate the gluconeogenic pathway. These data indicate that I does significantly reduce gluconeogenesis at conc. which occur physiologically, and that the response to variations in the I conc. is independent of substrate supply.

EFFECT OF BETA BLOCKADE ON RENIN SECRETION ASSOCIATED WITH RENAL NERVE STIMULATION AND ISOPROTERENOL INFUSION. C. H. Sloop,* R. G. LaGrange,*, O. Beaty* and H. E. Schmid. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

Renin secretion, in response to low frequency nerve stimulation and isoproterenol infusion, was studied in acute dog experiments. Renal blood flow (measured by a non-cannulating electromagnetic probe), GFR (derived from a continuous determination of the extraction of I^{131} iothalamate or ^{99m}Tc labeled inulin) and urine electrolytes, were studied at several levels of reduced renal artery pressure (control to 75 mm Hg). Stimulation of isolated renal nerves (0.8 msec, 10v, 0.1-0.2/sec) increased renin production over control values at all pressure levels. Intra-arterial administration of practolol (AY-21,011)(8 mg/kg) blocked the renin release to nerve stimulation but did not abolish the increased renin release to graded artery constriction. Practolol appeared to have no effect on the decrease in sodium excretion which occurred with graded artery constriction or nerve stimulation.

Intra-arterial infusion of isoproterenol (0.01-0.05 μg/kg/min) significantly increased renin release at dose levels which did not decrease GFR or sodium excretion; the increased renin release was blocked by both practolol and propranolol (1 mg/kg).

The results indicate that the renal sympathetic nerve stimulation increased renin secretion via an intrarenal adrenergic receptor site which can be inhibited by β-blocking agents.

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DISTRIBUTION OF LYSOSOME POPULATIONS IN CARDIAC TISSUE. Amelia L. Smith* and John W. C. Bird. Department of Physiology, Rutgers University, New Brunswick, New Jersey 08903.

Rat heart tissue was fractionated by isopycnic zonal centrifugation of the post-nuclear fraction, followed by differential centrifugation of the individual fractions. The distribution of 5 lysosomal hydrolases, neutral (pH 7.4) and alkaline (pH 8.5) proteases, and several marker enzymes for cell organelles (catalase, Ca-ATPase, cytochrome oxidase, glucose-6-phosphatase, and muramidase) were studied. Three major lysosomal populations were described with equilibrium densities of 1.09, 1.18, and 1.23. Acid, neutral and alkaline proteases were further purified by gel filtration on Sephadex G-100 columns. Each protease was found to have three subspecies, and K_m and V_{max} studies showed the lowest molecular weight subspecies to be the most active. The distribution of the proteases within the cell indicates that the neutral and alkaline proteases are mainly soluble, whereas the acid protease is membrane-bound. (Supported in part by U.S.P.H. grant NS-07180.)

RELATIONSHIPS BETWEEN SPONTANEOUSLY OCCURRING AND EVOKED SYMPATHETIC NERVOUS DISCHARGES. D. W. Snyder and G. L. Gebber (intr. by D. A. Reinke) Dept. of Pharmacol., Mich.State Univ., E.Lansing, Mich. 48823.

A study was made of the relationships between the level of spontaneously occurring discharges (SOD's) and the amplitude of evoked action potentials (EAP's) recorded from a "vasoconstrictor" postganglionic branch of the cat superior cervical ganglion. EAP's were elicited by 10 msec trains of 3 pulses applied to pressor sites in the medulla. Electrical activation of the medial medullary depressor region (DR) (1) reduced SOD's and EAP's with onset latencies of 50-100 msec and (2) enhanced EAP's with onset latencies of 30-45 msec. The degrees to which the SOD's and the short and long latency EAP's changed were related similarly to the intensity of DR stimulation. The reciprocal actions of DR stimulation also were observed when the short and long latency EAP's were elicited from descending spinal pressor tracts and recorded from the preganglionic cervical sympathetic nerve. Alterations in systemic blood pressure produced changes in SOD's and EAP's which were predicted on the basis of the DR stimulation experiments. The pressor action of i.v. norepinephrine was accompanied by (1) reduction of SOD's and long latency EAP's and (2) enhancement of short latency EAP's. The depressor action of i.v. histamine was accompanied by (1) enhancement of SOD's and long latency EAP's and (2) reduction of short latency EAP's. This study supports the contention that pressor influences are distributed over parallel pathways from the brain to the cells of the spinal sympathetic columns. The data suggest that (1) long latency EAP's were elicited from the pathway mediating SOD's and (2) transmission in the pathway from which the short latency EAP's were elicited is influenced at a spinal site by the level of SOD's in the pathway mediating the long latency EAP's. (Supported by PHS Grant No. 5-R01-HL 13187).

ROLE OF BODY FAT IN RESPONSE TO HEAT. *R.G. Soule*, R.F. Goldman, and W.L. Sembrowich**. US Army Research Institute of Environmental Medicine Natick, MA 01760

Although Miller and Blyth reported (1955) a lack of insulating effect of body fat during internal and external heat load, most studies of men working in the heat suggest that a high percentage of body fat reduces heat tolerance. During a recent field study, body fat and rates of rise of T_{re} were determined for over 200 men marching in the heat; no correlation ($r \sim 0.01$) was found for the whole group, or for just the 10 fattest and 10 leanest. In the present study, 14 men selected from a group of over 200 fit but "thin" or "fat" volunteers to provide a range of body fat from 11.9 to 30.5%, worked under 5 conditions: climatic chamber on a treadmill (25 min walk, 25 min rest, 25 min walk, 45 min rest) at 5.6 km/hr at, 1) 24°C, 50% RH in shorts; 2) 35°C, 50% RH in vapor barrier coveralls; 3) 49°C, 20% RH in shorts; outdoors in standard fatigues, ($T_a \simeq 27$°C, RH $\simeq$ 50%) on a blacktop circuit, 4) as a group at 5.6 km/hr; 5) individually, self-paced. The analyses were carried out on the T_{re} and HR change during each work and each rest period. There was a significant correlation for the self-paced condition, with fatter men walking slower ($p < 0.05$) than thinner. There were few significant correlations between T_{re} (or heart rate) and body fat during rest or work. In both heat conditions [2) and 3)], the change in HR during the first 25 min walk was correlated with % body fat ($p < 0.05$), with fatter men having the greater increase; the only other significant correlation was for HR fall for the first rest period at 49°C, where fatter men started significantly higher. Thus, at least for conditions producing $T_{re} \simeq 39.1$°C and HR $\simeq$ 145, relative fat had little influence on these responses to heat, except for a more rapid initial ΔHR. This may not be true for less fit fat men.

cAMP AND CATECHOLAMINE RESPONSE OF CORONARY VASCULAR SMOOTH MUSCLE. H.V. Sparks and R.L. Schnaar*. Univ. of Mich., Ann Arbor, Mich. 48104

The present study was designed to determine whether tension responses of coronary smooth muscle to catecholamines are mediated by cAMP. For tension studies, canine coronary artery strips (2mm OD) were mounted in a muscle bath containing physiological salt solution with increased KCl (30mM) to produce tonic contraction. Isometric tension was measured. Dibutyryl cAMP (5×10^{-4} to 2×10^{-3}M) caused relaxation of the vessels. Epinephrine stimulates both α(contraction) and β(relaxation) adrenergic receptors of large coronary vessels. Epinephrine (10^{-8} to 3.13×10^{-5}M) alone caused contraction (max=348±50 mg). In the presence of propranalol (10^{-6}M) the contraction was enhanced (max=478±57 mg). In the presence of phentolamine (10^{-5}M) epinephrine caused relaxation (max=-98±11 mg). For cAMP studies 5-10 mg coronary artery slices were incubated in PSS, and exposed to appropriate drugs and blockers. Tissues were quickly frozen and cAMP was extracted in TCA and measured using the Gilman protein binding assay (Proc. N.A.S. 67:305, 1970). Control values were 5.7±0.8 pmoles/mg protein. Significant increases ($p < .05$) in cAMP levels were caused by the addition of: 1) 10^{-5}M epinephrine & 10^{-5}M phentolamine (cAMP=12.4 pM/mg); 2) 10^{-6}M isoproterenol (9.8pM/mg); and 3) 4.5×10^{-5}M isoproterenol (16.5pM/mg). Addition of epinephrine (10^{-5}M) alone also caused a significant increase in cAMP levels (9.8pM/mg). No significant change in cAMP levels was found with addition of 10^{-5}M epinephrine & 10^{-6}M propranalol (7.9pM/mg; p=.53). These data are consistent with the hypothesis that β-stimulation is mediated by increased tissue cAMP levels. However, the results with epinephrine alone and epinephrine & propranalol do not support cAMP mediation of the α-response. (Supported by USPHS Grants HE-13538 and HE-05682).

EFFECTS OF CHRONIC LITHIUM ADMINISTRATION ON CANINE RENAL FUNCTION. H.W. Spencer, T.K. Auyong, and T.W. Nielsen (intr. by H.E. Ederstrom), Department of Physiology and Pharmacology, School of Medicine, University of North Dakota, Grand Forks, No. Dak. 58201.

Mongrel female dogs weighing from 7-18 kg were used in this study. Each animal was surveyed for renal function including concentrating and diluting ability. The animals were then placed on oral dosages of lithium carbonate ranging from 30-90 mg/kg body weight b.i.d. with food and water ad lib. Renal function tests were performed biweekly. Thirty mg/kg body weight produced no overt renal changes, whereas 90 mg/kg b.i.d. was fatal after a brief anorexic episode. Animals invariably exhibited spontaneous diuresis in the dosage range of 50-60 mg/kg body weight. The degree of diuresis varied but was as high as 6 L/day. The diuresis was reversible and concentrating ability returned when lithium administration ceased. The animals became refractory to vasopressin, USP within 12 days after lithium administration, with the degree of refractoriness varying with the dosage of lithium. The above changes occurred without demonstrable changes in glomerular filtration rate (GFR) or renal plasma flow (RPF) as measured by inulin and para-aminohippuric acid (PAH) clearances, respectively. Alterations in free water reabsorption ($T^C_{H_2O}$) and free water clearance (C_{H_2O}) suggest that the aberrations produced by lithium are located in the distal portions of the nephron i.e., the ascending limb of the loop of Henle, the distal convoluted tubule, and the collecting duct. Supported by USPHS Grant MH20788-01.

REMOVAL OF RECENTLY DEPOSITED AND CHRONICALLY INGESTED RADIOSTRONTIUM IN MAN. Herta Spencer, Lois Kramer*, and Joseph Samachson*. Metabolic Research Unit, VA Hospital, Hines, Illinois.

A relationship has been observed between the urinary excretion of calcium and of radiostrontium in man. Therefore, certain agents which increase the urinary calcium were used to enhance the excretion of acutely administered radiostrontium in man using $^{85}SrCl_2$ as the tracer. The compounds which were effective were then used for the removal of chronically ingested ^{90}Sr which enters the body with the food due to nuclear fallout. However, some of these compounds increased the urinary ^{90}Sr excretion but others were not effective. While intravenous calcium significantly increased both the urinary excretion of calcium and of recently administered ^{85}Sr, the urinary excretion of ^{90}Sr did not increase despite the marked increase of the calciuria. In contrast, orally administered ammonium chloride increased the excretion of both the urinary excretion of recently administered ^{85}Sr and of chronically ingested ^{90}Sr, although the increase in calciuria was less than that induced by intravenous calcium. Intravenously administered stable strontium led to a 2- to 3-fold increase of the urinary calcium, of the urinary ^{85}Sr, and of the urinary ^{90}Sr excretion. The difference in effect of the different agents on the enhancement of excretion of ^{85}Sr and ^{90}Sr is not due to differences in metabolic behavior of these two radioisotopes but can be explained on the basis of the difference of the action of the enhancing agents on bone. (Supported by Contract AT(11-1)-1231-84 from the U.S. Atomic Energy Commission.)

A STUDY OF SOME INTERACTIONS AND COMPARISONS OF THE PULMONARY AND BRONCHIAL CIRCULATIONS. Richard P. Spencer, Robert J. Touloukian,* Pallas Sun Lo,* Section of Nuclear Medicine and Department of Surgery, Yale University School of Medicine, New Haven, Connecticut. 06510

While the pulmonary blood volume can be calculated from the mean transit time and the cardiac output, the procedure can not be applied to estimating the residual volume in the bronchial circuit. However, by use of the cardiac output and determination of the fraction of the output in the bronchial vessels, flow through the system can be calculated. Adult dogs were prepared with a catheter in the left heart, or with 2 catheters (one in the right heart, one in the left). Radiolabeled microspheres (50 microns diameter) were injected into the left heart catheter; at sacrifice, the amount in the lungs and bronchial tree represented bronchial circulation. When both sides of the heart were catheterized, microspheres of one radiolabel were injected into one side, while a distinct radiolabel was used on the other side. Hence it was possible to look at the relationship of bronchial blood flow to pulmonary flow. The gravity dependence of the pulmonary blood flow is well known. A superior to inferior gradient, with dogs injected upright, could be shown for both the pulmonary and bronchial circulations. The ratio of bronchial/pulmonary flow in an area was approximately constant, deviating only as the larger segments of the bronchial tree were approached. The dual microsphere technique appears to offer a useful approach to studying bronchial/pulmonary interactions. Supported by USPHS 14179 (Yale University Lung Research Center), by USPHS CA 06519 and by ET-44B from the American Cancer Society.

HYPERSECRETION OF RENIN IN DOGS WITH HIGH OUTPUT HEART FAILURE. W.S. Spielman*, J.O. Davis, and R.W. Gotshall*. Dept. of Physiology, University of Missouri School of Medicine, Columbia, Missouri 65201.

In experimental high output failure secondary to a large infrarenal aortic-caval fistula, increased aldosterone secretion has been related to elevated plasma renin activity (PRA). Decreased metabolism of renin contributes substantially to the increase in PRA (Schneider, et al. Circ. Res. 24:213, 1969). The present study was designed to investigate the possibility that an increased rate of renin secretion also contributes to the elevated level of PRA. Six dogs with large aortic-caval fistulas and evidence of cardiac failure (i.e. elevated central venous pressure, sodium excretion less than 5 mEq/day on an intake of 68 mEq/day of sodium, peripheral edema and/or ascites and decreased arterial pressure) were studied. The rate of renin secretion was determined as the product of renal plasma flow, measured by electromagnetic flowmeter, and the difference in PRA across the kidney (renal venous renin activity - arterial renin activity). PRA was measured by methods described previously. Renin secretion data in the high output failure model compared to that in normal dogs are presented in this table.

	ARTERIAL PRA (ng. angiotensin/ml)	RENAL VENOUS PRA (ng. angiotensin/ml)	RENIN SECRETION (ng. angiotensin/min)
Normal	15.3±2.1	18.6±2.5	607±101
High Output Failure	55.7*±14	78.6*±22	1978*±496

(Mean ± SEM; *p<.01)

These observations provide evidence that an increased rate of renin secretion by the kidney contributes to the increase in PRA in experimental high output heart failure. (Supported by HL05810 and HL10612).

MODIFICATION OF FROG COLD RECEPTORS BY SYMPATHETIC STIMULATION. D. C. Spray* (intr. by J. B. Munson). Depts. of Physiology and Neuroscience, College of Medicine, University of Florida, Gainesville, Florida 32601.

This study was undertaken to investigate the interaction between stimulation of sympathetic fibers and responses of peripheral cold receptors in the frog. A preparation was made consisting of dorsal musculature and skin from collar to urostyle placed dorsum down atop a thermoelectric cooler. Stimulation of the first sympathetic ganglion was in 200 msec trains of 5, 10, 20/sec, 0.2 V, 5 msec pulses presented at 5 sec intervals; recordings were made from the four or five ipsilateral dorsocutaneous nerves. The present study shows that the frog dorsum possesses nerve endings which fulfill the criteria for cold receptors (Hensel, Erg. Physiol., 1952). Both threshold and sensitivity (Impulse frequency/°C) of dorsocutaneous cold receptors varied with the rate of sympathetic stimulation. These results are consistent with findings of sympathetic enhancement of lingual cold receptors (Chernetski, J. Neurophysiol., 1964) and cutaneous mechanoreceptors (Chernetski; Loewenstein, J. Physiol., 1956), suggesting that this is a generalized effect on peripheral receptors. (Supported by NIMH traineeship 10320 and Grass Foundation Fellowship).

EVIDENCE FOR THE EXISTENCE OF SPONTANEOUSLY DISCHARGING RESPIRATORY RELATED NEURONES IN THE ANTERIOR HYPOTHALAMUS OF THE CAT. H.A. Spurgeon, G. Weiss* and K. Kastella. Dept. of Physiology, University of New Mex. School of Medicine, Albuquerque, N.M. 87106.

