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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.

PERMISSIVE ROLE OF GASTRIN IN VAGALLY MEDIATED ACID SECRETION

L.S. Adair*, J.E. Shaw, J. Urquhart, and F.P. Brooks. Dept. of Physiol. University of Pennsylvania, Philadelphia, Pa., and Alza Research, Palo Alto, Ca. 93404

It is our hypothesis that gastrin plays a permissive role in vagally mediated acid secretion. We have previously shown that antibodies to synthetic human gastrin, SHG:2-17 raised in rabbits, inhibited vagally stimulated acid secretion in the isolated perfused canine stomach. (Fed Proc. 33:596, 1974) Since it is not possible to measure free endogenous gastrin when antibody is present in the system, the following study was designed as an alternative method of defining the role of gastrin in a vagally mediated acid response. The pyloric antrum was excluded from the isolated stomach, and the entire stomach removed from the large donor dog in the preparation of Shaw and Urquhart (J. Physiol. 226:107P, 1972) to prevent the release of antral gastrin. Under these circumstances, electrical stimulation (8V, 5 msec, 2 Hz) of the left vagal trunk elicited a maximum acid output in the isolated stomach of 0.24 mEq/hr, and a gastric blood flow (GBF) of 10-12 ml/min. 30 min after vagal stimulation was stopped, SHG:2-17 was infused into the arterial input to the isolated stomach at either 100 pg/min or 4ng/min. No acid response to either dose of gastrin was observed, but GBF increased to 15-16 ml/min. When the infusion of gastrin at 4 ng/min was combined with electrical vagal stimulation, a maximum acid output of 6.02 mEq/hr was observed. This level of acid secretion is comparable to that of the vagally stimulated isolated stomach with antrum intact. GBF increased to 30 ml/min in response to the combined stimuli. We conclude that some permissive level of gastrin, which is in itself subthreshold for stimulating acid output, may be required for a vagally stimulated acid response in the canine stomach.

THE EFFECT OF STEROIDS ON INSULIN-STIMULATED XYLOSE TRANSPORT IN SOLEUS MUSCLE. N.S.Adzick*, L.J.Fishman*, M.M. Sayeed, A.E.Baue and I.H. Chaudry. Dept. of Surgery, Washington Univ. School of Med. and the Jewish Hosp. of St. Louis, Missouri 63110.

Previous work from our laboratory has shown that tissues from animals subjected to severe hemorrhage were resistant to insulin. Since the blood level of corticosteroids is known to increase during shock, it is possible that the insulin resistance could have been due to the interaction of steroids with insulin. To test this possibility, Holtzman rats (70-90g) were bilaterally adrenalectomized (ADX) 3-4 days prior to the study. Two soleus muscles from each animal were quickly removed and placed in 1.0 ml of medium containing Krebs-HCO_3 buffer (pH7.4) and xylose (6mg/ml). Insulin and steroids when used were added to concentrations ranging from 100μU-200mU/ml and 10^{-4}M-10^{-2}M respectively. Incubations were carried out in a metabolic shaker for 30 min at 37°;shaking rate 110 cycles/min; atmosphere 95% O_2-5% CO_2. The muscles were then rinsed, blotted, frozen and homogenized in $Ba(OH)_2$-$ZnSO_4$ and the supernatant was analyzed for xylose. The results indicate that in control as well as in muscles from ADX animals, 100mU/ml insulin was required for maximal xylose transport. Hydrocortisone (10^{-4}M), Dexamethasone (10^{-4}M) or Hydrocortisone-21 Na succinate (10^{-2}M) had no effect on basal transport. In the presence of 10^{-4}M of any of the above steroids insulin-stimulated transport was not affected at any insulin concentration. When Hydrocortisone-21 Na succinate was used at 10^{-2}M, insulin-stimulated transport was decreased with a maximal inhibitory effect in the presence of 100mU/ml insulin. In this study, steroids failed to inhibit insulin-stimulated transport at concentrations higher than known blood steroid levels during shock (10^{-5}-10^{-6}M). Thus, it is unlikely that during shock steroids were responsible for the observed tissue insulin resistance.

EPILEPTIC SEIZURE MECHANISMS IN PREPYRIFORM CORTEX OF RABBITS Soo-Myung Ahn (intr. by W.J. Freeman), University of California, Berkeley, Calif. 94720

A study is made of epileptic seizure in the prepyriform cortex of rabbits. A square pulse train with pulse width 0.05 - 1 msec, amplitude 10 - 40 volts and repetition rate 100 - 1000 pulses/sec delivered to the lateral olfactory tract easily induces an epileptic seizure in the prepyriform cortex. The seizure is manifested by ipsilateral twitching of the eyelid and muzzle, by the loss of the normal escape or avoidance responses to visual or tactile stimuli, and by the absence of normal locomotor activity. The cortical spike during the seizure is uniform in that each monotonically approaches to a deep-negative (surface-positive) crest which is the manifestation of the inhibitory postsynaptic potentials (IPSP) of the superficial pyramidal population and from the crest it falls to a small peak with reversed polarity. From this deep-positive (surface-negative) peak which is the manifestation of the excitatory postsynaptic potentials (EPSP) of the superficial pyramidal population it slowly decreases monotonically to the onset of the next cortical spike. The amplitudes of the cortical spikes during the seizure are abnormally higher than those of the normal evoked potentials or the normal EEG (10 - 1000 times). The seizure lasts 10 - 70 seconds. It is argued that if during the seizure the inhibitory cortical granule population did interact with the excitatory superficial pyramidal population with the normal interaction strength there would exist an oscillatory behavior as shown in the normal evoked potentials. It does not. It is also argued that the high amplitude inhibitory activity is caused by high interaction strength manifested by the hypersynchrony. Therefore it is concluded that the seizure is the result of the instability of the cortical granule population owing to the abnormal increase of the interaction strength.

EFFECT OF NOREPINEPHRINE ON THE CAROTID SINUS. J. Edgar Alarcon*, Kenneth B. Campbell*, and Lysle H. Peterson, Bockus Research Institute, University of Pennsylvania, Philadelphia, Pennsylvania.

Norepinephrine (NE) locally applied to the carotid sinus (CS) wall is known to modify the carotid sinus reflex (CSR). Whether this modification is primarily induced through changes in CS strain caused by CS smooth muscle contraction and/or by a direct effect of NE on the carotid sinus mechanoreceptors (CSMR) is the question which was investigated. The vascularly isolated CS of anesthetized dogs [chloralose] was perfused with physiological salt solution (PSS) and with PSS containing NE in concentrations of 1 and 5 μg/cc. The carotid sinus pressure (CSP) was increased from 60 to 210 mmHg in steps of 30 mmHg. Systemic arterial pressure (SAP) and carotid sinus diameter (CSD) were monitored. When compared to CS perfusion with PSS, the presence of NE in the perfusate caused: 1) a reduction of as much as 50% in the mean SAP for any given CSP; 2) a reduction of as much as 42% in the pressure level of CSR operating point; 3) an overall decrease in the open loop gain of the CSR but with no change in the range (120-150 mmHg) of CSP at which maximal open loop reflex gain was observed; and 4) a reduction in CSD. All of the effects noted above showed a monotonic dependence on the concentration of NE in the perfusate. These results demonstrated that in the presence of NE there was an increase in the CSMR activity even though there had been a decrease in CS circumferential strain. These findings are consistent with a direct stimulating effect of NE on the CSMR.

PHYSIOLOGICAL AND ANATOMICAL DISTURBANCES AFTER TEMPOROPARIETAL HEAD IMPACT, William A. Alter III, Stanley A. Shatsky*, Delbert E. Evans* Richard L. Donovan* and Vernon Armbrustmacher*. Armed Forces Radiobiology Research Institute, Bethesda, Md. and Armed Forces Institute of Pathology, Washington, D. C.