Using tungsten microelectrodes (4-10μ tips) unit discharges correlated with respiratory air flow velocity have been recorded from the anterior hypothalamus of the vagotomized, spontaneously respired cat. Discharge patterns appear equally distributed between inspiratory, expiratory, and phase spanning unit types. Relatively few units have been found in a given animal. Small unit amplitudes suggest that the cells represented are small, and the discharge patterns recorded are often difficult to separate from background activity. Special computer techniques have been used to extract the discharge patterns. Activity apparently is inhibited by the vagus. Anesthesia levels appear critical for success in finding these units. The highest probability of success has been found using pentothal narcosis, a finding consistent with other reported respiratory data. The exact role of these units has not been established but it seems likely that they represent respiratory efferent activity, since our findings are consistent with previously reported stimulation data (Physiologist 13: 313, 1970). In view of the high degree of integration ascribed to the hypothalamus, it is possible these cells represent a site of respiratory integration. Some evidence has been seen regarding a possible inspiratory rate sensitive neurone which could provide feedback regulation for air flow velocity. Because these cells discharge spontaneously, it is probable that they are actively involved in respiratory control.
(Supported by Grant No. 71 836 from American Heart Assoc., and Grant No. HL 13783 from NHLI.)

DIRECT EVIDENCE IN A MAMMALIAN SKELETAL MUSCLE THAT OXYGEN TRANSPORT DOES NOT LIMIT OXYGEN UPTAKE. W. N. Stainsby, J. K. Barclay, and P. D. Allen. Dept. of Physiol., Coll. of Med., Univ. of Fla., Gainesville.

Because lactate production is transient and mitochondrial NAD/$NADH_2$ becomes more oxidized at maximal metabolic rate, it has been suggested that oxygen transport does not limit the metabolic rate of circulated mammalian skeletal muscle. To test this possibility directly the circulation to the gastrocnemius-plantaris muscle group of the dog was isolated and perfused with the animal's own blood. The muscles were stimulated indirectly to contract at 5.0 twitches/sec., and the contractions were measured using a pneumatic myograph. This stimulation frequency produces maximal sustained metabolic rate, but the metabolic rate is much less than 5x the sustained metabolic rate at 1.0 twitch/sec., indicating that the metabolic rate is limited by some process. Increasing the blood flow above spontaneous values during continuous contractions did not increase contraction strength. The flow could be reduced about 10 percent before contraction strength decreased, indicating a true flow dependent metabolic rate. At spontaneous flows, increasing blood oxygen tension by 100 percent O_2 breathing gas during the contractions did not increase contraction strength. The breathing gas could be reduced to 12 percent O_2 before contraction strength decreased. These data support the hypothesis that oxygen transport does not limit metabolic rate unless O_2 transport is reduced below spontaneously occurring levels. The metabolic rate limiting process must be within the muscle. (Supported by NIH Grant GM06264-13)

INTERACTION OF LUNG VOLUME AND CO_2 TENSION ON BREATH HOLDING TIME. N.N. Stanley*, M.D. Altose* and N.S. Cherniack. Cardiovascular-Pulmonary Division, University of Pennsylvania, Philadelphia, Pa.

We studied the effects of lung volume and P_{CO_2} on breath holding time (BHT) during hyperoxia. Apnea was commenced over a wide P_{CO_2} range by using hyperventilation or CO_2 rebreathing to vary the initial P_{CO_2} of each breath hold. For apnea started at hypocapnic levels, BHT was unaffected by lung volume and the breaking point P_{CO_2} always fell within narrow limits (48-52 mm Hg) whatever the initial P_{CO_2}. This contrasted with breath holding after rebreathing in which (1) BHT increased with lung volume and (2) increases of initial P_{CO_2} were accompanied by higher breaking point P_{CO_2} levels, despite reduced BHT. Consecutive breath holds performed during the course of rebreathing were also longer at TLC than at FRC, but the effect of lung inflation was reduced when only one breath separated the periods of apnea. The number of breaths between serial breath holds at FRC had no effect on BHT. Phasic electrical activity of the diaphragm was usually completely suppressed during breath holding, but voluntary phasic contractions of the respiratory muscles with a closed glottis prolonged BHT. Thus, breath holding may be terminated by P_{CO_2} only when a threshold value is exceeded. Above this CO_2 threshold a lung volume factor interacts with the CO_2 stimulus, but the factor facilitating breath holding at TLC may adapt during prolonged apnea and fails to recover immediately. (Supported by NIH grant HE-08805.)

INTERACTION OF LANTHANIDES WITH Na^+ AND K^+ ACTIVATION IN SQUID AXONS. Michael Starzak*, Joseph P. Senft, and William J. Adelman, Jr. Marine Biological Laboratory, Woods Hole, Mass., State Univ. of N. Y. at Binghamton, Binghamton, N. Y., Rutgers - The State Univ., New Brunswick, N. J., Laboratory of Biophysics, NINDS, NIH, Bethesda, Md.

Ca^{2+} must be present for normal excitability in squid axons. Ca^{2+} interact with both the Na^+ and K^+ conductance changes which occur during excitation. The approach followed in this study to investigate this interaction was to substitute ions of the lanthanide series for Ca^{++}. These ions have many chemical properties in common with Ca^{2+}; in particular their crystal radii are similar. Voltage clamp techniques were used to analyse membrane currents when axons were exposed to 10 mM concentrations of these ions as replacement for the usual Ca^{2+} concentration. All ions gave a two rate constant decrease in resting potential; an initial rapid fall, during which the action potential overshoot remained nearly constant, followed by a slow decline. The rapid fall appeared to be almost completely reversible while the slow decline was not. The effectiveness of lanthanides in inhibiting membrane currents was $Sm^{3+} = Eu^{3+} > Yb^{3+} > Eu^{2+} > La^{3+}$. Current measurements showed that during the rapid resting potential decline K^+ conductance was reduced more rapidly than the Na^+ conductance. The kinetics of the interaction of these ions, as well as that of Ca^{2+}, with the Na^+ and K^+ conductances will be presented and discussed with particular reference to the Hodgkin and Huxley parameters which describe these conductances.

Supported in part by funds from NINDS, NIH, PHS.

ACID HYDROLASE ACTIVITY IN THE SARCOPLASMIC RETICULUM OF RAT SKELETAL MUSCLE. William T. Stauber* and John W. C. Bird. Department of Physiology, Rutgers University, New Brunswick, New Jersey 08903.

Fractions (M+L) rich in acid hydrolase activity, isolated by differential centrifugation from rat skeletal muscle tissues, were subfractionated by S-ρ zonal separations in sucrose gradients containing 0.02 M KCl. Zonal fractions were assayed for protein, cytochrome oxidase, 3 acid hydrolases (cathepsin D, pNPPase, and β-glucuronidase), catalase, and 2 ATPases (Ca^{++}-activated and "extra" ATPase). The results indicate the presence of 2 lysosome populations having different S-ρ coordinates, but both containing calcium activated ATPase activity. Zonal fractions incubated with 3 mM $CaCl_2$-EGTA, 5 mM ATP, and 5 mM $MgCl_2$ in 5 mM imidazole buffer (pH 7.2) produced an increase in density of a portion of both lysosome populations similar to the effect described for isolated sarcoplasmic reticular membranes. Our results suggest that the lysosome indiginous to the muscle fiber and the sarcoplasmic reticulum belong to the same subcellular compartment in rat skeletal muscle. (Supported in part by U.S.P.H. grant NS-07180.)

A UNIFYING AND COMPREHENSIVE HEMODYNAMIC EQUATION INDICATIVE OF MYOCARDIAL CONTRACTILITY. Paul D. Stein and Edward F. Blick*. Univ. Oklahoma School of Med. and V. A. Hosp., Oklahoma City, Okla.

A physiologically meaningful equation that combines previously unrelated indices of contractility was derived from analysis of the rate of change of ventricular power. This equation, indicative of the fractional rate of change of ventricular power, is $1/p\ dp/dt + 1/\dot{Q}\ d\dot{Q}/dt$ where p is pressure, $\dot{Q}$ is flow, dp/dt and $d\dot{Q}/dt$ are their respective rates of change. Contractile element velocity (V_{CE}) and circumferential fiber shortening rate (V_{CF}) are factors which mathematically can be derived from the flow term. The equation can be extrapolated to Vmax (times a known constant) during isovolumetric contraction. Since dp/dt, $d\dot{Q}/dt$, V_{CE}, and V_{CF}, are indices of contractility, their incorporation within this equation suggests that it may be a more meaningful indicator of performance than any of these component factors. The validity of the expression was tested in dogs following pharmacological interventions. Both the fractional rate of change of power, (and rate of change of power from which it was derived) quantitatively reflected myocardial performance. Peak values of each changed concordantly with previously utilized indices. Graphic representation of the curves indicative of power velocity and of the fractional rate of change of power appeared to give meaningful information beyond that which was provided from analysis of the peak values. In summary, an equation was derived which incorporates the major indices of contractility into a unifying expression of myocardial performance. These diverse indices, therefore, conceptually can be related to each other as components of the fractional rate of change of power. Application of the equation shows that it is a meaningful and comprehensive indicator of contractility.

INCREASED VENOUS RETURN WITH HYPERCAPNIA. J.K. Stene,* S. Permutt, B. Burns.* Johns Hopkins University, Dept. of Environmental Medicine, Baltimore, Maryland 21205.

Using dogs prepared with a right heart bypass to control the right atrial pressure, we studied the effects of breathing 10% CO_2 in air on venous return. As the $PaCO_2$ increased from 24 to 67mmHg in 15 dogs, the venous return increased from 1877 to 2472ml/min($P<.01$) and the mean systemic pressure increased from 5.9 to 7.7mmHg($P<.01$). Thus, hypercapnia produced a parallel shift in the Guyton venous return curve similar to the shift caused by adding volume. In 8 dogs 20% of the blood volume was removed before hypercapnia. The increase in venous return and the shift in the venous return curve were more pronounced in the hemorrhaged dogs. Venous return did not increase if CO_2 was given during thoracic aortic occlusion. Occlusion of the thoracic aorta produced a significant increase in venous return of normocapnic dogs by transferring volume from the very compliant splanchnic veins to the less compliant cranial-forelimb veins. However, occluding the aorta while breathing 10% CO_2 decreased venous return from 2396 to 2005 ml/min ($P<.01$). Hypercapnia apparently reduces the volume contained in the splanchnic veins. The increased venous return with hypercapnia was abolished by pretreating the dogs with dibenzyline. We feel that the increased venous return of hypercapnia is due to a sympathetically mediated splanchnic veno-constriction which redistributes the blood volume and increases mean systemic pressure. (This work was supported by PHS Grants # ES000454 and # HL10342)

CYTOPHOTOMETRY OF FEULGEN-DNA IN MYOCARDIAL TISSUE FROM HYPOXIA EXPOSED RATS. Athleen J. Stere* and Adam Anthony, Dept. of Biology, Pennsylvania State University, University Park, Pa.

Cytophotometry used in conjunction with histochemical staining specific for a given chemical constituent provides a means of determining the relative concentration of that constituent in individual cells and also reveals whether a cell population is uniform with respect to the parameter in question. Cardiac hypertrophy, due to the increased work load imposed in an attempt to maintain adequate oxygen supply at the cell level, is an obvious systemic response to hypoxia exposure. Since hypertrophy implies increased protein synthesis, the primary aim of this study was to determine whether cardiac hypertrophy is accompanied by a concomitant change in metabolic state of DNA as reflected in increased affinity for Feulgen stain and, also, whether there is a change in DNA content of myocardial nuclei as cells increase in size. Myocardial tissue from rats exposed to reduced barometric pressure (380 mm Hg) for 0,1,4,7,14,21,28,42 and 56 days was stained by the Feulgen technique. When the DNA content was plotted in histogram form, there was no evidence of a shift in the profile, indicative either of increased Feulgen staining due to chromatin uncoiling when DNA is actively transcribing RNA or of increased mitotic activity as a result of hypoxia exposure. The DNA profile does show that roughly half of cardiac muscle nuclei are tetraploid (4C), only 10-20% are diploid, the remainder have greater than 4C amounts of DNA. It was concluded that lack of change in the physicochemical nature of cardiac muscle chromatin as a result of hypoxia exposure is due to the fact that chromatin in these cells is customarily diffuse and in a reactive state because cardiac muscle must maintain a high metabolic level at all times.

A MODEL OF AN EARLY 'OFF' RESPONSE IN FROG OPTIC TECTUM. Richard J. Stevens (intro. by Wm. C. Kaufman). College of Human Biology, Univ. of Wisconsin-Green Bay, Green Bay, Wisc.

In a study of visual information processing in the frog optic tectum, microelectrodes were used to measure action potentials (AP's) and field potentials (FP's) of the tectal response to a 10' of arc white light stimulus. With moderate dark-adaptation a short duration stimulus (15-200 msec) produced only an 'on' response. When the frog was highly dark-adapted and when the intensity of the stimulus was near threshold, it was found that the response developed a second, longer latency component which was very sensitive to degree of dark-adaptation and which was not observable for durations greater than 1.5 sec. The second component is termed the "early 'off'" since it was linked to the 'off' of the stimulus and since it was distinct from the 'off' response which occurred for all degrees of dark-adaptation and only for durations greater than 200 msec. Typical latency values measured from the onset of a 200 msec stimulus to the onset of the response are 140 msec for the 'on' response, 775 msec for the early 'off' and 1650 msec for the 'off'. The early 'off' was not observed in the retina with simultaneous tectal and retinal recordings. Only 'on' responses occurred in the retina for durations of less than 200 msec and only 'on' and 'off' retinal responses occurred for longer durations. The 'on'/early 'off' complex was highly sensitive to ACh and curare applied to the tectum, whereas only the early 'off' was sensitive to atropine. It appears the early 'off' is produced in the tectum and not in the retina. Assuming that phasic 'on' tectal afferents are excitatory and that sustained 'on' afferents are inhibitory, a model of tectal processing which explains the occurrence and properties of both the AP's and FP's observed for the early 'off' tectal response is presented.

METABOLISM OF ISOLATED ADIPOCYTES FROM VARIOUS TISSUE SITES IN THE RAT: INFLUENCE OF HEMORRHAGIC SHOCK. Richard Storck* and Judy A. Spitzer. Hahnemann Med. Col., Philadelphia, Pa.

Isolated adipocytes were prepared and their cell size distribution determined from epididymal (E), subcutaneous (SC), perirenal (PR), mesenteric (M), and omental (O) adipose tissue sites obtained from overnight fasted rats (300-350 g). Each animal was anesthetized with Nembutal and received 200 units of heparin. Norepinephrine-stimulated (0.2μg/ml.) glycerol (G) and free fatty acid release were determined. M and O adipocytes released significantly more G (per mmole triglyceride content) than did E, SC, and PR. M and O adipocytes were smaller (40-45μ in diameter) than E, SC, or PR (60-65μ in diameter). G release per 10^6 cells was not different in any of the five sites. Heparin administered in vivo did not alter the in vitro lipolytic response. Hemorrhagic shock (40 mm Hg for 2½ hrs.) caused a 50-60% decrease in the lipolytic rate (per 10^6 cells) of E, SC, PR, and M adipocytes. Cells of O origin maintained their lipolytic activity at the pre-hypotensive level. The results indicate that metabolic adjustments brought about by hemorrhagic shock are not uniform at all adipose tissue sites. (Supported by grant HE 03130 from the National Heart and Lung Institute.)

THE INTRARENAL DISTRIBUTION OF BLOOD FLOW IN SPONTANEOUSLY HYPERTENSIVE RATS. N.T. Stowe*, E.S. Chernak*, S. Sen*, and P.A. Khairallah, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio 44106.

Spontaneously hypertensive rats (SHR) exhibit an erythrocytosis which parallels the increase in blood pressure. The purpose of the present study was to determine if the intrarenal distribution of blood flow (ID BF) was altered in SHR and if this change could be a factor in the elevated erythropoietin levels. All rats were anesthetized with sodium pentobarbital (30 mg/kg) and the left kidney placed under a gamma counter. ^{133}Xe was injected through a cannula placed in the aorta. Normotensive Wistar rats (NWR) of the same weight were used as controls. Since α-methyldeoxyphenylalanine (α-methyldopa, 200 mg/kg I.P.) reverses the hypertension and erythrocytosis in SHR, these were also studied. The renal washout of ^{133}Xe in SHR and NWR was described by a four component exponential curve. In SHR treated with α-methyldopa, the renal washout curve was described by three components. The rate of disappearance of the first two components was slower in SHR than in NWR. The relative volume of distribution (RVD) of tissue perfused at the fastest flow rate was reduced by 38% in SHR. The RVD for the compartment corresponding to the second fastest component in SHR was 23% larger than the same compartment in NWR. The blood flow rates through compartments 1 and 2 was 51% less than the flow rates in the same compartments of NWR. Preliminary results from ^{85}Kr autoradiographs suggest that compartment 1 corresponds to the outer cortex in SHR. These data in SHR suggest that the total blood flow through the cortical compartment as well as the volume of distribution of this compartment is reduced, consistent with the report that renal vascular resistance is increased. Such an alteration in the IDBF may cause the release of an erythropoietic factor which is responsible for the erythrocytosis. (Supported in part by NHLI Grant HL6835).