The mechanisms of injury in blunt head trauma have yet to be defined. This study was undertaken to determine movements of cerebral structures during blunt head trauma and to correlate displacements with physiological and pathological changes observed postimpact. One thousand frame per second contrast radiography was used to study movements of cerebral vasculature. Anesthetized rhesus monkeys received a blow to the temporoparietal skull surface after accelerating to 7 m/sec. Impact forces ranged from 400 to 1000 lbs with a pulse duration of 3 to 6 msec. Temporoparietal impact resulted in an immediate reduction in skull diameter (1.5 to 4 mm) in the plane of impact. At 5 msec postimpact, the common pericallosal artery was displaced 3 to 6 mm towards the impact surface. The period of this oscillation was 3 to 5 sec. Initial movements included complex oscillations of bifurcations of the internal carotid arteries. Subsequent to these movements nodal and ventricular arrhythmias were observed and persisted for up to 3 min. Blood pressure remained near preimpact levels, suggesting intact baroreceptor mechanisms. Pretreatment with atropine (0.4 mg/kg) eliminated all changes in cardiac rhythm following head trauma, suggesting that these arrhythmias were due to vagal hyperactivity. Pathological findings were parasaggital petechial hemorrhage, subarachnoid hemorrhage at the brain stem level and contusions of temporoparietal cerebral surfaces. Preliminary data indicate that discrete movements of cerebral structures are related to the extent of physiological and pathological changes observed after blunt head trauma.

HEMORRHAGIC SHOCK (HS) AND RETICULOENDOTHELIAL SYSTEM (RES) FUNCTION IN SPECIFIC PATHOGEN-FREE RATS. Burton M. Altura. Albert Einstein Col. Med., Bronx, New York.

Previous reports have indicated that pathogenic bacterial and viral organisms can affect the ability of hosts to survive circulatory shock. More recently, we reported that certain broad spectrum antibiotics can depress RES phagocytic function in normal rats and sensitize such animals to circulatory shock (RES: J. Reticuloendothelial Soc. 3: 477, 1966). In view of these findings, experiments were undertaken with specific pathogen-free rats (SPFR) to determine whether: a) such animals exhibit changes in RES function compared to conventional rats; and b) SPFR are more susceptible (or resistant) to HS (3% blood loss) than conventionals. The results indicate that RES phagocytic function (carbon clearance) is depressed 35% in unshocked SPFR which, on analysis of RES organ weights (α values), suggests that the hypophagocytosis is due to decreased tissue activity of the RES phagocytic elements rather than to cellular atrophy. The SPFR after HS and transfusion fail to clear carbon. In addition, the SPFR showed significantly lower survival rates after HS and an inability to either a) maintain a stable blood pressure (BP) after HS, or b) attain a normal, pre-HS BP after transfusion. Although these findings do not identify the mechanism (s) whereby the pathogen-free state decreases RES phagocytic function and resistance of rats to HS, they do suggest that the normal presence of certain pathogenic microorganisms may play roles in maintaining RES function and host defense against circulatory shock. (Supported by N.I.H. Research Grants.)

INCREASE OF CATECHOLAMINES IN THE NORMAL PARTS OF THE HEART FOLLOWING ACUTE CORONARY OCCLUSION IN THE PIG. E.T.Angelakos, R.A.Bonner,* & R.Sapawi*. Hahnemann Medical College, Phila., Pa. and Biomedical Research Institute, Portland, Maine.

Tissue norepinephrine(NE) was determined(chemically fluorometrically) in seven parts of the heart in 30 young anesthetized domestic pigs 30 min. to 4 hrs. after acute coronary ligation(ACL) (left descendans) and compared to similar determinations made in 10 sham operated animals kept for the same periods of time. All normal parts of the heart (RA,LA,RV,SEPT,LV) showed marked (2x-3x) NE increases which were significant 30 min. after ACL and peaked at about 1 hr. after ACL. No significant changes in cardiac NE were found in the sham controls. Plasma catecholamines were elevated in only a few ACL animals and did not bear any relationship to the tissue levels. Fluorescence histochemical studies confirmed an increase in intraneuronal NE in all parts of the heart and a more marked increase in the peri-ischemic regions. Chemical determinations in the ischemic areas showed no change (initially) or a slowly progressive decrease in tissue NE. These results are consistent with an increased adrenergic drive of the uninvolved parts of the heart after acute coronary occlusion.

BILE ACID METABOLISM IN PONIES. M.S. Anwer*, L.R. Engelking*, R. Gronwall, Dept. of Physiological Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas.

Bile acid metabolism was studied in ponies with chronic external biliary fistulas. Bile was collected by gravity drainage to determine flow rate (29.7 ml/day/kg) and rate of bile acid excretion (320 µMoles/day/kg). Bile acid pool size (8.4 µMoles/kg) and hepatic synthesis rate (7.9 µMoles/day/kg) were estimated by a washout technique. Turnover of the bile acid pool, as calculated from the rate of excretion and pool size, was 38 times per day. Plasma bile acid (0.03 µMoles/ml) represented 14% of the total bile acid pool. The pool size, hepatic synthesis rate and excretion rate were lower and the turnover rate was higher in ponies when compared to reports for other species. Chenodeoxycholic acid (major bile acid in equine bile) produced a more pronounced choleresis than taurocholic acid, without a significant change in the bile acid-independent bile flow.

AUTOREGULATION OF BLOOD FLOW IN THE RAT KIDNEY. William J. Arendshorst*, William F. Finn* and Carl W. Gottschalk**. Univ. of North Carolina School of Medicine, Chapel Hill, N.C.

Previous attempts to quantitate renal blood flow (RBF) in rats using noncannulating flow probes have been unsuccessful largely because probes with the desired lumen diameter were not available. A noncannulating electromagnetic flow transducer having a small lumen diameter (about 0.5 mm) is now available which is capable of reliable and accurate measurements of RBF in anesthetized nondiuretic rats. In vitro calibration yielded a linear relationship (r=0.998) between flowmeter output voltage and variations in blood flow rate from 0.2 to 10.3 ml/min. Excellent agreement was observed between simultaneous determinations of RBF by the flowmeter system (RBF-Direct) and the PAH clearance-extraction technique (RBF-PAH); the mean ratio of RBF-Direct/RBF-PAH, 1.01 $\pm$ 0.02, is not different from unity. Glomerular filtration rate and RBF for the left kidney with a flow transducer around its renal artery did not differ significantly from corresponding values for the undisturbed contralateral kidney.

The relationship of mean RBF with steady-state variations in perfusion pressure was evaluated in 13 nondiuretic rats. RBF averaged 6 ml/min · g KW at arterial pressures (AP) above 100 mm Hg. A high degree of autoregulatory efficiency was observed when mean AP varied between 105 and 145 mm Hg. Over this pressure range RBF changed only 3% as changes in intrarenal vascular resistance and AP were directly related (r= 0.994). Below 95 - 105 mm Hg RBF decreased in a curvilinear fashion with the concavity toward the pressure axis.

INSTANT TO INSTANT REFLEX CARDIAC REGULATION. J. A. Armour. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Mechanical distortion of specific receptor fields of the atria, ventricles or aorta reflexly activated preganglionic and postganglionic efferent sympathetic fibers in the ansae subclavia or cardiac nerves. Thus efferent cardiac sympathetic fibers are primarily activated reflexly by receptors from the thoracic cardiovascular region. On the other hand, efferent parasympathetic fibers in cardiac nerves were activated by mechanoreceptors in the carotid arteries and lungs. Electrical stimulation of the afferent ends of cardiac nerves reflexly activated thoracic sympathetic preganglionic and postganglionic efferent fibers and suppressed vagal fibers; above 30 cps the sympathetic efferents were suppressed. Afferent stimulation of cardiac nerves initiated reflexes from 20 to over 300 milliseconds later in sympathetic postganglionics. Early reflex activation occurred via sympathetic afferents whereas late reflexes were activated via vagal afferents. Normally postganglionic sympathetic efferent traffic is cyclically related to heart rate and very dependent on local reflex modulation. Highly localized cardio-cardiac reflexes modulate cardiac sympathetic control. In addition, mass discharges of the sympathetic nerves during each cardiac cycle are very dependent upon thoracic reflexes and modulation via the cord and higher centers. Cardiac control is initiated via positive and negative feedback mechanisms of the autonomic nerves which are modulated on an instant to instant basis effecting coordination of cardiac contraction and thus the efficiency of the heart. *(Supported by NIH Grant HL 08682)*

PHASIC CHANGES IN THE CONTRACTILE PROPERTIES OF RAT FEMORAL VEINS DURING THE ONSET OF RENAL HYPERTENSION. Neal R. Bandick and Suzanne I. Kuwahara* Oregon College of Education, Monmouth, Oregon.

Helically cut femoral venous strips (o.d. = 1.1mm) from albino rats made hypertensive by unilateral nephrectomy and contralateral renal artery clamping were studied in a common muscle bath with strips taken from normotensive rats. Venous strips taken from rats that had been hypertensive from 1 to 15 days developed greater maximum contractile tension in response to norepinephrine (5×10^{-7}g/ml) than those from control rats ($P<0.05$). There was no difference between the strips if hypertension were prolonged beyond 15 days ($P>0.1$). Strips from normotensive rats and rats that had been hypertensive for longer than 15 days equally divided their peak response to norepinephrine between 50 and 75% stretch. However, the peak occured most commonly at 50% stretch (14 of 20) if the strips were taken from rats that had been hypertensive for 15 days or less. Norepinephrine threshold levels were the same for strips from normotensive and hypertensive rats. These results show that venous contractile properties are changed at the onset of renal hypertension. However, these changes do not appear to continue during prolonged hypertension. (Supported by NIH HL-14874 and the H. R. Kaiser Foundation)

CADMIUM STIMULATION & CADMIUM-CYSTEINE INHIBITION OF ACTIVE Na TRANSPORT BY THE FROG SKIN. R.O. Banks (intr. by D.L. Kline), Dept. of Physiology, Univ. Cincinnati Coll. of Med., Cincinnati, Ohio 45219.

The effects of 10mM Cadmium on active sodium transport were evaluated on isolated R. pipiens skins mounted between leucite chambers. With Cl-Ringers on both sides, addition of Cd to the external solution results in an immediate increase in the short-circuit current (SCC) and transmembrane potential (Pd) with both reaching a plateau in 6-10 minutes. Skin resistance (R_T) increases 45% (n=7, range 31 → 79%) during the same time period. With SO_4-Ringers on both sides, externally applied Cadmium increases SCC and Pd but R_T decreases 28% (n=4, range -11% → -50%). If equimolar concentrations of cysteine (10mM) are added to the external solution during the plateau phase of Cd stimulation, the SCC rapidly falls below control values and then decreases to zero with a decay constant of about 30 minutes. The Pd also decreases to zero with a similar decay constant. R_T increases markedly following cysteine addition and remains elevated as SCC and Pd decrease. The effects of cysteine on SCC, Pd and R_T occur in both Cl-and SO_4-Ringers. When cysteine is added to the serosal solution during the plateau phase of external Cd stimulation, inhibition occurs after a delay of 20-30 minutes. Effects of serosal addition of Cd on SCC and Pd are variable. However, with Cd + cysteine on the serosal side, inhibition of SCC and Pd occurs after a delay of about 15 minutes. Cysteine alone on either side has little effect on SCC and Pd. These results suggest that Cd, when added to the external surface of the frog skin, increases Na transport by increasing Na permeability of the outer facing membrane. Coincidentally, Cd also decreases Cl permeability. In the presence of cysteine, Cd can apparently enter the cell and directly interfere with cellular transport processes. Supported by NIH grant HL 14348.

INTERACTION OF DESCENDING SPINAL SYMPATHO-EXCITATORY AND SYMPATHO-INHIBITORY PATHWAYS. S. M. Barman* and R. D. Wurster. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Descending sympatho-excitatory and sympatho-inhibitory pathways have been localized on the dorsolateral and ventrolateral funiculi, respectively, in the cat spinal cord (Illert and Gabriel, Pflugers Arch 335: 109, 1972; Foreman and Wurster, AJP 225: 212, 1973; Illert and Seller, Pflugers Arch. 313, 343, 1969). Stimulation of the excitatory pathway elicits an increase in blood pressure and preganglionic nerve activity, while stimulation of the inhibitory pathway decreases blood pressure and preganglionic nerve activity. The purpose of this investigation is to determine the interaction of these two pathways on blood pressure and preganglionic nerve activity. Systemic arterial blood pressure is recorded in anesthetized or decerebrate cats during stimulation of the pathways in the lower cervical or upper thoracic spinal cord. Stimulation of the sympatho-excitatory pathway (3-10 volts, 1 msec, 50 Hz) elicits an increase in mean blood pressure of 25-100 mm Hg. When the increase in blood pressure has stabilized, the sympatho-inhibitory pathway is also stimulated (1-6 volts, 1 msec. 50 Hz). This results in a decrease in mean blood pressure of 10-40 mm Hg. When the inhibitory stimulus is terminated, the blood pressure again rises to its peak level, or even higher. Our laboratory is currently investigating the electrophysiological characteristics of the interaction of these two pathways on preganglionic nerve activity. *(Supported by NIH Grant HL 08682)*

SUBCELLULAR DISTRIBUTION AND SOME PROPERTIES OF ENZYMES RELATED TO ADH ACTION IN RENAL MEDULLA. L.D. Barnes*, Y.S.F. Hui*, P.P. Frohnert*, and T.P. Dousa, Mayo Clinic and Foundation, Rochester, Minnesota 55901

Major subcellular fractions were prepared from bovine renal medulla, and were characterized by the presence of marker enzymes. The highest specific activity of adenylate cyclase was found in plasma membranes. The specific activity of basal adenylate cyclase increased two times above homogenate, ADH-stimulated and NaF-stimulated activities both increased five times. The highest specific activity of cyclic AMP phosphodiesterase was found in the cytosol when assayed with 0.5 mM or 5 μM cAMP. However, with 5 μM cAMP three times as much of the specific activity remained associated with all membrane fractions as when assayed with 0.5 mM cAMP. Cyclic AMP phosphodiesterase assayed with 0.5 mM cAMP was less inhibited by theophylline than when assayed with 5 μM cAMP, and isobutyl methylxanthine was a tenfold better inhibitor than theophylline at 5 μM cAMP. The cAMP-stimulated protein kinase activity was found predominantly in the cytosol. Protein phosphatase activity was assayed using as substrates histones, plasma membrane proteins, or cytosolic proteins labelled with ^{32}P. The highest specific activity was localized in the cytosol. Cytosolic protein phosphatase activity was unaffected by 10^{-6}M cAMP or 10^{-6}M cGMP; it was inhibited about 80% by 10 mM $ZnSO_4$ and 10 mM $CuSO_4$ when ^{32}P-histones served as the substrate. The results indicate that ADH-sensitive adenylate cyclase is associated with the plasma membrane fraction while all other enzymatic activities related to the cellular action of vasopressin in mammalian kidney are predominantly localized in the fraction of soluble proteins. (Supported by NIH Grant AM-16105, AHA Grant-in-Aid and by the Mayo Foundation.)

LIVER REGENERATION IN ALLOXAN INDUCED DIABETIC RATS. Rosemary Barra* and James C. Hall, Dept. of Zoology and Physiology, Rutgers Univ. Newark, N.J.

This study was carried out to determine the possible effects of alloxan-induced diabetes on the process of rapid liver regeneration initiated by partial hepatectomy. Normal and diabetic animals were sacrificed at 8 time periods between 16 hrs. and 4 wks. following the removal of approximately 65-70% of the liver. Two hours prior to sacrifice the animals were injected with 2 Ci of orotic acid-6-C^{14} and 5 Ci of glycine-2-H^3 for the labeling of RNA, DNA, and protein. The regenerative response was evaluated by comparing the total concentrations and the incorporation of labeled precursors into these three constituents. In both normal and diabetic animals, two peaks occurred in the DNA concentrations and in the specific activities. These were at 24 and 48 hrs. in the normals and at 36 and 72 hrs. in the diabetics. The maximum concentration of RNA occurred at 24 hrs. in the normals, while the specific activity did not show a definite peak but remained at high levels in the 16 through 72 hr. samples. In the diabetic, the RNA concentration increased to an initial peak at 36 hrs., decreased, and then increased to a maximum at 72 hrs. The pattern for the specific activity of RNA also differed from the normals. It was high at 24 hrs., decreased, and then increased to a second peak at 48 hrs. The values at these two times were significantly greater than those obtained at any of the time intervals in the normals. The protein concentration reached its maximum level at 24 hrs. in the normals and at 48 hrs. in the diabetics. The incorporation of glycine in the normals was greatest at 24 hrs. with a second peak at 48 hrs., while in the diabetic it was high in both the 36 and 48 hr. samples. These results indicate that diabetes does not prevent the process of liver regeneration. However, all three parameters tested indicate that the regenerative process is delayed by at least 12 hrs., and that the recovery period is more prolonged. Supported by U.S.P.H. Grant #RR7059.