EFFECT OF α-ADRENERGIC BLOCKADE AND β-ADRENERGIC STIMULATION ON PROXIMAL SODIUM REABSORPTION. J.W.Strandhoy*, L.R.Willis*, E.G.Schneider, and F.G.Knox. Nephrology Research Laboratory, Department of Physiology, Mayo Clinic, Rochester, Minnesota.

The adrenergic nervous system has been implicated in the regulation of proximal sodium reabsorption independent of renal hemodynamic changes. The effects of renal α-adrenergic blockade and β-adrenergic stimulation on proximal Na reabsorption were measured with micropuncture techniques. As an additional index of proximal Na reabsorption, the fractional excretion of phosphorus (C_{PO4}/C_{In}) was measured. In 11 dogs, phenoxybenzamine (POB, α-adrenergic blocking agent), .09 μg/kg/min was infused into the renal artery after an initial period of hydropenia, increasing urine flow, V, by .15 ± SE.04 ml/min ($p<.005$) and Na excretion, $U_{Na}V$, by 35 ± 5 μEq/min ($p<.001$). There were no changes in glomerular filtration rate (GFR), renal plasma flow (RPF), filtration fraction (FF), nephron gfr, tubular fluid/plasma inulin concentration (TF/P_{In}) (-.04 ± .04) or C_{PO4}/C_{In} (-.05 ± .26). In another series of 7 dogs, renal α-blockade (POB) was compared to α-blockade + β-stimulation (POB + isoproterenol, .018 μg/kg/min into the renal artery). Additional increases in V (.17 ± .09 ml/min) and $U_{Na}V$ (37 ± 19 μEq/min) were found. No significant alterations were found in GFR, RPF, FF, nephron gfr, TF/P_{In} (0 ± .04) or C_{PO4}/C_{In} (.30 ± 1.93). In a control group of 11 dogs studied during continued hydropenia, none of the measured clearance or micropuncture parameters were changed. We conclude that α-adrenergic blockade and β-adrenergic stimulation increase $U_{Na}V$ to a modest degree independent of detectable hemodynamic alterations, but have no detectable effect on proximal Na reabsorption as measured by both direct and indirect methods.

COLCHICINE, CYCLOHEXIMIDE AND SEROTONIN INHIBITION OF INTESTINAL FLUID PRODUCTION CAUSED BY CHOLERA TOXIN. D. R. Strombeck (intr. by R. C. Ingraham). University of Illinois, College of Medicine, Chicago, Illinois 60680.

Cholera toxin binds rapidly and irreversibly to intestinal mucosa yet marked hypersecretion of intestinal fluid does not occur for several hr. Since the basis for this latent period is not fully understood, inhibitors of various physiological processes were employed to study this phenomenon. Rats in which cholera toxin (Wyeth, NIH Lot 001, 30 mg/ml) was placed in closed loops of the upper small intestine were used. The loops were removed 5 hr later and the fluid contents weighed. Colchicine (IV) inhibited (57% to 63%) the production of fluid stimulated by cholera toxin when the drug was given 90 min before toxin treatment to 45 min after. When colchicine was given 90 min after the toxin, inhibition was only 14%. Cycloheximide (IV) inhibited fluid production 57% when given 90 min before toxin treatment but when the drug was given simultaneously with the toxin, 15 min or 90 min after the toxin, inhibition was 37%, 28% and 12%, respectively. Serotonin (IP) given 90 min after toxin treatment inhibited fluid production 71%. These results suggest that colchicine, which is known to disrupt the microtubular system, could prevent the intracellular transport of cholera toxin to its site of action. Maximum inhibition by cycloheximide occurs only when given early, and this suggests that the drug may inhibit toxin binding to the mucosa or entry of the toxin across the mucosal border. The inhibitory action of serotonin still present 90 min later supports an earlier suggestion that it acts upon the microcirculation for its effect.

Dietary Influences on the Activity of Gulonolactone Hydrolase in Rats. Don W. Stubbs. Department of Physiology, The University of Texas Medical Branch, Galveston, Texas 77550.

Rats excrete about half of the ascorbic acid they synthesize, the remainder being metabolized to smaller products. In comparison to the rate of utilization this synthesis is a substantial surplus and appears to be more than sufficient to saturate the tissues with ascorbic acid. Further increases in availability of ascorbic acid by adding it to the diet raise the levels of ascorbate in blood and urine but do not substantially elevate tissue concentrations. Dietary feeding of ascorbic acid does not influence the activity of gulonolactone hydrolase (GLH), the rate-limiting enzyme within the biosynthetic pathway to ascorbic acid from glucuronic acid. This finding argues against a possible role of ascorbic acid in endproduct feedback control on this part of the pathway. Translational control of GLH is apparently primarily dependent on amino acid uptake by hepatic ribosomes as influenced by growth hormone and dietary protein. Both are required: in the absence of growth hormone a 27% protein diet is unable to maintain normal GLH activity in hypophysectomized rats, and in the absence of dietary protein growth hormone is unable to increase GLH activity. (NIH AM 09669)

BEHAVIORAL AND PHYSIOLOGICAL TEMPERATURE REGULATION IN BOX TURTLES (Terrapene ornata). B.A. Sturbaum* and M.L. Riedesel, Dept. of Biol., Univ. of New Mexico, Albuquerque, New Mexico.

Behavioral responses including seeking shaded areas and water were efficient in lowering core temperature; however when placed in thermal environments where behavioral responses were inadequate, the physiological responses to heat included increased heart rate, panting, buccal-pharyngeal movements, excessive salivation and urination. Animals preheated to 38 to 40C core temperature placed in an environment with 38C Ta and Tg reduced core temperature ranging from 6.4 to 0.6C below the ambient temperature. The major avenue of heat loss was by evaporation from the oral cavity as the oral temperature of these animals was as low as 25C.

In thermal equilibration experiments, animals maintained a gradient between core and environment near zero in 38C environments and a gradient as great as 10C in 51C environments. Additional experiments conducted include comparing rates of heating and cooling of live and dead animals. The efficiency of preferential distribution of blood flow and efficiency of evaporation will be discussed.

AVIAN CARDIAC NEUROTRANSMITTER. Paul D. Sturkie and David Poorvin*, Department of Environmental Physiology, Rutgers University, New Brunswick, New Jersey.

Levels of Norepinephrine (N) and Epinephrine (E) in blood and heart of chickens are high and variable depending on degree of excitement, stress, anesthesia; circulating E which is higher than N comes from adrenals and is very loosely bound in heart, but N is tightly bound. In the isolated perfused heart E is washed out soon, but N is not released until the cardioaccelerator nerve is stimulated. Histofluorescence studies revealed adrenergic nerve terminals in all 4 chambers of heart, containing N which was absent after denervation or depletion with reserpine and decaborane. Cardioaccelerator nerve (CA) stimulation releases not only N, but also a cholinergic component which is blocked with atropine. Post vagal tachycardia could be abolished by propranolol in even sympathectomized birds. The right CA nerve innervates mainly the right atria and left CA the ventricles.

IDENTIFICATION AND LOCATION OF INHIBITORY INTERNEURONS WHICH SYNAPSE ON HYPOGLOSSAL MOTONEURONS. R. Sumino and Y. Nakamura (intr. by R. Dubner). Institute of Brain Research, University of Tokyo, Tokyo, Japan.

In the region of the hypoglossal nucleus, intracellular and extracellular recordings were made from a group of neurons which could not be antidromically activated by stimulation of the hypoglossal nerve. These neurons fired in regular bursts of 3 to 18 spikes, with frequencies of up to 900/sec, following suprathreshold stimulation of the inferior alveolar nerve (IAN), the masseter nerve (MN), and the hypoglossal nerve. In response to increases in stimulus intensity applied to the IAN and the MN, the number of spike discharges correlated closely with the amplitude of induced IPSPs recorded from hypoglossal motoneurons. With a single shock applied to the ipsilateral IAN, the mean latency of onset of the initial spike (3.28 ± 0.33 msec, n=19) was 0.56 msec shorter than the mean latency of onset of IPSPs of hypoglossal motoneurons (3.84 ± 0.44 msec, n=28). Electrophoretic injection of dye (methylene blue) through the recording microelectrode revealed that all these neurons were localized in the region ventral to hypoglossal motoneurons around the radix of the hypoglossal nerve. These data suggest that small cell groups ventral to the hypoglossal nucleus, such as the nucleus of Roller and the nucleus interfascicularis, function as inhibitory interneurons in the trigemino-hypoglossal reflex.

HEPATIC AND SPLENIC BLOOD FLOWS DURING ENDOTOXIC SHOCK IN BABOONS. K. G. Swan, L. W. Evans* and D. G. Reynolds*. Walter Reed Army Institute of Research, Washington, D. C.

Mesenteric blood flow is well maintained during early endotoxic shock in the monkey but not the dog (Swan, Gastroenterology 61: 872, 1971). Under the same circumstances blood flow through the liver and spleen were compared in the two species. Under pentobarbital anesthesia electromagnetic blood flowmeter transducers were placed on the hepatic and splenic arteries. Arterial (AP) and venous (VP) pressures were recorded. Intravenous endotoxin (E. coli, LD_{80}) reduced AP in the baboon from a control of 122 $\pm$ 3 (S.E.) to 67 $\pm$ 5 mm Hg within 150 minutes ($p < .001$). Hypotension was sustained. Splenic blood flow (SBF) underwent a gradual and progressive fall which paralleled changes in AP. Hepatic blood flow (HBF) and VP were not significantly changed ($p > .10$) from their control values (106 $\pm$ 19 ml/min, and 4.0 $\pm$ 0.6 mm Hg). Calculated hepatic vascular resistance (R) fell from 1.11 to 0.71 peripheral resistance units within 30 minutes following endotoxin and the fall in resistance was sustained. In contrast, the dog exhibited similar changes in arterial pressure, however, a marked fall in HBF and SBF accompanied a progressive increase in R across both vascular beds. The liver and spleen of the dog appeared to be "target organs" of experimental shock. These findings contrast the subhuman primate in which hepatic blood flow is maintained despite marked hypotension. Although blood flow to the monkey spleen falls during endotoxic shock, the contribution to total splanchnic circulation is small. These findings provide no support for the concept of the splanchnic visceral circulation as a target of experimental or clinical shock.

EFFECT OF [1-SARCOSINE, 8-ISOLEUCINE]-ANGIOTENSIN II IN NORMOTENSIVE, ACUTE RENAL HYPERTENSIVE AND CHRONIC PERINEPHRITIC HYPERTENSIVE DOGS. C.S. Sweet*, C.M. Ferrario, M.C. Khosla*, and F.M. Bumpus*, Research Div., Cleveland Clinic, Cleveland, Ohio 44106.

[1-sarcosine, 8-isoleucine]-angiotensin II [Sar^1, Ile^8]-Ang II, a competitive antagonist of angiotensin II (Ang II), has been used in the present experiments to assess the contribution of the renin-angiotensin system in two hypertensive states. Three series of experiments were performed to evaluate (1) the antagonistic effect of [Sar^1, Ile^8]-Ang II against the pressor response (PR) to exogenous Ang II in anesthetized, normotensive dogs, (2) its effect on the sustained pressor response following acute renal artery constriction (1-2 hours) and (3) the response of the antagonist in unanesthetized dogs with chronic perinephritic hypertension. In the first series of experiments, the PR to a range of doses of Ang II was significantly reduced during intravenous infusions of the antagonist (200 ng/kg/min) lasting 55 minutes. PR had returned to 75% of control 60 minutes after the infusion. The PR to i.v. norepinephrine (NE) did not change. [Sar^1, Ile^8]-Ang II (400 ng/kg/min, i.v.) completely antagonized the hypertensive response to Ang II released endogenously during acute reduction (50%) of renal blood flow in the second series of experiments. The PR to Ang II, but not NE, was completely blocked. In contrast, acute i.v. infusions of the antagonist (> 2γ/kg/min x 90 min) in chronic perinephritic hypertensive dogs did not reduce mean arterial blood pressure, although the PR to exogenous Ang II was completely suppressed. Experiments are now in progress to assess the long term effect of [Sar^1, Ile^8]-Ang II in chronic hypertensive dogs. The results suggest that [Sar^1, Ile^8]-Ang II is a long acting specific antagonist against Ang II in dogs and may be useful in ascertaining the contribution of angiotensin in various hypertensive states. (Supported by NHLI, Grant #HL-6835).

EFFECTS OF PERIPHERAL CHEMORECEPTOR DENERVATION ON THE RAPID VENTILATORY RESPONSES TO BRIEF, ASCENDING AORTA INFUSIONS OF CO_2- EQUILIBRATED BLOOD IN LIGHTLY ANESTHETIZED DOGS. J. T. Sylvester*, B. J. Whipp, and K. Wasserman. Dept. of Med., Harbor Gen. Hosp., Torrance, Calif. 90509 and UCLA School of Med., Los Angeles, Calif. 90024.

In order to determine the sites responsible for the rapid ventilatory responses to small increases in arterial CO_2 tension, the carotid bodies and cervical vagus nerves of dogs, lightly anesthetized with thiopentol, were sequentially denervated, bilaterally. Before and after each stage of denervation, CO_2 - equilibrated blood was infused for 20 seconds into the ascending aorta (AA). The ventilatory responses were determined breath-by-breath a) in the intact animal, b) after bilateral carotid body resection (CBR), and c) after CBR and bilateral cervical vagotomy. Peripheral chemoreceptor denervation was confirmed by histological examination of the excised tissue, characteristic changes in arterial blood pressure and in the pattern of ventilatory responses to hypoxia. In the intact, lightly anesthetized animal AA infusions produced increases in $\dot{V}_E$ with a latency of 9.1 seconds, time to peak response (from the beginning of the response) of 17.5 seconds and response sensitivity (S) of 0.33 L/min/mm Hg. After CBR, latency was doubled but peak response time and S were not changed. Following subsequent vagotomy, peak response time and S remained unaltered and latency was not further changed. The duration of response, however, became significantly prolonged. These results indicate that the aortic and carotid bodies are not the unique chemoreceptors responsible for the rapid ventilatory responses observed during brief increases in arterial CO_2 tension. Supported by PHS Grant HL-11907.

ANTICATATOXIC EFFECT OF SOMATOTROPHIC HORMONE (STH) AND L-THYROXINE. S. Szabo* and H. Selye. Institute of Experimental Medicine and Surgery, University of Montreal, Montreal, Que., Canada.

Certain steroids [e.g., pregnenolone-16α-carbonitrile (PCN), progesterone] and polypeptide hormones (e.g., ACTH) possess a resistance-increasing or catatoxic effect, which is often mediated through the induction of drug-metabolizing enzymes of hepatic microsomes. This prophylactic action can be counteracted by STH or L-thyroxine. Thus, pretreatment of female Sprague-Dawley rats (100 g) with PCN (50 μg twice daily po.) for three days completely prevents the fatal convulsions caused by digitoxin (2 mg po. on the 4th and 5th day) as well as the jejunal ulcers and mortality elicited by indomethacin (1 mg sc. from the 4th to the 8th day of the experiment). This protective effect of PCN is blocked by bovine STH (1 mg twice daily sc.) or L-thyroxine (200 μg once daily sc.). Pretreatment with ACTH (50 I.U. thrice daily) for seven days prevented the bilateral adrenal apoplexy and mortality produced by acrylonitrile (15 mg iv.). STH + ACTH still protected against acrylonitrile-induced adrenal lesions but not against mortality. Under our experimental conditions STH, given alone, failed to influence the action of the three toxicants. (Supported in part by the Medical Research Council of Canada, and the Ministère des Affaires Sociales, Quebec.)

* Fellow of the Medical Research Council of Canada

THE PITUITARY-ADRENAL RESPONSE TO STIMULATION OF THE MEDIAL BASAL HYPOTHALAMUS (MBH) IN AWAKE, UNRESTRAINED MALE CATS. Henry Szechtman*, E. Edwin Fahringer*, and Edward S. Redgate. Depts. of Psychology and Physiology, University of Pittsburgh, Pittsburgh, Pa.