USE OF ELEMENTARY SIGNALS IN RESEARCH ON COCHLEAR POTENTIALS. T.W. Barrett, Department of Physiology & Biophysics, University of Tennessee Medical Units, 894 Union Avenue, Memphis, Tennessee 38163.

The cochlear microphonic potential (CM) and summating potential (SP) elicited by elementary signals defined by the bounding conditions: $\Delta f.\Delta t = f_o.t_o = \frac{1}{2}$, where Δf is signal bandwidth, Δt is signal duration, f_o is signal midfrequency and t_o is signal midperiod (Barrett, J. Acoust. Soc. Am. 54 (1973) 1092-1098) increase their temporal wavelength (w_t) as the signal parameter f_o is increased obtaining a constant waveshape or wavelength (Barrett, Biophysical Soc. Abstr. (1974)). It is well known that spatial wavelength (w_s) is inversely related to the velocity (v) of cochlear fluids, i.e., $(v_o/v_i)\cdot(w_{s_o}/w_{s_i}) = c$ (where o = output, i = input, c = a constant). By means of the CM and SP response we demonstrate experimentally that the amplitude (a) and temporal wavelength are related: $(a_o/a_i)\cdot(w_{t_o}.w_{t_i}) = c$ for radial shear movement of the cochlear partition. It is also well known from studies using sinusoidal signals that the velocity of the cochlear fluids is independent of frequency. Therefore, the well-known relation $f_o\cdot(w_{s_o}/w_{s_i}) = (v_o/v_i)$ indicates the dependence of changes in wavelength solely upon changes in velocity and thus upon the partition stiffness gradient for radial shear force. We demonstrate that the relation of f_o to w_{t_o}/w_{t_i} parallels the $(v_o/v_i) - (w_{s_o}/w_{s_i})$ relation for radial shear force, i.e., $f_o\cdot(w_{t_o}/w_{t_i}) = -c$ and $w_s = w_t$ as prolongation of temporal wavelength occurs in all four turns. In the case of longitudinal shear force, $(v_o/v_i)\cdot(a_o/a_i) = c$ effecting the well known spatial dispersion of maximum basilar membrane displacement according to frequency. As w_t is identical with Δt and both longitudinal and radial shear forces are cochlear stimuli, which are elicited optimally by elementary signals and not sinusoidal signals, cochlear mechanisms appear designed primarily for elementary signal analysis.

NONSTEADY STATE RESPIRATORY RESPONSES TO VERTICAL LADDER CLIMBING. F. Wesley Baumgardner, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Untrained human volunteers climbed a vertical ladder at ascent rates ranging from 60 ft/min to 120 ft/min. Others also climbed on a vertical treadmill at ascent rates up to 135 ft/min. The subjects were between 23 and 44 years of age and their weight ranged from 67 to 91 kilograms.

Expired gas was collected in neoprene balloons. Minute ventilation, oxygen uptake, and carbon dioxide output were calculated. During intermittent climbing of a ladder 30 ft in height, measurements taken from gas expired during the third consecutive ascent gave the following average results (±1 S.D.):

Ascent Rate	$\dot{V}_{O_2}$	$\dot{V}_E$	No. of
ft/min	STPD L/min	BTPS L/min	Subjects
60	2.3 (±0.4)	69.4 (±16.8)	15
80	2.9 (±0.4)	86.3 (±20.7)	13
100	3.3 (±0.3)	110.1 (±17.7)	12
120	3.8 (±0.3)	135.0 (±23.6)	10

During continuous climbing on a vertical treadmill inclined at 10° from the vertical, 4 subjects climbed at the rate of 135 ft/min for 40 sec. Oxygen uptake and minute ventilation of these subjects ranged from 2.6 to 3.7 STPD L/min and 79.2 to 107.7 BTPS L/min respectively, during the second half of the time period. These oxygen costs, which are comparable to reported maximum values for untrained, exercising subjects in this age group, were attained with unexpected rapidity.

PROSTAGLANDIN MEDIATED SPARING OF RENAL BLOOD FLOW IN THE ANESTHETIZED DOG. R. D. Bell, R. J. Sinclair* and W. L. Parry*. Veterans Administration Hospital, Oklahoma City, Okla.

The objective of the present study was to determine to what extent intrarenal prostaglandin (PG) synthesis alters the renal response to acute hemorrhage, and to compare the results obtained using two different anesthetic agents. A surgical plane of anesthesia was induced in mongrel dogs (20-30 kg) using either sodium pentobarbital or a combination of chloralose and urethane. Hemorrhage (30 ml/kg B.W.) was accomplished via the carotid artery. It was found that acute hemorrhage was followed by an initial decrease in renal blood flow (RBF) followed by a rapid recovery, regardless of anesthetic agent. In contrast, RBF remained well below control following hemorrhage when renal PG synthesis was inhibited by indomethacin. A similar effect was observed on renal vascular conductance, but the decrease observed was most dramatic in dogs anesthetized with chloralose-urethane. In addition, it was found that indomethacin treatment caused a small, but consistent decrease in renal conductance even in the absence of hemorrhage. Exogenous creatinine clearance (C_{cr}) was observed to follow a pattern similar to RBF in pentobarbitalized dogs, but was unaltered by indomethacin treatment. It was concluded that intrarenal PG synthesis effectively opposes renal vasoconstriction following acute hemorrhage in dogs under both anesthetic agents used. In contrast, the evidence suggests that maintenance of GFR following hemorrhage may be independent of PG mediated mechanisms.

TIME COURSE OF CHANGES IN MYOCARDIAL OXYGEN CONSUMPTION AND CORONARY RESISTANCE FOLLOWING STEP CHANGES IN HEART RATE. F. L. Belloni, D. E. Mohrman, P. A. Murray* and H. V. Sparks. Univ. of Michigan, Ann Arbor, MI.

Steady state correlations between myocardial oxygen consumption ($M\dot{V}O_2$) and coronary vascular resistance (CVR) suggest a causal role for some factor closely associated with $M\dot{V}O_2$ (e.g., adenosine release) in the regulation of CVR. This hypothesis requires that changes in $M\dot{V}O_2$ precede changes in CVR. We have tested this requirement using in situ canine hearts perfused with blood at constant flow through the left coronary artery. Coronary perfusion pressure and coronary sinus O_2 content were monitored continuously. Step changes of approximately 20 bpm in heart rate were induced by pacing and the changes in CVR and $M\dot{V}O_2$ were observed. The time course of changes in CVR was taken directly from the pressure recording but changes in $M\dot{V}O_2$ could not be estimated directly from venous O_2 content because of the dispersive effects of flow between the capillary exchange area and the venous measurement site. The distribution of vascular transit times to this site for an intravascular dye injected as a close-arterial bolus was used to estimate this dispersive process. Using curve fitting techniques we found the time course of tissue $M\dot{V}O_2$ which would cause the observed change in venous O_2 content. CVR responded to a step change in heart rate with a time constant of 10.8 ± 0.9 seconds (mean $\pm$ S.E.M.) whereas $M\dot{V}O_2$ changes with a time constant $\leq 7.9 \pm 0.4$ sec. ($p < 0.05$, student-t, $n = 4$ dogs). We conclude that, under the conditions of our experiment, $M\dot{V}O_2$ changes rapidly enough to initiate events leading to the changes in CVR associated with changes in heart rate. (Supported by USPHS Grants HL13538 and HL16760.)

SODIUM TRANSPORT BY RAT CEACUM IN VITRO. Gregory Bennett* and Andrew M. Goldner. Dept. of Human Physiology, Univ. of California, School of Medicine, Davis, California 95616.