A non-stressful environment was established for freely behaving cats to test the excitability of hypothalamic sites mediating ACTH release. Each subject (S) was chronically implanted with bilateral electrodes and catheterized in superior vena cava. Plasma corticosterone (B) and cortisol (F) concentration was determined by fluorometry after chromatographic separation. Blood samples were collected at 5 and 30 minutes after entering the experimental room. Cats were housed and permitted to exercise in this room. Samples were taken during both sham and electrical stimulation (ES) while the Ss, of their own volition, reclined in a tray. Mean plasma F but not B steroids were significantly elevated after ES. B values during control and ES sessions were low, the changes were small and not correlated with F. The F response to ES was approximately equal to the response to a pharmacological dose of ACTH. Samples collected early in the 3 month experimental period showed F values as high as the F response to ACTH. Repetition of the sampling procedure produced low F levels in 3/3 cats. No discernible change in the cats' overt behavior accompanied this decrease in F. ES which produced a rise in plasma F, did not necessarily result in an overt behavioral reaction. When an overt response occurred, steroid elevation occurred. When control F values were high, stimulation was followed by a decrease in F; stimulation when F values were low resulted in increased F. The excitatory influence of MBH on F was confirmed under barbituate anaesthesia. It is concluded that ES of the MBH maximally elevates F when control values are low. Repeated training lowers initially high F levels. (Supported by NIH04095, U. Pgh. Medical Alumni Fellowship, PHS grant MH16581).

INTERCAUDATE RESPONSES AND RETICULAR FORMATION CONTROL. Emery G. Szekely and Gunter R. Haase*. Dept. of Neurology, Temple University School of Medicine, Philadelphia, Pa. 19140

It is known (e.g. Davison) that in Parkinsonism, including the so-called hemiparkinsonian cases, bilateral involvements are present in the substantia nigra and in the basal ganglia. This was the basis for our first series of metabolic investigations in cats and rats which indicated that lesions placed into the heads of the caudate nuclei changed the chemical and physiological status of the contralateral caudate nuclei. We studied electrographically the interstriatal relationship and the interconnecting bridge. Severance of the midline-fibers of the anterior, Meynert's, the supraoptic and Forel's commissures or the diagonal band of Broca did not noticeably influence the intercaudately evoked potentials. The corpus callosum(containing the part of the anterior forceps) and the fasciculus subcallosum form apparently the bridge for transmitting intercaudate communications, with or maybe without cortical involvement. During this study we made experimental sections at the superior collicular level (cerveau isolé), which increased greatly the amplitude of the intercaudate responses. Similarly Spiegel et al. observed changes in the caudate responses during stimulation of the vestibular nuclei after lesions had been placed in the dorsal part of the reticular formation of the midbrain. The two similar observations are perhaps due to interruption of inhibitory systems located in the dorsal parts of the midbrain reticular formation. Similar inhibitory functions of the reticular formation have been reported by others.

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CONTROL OF POSTURE BY DOGS WITHOUT VISUAL AND VESTIBULAR INPUT. R. E. Talbott and J. M. Brookhart. Univ. of Oregon Medical School, Portland, Oregon.

The extent to which visual and vestibular input enables the dog to maintain normal standing posture was quantitatively assayed. Dogs were trained to stand upon a moveable platform. The platform was moved sinusoidally in the headward-tailward direction (8 cm pk-to-pk; 0.2 to 2.0 Hz). Postural adjustment to this imposed motion was assessed from the changes in the angles found at the hip, knee, ankle and hind paw phalangeal joints and from the horizontal movements of the pelvis. Four states of the dogs were tested: normal, normal-blindfolded, chronic labyrinthectomized, and labyrinthectomized-blindfolded. The dynamic changes in posture required to maintain upright stance were quantitatively described by the use of Fourier analysis yielding the amplitude and phase coefficients of the driving frequency and its first four harmonics. Blindfolding both normal and labyrinthectomized dogs resulted in marked changes in the postural response at the lower frequencies. These were found in the movements about the knee, ankle and phalangeal joints and in the motion of the body with little change in hip motion. Chronic labyrinthectomized dogs differed markedly from normals in body movement, phalangeal joint angles, and in the harmonic content of hip angle signals. It is concluded that visual input contributes an important influence to the nervous system necessary for normal integrated postural response to low frequency disturbances. The effects of vestibular input are evident over a broader frequency range; its loss is never completely compensated. (This research was supported by N.I.H. Grant NS-04744).

RELATIVE ROLES OF VASCULAR RECRUITMENT AND DISTENSIBILITY IN MEASUREMENT OF EXTRAVASCULAR LUNG WATER. R. Tancredi*, P. Caldini, M. Shanoff* and S. Permutt. School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Maryland.

Pulmonary blood volume (PBV) and extravascular lung water (EVW) were measured in dog lungs perfused by double heart by-pass over a wide range of flows (F) at low and high left atrial pressures (P_{LA}). Pulmonary artery pressure (P_{PA}) was measured and airway pressure held constant. At each flow, a vascular reference tracer (I^{131}-albumin, RISA) and a diffusible tracer (I^{125}-antipyrine, IAP) were injected simultaneously into pulmonary artery, and mean transit times ($\bar{t}$) for each tracer were calculated from isotope dilution curves recorded by a gamma probe on the outflow line from left atrium. PBV [$F \cdot \bar{t}_{RISA}$] and EVW [$F \cdot (\bar{t}_{IAP} - \bar{t}_{RISA})$, with correction for plasma water] both increased as functions of P_{PA}, and were unaffected by changes in P_{LA} at any given P_{PA}. EVW/PBV was 0.8 at P_{PA} = 9 mmHg but decreased to a plateau of 0.5 at $P_{PA} \geq 20$ mmHg. In separate isolated lobe perfusion studies, changes in lung weight nearly equaled changes in PBV. Therefore, changes in measured EVW were not associated with any changes in total lung water. The constant EVW/PBV seen at $P_{PA} \geq 20$ mmHg suggested that recruitment of vascular channels was the primary mechanism for increasing PBV at high P_{PA}. Below 20 mmHg, both recruitment and distensibility contributed to measurement of PBV.

Substrate Utilization in the Isolated Perfused Dog Kidney. Marvin Tark*, Terrence Hoffer* and Howard M. Randall, Jr. Department of Physiology, Louisiana State University Medical Center, New Orleans, La. The metabolic activity of the isolated, perfused kidney was studied to: 1) quantify the effect of the rate of renal blood flow (RBF) on substrate utilization; and 2) study the relationship between the renal handling of FFA and glucose. Kidneys from donor dogs were placed into a pump-oxygenator system and perfused with freshly drawn whole blood. Clearance experiments were done in which GFR, RBF, $\dot{Q}$FFA, $\dot{Q}$glucose and Na^+ transport were determined. The perfused kidney appeared to be in an adequate physiological condition as indicated by its initial rates of RBF and its utilization rates of O_2 and FFA; all were comparable to that of an in vivo kidney. However, GFR was below in vivo values. The rates of RBF were reduced sequentially to 67% and 15% of control rates by reducing the perfusion pressure. The results demonstrate that the rates of FFA utilization were proportional to concentrations of arterial FFA as demonstrated previously in the in vivo kidney. The rate of FFA utilization was found also to be proportional to the rates of RBF, Na^+ transport and O_2 consumption suggesting that FFA is handled by the kidney in a manner similar to that of O_2 and that FFA oxidation may in part directly supply the energy necessary for the transport of Na^+, as observed in the in vivo kidney. The utilization of glucose, a substrate that can be utilized by the kidney, was found to be inversely proportional to the rate of FFA utilization, suggesting that glucose may substitute for FFA as an energy source. (Supported by USPHS Grant No. HE 11987).

SYNAPTIC EVENTS IN PUDENDAL MOTOR NEURONS OF THE CAT. Charles T. Teague, Gerald W. Timm and William E. Bradley (intr. by G.F. Ayala). University of Minnesota Medical Center, Minneapolis, Minnesota.

Two effects of pelvic nerve activity on pudendal motoneurons have been demonstrated in spinal cats. The first is an excitatory reflex of brief duration evoked by pelvic afferent nerve stimulation with the bladder empty. The second is an inhibitory reflex evoked by pelvic afferent nerve stimulation during bladder distension. The presence of these two different effects suggested the possibility of both pelvic nerve afferent inhibitory and excitatory synaptic endings on pudendal motoneurons. Therefore, cats with spinal cords acutely transected at the level of T-10 were used in a microelectrode analysis of pudendal motoneurons identified by antidromic stimulation of the pudendal nerve. Some pudendal motoneurons responded to pelvic nerve afferent stimulation with an EPSP, while other pudendal motoneurons responded with an IPSP. These results suggested the possibility of both presynaptic and postsynaptic interaction of pelvic nerve afferents with pudendal nerve afferents on pudendal motoneurons.

INTRACELLULAR STUDIES OF SYNCHRONIZING SYNAPTIC EVENTS IN IMMATURE THALAMIC NEURONS. R.W. Thatcher* and D.P. Purpura. Albert Einstein College of Medicine, Bronx, N.Y.

Low-frequency (3 cps) stimulation of medial thalamic regions (MTh) initiates 6-45 msec ($\bar{x}$=15 msec) latency IPSPs of 30-150 msec duration ($\bar{x}$=59 msec) in 75% of 106 cells impaled in the rostral thalamus of kittens less than 8 days old. In older kittens (2 weeks) IPSP mean latency was 15 msec and mean duration 130 msec in neurons examined at this stage. EPSPs preceding IPSPs are poorly represented in MTh-induced synaptic events but become more prominent with increasing age. Little correlation is observed between cortical surface and thalamic intracellular activities in very young kittens. Typical thalamocortical recruitment occurs by the second week. IPSP-summation is observed in immature thalamic neurons during high-frequency MTh-stimulation.This is generally succeeded by initial IPSP-attenuation during subsequent low-frequency stimulation. In older kittens high-frequency MTh-stimulation initiates brief IPSP-summation which is terminated by prominent sustained EPSP-summation as in adult animals. The data indicate that inhibitory synaptic activities are prominent though poorly developed in thalamic neuronal operations in the first postnatal week. Functional maturation of these activities and parallel development of excitatory synaptic events underlie the postnatal ontogenesis of thalamocortical synchronization.

COMPARISON OF ADENOSINE PRODUCTION IN ATRIAL AND VENTRICULAR MUSCLE. Rosemary Thomas*, Rafael Rubio, and Robert M. Berne. Department of Physiology, University of Virginia, School of Medicine, Charlottesville, Virginia 22901

In response to ischemia, ventricular myocardium is capable of a graded release of adenosine, a possible mediator in the control of coronary blood flow. The enzyme 5'-nucleotidase, which catalyzes the hydrolysis of AMP to adenosine, is located on the external membranes of ventricular myocardial cells (sarcolemma, intercalated discs, T-tubules). Since atrial cells lack T-tubules and hence have a smaller surface to volume ratio, it is possible that they contain lesser amounts of 5'-nucleotidase per unit volume and, with ischemia, would produce adenosine and its degradative products inosine and hypoxanthine at a slower rate than ventricular cells. To test this hypothesis, dog hearts were rendered ischemic for periods of 0 to 60 min. In atrium, at all times except 0 min., adenosine and inosine levels were less than those in ventricle (as little as one-tenth), and hypoxanthine reached ventricular levels only after 60 min. "In vitro" studies have shown ATP and ADP to be inhibitors of 5'-nucleotidase. Therefore, ATP, ADP and AMP levels (μmoles/g) were measured in both atrium and ventricle. At 0 min. ATP levels were 2.9 and 5.3, ADP levels 0.5 and 0.6, and AMP levels 0.08 and 0.06 μmoles/g in atrial and ventricular muscle respectively. These atrial, ATP and ADP levels would favor less inhibition of 5'-nucleotidase and therefore a greater rate of adenosine production. Therefore, the slower rate of production of adenosine, inosine and hypoxanthine is consistent with fewer AMP hydrolyzing sites per unit cell volume in atrial muscle.

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P_{50} CHANGES AT EXHAUSTION FOLLOWING AN HOUR OF INTENSE, MUSCULAR WORK. J. Thomson*, J.A. Dempsey, F. Cerny*, L. Chosy*. Pulmonary Physiology Lab, University of Wis., Medical School, Madison, Wis.

This study was concerned with the effects of prolonged work upon oxy-hemoglobin affinity determined under standard conditions (i.e. pH=7.4, temp. = 37°C, pCO_2=40mmHg). Six healthy, male volunteers (age 25-43 yrs.) walked at 3.5 mph on a graded treadmill at 61.8% to 68.3% of their maximal O_2 consumption to exhaustion ($\bar{x}$ time to exhaustion = 73.6 minutes). Brachial arterial and deep femoral venous blood was sampled simultaneously at intervals throughout the exercise period and at exhaustion. Results: Three subjects experienced a rightward P_{50} shift in femoral venous blood at exhaustion ($\bar{x}$ = 1.7mmHg). This reduction in O_2 - Hg affinity was also reflected in their final femoral blood sample which was right-shifted, in vivo, in excess of both the "calculated" effects of pH, intra-vascular temperature and pCO_2 and their in vivo O_2 dissociation curve "simulated" in vitro via tonometry. Conversely, the 3 subjects who did not experience a P_{50} shift at exhaustion did not experience a disproportionate in vivo shift. These results support the hypothesis, suggested by two previous studies, that in muscle tissue a "mechanism" exists for reducing O_2-Hemoglobin affinity.

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AMNIOTIC FLUID OF THE FOUR AND ONE-HALF DAY CHICK EMBRYO Kent L. Thornburg*, Thomas J. Green*, Charles F. Gault*, J. Job Faber. Department of Physiology, University of Oregon Medical School, Portland, Oregon 97201

Radio chloride was injected into an extraembryonic vitelline vein with the embryo in ovo. The eggs were analyzed at various intervals after injection. Plasma concentration of radio chloride fell to about one-tenth of its initial value in eight hours. Amniotic fluid concentration rose initially, continued to rise after reaching equality with plasma concentration, and then fell but remained in excess of plasma concentration.

The electrical potential of the amniotic fluid was 4.4 (± 0.6 SEM) mV below that of the blood plasma. Chloride concentrations were 128.5 (± 1.9 SEM) and 113.0 (± 3.0 SEM) meq/l in amniotic fluid and plasma respectively, and independent of embryo age.

On this basis a chloride pump was postulated. The transfer effected by the pump was calculated to be +0.0138 μeq/min. The diffusional flux was calculated to be -0.0086 μeq/min and the net influx to be 0.0052 μeq/min. The chloride already present at the beginning of the experiments was 5.41 μeq. The "growth" of chloride was therefore 0.097%/min. The growth of the amniotic fluid volumes directly measured was 0.102%/min. No sodium pump was demonstrable by experiments with sodium.

The pump flux of chloride may be an early step in the generation of the amniotic fluid.

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1,3-BUTANEDIOL EFFECTS ON GLUCOSE METABOLISM IN HUMAN SUBJECTS. R.B. Tobin, M.A. Mehlman, C.V. Kies*, H.M. Fox* and J.S. Soeldner. Omaha Veterans Administration Hospital, University of Nebraska College of Medicine, University of Nebraska School of Home Economics, and Harvard Medical School.

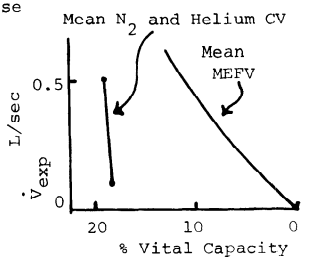
Synthetic sources of dietary calories are of interest as potential food reservoirs for an expanding world population, and may also have value in control of diseases such as diabetes, obesity, and atherosclerosis. Feeding 1,3-Butanediol (BD) is known to decrease blood sugar in rats and in human beings. BD feeding causes increased content of the gluconeogenic enzymes PEP carboxykinase and pyruvate carboxylase in rat liver. Livers perfused with BD however show decreased production of glucose from lactate. To understand better the mechanisms of influence of BD on carbohydrate metabolism in humans, additional studies of BD feeding were undertaken. Female volunteers were fed diets with either 40 gm BD per day, or a calorically equal quantity of sucrose for five day periods. Fasting blood samples were collected before and after each period, and analyzed for glucose, insulin, growth hormone, cholesterol, and triglycerides. BD feeding caused no change in glucose, triglycerides, or cholesterol values. Serum insulin and growth hormone were slightly increased after feeding BD. The lack of effect of BD on glucose in this study may be the result of giving it in a single dose. Previously, BD was mixed in diets (rats) or bread (humans) being consumed with all feedings. This project has been reviewed and approved by the Committee on Human Investigation, University of Nebraska Medical Center and of the V.A. Supported by the Veterans Administration and a grant from Celanese Chemical Company: No. WOO-3511-49A.

A MOLECULAR MECHANISM OF HYPERPOLARIZATION GENERATED BY CYCLIC AMP. Clara Torda. Mount Sinai School of Medicine, New York, N.Y., 10029.

During increased activity the cyclic AMP content of neurons increases and this generates hyperpolarization (see Adv. Biochem. Psychopharmacol., 3, (1970). The hyperpolarization begins with formation of a complex between cyclic AMP and its specific receptor. This specific cyclic AMP receptor inside the postsynaptic neuron was identified in the present study as the regulatory subunit of diphosphoinositide kinase (DPIK). On combination with cyclic AMP, this regulatory subunit releases the catalytic subunit of DPIK to phosphorylate DPI (diphosphoinositide) to TPI (triphosphoinositide). Since TPI has greater chelating ability than DPI, the membrane-bound Ca^{++} also increases. This leads to closure of membrane pores and decreased ion transport. Membrane hyperpolarization (with the inhibitory postsynaptic potential) are the expression of the momentary sums of the equilibrium potentials of the still migrating Cl^- and K^+ ions (see Nernst equation). Therefore, the coupling mechanism between formation of cyclic AMP-receptor complex, ion transport and bioelectric processes is the activation of DPIK by cyclic AMP. EXPERIMENTAL: DPIK was purified and its activity was tested by the method of Kai et al., Bioch. J., 106, 791 (1968). DPIK was fractionated into a catalytic and regulatory subunit by chromatography on a Sepharose 4B column (following the method of Reimann et al., Biochem. Biophys. Res. Comm., 42, 187 (1971). The fractions were studied by the method of Kai et al. The in vivo effects of these subunits were tested on the bioelectric processes of the postsynaptic neuron (sympathetic ganglia of rabbit and frog). Intrapostsynaptic microinjections of the catalytic subunit of DPIK induced membrane hyperpolarization. Intrapostsynaptic microinjections of the regulatory subunit prevented hyperpolarization by either electrical means, or intrapostsynaptic microinjections of cyclic AMP or the catalytic subunit of DPIK.

RELATION BETWEEN EXPIRATORY FLOW RATE AND CLOSING VOLUME BY HELIUM AND NITROGEN METHODS. David M. Travis, Malcolm Green* and Hillary F. Don*, Harvard Sch. Public Health & Peter Bent Brigham Hosp., Boston.

If a subject inspires a bolus of helium at RV followed by oxygen to TLC and expires slowly (less than 0.5L/sec) to RV, expired concentrations of helium and N_2 rise abruptly (phase IV) at a low lung volume called "closing volume" (CV) by Holland et al.(1968). At expiratory flow ($\dot{V}_{exp}$) rates greater than 0.5L/sec. phase IV occurs at a larger volume. Hyatt and Okeson (1971) have suggested on this basis that the cause of CV as usually measured is flow limitation and not closure of airways. To test this we measured CV's at expiratory flow rates between 0.1 and 0.5L/sec (the range used in practice) in 5 healthy subjects, ages 23-45. CV occurred at lung volumes greater than volumes delineated by the maximum expiratory flow-volume (MEFV) curve (see figure). Mean CV's were not significantly different between expiratory flow rates of 0.1 and 0.5L/sec. There was no difference in mean CV's between the two methods at the flow rates used in the 5 subjects or at 0.3L/sec in a study of 13 other subjects, but onset of phase IV in the N_2 records was, in some subjects, less distinct, and, in 3 of the 13 subjects, occurred at a lower lung volume than in helium tracings. The results by both methods show that CV is relatively independent of expiratory flow at slow rates and do not support the view that flow limitation is a major factor in determining normal CV's. (Supported by Fellowships from Univ. of Fla. and Oxford Univ., and by Grant #HL 14580).



BETA ADRENERGIC RECEPTORS IN THE CANINE INTRA- AND EXTRACRANIAL CIRCULATION. R.J.Traystman* and C.E.Rapela. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

The autoperfused cephalic vasculature of Na pentobarbital anesthetized dogs was studied to determine the responses of the intra (IV) and extracranial (EV) vasculature to β-adrenergic stimulating and blocking drugs injected intra-arterially (i.a.). Cerebral venous blood flow was measured at the confluence of the sagittal, straight, and lateral sinuses with the lateral sinuses occluded. Extracranial blood flow was estimated via electromagnetic flow probes placed around each carotid artery. Common carotid blood pressure was measured via indwelling catheters in each carotid artery. All drugs, dissolved in saline, were injected directly into the carotid arteries via a second set of indwelling catheters. While the doses of the drugs administered differed, the volume delivered remained the same (1 ml). The effects of i.a. injections of isoproterenol (ISO) in doses of 0.1 μg, 1 μg, and 10 μg were determined on both intra (IBF) and extracranial (EBF) blood flow; EBF increased in direct proportion with increasing doses of ISO, whereas IBF showed no change. Intra-arterial injections of propranolol in doses of 0.1 mg, 1 mg, and 10 mg were then made. Each injection of propranolol was followed with all three doses of ISO to determine the amount of β-blockade present at any given dosage of propranolol. The effects of ISO in the EV were decreased in proportion to the dose of propranolol. Propranolol per se does not appear to affect IBF. We conclude that β-receptors exist in the EV and that these receptors may be blocked with propranolol. The lack of response in the IV may be due to: 1) a lack of β-receptors in the IV, or 2) that the drugs administered i.a. cannot cross the 'blood brain barrier' to stimulate the β-receptors. Supported by: NHLI grants H-487, 5392 and N. C. Heart Assn.

ENHANCED ENDOTOXIN DETOXIFICATION ABILITY OF LIVER AND SPLEEN DURING THE STATE OF ENDOTOXIN TOLERANCE. Rafael A. Trejo* and N. R. Di Luzio. Department of Physiology, Tulane University School of Medicine, New Orleans, Louisiana

Recent studies have demonstrated that liver and spleen are the major sites of endotoxin detoxification. The cellular population implicated in endotoxin inactivation, as well as clearance of endotoxin from the vascular compartment is the reticuloendothelial component. In order to delineate the role played by the liver and spleen in the development of endotoxin tolerance, the influence of daily intraperitoneal administration of sublethal doses of S. enteritidis endotoxin on the detoxifying capacity of mouse liver and spleen was evaluated. Endotoxin detoxifying activity of liver and spleen was bioassayed by a reduction in the mortality of endotoxin sensitive Actinomycin D-treated mice which received endotoxin incubated in normal liver and spleen homogenate preparations as compared to the mortality of mice injected with endotoxin incubated in buffer alone. Homogenates were also prepared from endotoxin tolerant mice and assayed for their ability to detoxify endotoxin. Liver and spleen homogenates from endotoxin tolerant mice possessed significantly greater endotoxin detoxifying ability than liver and spleen homogenates from saline-treated mice. These findings further accent the importance of the liver and spleen in host defense against endotoxemia and indicate that the development of endotoxin tolerance is associated with the enhanced capacity of the liver and spleen to detoxify endotoxin. (Supported, in part, by American Heart Association and Atomic Energy Commission).

SUBSTRATE UTILIZATION AND SODIUM TRANSPORT IN THE ISOLATED PERFUSED RAT KIDNEY. M.E. Trimble and R.H. Bowman, V.A. Hospital, Syracuse, N.Y.

The role of substrate metabolism in the transport of sodium ($\dot{T}Na$) by the kidney has been studied with the aid of α-bromopalmitate (αBP), an inhibitor of palmitate oxidation. Kidneys were perfused with bicarbonate buffer equilibrated with 95% O_2/5% CO_2 and containing 7.5% bovine serum albumin. Data presented are from terminal 10 min. clearances begun after 60 min. of perfusion. Oxygen consumption ($\dot{Q}O_2$) was measured continuously with polarographic electrodes. In the absence of exogenous substrate, $\dot{T}Na$ averaged 22±2 μEq/min/g and fractional reabsorption (FNa) was 84±2%. $\dot{Q}O_2$ was 2.9±0.4 μmoles/min/g. In the presence of 0.4mM αBP, $\dot{T}Na$ = 7±2 μEq/min/g, FNa = 61±1% and $\dot{Q}O_2$ = 2.5±0.4 μmoles/min/g. No further inhibition was noted with 0.8mM αBP. With glucose (5.5mM) added to perfusate, $\dot{T}Na$ = 31±4 μEq/min/g, FNa = 95±1% and $\dot{Q}O_2$ = 1.9±0.4 μmoles/min/g. In the presence of glucose plus 0.4mM αBP, $\dot{T}Na$ = 18±3 μEq/min/g and FNa = 85±3%. Although, in this case, the $\dot{T}Na/\dot{Q}O_2$ ratio remained constant, a rise in basal $\dot{Q}O_2$ was noted. It is tentatively concluded that under the conditions of these experiments, the metabolism and/or transport of glucose supports the reabsorption of approximately 9-11 μEq Na/min/g while palmitate metabolism accounts for transport of at least 13-15 μEq Na/min/g. (Supported by USPHS Grant AM 14401)

ALPHA-BLOCKADE DURING SHOCK: EFFECTS ON CORONARY HEMODYNAMICS AND CARDIAC OUTPUT. M. E. Turbow (intr. by S. N. Kolmen). The University of Texas Medical Branch and Shriners Burns Institute, Galveston, Texas.

Effects of alpha-blockade on coronary hemodynamics and cardiac output (CO) during endotoxic and hypovolemic shock were examined. Coronary flow (CBF), CO, aortic pressure, left ventricular pressure and dP/dT were recorded. Dogs were given 0.75 mg/kg of endotoxin or were rapidly hemorrhaged by 2% of their body weight. Control CO and CBF averaged 125 ml/min/kg and 120 ml/min, respectively. Significant reductions of CO occurred (down to 52% of control by hypovolemia and down to 49% of control by endotoxemia). Reductions of CBF were less profound (down to 90% of control, hypovolemia and down to 85% control, endotoxemia). Two hours after toxin or hemorrhage 2 mg/kg of phenoxybenzamine were infused. Phenoxybenzamine significantly improved CO (up to 91% of control, hypovolemia and up to 83% of control, endotoxemia) and caused even further decreases in CBF (down to 55% of control, hypovolemia and down to 65% of control, endotoxemia). Thus, phenoxybenzamine improves cardiac output during shock. However, in absence of fluid resuscitation, CBF can be severely impaired during the hypotension which follows alpha-blockade.

Imidazole and Myocardial Contraction. Richard S. Tuttle, Masonic Medical Research Laboratory, Utica, N.Y.

Imidazole (Imid) and its derivatives have a number of enzymatic and pharmacologic activities including stimulation of myocardial phosphodiesterase and adrenalytic effects. The effect of imidazole on myocardial rate and force of contraction has not been investigated. The present study was designed to measure the effect of imidazole on the isolated as well as the intact heart. Isolated right and left atria of rabbits were exposed to the compound as well as the failing heart-lung preparation. In spontaneous contracting right atria incubated in Tyrode's solution, Imid (.5 mg/ml) increased contractile force by 1-300% without effecting rate. In left atria, the increase in contractile force did not abolish the frequency-force relationships. In the failing heart lung previously exposed to 180-200 mg of pentobarbital, Imid 50-100 mg more than doubled cardiac output. The effects are not blocked by propanolol or antihistamine. Aminophylline (.5-5mM) had no effect on the inotropic action. The results suggest that Imid has a glycoside-like effect on myocardial contraction. Supported by USPHS # NS 07767-05.

EFFECTS OF CONTINUOUS POSITIVE PRESSURE BREATHING ON ABDOMINAL EXPIRATORY ACTIVITY, MINUTE VENTILATION, AND END-TIDAL CO_2 IN CONSCIOUS MAN. Nancy Urbscheit*, Beverly Bishop, and Hans Bachofen*. Dept. of Physiology, State University of New York at Buffalo, Buffalo, New York 14214.

Acute ventilatory responses of conscious man to continuous positive pressure breathing (CPPB) on air, 5% CO_2 and 12% O_2 were studied. Tidal volume, frequency of breathing, end-tidal CO_2 and the electrical activity of the abdominal muscle were continuously recorded. Minute ventilation increased and end-tidal CO_2 decreased in proportion to the pressure applied. The degree of hyperventilation was independent of the inspired gas mixture and primarily due to an increase in tidal volume. Below +10 cm H_2O of pressure, abdominal expiratory activity was delayed or absent. At +20 and +30 cm H_2O, abdominal muscle activity appeared on the first expiration and increased in proportion to the applied pressure. In addition, at these higher pressures the amplitude of the abdominal activity increased progressively with time during the application of the pressure. Thus, in response to CPPB, conscious man hyperventilates and has a complex abdominal muscle response. In contrast, previous studies showed that anesthetized cats tend to hypoventilate and have more stereotyped expiratory activity of the abdominal muscles. **(Supported in part by the American Physical Therapy Association, the U.S. Air Force, and the Office of Naval Research.)**

FACTORS AFFECTING TESTICULAR MONOAMINE OXIDASE (MAO) ACTIVITY: AGING, IRRADIATION, HYPOPHYSECTOMY, ADRENALECTOMY, FSH, LH, PROLACTIN, HCG, ESTROGEN, TESTOSTERONE, AND MELATONIN. R. L. Urry* and L. C. Ellis. Utah State University, Logan, Utah.

Rat testicular MAO activity was studied using 5-HT-^{14}C as a substrate to establish a functional role for this enzyme in the male gonad. Animals sacrificed at various ages showed that MAO activity was high at birth, low at 30 days of age, elevated during sexual development, and diminished during senescence at 410 days of age. Irradiation decreased MAO activity from 42 through 152 days after treatment. Senescence with respect to MAO activity was evidenced in the control animals by 152 days of age. Hypophysectomy of sexually mature animals reduced MAO activity, while neither adrenalectomy or estrogen treatment had any effect. Injecting immature hypophysectomized rats with HCG or prolactin failed to increase MAO activity. FSH increased MAO activity more than LH, but a combination of FSH, LH and prolactin resulted in an activity slightly lower than that observed with FSH. No correlation was observed between androgen biosynthesis and MAO activity for FSH, LH, prolactin, HCG, or a combination of FSH, LH, and prolactin treated animals. MAO activity was increased *in vitro* by melatonin at 10^{-6} and 10^{-5} M concentrations, but inhibited at 10^{-4} M. MAO activity was also elevated after injecting mature hypophysectomized animals with either 1 or 2 mg of melatonin. Thus our data show a functional relationship of MAO activity to aging and irradiation and their effects on the testis. Supported by U. S. Atomic Energy Commission Grant No. AT(11-1)-1602.

RECOVERY OF TEMPERATURE REGULATION AFTER PREOPTIC-HYPOTHALAMIC DAMAGE. D. A. Valentino°, E. Satinoff and P. Teitelbaum. Department of Psychology, University of Pennsylvania, Philadelphia, Pa.

Rats with preoptic-anterior hypothalamic lesions cannot maintain normal body temperature in the cold. Initially, this is due to a complete absence of any thermoregulatory responses. Recovery proceeds in stages. First, non-shivering thermogenesis, then shivering, returns. Paradoxical hyperthermia (elevated O_2 consumption and rectal temperature) occurs at room temperature even though the rats are still unable to keep warm in the cold. Respiratory and cardiovascular thermoregulatory responses are also impaired, but show some recovery.

BLEOMYCIN EFFECT ON PULMONARY FUNCTION IN BEAGLES. J.F. Valicenti*, R.A. Redding*, M. Stein. The Memorial Hospital, Pawtucket, Rhode Island 02860 and Brown University, Providence, Rhode Island.

Pulmonary function studies were performed in 4 pure bred Beagles treated with Bleomycin, a potential chemotherapeutic for epidermoid carcinoma. The Beagles received I.V. Bleomycin in low dose (0.625 mg/kg at 4 day intervals for 22 doses) and in high dose (1.25 mg/kg at 4 day intervals for 11 doses). Each group comprised one male and one female. Pulmonary function was studied before, during and after drug administration over a period of 8 months. Two mongrel dogs, studied in similar fashion, received no drug. During each session, measurements of total lung capacity, (TLC), functional residual capacity, (FRC), single breath diffusing capacity, (DL_{CO}), static lung compliance, (C_L), chest x-rays and arterial blood gases breathing room air and 100% O_2 were obtained. Chest x-rays in all animals showed no abnormalities. The mongrel dogs demonstrated no significant changes in pulmonary function during the eight month period, indicating tolerance to frequent anesthesia and testing. The treated Beagles had significant reductions in FRC, TLC, and DL_{CO} with return to normal values when the drug was stopped. C_L decreased and remained abnormal throughout the study. Blood gases on room air and 100% O_2 were not affected. Histologic study of the lungs showed interstitial inflammation and fibrosis in the Bleomycin dogs. This study suggests that non-reversible changes in lung mechanics may occur in Beagles treated with Bleomycin. (Supported in part by NIH#71-2055 and a grant from the Hines Estate)

EFFECT OF ACETYLCHOLINE ON REACTIONS OF ISOLATED CUTANEOUS VEINS TO SYMPATHETIC STIMULATION. Paul M. Vanhoutte* and John T. Shepherd. Mayo Foundation, Rochester, Minnesota.