The mammalian ceacum in vivo is involved in fluid and electrolyte absorption and exhibits a transepithelial electrical potential difference (P.D.). The nature of the P.D. was investigated in vitro. Rat ceacum was mounted as a flat sheet between two lucite chambers, bathed by identical sodium containing bicarbonate Ringers solution + 10 mM glucose at 37°C. The mean (± S.E.) P.D. was 3.7 ± 0.1 mV, mucosa negative, the short circuit-current (SCC) 59.4 ± 4.1 $\mu Amp/cm^2$ and the resistance, 64.0 ± 2.5 $ohm \cdot cm^2$. Unidirectional sodium fluxes in the short-circuited ceacum in $\mu Eq/hr \cdot cm^2$ were $Jm \rightarrow s$ 9.7 ± 0.4, $Js \rightarrow m$ 6.0 ± 0.3 and Jnet 3.6 ± .14. The sodium flux accounts for approximately 60% of the simultaneously measured SCC. When the ceacum was bathed in Na free Ringers in which choline was substituted for Na, the SCC decreased to approximately 5 $\mu Amp/cm^2$ but the resistance remained at the control level. Neither the SCC nor the net sodium transport were inhibited in the presence of 10^{-4} to $3x10^{-3}$M ouabain. The major proportion of the electrical properties of this tissue appear to be determined by active sodium transport from the mucosal to the serosal compartment. The transport across this tissue resembles that across other areas of the intestine. The ouabain insensitivity has previously been reported in rats and may be a species variation.

SPIRAL GANGLION RNA CHANGES IN RATS EXPOSED TO ACUTE NOISE STRESS. Thomas E. Bennett*, Robert W. Farwell*, and Adam Anthony. Department of Biology, Physiology Laboratories, The Pennsylvania State University, University Park, Pennsylvania 16802.

Twenty adult male Wistar rats were exposed to high intensity (120 dB, re: 0.0002 μbar), wide band (800 - 20,000 Hz) noise for 60 minutes. Ten controls were maintained at an ambient sound pressure level of 60 dB. Rats were sacrificed by decapitation at 1, 4, 8 and 24 hours post exposure; the tympanic bulla was excised, fixed in cold Carnoy's and decalcified with EDTA. Each bony cochlea was subsequently excised, paraffin processed, sectioned at eight microns and stained with azure B after DNase pretreatment. Cytophotometric determinations of spiral ganglion RNA levels were made with a single beam microspectrophotometer using the two wavelength method. A significant decrease in azure B-RNA levels was evidenced at 4, 8 and 24 hours post noise exposure. A decrease in ganglion cell volume at 1, 4, 8 and 24 hours was also found. Previous work in our laboratory established that noise evokes a transient increase in RNA activation in higher brain elements (auditory cortex, optic cortex and hippocampus) and in adrenal cortical cells over a corresponding 24 hour post exposure time interval. A decrease in spiral ganglion nucleic acid metabolism may reflect an increase in the excitation threshold of receptor nerve pathways. This could prove beneficial since it occurs when corticoid induced enhancement of excitability of higher brain centers appears to be maximal. (Research aided by the Office of Environmental Quality Programs and the Center for Air Environment Studies).

THE FLUX OF VALINOMYCIN AND PEPTIDE PV ACROSS BLACK LIPID MEMBRANES.
D.J. Benos* and D.C. Tosteson, Department of Physiology and Pharmacology Duke University Medical Center, Durham, North Carolina 27710.

When valinomycin ([(DVal-LLac-LVal-DHyv)$_3$]) is added to one side of a bilayer system separating identical KCl or NaCl solutions, membrane conductance increases but there is no zero-current potential. If PV ([(DVal-LPro-LVal-DPro)$_3$]), synthesized by Gisin and Merrifield (J. Am. Chem. Soc., 1972, 94: 6165), is added asymmetrically, a zero-current potential does develop with the side opposite to the PV positive. Ting-Beall et al. (J. Gen. Physiol, 1974, 63: 492) suggested that this potential is due to a very low membrane permeability to the uncomplexed form of PV, resulting in a concentration gradient of PV-cation complexes across the membrane. They also argued that the bilayer permeability to valinomycin is so high that no such gradient exists. Our experiments were designed to measure directly the permeability of bilayers to these macrocyclic carrier compounds. Using a radiotracer technique, the flux of valinomycin was found to be unstirred layer limited, i.e., the measured permeability coefficient was 4.5 (±1.5) x 10^{-4} cm/sec (N = 10). The permeability coefficient of the membrane to free PV was determined by an electrical technique to be 4.5 (±0.9) x 10^{-5} cm/sec (N = 17). These results are consistent with the hypothesis that the zero-current potential produced by unilateral addition of PV is referable to a low membrane permeability to this compound. (Supported by NIH Grant No. 5 P01 HL-12157 and USPHS Training Grant No. 5 T01 GM-00929.)

EVOKED PHRENIC NERVE RESPONSES TO ELECTRICAL STIMULATION OF THE VENTRAL MEDULLA IN ANESTHETIZED CATS

A.J. Berger* and R.A. Mitchell, Depts. of Physiology and Anesthesia University of California, San Francisco CA 94143

We stimulated various points over the ventral surface of the medulla with a bipolar electrode to a depth no greater than 0.5 mm from the surface in anesthetized, paralyzed, artificially ventilated cats. We recorded the evoked response to this stimulus simultaneously from both whole phrenic nerves. The response was averaged for 20 shocks delivered randomly during inspiration and at various voltages. We prepared an evoked response map extending from about 1 cm rostral to 1 cm caudal to the XII nerve roots, and from 1 mm to 4 mm lateral to midline. Unilateral stimulation of the area originally described as the site of the central chemoreceptors by Mitchell et al. (J Appl Physiol 18:523-533, 1963) consistently resulted in a bilaterally evoked response with 9.4 ± 0.3 msec latency and 14.0 ± 0.3 msec duration to peak. The conformation and latency of this evoked response is similar to that obtained by unilateral electrical stimulation of either the carotid sinus or glossopharyngeal nerves. Stimulation of other points over the ventral surface usually resulted either in no evoked response or a short latency response with 2.6 ± 0.4 msec duration to peak. This latter response is primarily evoked ipsilateral to the stimulus and could be associated with descending respiratory tracts. We suggest that from the area of the superficial chemoreceptors there is an excitatory neural pathway to the respiratory center at depth within the medulla. (Supported by USPHS Grants 5 F03 GM53152-02, GM15571, and 5-K3-H1319411)

DEVELOPMENT OF AN ANIMAL MODEL FOR THE STUDY OF HUMAN RED BLOOD CELLS. Herbert J. Berman and Margaret A. Cassidy*. Dept. of Biology, Boston Univ., Boston, Mass.

In vitro work here on the inherent capacity of hamster and human RBC to aggregate has shown a distinct difference. Human RBC have a greater tendency to aggregate than do hamster RBC, and this capacity is mainly inherent in the RBC and not in the plasma. These findings demonstrate the desirability if not need to study human RBC in vivo in an animal model by quantitative techniques. Freshly drawn human whole blood, plasma, or washed RBC were infused intrafemorally into the golden hamster either as an exchange or hypervolemic infusion. Of the hamsters infused with washed human RBC, 89% survived for the 8 day period of observation. Of those infused with human plasma and whole blood, 22% and 11%, respectively, survived 8 days. When human and hamster whole blood were mixed in vitro and observed microscopically, in most cases (87%) no RBC agglutination was observed. Known blood types of human RBC were injected into the hamster and their rates of disappearance from the circulation followed by routine blood typing tests. (Typing sera A or B do not agglutinate hamster RBC.) When samples of blood were taken and typed at 24 and 48 hrs, appreciable amounts of agglutinated cells were observed. By day 4 there was no evidence for the presence of circulating human RBC. The results with blood typing sera were checked by tagging 3 week old human RBC with Cr^{51} as sodium chromate. Most of the activity disappeared by 24 hrs. However, the activity in 60 min samples indicated that at that time practically all the human RBC were present in the circulating blood. These experiments demonstrate that human whole blood and plasma are toxic when infused into the hamster, washed human RBC are not, and that human RBC can be studied in the hamster circulation for several hours after their infusion. (Supported by HLI grants 00902 and 09447.)

THE 12,000 DALTON PEPTIDE OF APLYSIA NEURONS: LACK OF CORRELATION WITH PACEMAKER OR NEUROSECRETORY ACTIVITY. Robert W. Berry (intr. by F. Gonzales). Northwestern Univ. School of Med., Chicago, Ill.

Earlier workers have shown that extracts of leucine-labeled protein from certain identified neurons of the abdominal ganglion of Aplysia contain a prominent peak migrating at an apparent molecular weight of 12,000 on SDS-polyacrylamide electrophoresis, but its function is unknown. The fact that all neurons which synthesize this material are apparently spontaneously active pacemakers (R3-15, L11), whereas the neurons which do not are silent (R2, LPG), suggests that this peptide could have a role in endogenous electrical activity. Alternatively, since there is evidence that R3-15 are neurosecretory, whereas R2 and LPG are not, the material could function in secretion. I here report that the spontaneously active neurons L7-9 and RC do not synthesize the 12,000 dalton peak. Since spike resetting and lack of visible epsp's during hyperpolarization indicate that at least L8 is endogenously active, the protein is not likely to be involved in the generation of pacemaker activity. In addition, I find that the interneuron L10 does synthesize this material; thus a neurosecretory role for the 12,000 dalton protein is also unlikely.

DIGESTIVE MYOELECTRIC ACTIVITY IN THE CANINE SMALL INTESTINE. G. Bertiger, J. A. Flamini and G. M. Carlson (intr. by F. P. Brooks). Dept. of Physiology, Univ. of Pennsylvania School of Medicine, Philadelphia, Pa. 19174

The effects of a standard meal (Purina Dog Chow, Ralston Purina, 200 Gm mixed with 200 ml H_2O) and of a gastric H_2O instillate (400 ml, 38°C) upon canine small intestinal myoelectric activity were studied. Four dogs were chronically implanted with monopolar Ag-AgCl electrodes located approximately 1, 20, 40, 65 and 98% distant from the gastro-duodenal junction (total length of small bowel = 100%). Records were analyzed to determine the frequency of slow waves (SW) and action potentials (AP). Mean SW and AP frequencies (#/min) were determined for the 0-15, 15-30, 30-45 and 45-60 min intervals following the standard and H_2O meals. In addition, the 105-120 and 165-180 min intervals were analyzed following the standard meal. In all dogs, a decremental SW frequency gradient from duodenum to ileum was observed during each analysis period which confirms the observations of Szurszewski et al. (Am. J. Physiol., 218:1468, 1970). No decremental frequency gradient was observed for AP activity following either the standard or the H_2O meal during any of the analysis periods. The AP frequency was never as great as the SW frequency at any point in the small bowel during any of the analysis periods. Since AP activity can be used as an index of contractile activity (Bass and Wiley, Am. J. Digest. Diseases, 10:183, 1965), we conclude that aborad movement of small intestinal luminal contents following a meal is not dependent upon a decremental contractile frequency gradient.

EFFECT OF PHLORIZIN AND PHLORETIN ON THE KINETICS OF UNIDIRECTIONAL GLUCOSE TRANSPORT INTO THE ISOLATED DOG BRAIN. A.L. Betz* & D.D. Gilboe. Depts. of Neurosurg. and Physiol., Univ. of Wis., Madison, Wis. 53706.

The effect of phlorizin and phloretin on the unidirectional uptake of D-glucose-6-^{3}H was studied in 10 isolated dog brains by means of a single pass indicator dilution technique using ^{22}Na as the intravascular reference. The fractional extraction of labeled glucose, E, was calculated from the ratio of ^{3}H to ^{22}Na recovered in the venous blood after a 50ul arterial injection of the isotope mixture. The rate of unidirectional glucose transport, v, was calculated from the equation (v = (E-0.036) AF_p/W,) where A is the arterial plasma glucose concentration, F_p/W is the plasma flow rate per unit weight of brain, and 0.036 is a correction for glucose diffusion that had been obtained previously (Am. J. Physiol. 225:586, 1973). Indicator dilution injections were made over a range of arterial glucose concentrations and at constant blood levels of phlorizin (1.0 or 1.5mM) or phloretin (0.10 or 0.20mM). Data obtained in the presence of each inhibitor were combined with data previously obtained under control conditions (Am. J. Physiol. 225:586, 1973) and then fitted in Michaelis-Menten equations describing competitive or non-competitive inhibition. This analysis suggests that both phlorizin and phloretin are competitive inhibitors of glucose transport from blood to brain. Comparison of the K_i's shows that the phenol (K_i for phloretin = .096mM) is a more potent inhibitor than its glucoside derivative (K_i for phlorizin = .586mM). This work supported by Grant NS 05961

CEREBROSPINAL FLUID ACID-BASE BALANCE IN CHRONIC HYPERCAPNIA FOLLOWING CAROTID BODY DENERVATION. G. E. Bisgard, H. V. Forster, C. A. Rawlings* J. A. Orr*, B. Rasmussen* and D. D. Buss*. Univ. of Wis., Madison, Wis.

Seven ponies were subjected to carotid chemoreceptor denervation (CD) and 2 were sham operated. Studies were carried out prior to and 1, 2, and 4 weeks after surgery. All physiologic measurements were carried out in unanesthetized unsedated animals. Arterial blood was sampled from an indwelling aortic catheter and cerebrospinal fluid (CSF) was sampled from the cisterna magna. Successful denervation was confirmed in all CD ponies by total lack of ventilatory response to intravenous NaCN and to acute hypoxia. The mean acid-base data:

	Control	1 week	2 weeks	4 weeks
pHa	7.405	7.430*	7.385	7.411
$PaCO_2$	40.5	55.0*	51.8*	46.0*
$[HCO_3^-]_a$ mEq/l	24.8	35.5*	30.3*	28.8*
PaO_2	87.0	77.0*	72.0*	90.0
pHcsf	7.328	7.304*	7.304*	7.300*
$P_{csf}CO_2$	50.3	63.6*	59.1*	54.9*
$[HCO_3^-]_{csf}$ mEq/l	24.7	29.6*	27.5*	25.2

*Significantly different from control($P<0.05$)

Sham operated animals maintained normal acid-base status. These data indicate that CD causes respiratory acidosis indicating that the carotid chemoreceptors are active in regulating normal resting ventilation. The respiratory acidosis is compensated more quickly and more adequately in blood than in CSF. This finding and other studies we have reported previously indicate that arterial blood pH is better regulated than is CSF pH in respiratory acid-base disturbances. (Supported by USPHS Grant HL 15473)

ANALYSIS OF MULTIPLE PARAMETERS OF ANKLE CLONUS EVOKED AND SUSTAINED BY DIFFERENT PERTURBATIONS. B. Bishop and R. Johnston*. Dept. Physiol., State University of New York at Buffalo, and Veterans Admin. Hospital, Buffalo, N. Y. 14214

Clonus is one outstanding clinical manifestation of spasticity, yet its exact neural mechanisms are inadequately defined. Hence, we analyzed multiple parameters of sustained clonus under a variety of conditions in six patients with various CNS involvements. Gastroc-soleus EMG was detected with surface electrodes. Angle displacement and velocity of ankle movements were obtained from a potentiometer mounted at the ankle. Clonus was elicited by graded taps to the Achilles tendon, or by dorsiflexing the ankle at different velocities, through different angles, and for different durations. Clonus was sustained by applying different bias forces to the ball of the foot. The results showed that in any given subject the duration of the clonic beat (i.e., duration of the EMG burst) remained constant regardless of the initiating stimulus, imposed perturbations, or extent of motor unit recruitment. In contrast, amplitude of the beat, extent and velocity of ankle movement were all altered by the perturbations. Progressive increases in bias force initially shortened the pause and cycle durations, but further increments in bias force increased pause duration and ultimately stopped clonus. Procaine block of the peroneal n. or ischemia induced by above-knee inflation converted clonus to tonic gastrocnemius activity. The results demonstrate the importance of temporal and spatial patterns of multiple sensory inputs to the maintenance and timing of clonus.

Control of vascular volumes in the sheep umbilical circulation. Bissonnette, J.M., Department of Obstetrics and Gynecology, University of Oregon Medical School, Portland, Oregon.