A comparison has been made of the responses of isolated cutaneous veins to acetylcholine both under resting conditions and when constricted by electric stimulation, norepinephrine and other vasoactive agents. Changes in isometric tension of helical strips of dogs' saphenous veins were recorded. Addition of 0.01 ng to 0.01 μg/ml of acetylcholine did not affect basal tension, while 0.05 to 0.5 μg/ml caused an increase in tension. Electric stimulation (0.5 to 10 cycle/sec), which acts through liberation of endogenous catecholamines, caused the strips to contract. Acetylcholine, in concentrations which caused no or minimal increases in basal tension, evoked a dose-related depression of the contraction to electric stimulation. This depression was reversed on washing-out the drug; it was not influenced by propranolol or hexamethonium, but was abolished by atropine (0.01 μg/ml) indicating that a muscarinic receptor mechanism is involved. By contrast the same doses of acetylcholine augmented the contractions due to norepinephrine (0.005 to 0.5 μg/ml), tyramine (0.5 μg/ml), KCl (25 mM) and $BaCl_2$ (0.25 mg/ml); this effect of acetylcholine was not changed by tetrodotoxin but was abolished by atropine. These experiments suggest that doses of acetylcholine smaller than these known to have a direct constrictor effect cause relaxation of cutaneous veins probably through a presynaptic inhibition of neurotransmitter release. (Supported in part by NIH Grant HL 5883).

THE EFFECTS OF NOREPINEPHRINE AND CYCLIC AMP ON ($Na^+ + K^+$)-ACTIVATED ATPase. M. Vassalle, R. Carpentier* and P. C. Chan*. Departments of Physiology and Biochemistry, State University of New York, Downstate Medical Center, Brooklyn, New York.

The ATPase activity in the microsomal fraction of pork brain has been studied under various conditions. The following effects on the ATPase activity have been observed to date: 1) norepinephrine at 10^{-4} M had consistently an inhibitory action in the presence of 8 mM K^+ and 100 mM Na^+ or 4 mM K^+ and 10 mM Na^+; 2) Ca^{++}, as expected, caused a depression which was counteracted by the addition of norepinephrine; 3) the stimulatory effect of norepinephrine in the Ca^{++}-inhibited preparation was maximal at 10^{-7} - 10^{-8} M norepinephrine; 4) the Ca^{++}-induced inhibition was enhanced by 10^{-3} M norepinephrine; 5) adenosine 3',5'-monophosphate (cyclic AMP) consistently had stimulatory effect at both the high and the low concentrations of Na^+ and K^+ stated above; 6) such stimulatory action of cyclic AMP was observed both in the presence and in the absence of Ca^{++}. Tests were also carried out in microsomal fractions obtained with two different methods from the myocardium of dogs and guinea pigs. So far it has been found out that in the absence of Ca^{++}, 10^{-4} M norepinephrine had an inhibitory effect, while 10^{-4} cyclic AMP had a stimulatory effect as in the pork brain preparation. The results suggest that under the conditions prevailing in vivo, when Ca^{++} presumably exerts some degree of inhibition on the Na^+-K^+ transport ATPase, norepinephrine may be expected to have a stimulatory effect. The mechanism of such an effect is likely to be an increase of the intracellular level of cyclic AMP, since in the present experiments cyclic AMP consistently stimulated the ATPase activity.

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AUTONOMIC COMPONENTS OF REFLEX TACHYCARDIA INDUCED BY HYPOTENSION. Stephen F. Vatner,* Charles B. Higgins,* Dean Franklin, and Eugene Braunwald. Dept. of Med. UCSD, LaJolla.

It is now generally agreed that the reflex bradycardia induced by baroreceptor hypertension in conscious animals and man is mediated predominantly through cholinergic mechanisms, but the autonomic components of the tachycardia response to hypotension remain controversial. Experiments were conducted in 10 healthy conscious dogs 2 to 6 weeks after implantation of catheters in the aorta (A) for pressure (P) and hydraulic occluders on the inferior vena cava (IVC). Nitroglycerin, 40 μg/kg, i.v. decreased mean AP from 98 to 70 mm Hg and increased heart rate (HR) from 77 to 175 beats/min. After propranolol, 1-3 mg/kg, nitroglycerin decreased mean AP from 99 to 70 mm Hg and increased HR significantly ($p<.01$) from 75 to 118 beats/min. After atropine .1-.3 mg/kg, nitroglycerin decreased mean AP from 101 to 72 mm Hg and increased HR significantly ($p<.01$) from 180 to 212 beats/min. IVC occlusion without autonomic blockades decreased mean AP from 98 to 72 mm Hg and increased HR from 77 to 153 beats/min. The proportion of tachycardia mediated by sympathetic and cholinergic mechanisms was similar to that following nitroglycerin. Combined sympathetic and cholinergic blockades prevented tachycardia following either nitroglycerin or IVC occlusion. Thus, in the conscious dog the reflex tachycardia induced by hypotension from either nitroglycerin or IVC occlusion is not due solely to sympathetic stimulation or to parasympathetic withdrawal but more likely to a combination of both influences.

INCORPORATION OF EXOGENOUS ADENOSINE INTO NUCLEOTIDES BY HUMAN ERYTHROCYTES. *Roger W. Voight and Donald P. McNamara*, Clinical Research Service, Fitzsimons General Hospital, Denver, Colorado 80240.*

Erythrocytes from fresh blood were washed twice with isotonic saline and once with Ringers' containing either 40 mM phosphate (hi-P) or 2 mM phosphate (low-P) + 20 mM bicarbonate (equilibrated with 5% CO_2), pH = 7.4. The cells were then suspended in fresh Ringers' to give a hematocrit of 10-11% and maintained at 37°. Aliquots were taken at intervals and added to boiling sodium borate buffer (20 mM, pH 5.5) to lyse the cells and denature the proteins. The extract was assayed for adenine nucleotides and pyruvate. In hi-P Ringers' containing 10 mM glucose, the erythrocytes maintained steady levels of nucleotides for 3 hours (ATP=5.0, ADP=0.5, and AMP=0.2 μM/g Hb); however, if adenosine (4 mM) was also present, ADP increased markedly (30.5 μM/g Hb), ATP increased moderately (8.0 μM/g Hb), but AMP declined (0.05 μM/g Hb). If the glucose was omitted, the ATP rose much more rapidly, requiring only 80 minutes to reach 7.8 μM/g Hb, but the increase in ADP was not as great. Since the ribose portion of the adenosine was the sole source of energy in this case, the reduction in total nucleotide synthesis probably reflects increased catabolism of the adenosine. In low-P Ringers' under these conditions the increase in ADP was not as striking (6.3 μM/g Hb) but was still highly significant ($p<<0.001$); however, the ATP concentration dropped during the first 40 minutes when most of the new nucleotide was being formed, then slowly returned to initial levels after 2 1/2 hours. Adenine and ribose were without effect. Cytidine did not stimulate ATP synthesis, but did cause an accumulation of large amounts of pyruvate. We conclude that the efficacy of adenosine in maintaining red cell viability during blood bank storage may be due more to its incorporation into new nucleotide than to its contribution to the pentose phosphate pool.

REGIONAL UPTAKE AND IN VIVO DECARBOXYLATION OF L-DOPA IN RAT BRAIN. Lester A. Wade* and Robert Katzman, The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, New York.

The regional uptake of L-DOPA-3-^{14}C in rat brain was measured using the technique of Oldendorf. A mixture of the labelled DOPA and ^{3}H-H_2O was injected into the carotid artery; the rat decapitated at 15 seconds, and the brain dissected prior to counting. At all concentrations, the uptake by the striatum was about the same as in adjacent cortex, although the total catecholamine content of the striatum is five times that of the cortex. This is in accord with the finding on histofluorescence that DOPA is primarily taken up by capillary endothelium. If the total DOPA in the injection mixture was 100 mg%, the percent uptake of L-DOPA-3-^{14}C referred to the uptake of ^{3}H-H_2O was significantly less than if 5 or 20 mg% were used, confirming the self-saturation of L-DOPA transport as previously suggested. Minor regional variations in L-DOPA uptake measured by this method probably result from different effective concentrations in the capillaries due to variations in blood flow. We have now extended this method to study regional differences in L-DOPA decarboxylation by use of an injection mixture containing L-DOPA-COOH-^{14}C and L-DOPA-2,3-^{3}H.

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MECHANISM OF INTRAPULMONARY GAS MIXING DURING BREATHHOLDING IN MAN. P. D. Wagner*, R. A. Gaines*, R. W. Mazzone*, and J. B. West Dept. of Medicine, University of California, San Diego, La Jolla, California

The anatomic dead space as measured by the Fowler single breath technique (V_D) falls rapidly during breathholding, and it is generally held that the mechanism is gaseous diffusion between the airways and alveolar regions. We measured V_D after breathholding first for helium ($V_{D_{He}}$) and sulphur hexafluoride ($V_{D_{SF_6}}$) inspired together, and then for nitrogen ($V_{D_{N_2}}$) and carbon monoxide ($V_{D_{CO}}$) inspired together. Breathholding was performed at FRC + 1 liter for 0, 5, 10, and 30 seconds, and expiratory flow rates were controlled. In four normal subjects, $V_{D_{He}}$ was 91% of $V_{D_{SF_6}}$ without breathholding, but this difference progressively diminished with breathholding, vanishing after 30 seconds. In five isolated dog lungs, $V_{D_{He}}$ was also less than $V_{D_{SF_6}}$ initially, but the difference increased after breathholding. In three normal subjects, $V_{D_{N_2}}$ and $V_{D_{CO}}$ were similar both initially and after breathholding. For both man and dog, the initial differences between $V_{D_{He}}$ and $V_{D_{SF_6}}$ can be explained by diffusional separation of the gases during inspiration and expiration. However, the changes with breathholding in man are not compatible with the mechanism of diffusion. This would predict a faster fall in $V_{D_{He}}$ than in $V_{D_{SF_6}}$ due to molecular weight differences and a faster fall in $V_{D_{CO}}$ than in $V_{D_{N_2}}$ because of the rapid uptake of CO by the blood and the consequent fall in alveolar CO concentration. The behavior in the isolated dog lungs with breathholding does follow the laws of diffusion, and it is therefore suggested that the mechanism by which V_D is reduced on breathholding in intact man is convective mixing, probably on the basis of cardiovascular agitation.

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INHIBITION OF PARATHYROID HORMONE BY INHIBITORS OF CARBONIC ANHYDRASE. Len C. Waite (intr. by K. C. Huang). Department of Pharmacology, Health Sciences Center, University of Louisville, Louisville, Kentucky.

The ability of a series of carbonic anhydrase inhibitors to inhibit parathyroid hormone (PTH) induced bone resorption has been studied in nephrectomized rats. Three enzyme inhibitors (acetazolamide, methazolamide and ethoxzolamide) inhibit the action of endogenous and exogenous PTH. Maren (Physiol. Rev. 47:595, 1967) states that ethoxzolamide is 65 times as potent as methazolamide when in vitro enzyme inhibition is measured and 48 times as potent when in vivo inhibition of kidney carbonic anhydrase is used as the reference point. The present study shows that ethoxzolamide is 41 times as potent as methazolamide with respect to PTH inhibition when the concentration of unbound drug in plasma (2 hours post injection) is used for comparison. An acetazolamide analogue (CL 13,850) devoid of carbonic anhydrase inhibitory properties is inactive as a PTH inhibitor when given at a dose of 9 mg/100 g. The same dose of acetazolamide results in PTH inhibition.

DRUG	DOSE mg/100g	PLASMA DRUG CONCENTRATION (TOTAL) μg/ml ± S.E.	PLASMA DRUG CONCENTRATION (UNBOUND) μg/ml ± S.E.	PLASMA CALCIUM DECREASE mg/100ml ± S.E.
METHAZOLAMIDE	1	13.8 ± 1.2	7.28 ± 0.7	0.4 ± 0.2
	3	44.8 ± 3.7	26.20 ± 3.1	1.0 ± 0.2
	9	121.6 ± 15.6	65.80 ± 8.6	2.2 ± 0.4
ETHOXZOLAMIDE	1	3.9 ± 0.2	0.28 ± 0.04	0.8 ± 0.3
	3	13.2 ± 1.4	0.92 ± 0.16	1.4 ± 0.2
	9	36.4 ± 5.1	2.48 ± 0.31	2.7 ± 0.5

TRANSVENOUS PHRENIC NERVE STIMULATION IN ANESTHETIZED DOGS. Adam Wanner* and Marvin A. Sackner. Division of Pulmonary Diseases, Mount Sinai Medical Center, Miami Beach, Florida.

In anesthetized dogs, prolonged spontaneous breathing or mechanical ventilation often leads to atelectasis and hypoxemia. Further, tests of pulmonary function which require special respiratory maneuvers usually cannot be carried out without the aid of positive or negative pressure breathing. For these reasons, we adapted the transvenous phrenic nerve stimulation (PNS) method of Daggett et al (J.Thor.Cardiovasc. Surg. 51: 676, 1966) to permit either controlled unilateral or bilateral PNS. In 45 dogs anesthetized with Pentobarbital, arterial blood gas analysis at hourly intervals for 6 hours revealed the following: 1) pO_2 92.4-.7mmHg/hour, 2)pCO_2 28.3 + .3mmHg/hour and 3)pH 7.50-.01 units/hour (p = N.S.). The nitrogen washout technic revealed a single exponential curve over the range of 10 to 38 respirations per minute during both bilateral and unilateral PNS. Static lung compliance was obtained by varying voltage of PNS to produce stepwise changes of inspiratory volume. In 22 prone dogs, static lung compliance was .086 L/cmH_2O, S.D. .026, and dynamic lung compliance at 20 breaths per minute .078L/cmH_2O,S.D. .024(p = N.S.) In 12 dogs, thoracic gas volume and airway resistance were determined by a body plethysmographic method during rapid PNS (panting). Functional residual capacity was 45.8 ml/kg,S.D. 8.1 and specific lower airway conductance (from the trachea upstream): .93 L/sec/cmH_2O/L, S.D. .31. Inspiratory resistance-volume curves were obtained by changing lung volume through expiratory resistances and chest strapping. We conclude that PNS is a reliable means to maintain adequate ventilation and to control breathing patterns in anesthetized dogs, and therefore superior to mechanical ventilation. (Supported by HL 10622)

PLASMA PROTEIN-INSULIN COMPLEX. Yen Wang, Homestead Hospital and the University of Pittsburgh, Pittsburgh, Pennsylvania.

In the previous work with thyroxine (Acta Endocrinol. Suppl. 76: 1-46, 1963; Federation Proc. 21:216a, 1962; Am. J. Physiol. 210: 715-717, 1966), two specific plasma protein fractions have been identified to form the active form of Cohn fraction IV_1-thyroxine complex and the inactive form of Cohn fraction $IV_{5,6}$-thyroxine complex. These same proteins were used in evaluating the relationship between the protein fractions and insulin and is reported here.

Insulin (Lilly, Iletin insulin injection, concentrated, 500 u/cc) and both fresh and old Cohn fraction IV_1 and $IV_{5,6}$ were used in a series of in vitro experiments with human RBC and in vivo with white rats. Solutions of various concentrations of the IV_1 and $IV_{5,6}$ mixed with different concentrations of insulin were injected I.V. to the rats and blood samples were drawn prior to and 1 hour after injection. The change of serum glucose level was evaluated. These two Cohn fractions showed a similar effect with insulin as with thyroxine. A IV_1-insulin complex enhances the insulin effect on serum sugar, while a $IV_{5,6}$-insulin complex inhibits the insulin effect. The degree of effect is proportional to the concentration of protein fraction.

The data from the experiment to be presented and the previously reported thyroxine-protein experiment have revealed similar enhancing and inhibiting effects with IV_1 and $IV_{5,6}$ on both insulin and thyroxine. It may be postulated that the two different protein fractions with opposite affects on thyroid hormone metabolism is probably similar to that of insulin metabolism, either on the basis of mechanism, nature of the protein or both. It is of interest to further prove that the described effect of the protein hormone complex could be relevant to other hormones.

HUMORAL INHIBITION OF Na TRANSPORT BY Cl PERMEABILITY ALTERATION. C.O. Watlington and L.B. Taylor*. Endocrin. Div., Med. Coll. Va., Va. Commonwealth Univ., Richmond, Va.