Experiments were performed in 10 near term ewes using a perfused umbilical circulation in which umbilical artery (P_{fa}) and umbilical vein (P_{fv}) pressures, and umbilical blood flow could be independently regulated. Vascular and extravascular volumes were measured using a single injection double indicator (Albumin T-1824 and glycerol ^{14}C) method. With P_{fv} constant at 5 mm Hg. increasing P_{fa} from 25 to 45 mm Hg resulted in a 24.4 ± 7.0 (mean ± S.D.) ml increase in vascular volume; 35 to 45 = 11.6 ± 4.3 ml; 45 to 55 = 9.9 ± 3.1 ml and 45 to 65 = 22.3 ± 4.8 ml. Over the range of P_{fa} 25 to 35 mm Hg the extravascular volume increased but then remained constant from 35 to 65 mm Hg. When P_{fv} was raised to 15, 20, and 25 mm Hg, while P_{fa} was held constant by decreasing flow, the vascular volume increased 12.2 ± 5.6, 22.2 ± 5.4 and 28.0 ± 12.5 ml., respectively. No change in extravascular volume occurred when P_{fv} was raised at a constant P_{fa}. The simultaneous increase in both vascular and extravascular spaces in the lower pressure range (P_{fa} = 25-35 mm Hg.) is consistent with recruitment of previously unperfused vascular beds. The increase in only vascular volume over the range between P_{fa} 35 and 65 mm Hg and the changes seen when P_{fv} was increased can be explained by a model which allows for capillary distension.

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EFFECT OF OUABAIN ON ADRENAL POTASSIUM BALANCE IN SHEEP. E. H. Blaine, J. P. Coghlan, D. A. Denton, K. J. Hardy and B. A. Scoggins (intr. by J. H. Howell). University of Pittssburgh School of Medicine, Pittsburgh, Pa. and Howard Florey Institute, Melbourne, Australia.

We have recently shown that ouabain administered into the arterial supply of an autotransplanted adrenal gland of conscious sheep produces a profound reduction in aldosterone secretion (Blaine, et al, Endocrinology 94:1304, 1974). The present study was undertaken to discover the time course of change in adrenal potassium balance when ouabain is administered into the arterial supply of the in-situ adrenal of conscious sheep. Seven crossbreed Merino ewes were studied in this experiment in which 2.4×10^{-4} M ouabain was infused into the adrenal arterial blood supply. Adrenal venous blood samples were collected simultaneously with systemic arterial samples for measurement of potassium balance across one adrenal gland. Ouabain was administered for thirty minutes with blood samples at ten minute intervals. After discontinuing the ouabain infusion, appropriate samples were obtained for the ensuing sixty minutes. Ouabain produced a striking negative adrenal K balance within ten minutes of beginning the infusion. The adrenal continued to lose K for thirty minutes of the infusion and for thirty minutes thereafter. All periods of negative K balance were highly or very highly significant. The mean total K loss from one adrenal for all animals studied was 42.3 7.9 uEq. Thirty minutes after ending the ouabain infusion the adrenal began taking up K but had not recovered its normal K complement by sixty minutes after ending the ouabain infusion. These data combined with our earlier observations suggest that turn-off of aldosterone is not chronologically symmetrical with turn-on of aldosterone secretion under the influence of K.

K-FREE CONTRACTURE AND K RELAXATION OF VASCULAR SMOOTH MUSCLE. Aurora Bonaccorsi* and David F. Bohr. Dept. of Physiology, University of Michigan, Ann Arbor, Michigan.

The mechanisms of K-free contracture and K relaxation were studied in vascular smooth muscle by observing the effects of specific interventions on these phenomena. Strips from rat tail arteries contract slowly in K-free solution and relax when K is added back. The higher the concentration of K in the preincubation solution, the longer is the time required for the development of K-free contracture. Substitution of lithium, sucrose, or choline for Na causes a faster contracture in the absence of K. K-free contracture is abolished in Ca-free solution and is antagonized by Mn. K-free contracture is immediately reversed by adding back K. 0.2 to 10 mM KCl causes a concentration-dependent relaxation; 20 to 40 mM KCl causes an immediate relaxation followed by a contraction. If K-free contracture is obtained in a Na-free environment the readmission of K fails to induce relaxation and often causes further contraction. K relaxation is also inhibited by 10^{-4} to 10^{-3} M ouabain in rat arteries and by 10^{-7} M in dog arteries. K-free contracture occurs under conditions that inhibit the electrogenic Na-K pump. Relaxation resulting from the readmission of K to K-free tissues does not occur under these conditions.
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MYOCARDIAL RESERVE IN RHESUS MACAQUES FED AN ATHEROGENIC DIET FOR 19 MONTHS. Robert F. Bond and Eva S. Manning*. Bowman Gray School of Med., Winston-Salem, N.C.

The objective of these investigations was to quantitate the extent of diminished myocardial reserve in eleven Rhesus Macaques rendered mildly atherosclerotic by placing them on a high cholesterol diet (Diet Test) for 19 months. Seven additional animals fed monkey chow acted as Diet Controls. The extent of coronary artery disease was evaluated while myocardial oxygen demand was increased by controlled atrial pacing. During the pacing procedure the following physiological parameters were recorded in open chested monkeys respired in such a way as to maintain the arterial pO_2 at 126±5 mmHg, pCO_2 at 30.5±2.5 and pH at 7.48±0.03: 1) aortic BP, 2) LVP, 3) contractility ($dlnP/dt$), 4) aortic flow, 5) cardiac power (CP), and surface ECG. Aside from gaining valuable cardiovascular control data, four critical pacing rates were obtained: a) the lowest rate before repolarization changes occurred in the ECG (ST-T wave changes), b) the rate at which CP decreased below control, c) the rate at which the contractility decreased below control and d) the fastest rate that the heart could follow on a 1:1 basis. The data below is expressed as mean heart rate ± 1 SEM.

	Intrinsic Rate	ST-T	CP↓	dlnP/dt↓	Max HR
Diet Control	166 ± 4	204 ± 2	223 ± 5	241 ± 7	252 ± 8
Diet Test	163 ± 8	181 ± 9	206 ± 6	228 ± 7	250 ± 6

There were significant decreases ($P<1\%$) in the maximum HR achieved before evidence of ischemia was seen; and the maximum HR before a cardiac power drop occurred ($P<5\%$) in the Diet Test animals suggesting that the atherosclerotic animals had a significant degree of coronary artery insufficiency. (Supported by USPH, NHLI Grants HL 14164 and HL 487.)

CARDIORESPIRATORY SEQUELAE IN A MODEL OF SUDDEN INFANT DEATH. R. A. Bonner*, R. W. Millard* and E. T. Angelakos. Biomedical Research Institute, University of Maine, Portland, Maine.

Human infants and most mammals are obligate nose breathers. Nasal obstruction followed by laryngospasm has been suggested as responsible for sudden infant death syndrome (SIDS). This study was performed to determine cardiovascular and respiratory events during and after short term (30 to 120 sec.) nasal obstruction in anesthetized young pigs (3-10 weeks). Heart rate (HR), electrocardiogram (ECG), intrathoracic (IT), left ventricular (LV), right ventricular (RV), and aortic (A) pressures (P) were recorded continuously. Three phases of cardiorespiratory responses to acute hypoxia were observed. Phase 1 (0-45 sec. hypoxia): HR decreased slightly from 185 to 165 beats/min. and mean AP rose sharply from 115 to 153 mmHg as did RVP (50/8 to 59/18 mmHg). ITP reached -50 mmHg during intense inspiratory attempts. Phase 2 (45-120 sec. hypoxia): HR fell to 135 beats/min. with intermittent A-V dissociation. Mean AP decreased to 128 mmHg as did LVP and RVP. No respiratory attempts were made during this period. Phase 3 (0-30 min. post nasal obstruction). Severe arrhythmias, elevated S-T potentials and large T waves occurred in ECG. Large oscillations in mean AP and irregular respiratory pattern with prolonged periods of apnea characterized this phase. Ten of 14 pigs studied died within 30 min. of having total A-V block with ventricular arrest. Postmortem findings included cardiac, pulmonary and pleural hemorrhages. Thus an otherwise non-life threatening event (acute hypoxia) initiated a series of physiological responses resulting in cardiac arrhythmias, apnea and death in young domestic swine. We conclude that inappropriate cardiovascular and respiratory reflex responses to nasal obstruction may be the principal cause of SIDS.