Adaptive decrease in passive Cl conductance (G^{Cl}) or permeability, as well as the expected decrease in active Na transport, occurs in skin of frogs after preconditioning in high concentration NaCl. Arginine chloride (Arg·Cl) conditioning allows the study of the Cl permeability inhibitory system, alone. It produces selective inhibition of G^{Cl} (Cl flux in the short-circuited state) with no change in active Na transport (short-circuit-current, I_S). Yet, net Na flux in the open-circuit state is decreased by Arg·Cl conditioning indicating an indirect mechanism of inhibition of Na transport through a Cl permeability "drag" effect (Clin. Res. 20:614). To demonstrate a humoral factor responsible for this regulatory system, plasma of frogs preconditioned for 5d in 100 mM Arg·Cl in tap water or tap water alone as a control was placed in the inside chamber of isolated test skins (dilution 1/8). This model was selected because alteration in humoral factors regulating active Na transport would less likely obscure the effects of the factor in question. Plasma of Arg·Cl conditioned animals produced a 28% decrease in G^{Cl} ($P<.02$) with no change in I_S. Plasma from tap water maintained frogs did not significantly alter G^{Cl}. The effect was best seen in isolated test skins subjected to adrenergic blockade. Despite no change in I_S, Arg·Cl plasma produced a relative decrease in net Na flux under open circuit conditions ($P=.025$) compared to plasma from frogs conditioned in tap water alone. Differences in plasma electrolyte composition, pH and osmolality in the two groups were insufficient to explain the transport effects of plasma from Arg·Cl conditioned frogs. These findings indicate the presence of a humoral factor producing inhibition of Na transport by Cl permeability alteration.

GASTRIN CONCENTRATIONS IN UPPER GASTROINTESTINAL MUCOSA. L.C. Watson*, D.D. Reeder*, H.D. Becker*, L. LaGrone* and J.C. Thompson. University of Texas Medical Branch, Galveston, Texas

It has recently been shown that antrectomy does not alter basal or food-stimulated serum gastrin, suggesting significant extra-antral sources of gastrin. Furthermore, we have found that gastrin can be released from the duodenum in response to topical acetylcholine. The present studies were undertaken to determine the concentration of gastrin as measured by radioimmunoassay in upper gastrointestinal mucosa. Method: The mucosas of the fundus, antrum and proximal and distal duodenum were obtained from five dogs. The tissue was boiled immediately in water for 30 min. Gastrin in the supernatant was measured by radioimmunoassay and fractionated into "big" and "little" gastrin by starch gel electrophoresis. Results: The average concentrations of gastrin (expressed as nanograms/gram of mucosa) were 112 ± 19 in the fundus, 19,900 ± 380 in the antrum, 188 ± 68 in the proximal duodenum and 41 ± 4 in the distal duodenum. 80% of the mucosal gastrin from the fundus, antrum and duodenum was in the form of "little" (heptadecapeptide) gastrin. Conclusion: The fundic and duodenal mucosa contain appreciable concentrations of gastrin which are stored mainly as little gastrin. These extra-antral sites would appear important in physiologic studies of the origin and release of gastrin.

Supported by grants from the National Institutes of Health, AM 15241 and the John A. Hartford Foundation, Inc.

THE AFFECT OF TEMPERATURE ACCLIMATION ON THE CIRCULATORY RESPONSES OF "WINTER" BULLFROGS TO TEMPERATURE. W. W. Weathers and S. J. Birchard (Intr. by J. J. McGrath). Depart. of Environmental Physiology, Rutgers, The State University, New Brunswick, 08903.

The relationship of heart rate and femoral arterial pressure to body temperature (Tb) was determined in unanethetized "winter" (Jan-Mar) bullfrogs, Rana catesbeiana, following acclimation to 5°, 20°, or 30°C (±1°C) for 2-3 weeks. Heart rate increased exponentially with increasing Tb (0-35°C) in all three groups. The slope of the line relating log heart rate to Tb was 27% steeper in the 5° group, suggesting an increased sensitivity of heart rate to temperature following cold acclimation. Arterial systolic pressure increased continuously with increasing Tb in the 20° and 30° groups, but remained constant in the 5° group. Pulse pressures increased with temperature in 20° and 30° acclimated frogs but continuously decreased in 5° frogs. Arterial capacitance, determined in vitro on segments of the right aortic arch, was unchanged by thermal acclimation. Determination of blood volumes by dye dilution (T-1824) revealed that cold acclimation resulted in a 28% reduction in blood volume. These data suggest that cardiac output of 5° acclimated frogs may remain constant as Tb increases, possibly due to continuously declining stroke volume.

EFFECTS OF MAGNESIUM ON CARDIAC OXIDATIVE METABOLISM. W. R. Webb and M. Massad. Dept. of Surgery, SUNY Upstate Medical Center, Syracuse, N.Y.

Previous studies showed magnesium to act as a metabolic inhibitor and extend the tolerance of rat hearts to ischemia at normothermia from 15 minutes to over 4 hours. Oxygen utilization rates were studied in vitro with Clark oxygen electrodes using cardiac tissue slides immersed in two different media, one containing a high (2%) magnesium concentration. Oxygen uptake was studied without added metabolites and after 10 mM pulses of glucose, lactate, pyruvate, succinate, acetate or B-hydroxybutyrate. Results are shown in the table below. Respiratory rates are in micro liters/gm of dry tissue.

		2 - 4 minutes				
SUBSTRATE	NO. OF RATS	$\bar{x}$ Mg	$\bar{c}$ Mg	R.R.DIFF.	%CHANGE	P
ENDOGENOUS	15	86.5 ul/gm	78.9 ul/gm	7.6 ul/gm	8.8%	$<.02$
GLUCOSE	12	62.8	55.8	7.0	11.2	$<.001$
LACTATE	18	79.6	63.9	15.7	19.7	$<.001$
PYRUVATE	13	106.8	79.4	27.4	25.7	$<.001$
SUCCINATE	13	119.6	104.0	15.6	13.1	$<.01$
B-HYD- BUTYRATE	12	139.9	117.7	22.2	15.9	$<.01$
ACETATE	11	101.4	81.6	19.8	19.5	$<.01$

These results show significant inhibition of all substrates by magnesium.

BARBITURATE-INDUCED APNEUSIS IN THE CAT. Charles L. Webber, Jr.* and Clarence N. Peiss. Department of Physiology and the Graduate School, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

Classically, apneustic breathing patterns can be induced by rostral pontine transection in vagotomized preparations. In contrast to this, data from spontaneously breathing anesthetized cats indicate that it is possible to initiate sustained inspiratory drive by additive intravenous injections of sodium pentobarbital or pentothal with or without vagal afferent feedback. This chemical block is indistinguishable from its neural transection correlate with respect to peripheral airflow velocity and interpleural pressure changes. To better understand this phenomena, single unit recordings have been made from medullary respiratory neurons during barbiturate titration. Although a consistent depression in the respiration rate has been observed with accumulative doses of barbiturate, interesting triphasic shifts in interspike interval histograms for single units suggest a differential drug action at rostral and caudal brainstem structures. For example, the inspiratory units are first depressed, then activated and finally depressed again as barbiturate is added with no significant alteration in the blood pressure. This data is consistent with the concept that the pneumotaxic region has a lower barbiturate depression threshold than the medullary area. However, the observation that barbiturate apneusis can be seen in cats with intact vagi suggests that a more general interpretation is tenable; namely, that inhibitory mechanisms are more susceptible to barbiturate depression than are facilatory ones with respect to respiratory control. (Supported by NIH Grants HE 08682 and GM00999)

STRENGTH-DURATION CHARACTERISTICS OF THE ESTROGEN STIMULUS FOR THE LH SURGE IN THE RHESUS MONKEY. R.F. Weick, F.J. Karsch, W.R. Butler, D.J. Dierschke, L.C. Krey, G. Weiss, J. Hotchkiss and E. Knobil. Department of Physiology, University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15213

A single subcutaneous injection of estradiol benzoate in oil during the early follicular phase of the menstrual cycle of the rhesus monkey elicits an initial depression in plasma LH followed by a sudden massive increase indistinguishable from the spontaneous preovulatory LH surge. To investigate the strength and duration of the estradiol stimulus necessary to induce this premature LH surge, Silastic capsules containing estradiol-17β were implanted subcutaneously for varying time periods during the early follicular phase of the cycle. When capsules producing plasma estrogen levels of 200-400 pg/ml were implanted for 24 hours or less, only the initial depression in plasma LH was seen with a prompt return to control levels following removal of the implants. When such implants were left in place for 36 hours, 6 of 11 animals responded with LH surges. When such implants were left in place for 42 hours, all of the monkeys showed LH surges. When capsules producing 1200-2000 pg/ml of plasma estrogen were implanted for 24 hours, all of the animals responded with LH surges. Implantation of capsules producing 100-200 pg/ml for 36 hours did not induce an LH surge in any of the animals tested; exposure to these levels for 96 hours resulted in LH surges in 5 of 6 animals tested. These results show that with higher plasma estrogen levels, a shorter time of exposure is required to induce an LH surge. Further, in every animal that showed an LH surge, LH had started to rise before estrogen levels had declined to base line suggesting that the stimulus must be applied until the response actually begins.

POSITIVE AND NEGATIVE FEEDBACK REGULATION OF GONADOTROPIN SECRETION IN THE POSTPARTUM RHESUS MONKEY. G. Weiss, D. J. Dierschke and E. Knobil. Department of Physiology, University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15213

Plasma concentrations of FSH and LH were studied in 8 lactating and 6 nonlactating postpartum rhesus monkeys. In the early postpartum period LH and FSH levels were undetectable in plasma by RIA. Return to detectable levels generally occurred in 3 to 6 weeks in nonlactating animals compared to an average of 3.5 months in lactating monkeys. An LH and FSH surge could be elicited by estrogen administration in most nonlactating animals 1 to 2 months postpartum. This response was delayed from 5 to 9 months in lactating monkeys. Spontaneous ovulatory LH and FSH surges were observed at 4 to 6 weeks postpartum in nonlactating animals only. The increase in circulating gonadotropins observed within 2 days following ovariectomy of cycling animals was delayed for 3 to 9 weeks in lactating monkeys. The rate of rise in plasma gonadotropin concentration was accelerated by weaning. In all of the foregoing circumstances, the reestablishment of the pre-gestational patterns of FSH secretion preceeded those of LH. It is concluded that, in the rhesus monkey, lactation maintains the suppression of basal gonadotropin secretion which is initiated during pregnancy and interferes with the negative and positive feedback control systems for the release of these hormones.

EFFECTS OF EXTRACELLULAR POTASSIUM CONCENTRATION AND CATECHOLAMINES ON RESTING MEMBRANE POTENTIAL OF MURINE NEUROBLASTOMA CELLS. Robert M. Weiss,* Michael R. Rosen,* Daniel M. Albert* and Brian F. Hoffman. College of Physicians and Surgeons, Columbia Univ., New York, N.Y. and Yale Univ. School of Med., New Haven, Ct.

Murine neuroblastoma cells (NC) from a clonal line maintained in tissue culture were studied to determine the effects of $[K^+]_o$ and catecholamines on resting membrane potential (RMP). NC, grown on glass cover slips in RPMI-1640 with glutamine (RPMI) were placed in a perfusion chamber mounted on an inverted image microscope and impaled with glass capillary microelectrodes. Replacement of RPMI with Tyrode's solution for 6 hr. did not alter RMP; NC then returned to tissue culture grew normally. The mean RMP for a series of 1200 impalements was -9.6mV (range -4 to -33mV). Maximal RMP was noted at $[K^+]_o$ = 2-4mM. At higher and lower $[K^+]_o$, RMP decreased. Replacement of Cl^- by $NO_3^=$ resulted in a fall in RMP but not to the extent seen with changes in K^+. These changes in RMP were not due to alterations in osmolarity, as no change in RMP occurred with Tyrode's solution containing dextrose in concentrations as high as 60 mM/L. Norepinephrine and epinephrine (E) had quantitatively similar effects on RMP. $E < 1 \times 10^{-5}$ M/L induced no change in RMP. $E = 1 \times 10^{-5}$M, induced depolarization of NC when control RMP > -9mV and hyperpolarization of NC when control RMP < -9mV. RMP returned to control level after 1 hr. washout of catecholamines. E (1×10^{-5}M) also hyperpolarized NC initially depolarized by Tyrode's solution containing $[K^+]_o$ =0.5 mM/L. These data indicate that RMP of NC, like that of other excitable tissues, shows a marked dependence on $[K^+]_o$, and that catecholamines may hyperpolarize or depolarize the NC, depending on the control level of RMP. Supported by NIH Program Project Grant 12738-04 and NIH Grant EY-00108-03.

EFFECTS OF CHRONIC ADMINISTRATION OF PROSTAGLANDIN E_1 (PGE_1) ON ARTERIAL BLOOD PRESSURE OF UNANESTHETIZED HYPERTENSIVE RATS. M. G. Wendling, D. W. DuCharme* and B. E. Graham*. The Upjohn Company, Kalamazoo, Michigan.

It has been reported that daily injections of PGE_1 (15 µg/kg I.P.) for 1 month normalized blood pressures of rats made hypertensive by impeding blood flow to both kidneys. The present experiments were done to study blood pressure responses to PGE_1 in 2 additional experimental models of hypertension. A rat colony was made hypertensive by subjecting each animal to an operation in which blood flow was restricted to one kidney and the contralateral kidney removed (GH). Indirect systolic arterial blood pressure (SBP) averaged 184 ± 7.7 mm Hg in 7 rats before daily administration of PGE_1 (15 µg/kg I.P.) and was 192 ± 9.1, 215 ± 14.0, 217 ± 13.1 and 209 ± 9.1 mm Hg following 1, 2, 3 and 4 weeks of treatment respectively. Corresponding averages in 9 control rats were 194 ± 7.8 before injections of carrier solution and 217 ± 7.0, 225 ± 6.2, 226 ± 7.8 and 233 ± 4.7 at 1, 2, 3 and 4 weeks respectively. SBP averaged 185 ± 2.6 mm Hg in 20 spontaneously hypertensive (SH) rats before daily injections of PGE_1 (15 µg/kg I.P.) and 182 ± 3.6, 187 ± 3.4 and 183 ± 3.3 mm Hg following 1, 2 and 3 weeks of treatment respectively. Comparable results were obtained when these rats were treated for 2 additional weeks with PGE_1 (30 µg/kg I.P.). Corresponding averages in a group of 20 control SH rats were 181 ± 3.4 before injection of carrier solution and 181 ± 3.2, 188 ± 3.5 and 185 ± 3.8 at 1, 2 and 3 weeks respectively. These experiments indicate that chronic administration of PGE_1 does not decrease SBP of either SH or GH rats, and suggest that the antihypertensive activity of PGE_1 may be manifest in only specific types of experimental hypertension.

ARTERIAL CONCENTRATION AND CEREBRAL REMOVAL OF METABOLITES IN FASTING PUPPIES. J.T. Weng*, Y. Nakamura* and John J. Spitzer. Hahnemann Medical College, Philadelphia, Pa.

Newborn puppies were fasted for 1-3 days. To ascertain the changes in arterial concentration and cerebral removal of various metabolites, simultaneous arterial and sagittal sinus blood samples were obtained under Nembutal anesthesia. Significantly lower concentrations of arterial FFA (0.225 vs 0.421 μmole/ml), triglyceride FA (0.152 vs 1.073), phospholipid FA (1.212 vs 2.537) and glucose (2.30 vs 7.76) were found in fasted, than in control (fed) puppies of similar age. Arterial β-hydroxybutyrate (βOHB) concentration was similar in the two groups (0.090 vs 0.077 μmole/ml), while acetoacetate (AcAc) appeared to be lower during fasting (0.089 vs 0.140). Oleic acid flux of the fasted animals was only 1/5 of the control rate. Significant cerebral removal of FFA (0.030±0.006 μmole/ml) was found in the fasting, but not in the control group. Cerebral A-V difference of AcAc was comparable in the two groups (0.024), while only brains of control animals removed βOHB consistently. Glucose A-V difference across the brain was much larger in control, than in fasted puppies (1.17 vs 0.42 μmole/ml). Cerebral A-V difference of O_2 was comparable in the two groups. Thus, in fasting puppies the arterial concentration of several oxidizable metabolites decreased markedly. The metabolic needs of the brain seemed to be met mainly by glucose even in these hypoglycemic animals, with lesser contribution from FFA and AcAc. (Supported by grant HE 03130 from the National Heart and Lung Institute.)

SUPPRESSION OF THE ROD LATE RECEPTOR POTENTIAL AT PHOTOPIC INTENSITIES IN THE MACAQUE MONKEY RETINA. David N. Whitten* and Kenneth T. Brown. Department of Physiology, University of California, San Francisco.

The late receptor potential (late RP) was isolated in macaque monkeys by clamping the retinal circulation at the optic disc, while maintaining the animal on light halothane anesthesia with well controlled arterial oxygenation and pH. Just after its isolation the late RP elicited from all retinal areas by flashes of photopic intensity was pure cone in origin, as indicated by well validated criteria of waveform and by spectral response curves. The pure cone late RP of the macular area was well maintained, but with time a rod contribution appeared in the late RP of the peripheral retina, as indicated both by response form and by spectral response curves. This was shown to result from local metabolic changes, principally anoxia. In another series of experiments the late RP was isolated by infusing pentobarbital into the vitreous humor. At levels of barbiturate just sufficient to isolate the late RP, responses were pure cone. As the level of barbiturate was increased, a rod contribution appeared progressively in both the response form and the spectral response curve. The barbiturate effect was reversible, while that of anoxia was not. A pure rod late RP could be seen in either series of experiments when stimulus intensity was lowered into the scotopic range. Hence these findings indicate that under normal physiological conditions the rod late RP is suppressed when cones are stimulated by intensities above the low photopic range. We suggest that this effect is mediated by a cone-rod lateral inhibitory pathway that may be functionally interrupted by either anoxia or pentobarbital, and which presumably involves the horizontal cell as inhibitory interneuron. (Supported by NIH grant No. EY 00468.)

EFFECT OF EXPOSURE TO HEAT ON THE OXYGEN UPTAKE OF THE CALIFORNIA SEA LION. G.C. Whittow and D.T. Matsuura.* Department of Physiology, School of Medicine, University of Hawaii, Honolulu, Hawaii.

A previous study revealed that the California Sea Lion has a limited capacity for evaporative cooling, in a hot environment (Matsuura and Whittow, Fed. Proc. 31, 826, 1972). The purpose of the experiments described in the present communication was to investigate the possibility that sea lions respond to heat in another way, that is, by a diminution in their heat production. Three sea lions were exposed to air temperatures between 12°C and 30°C, and their oxygen uptake was measured by an open circuit technique. Deep-body temperature and the skin temperature of the ventral abdomen were also recorded. Between air temperatures of 12°C and 21°C the oxygen uptake of the animals was substantially unchanged at approximately 18 ml/min. kg 3/4. Above an air temperature of approximately 21°C, the rectal temperature and oxygen uptake increased, the latter to a level of 26 ml/min. kg 3/4 at a rectal temperature of 39.3°C. The relationship between oxygen uptake and rectal temperature was logarithmic, suggesting that the increased oxygen consumption was the result of a Q_{10} effect. When the sea lions slept during exposure to heat, their oxygen uptake was approximately 24% less, at a rectal temperature of 38.9°C, than when they were awake. This finding is in accord with the previous observation that sea lions are considerably more heat tolerant during exposure to solar radiation, when they sleep (Whittow et al. Comm. Behav. Biol. 6, 87, 1971.)
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FFA AND KETONE UPTAKE BY MYOCARDIUM AND SKELETAL MUSCLE IN ALLOXAN-DIABETIC DOGS. Roslyn Wiener* and John J. Spitzer. Hahnemann Medical College, Philadelphia, Pa.

The pattern of myocardial and skeletal muscle substrate utilization was investigated in 8 mongrel dogs, alloxanized 3 days prior to study. To assess indices of fatty acid metabolism, a continuous infusion of 1-^{14}C palmitate was administered during the experiments. At initial blood ketone levels of ≈1 μmol/ml and plasma FFA concentration of ≈0.7 μmol/ml, FFA oxidation accounted for about 50% of the CO_2 production in both tissues. The uptake of endogenously produced ketones, if completely oxidized, would have provided about 40% of both myocardial and skeletal muscle CO_2 production. Upon further elevation of blood ketones (to 3.7 μmol/ml) by infusion of Na D,L β-OH butyrate, arterial FFA concentration and FFA flux decreased as did FFA oxidation by both tissues. The contribution of FFA to CO_2 production by both myocardium and thigh muscle fell to less than half of the preinfusion level. After βOHB infusion, ketone uptake by both tissues increased sharply, with correspondingly augmented percentile contribution to the CO_2 production. Myocardial and skeletal muscle RQs rose after ketone infusion. These studies in the diabetic dog indicate that substrate utilization by both myocardium and skeletal muscle appears to be influenced by relative substrate availability, independently of insulin, and that at sufficiently high arterial levels, ketones may replace FFA as the major fuel. (Supported by grant HE 03130 from the National Heart and Lung Institute.)

SENSORY AND MOTOR NEURON FIRING PATTERNS DURING CRAYFISH CLAW REFLEXES. Theodore J. Wiens* and George L. Gerstein. Departments of Biophysics and of Physiology, Univ. of Pa., Philadelphia, Pa. 19104.

The central mechanisms controlling claw reflexes in the crayfish may be studied by means of peripherial recordings made simultaneously from several identified motor and sensory fibers. Detailed analyses of pairs of spike trains by means of cross correlation and post-stimulus-time scatter diagram can be used to infer the central connections that are effective under various behavioral conditions. Our data show that: (a) the claw closer exitor motor neuron is strongly and directly driven both by the proprioceptive PD organ and by certain hair receptors; (b) there are excitatory and inhibitory interactions (connections) between the four motor neurons; and (c) the strength of all these neuronal interactions can depend on the history and current condition of the claw. Simple model neural networks based on these data can be used to explain some aspects of the behavior and behavioral plasticity of the crawfish claw. (Supported by USPHS, NIH Grant NS-05606.)

ANALYSIS OF THE BIOELECTRIC POTENTIAL ACROSS A FRESHWATER CLAM'S MANTLE. Donald S. Wood*, A.L. Sorenson* and L.B. Kirschner. Wash. State Univ., Pullman, Wash., Brooklyn Coll., Brooklyn, N.Y.

Measurement of membrane potentials, using intracellular micropipettes, has demonstrated that the sensitivity to both calcium levels and CO_2 of the voltage measured across a freshwater clam's mantle mainly reflects changes occuring at the cell membrane closest to the shell. Both *in vitro* and *in vivo* measurements showed a rest potential across the shell facing epithelial membrane of 43±2mV (inside of the cell negative) when the tissue was aerated with air (0.03% CO_2) in solution containing 12 meq Ca^{2+}/l. In separate experiments decreasing external Ca^{2+} to 1.2 meq/l or gassing with 96% O_2-4% CO_2 had little effect (45±3mV and 48±5mV respectively). However, reducing external Ca^{2+} in the presence of 96% O_2-4% CO_2 generated potentials of 63±2mV. Mantles in high Ca^{2+} (12meq/l) ringers gassed with air showed a potassium (K^+) dependence - 30mV/10 fold concentration change (1mM to 10mM K^+) across the shell facing membrane which increased to 40-50 mV/10 fold concentration change under low Ca^{2+} (1.2 meq/l), 96% O_2-4% CO_2 conditions. Reduction in Cl^-(KCl product kept constant by adding K propionate) produced a depolarization and return towards the resting potential while removal of Na^+ had no significant effect. The resting potential measured across the interstitial facing membrane of the same cells (41± 2mv) did not show a significant Ca^{2+} dependence in these experiments. (Supported by NIH grant from GM-04254)

Neural Correlates of the Prey-capture Response of Navanax

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The marine opisthobranch Navanax inermis responds to food stimuli with a characteristic sequence of motor behavior which involves rapid expansion of the "pharynx" followed by more or less rhythmic contractions which assist in food capture and ingestion. Recordings have been made from single identified neurons of the buccal ganglion of this animal, most of which show a stereotyped pattern of electrical activity correlated with the behavioral sequence. Their pattern of activity is essentially the same in whole animal and isolated ganglion-pharynx preparations. Normally the behavioral sequence is triggered by food or tactile stimuli to the oral area, which influence neurons in the buccal ganglion via connectives from the cerebral ganglion; but, portions of the response, including the cyclic components, can be triggered by intracellular stimulation of individual cells in the isolated ganglion. Intracellular recordings made in conjunction with recordings from the muscles and motor connectives indicate that although many neurons become active during the response, only a few send axons to the muscles. Several "multimodal" neurons have been observed capable of generating spikes in one region of the cell which are not propagated to the muscles (thus functioning in an interneuronal mode, interacting with other neurons synaptically and electronically) and generating spikes in other regions (in a motoneuron mode) which are propagated directly to muscles via axons leaving the ganglion through pharyngeal connectives.

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GRAVITATIONAL FORCE AS A NECESSARY DETERMINANT OF GROWTH AND OF SHELL SHAPE WITH BOX TURTLES (TERRAPENE CAROLINA) CHRONICALLY SUSPENDED FOR LOW-G SIMULATION OR CHRONICALLY CENTRIFUGED TO SIMULATE 1.4, 2, 3.5 AND 8 G AT 30°C.

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Nine young turtles (42 mm, 16 gm, actively growing at 1.10 ± 0.03 mm/wk, with normally flat or convex plastrons) exhibited drastic plastron concavity upon 3 days of suspension by foam or pedestal. Infolding peaked after 3 weeks to as great as 5 mm, and persisted for as long as 12 weeks. Neither this indentation nor the decrease (0.5 ± 0.2 mm/wk) in carapace growth could be confirmed during chronic water immersion with successful growth of 4 such land turtles. Centrifugation increased plastron convexity when approximately 100 turtles were not supported by the floor of their growth chamber, but flatening occurred when another 100, high-G turtles and 4, pack-supporting turtles had plastron support. Although a progressive effect upon growth as fields increased beyond 2 G could not be initially demonstrated, there was a general decrement of 0.35 ± 0.05 mm/wk with more recovery at lower fields toward the end of the 90 day exposure for the 200 high-G turtles. O_2 demand increased the first day and decreased toward the end of centrifugation. With return to one G, almost normal development resumed. Before these high-G results are extrapolated to zero G, more measurements at 1.0 to 1.4 G are necessary. Should such show the same accelerated growth as for aquatic turtles (Nature 197:922, 1963), then extrapolation would, in agreement with the suspension studies, suggest normal growth rates could not continue without gravity. Present results indicate gravity determines normal shell shape. This agrees with other studies, (ibid. 188:151, 1960) suggesting that normal skeletal shape of other vertebrates including man is determined by gravity.

BLOOD BRAIN BARRIER PARTICIPATION IN THE CNS RADIATION SYNDROME OF RATS. D. E. Wyant,* J. Kabal, S. J. Baum, L. J. Parkhurst,* and A. A. René.* Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20014.

The blood brain barrier (BBB) of rats was altered prior to exposure to 20,000 rads of whole-body gamma-neutron radiation. A transient BBB alteration was induced by injection of glycerol and a permanent BBB alteration was induced either by injection of mercuric chloride ($HgCl_2$) or by applying the technique of lymphatic cervical blockade (LCB). The effect of each of these alterations on post-irradiation survival time was tested. When the LCB, $HgCl_2$ and glycerol induced BBB alterations (alone or in combination) were superimposed by irradiation, this additional effect only slightly influenced the survival time. This phenomenon may possibly be explained by the following: (1) the BBB does not play a major role in the induction of the CNS syndrome; (2) the shortened survival time at high doses of irradiation may primarily be due to an accelerated GI injury (our data indicate that the magnitude of dehydration and its consequences, e.g. Hct increase, rectal temperature and body weight decrease, correspond well with the magnitude of dehydration observed in the GI syndrome); or (3) an interaction effect may take place, e.g. only a certain threshold of BBB alterations may be necessary to render the brain susceptible to the detrimental effects of certain substances, released outside the CNS, as a result of whole-body irradiation (i.e. abscopal effects).

THE EFFECTS OF BARORECEPTOR REFLEXES ON THE INOTROPIC STATE OF THE LEFT VENTRICLE IN CONSCIOUS DOGS. Chaim Yoran* and John Ross, Jr., University of California, San Diego, Sch. of Med., La Jolla, California 92037.

The effects of baroreceptor reflexes on heart rate (HR) and the inotropic state of the left ventricle (LV) in the anesthetized animal are well established. However, their role in conscious dogs has been questioned. Accordingly, integrated baroreceptor reflex responses were studied in awake dogs chronically instrumented with a miniature high fidelity gauge for LV pressure and an inflatable cuff around the inferior vena cava (IVC). Graded IVC obstructions for 10-15 sec decreased LV end-diastolic pressure (EDP), systolic arterial pressure (SAP) and increased HR. In 75 observations from 10 experiments in 5 dogs an increase in HR was related to the drop in SAP, $\Delta HR=2.23(\Delta SAP)+8.5$ beats/min, r=.81. Following propranolol (P), 1-2 mg/kg IV, this relation was significantly reduced to $\Delta HR=0.89(\Delta SAP)+9.4$ beats/min, r=.69 ($p<.01$). Peak LV dp/dt was obtained before and 2-6 sec after release of the IVC obstruction when HR, LVEDP and SAP had returned to control levels. The rise in LV dp/dt was related to the fall in SAP, $\Delta LV\ dp/dt=43.00(\Delta SAP)+223$ mmHg sec-1, r=.83. Thus a 25 mmHg decrease in SAP from basal levels was associated with a 42% increase in peak dp/dt. Following propranolol, the relation was significantly reduced to $\Delta LV\ dp/dt=11.07(\Delta SAP)+142.8$ mmHg sec-1, r=.73 ($p<.01$). With small IVC obstructions, when HR and SAP were unchanged, despite a drop in LVEDP by 6.3±.6 mmHg (5-9.5) there was a slight rise in LV dp/dt from 3118.4±100 to 3209.9±104.5 mmHg sec-1 ($p<.09$), suggesting an increase in contractility due to activation of low pressure baroreceptors. Although the afferent pathways remain to be determined, reflex augmentation of myocardial inotropic state plays a highly important role in the integrated response of the conscious animal.

INTERACTION BETWEEN CHEMICAL FACTORS AND DURATION OF APNEA FOLLOWING LUNG INFLATION. M.Younes*, P.Vaillancourt* and J.Milic-Emili. Department of Physiology, McGill University, Montreal, Canada.

The strength of the Hering-Breuer reflex has generally been assessed by the duration of apnea following lung inflation on the assumption that termination of apnea is exclusively a function of the reflex. We have studied the factors leading to termination of apnea in 7 cats anaesthesized with nembutal. For any given inflation volume the inspiratory excitatory activity (expressed as pressure generated by inspiratory muscles) was modified in the course of inflation through the use of inflation mixtures containing various combinations of O_2, CO_2 and N_2. It is concluded that 1) following inflation, vagal inspiratory inhibitory activity declines initially at a fast rate then stabilizes at a level that varies with lung volume and 2) the duration of apnea is the result of interaction between declining vagal inspiratory inhibitory activity and rising inspiratory excitatory influences (e.g., increasing arterial CO_2 resulting from breath holding); factors affecting the course of the latter following inflation can markedly affect the duration of apnea.

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EFFECTS OF CHANGES IN RENAL ARTERIAL OSMOLARITY ON RENAL BLOOD FLOW AND GLOMERULAR FILTRATION RATE. David B. Young* and Howard H. Rostorfer. Department of Anatomy and Physiology, Indiana University, Bloomington, Ind. 47401.

By infusing small volumes of hypertonic or hypotonic solutions of NaCl, dextrose or urea into the renal arteries of dogs, renal arterial osmolarity was changed over a range of +54 to -34 mOsm/L. Within seconds of the start of infusions, renal blood flow (RBF) measured by an electromagnetic flow meter, and glomerular filtration rate (GFR) measured by the extraction ratio technic responded, both varying directly with renal arterial osmolarity. The RBF responses were very consistent, the correlation coefficient for the regressions between percent of control RBF and change in osmolarity being near 0.9 for all three compounds, while the slopes of the regressions were 0.35, 0.30, and 0.22 for NaCl, dextrose and urea, respectively. Filtration rate responses were more variable. To investigate the mechanism of the osmolar effect, 3.2 ug/min norepinepherine was infused into the renal artery, first dissolved in isotonic NaCl then in hypertonic NaCl or dextrose. RBF, greatly depressed by the infusion of norepinepherine in isotonic NaCl, responded immediately upon substitution of infusion of the same amount of norepinepherine in hypertonic solution and increased to near control levels. The results suggest that arterial osmolarity can be a factor affecting renal hemodynamics having a direct effect on the membrane properties of the smooth muscle cells of the resistance vessels. Supported by PHS 5 F01 GM45681 03 and HE 05625

ARTERIAL-VENOUS DIFFERENCES ACROSS THE LUNGS IN PLASMA TRIGLYCERIDE CONCENTRATION. Christian W. Zauner, Måns Arborelius, Jr.*, and Gunnar Sundström*. Malmö Gen. Hosp., S-214 01 Malmö, Sweden.

Arterial-venous differences in plasma triglyceride across the lungs were determined in healthy human subjects before, during and following infusion of a soybean oil emulsion into the superior vena cava. Samples were acquired from the pulmonary and brachial arteries. A significantly greater mean concentration of triglyceride in venous as opposed to arterial blood was evident following 12 minutes of infusion ($P < 0.001$), with a tendency for the retained lipid to be released during the post-infusion period. It could be calculated that during infusion the lungs retained about 20 % of the available triglyceride, or 3 millimoles per minute. It was concluded that the lungs have the potential to at least act as triglyceride screens, and may be actively involved in triglyceride metabolism.