EFFECTS OF A WATER LOAD ON SINGLE NEPHRON GLOMERULAR FILTRATION RATE (SNGFR) IN DESERT QUAIL. Eldon J. Braun* and William H. Dantzler. Dept. of Physiol., Col. of Med., Univ. of Arizona, Tucson, Arizona 85724.

In previous studies on desert quail (Lophortyx gambelii), arginine vasotocin (AVT) administered during a mannitol diuresis reduced whole kidney glomerular filtration rate (GFR) primarily by reducing the number of filtering reptilian-type (RT) nephrons. In present studies, an attempt was made to suppress release of endogenous AVT by water-loading quail intravenously with a dilute (125 mOsm) solution of 75 mM glucose and 25 mM NaCl at 0.4 $ml \cdot kg^{-1} \cdot min^{-1}$ for 3 hrs. During the first 90 min of infusion, the plasma osmolality decreased by about 30% and then remained constant during the rest of the infusion. Plasma $[Na^+]$ decreased but plasma $[K^+]$ did not change. Urine remained isosmotic with plasma throughout infusion. Urine flow rate was only 50% of that observed previously during control 2.5% mannitol infusion. However, whole kidney GFR was 160% of that observed previously. About 94% of filtrate was reabsorbed during present water load compared with 78% during previous control mannitol infusion. The SNGFRs were estimated with a modified Hanssen's Na-ferrocyanide technique. In two birds, SNGFR averaged 23.4 nl/min for mammalian-type (MT) nephrons and 9.6 nl/min for the reptilian type (RT) nephrons. In a third animal, the mean SNGFR was 53.4 nl/min for MT nephrons and 15.1 nl/min for RT nephrons. Mean SNGFRs for the previous control studies with mannitol infusion were 14.6 and 6.4 nl/min for the MT and RT nephrons, respectively. In summary, although whole kidney GFR and SNGFR increased markedly during the water load, urine flow rate decreased, urine remained isosmotic, and only about 60% of the infusion was excreted. It appears that the GFR may have been freed of any suppressing effect of AVT during the water load, but that tubular permeability to water was not reduced and that isosmotic reabsorption of filtrate may have been enhanced. (Supported by AM 16294).

EFFECT OF AY-9944 OR HYDROCORTISONE ON PULMONARY O_2 TOXICITY. Jay B. Brodsky*, Richard W. Sheppe*, Susan M. Keegan*, and John Hedley-Whyte. (Intr. by G.S. Kurland). Dept. Anaesthesia, Harvard Medical School, Boston, Mass. 02215

AY-9944 (trans-1,4 bis(2-chlorobenzylaminomethyl) cyclohexane dihydrochloride) blocks cholesterol biosynthesis and may accelerate pulmonary surfactant synthesis. We administered AY-9944 (7.5-15.0 mg/kg bw in 0.5 ml N NaCl, i.p. q.d. x 21 days) to 100 gm, 5 week old Wistar-Lewis rats, and then studied their lungs as compared to normal, saline (0.5 ml N NaCl, i.p. q.d. x 21 days) and hydrocortisone (25-50 mg/kg bw in 0.5 ml N NaCl, s.c. q.d. x 7 days) treated rats. AY-9944 rats had significantly smaller body weights than N NaCl rats (means 173 vs 237 gm after 21 days of treatment, $p=.003$) although their lungs were heavier ($1.28\pm.07$ vs $1.03\pm.03$ gm (S.E.), $p=.018$). There were no significant differences in pressure-volume hysteresis area, deflation compliance or lung stability indices of excised lungs between groups. When exposed to ~100% O_2 at one atm (OAP), lung wts increased in all four groups by 48 hrs. Lung compliance decreased significantly ($p<.05$) in normal, AY-9944, and hydrocortisone groups at 56 hrs and in the saline group by 72 hrs OAP. The lung dry/wet wt ratios decreased in all groups at 24 and 48 hrs, but by 72 hrs OAP, had returned to non-O_2 exposed levels. Compliance, area of hysteresis, lung wt/bw ratios, lung dry/wet wt ratios and lung wts were similar in survivors between all groups at 24,48 and 56 hrs OAP, but hydrocortisone rats had increased compliance at 72 hrs compared to normals ($.091\pm.013$ vs $.056\pm.009$, $p<.05$). After 72 hrs OAP, 60.0% normal, 57.1% hydrocortisone, 50.0% N NaCl and 0% AY-9944 rats were alive. In conclusion, non-OAP exposed AY-9944 rats were smaller and had heavier lungs than normal, saline and hydrocortisone treated rats. OAP exposed AY-9944 rats survived for shorter periods probably on the basis of altered lipid metabolism. (Grants GM 15994 and HL 05422).

HEMODYNAMICS OF ARTERIOVENOUS FISTULAE. C.S.Brown*, J.E.Lavigne* and K.G.Swan. New Jersey Medical School, Newark, N.J.

The relationships between pressures and flows about arteriovenous fistulae have been described; however, for technical reasons, little attention has been directed to hemodynamic events within such fistulae. Utilizing a 4 cm length of autogenous common carotid artery interposed between artery and vein, we measured pressure and flow within femoral arteriovenous fistulae in five anesthetized dogs. A branch of the carotid artery was cannulated for pressure measurements. Flow was measured with an electromagnetic flowmeter. Pressures and flows within the limbs of the fistulae were measured and expressed in terms of their anatomic location with reference to the fistulae. When the fistula was closed, proximal femoral arterial blood flow (PAF) was 58 ± 14 (SE) ml min^{-1}. Proximal arterial pressure (PAP) was 156 ± 7 and proximal venous pressure (PVP) was 7 ± 2 mm Hg. Calculated femoral vascular resistance was 2.57 peripheral resistance units (PRU). When the fistula was opened PAF increased significantly ($p<.001$) to 417 ± 12 ml min^{-1}. Flow through the fistula (FF) was 408 ± 31 ml min^{-1} and this value was not significantly different ($p>.05$) from PAF or proximal venous flow (487 ± 52 ml min^{-1}). Opening the fistula caused PAP to fall significantly ($p<.01$) to 143 ± 7 mm Hg, but did not change PVP. Pressure within the fistula was 104 ± 4 mm Hg; calculated resistance across the fistula was 0.28 PRU. Proximal arterial occlusion reduced FF to 35 ± 4 ml min^{-1}, and this parameter was negligible following distal arterial occlusion. The findings indicate that flow across the fistula was generated by the proximal artery; "retrograde flow" from the distal artery was observed only when the proximal artery was occluded. Pressure within the fistula was relatively high; however, resistance was quite low and accounted for the seven fold increase in proximal arterial flow.

AMINO ACID AND AMMONIUM INFLUENCE ON HEPATIC ENCEPHALOPATHY
Henry Brown, Mary Evans*, James Hupp* and Frederick Reichle*
Harvard Surgical Unit, Boston City Hospital, Mass. 02118

Encephalopathy does not always accompany hyperammonemia after portacaval (PC) shunting theoretically because other compounds may be necessary to produce neurologic signs. This study presents evidence that abnormal concentrations (conc) of plasma amino acids (aa) may be one such group of compounds. 12 hyperammonemic PC shunted rats had no increased plasma aa conc and significantly, no encephalopathy. Certain aa were decreased, most notably, branched chain aa, Leu, Ile and Val. On the other hand, 3 hyperammonemic PC shunted cirrhotic patients had encephalopathy and increased conc plasma Met, Gln and aromatic aa Tyr and Phe. They also had decreased Leu, Ile and Val as the animal model. Feeding only minimal requirements of essential aa as sole nitrogen source for 5 days was associated not only with decreased ammonium and plasma aa Met, Gln, Tyr and Phe, but also clinical improvement documented by electroencephalographic changes.

It is concluded that in these studies decreased conc of plasma Leu, Ile and Val are associated with assymptomatic hyperammonemia, but when accompanied by increased Met, Gln, Phe and Tyr encephalopathy is observed. A new clinical approach to management of encephalopathy is suggested by controlling intake of specific amino acids.

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CHARACTERIZATION OF A PLASMA VASOCONSTRICTOR BY ITS ACTION ON VARIOUS TYPES OF SMOOTH MUSCLE.
Judith E. Bryant*, Mary C. Smith*, and David F. Bohr. Dept. of Physiology, University of Michigan, Ann Arbor, Michigan.

Normal plasma has been shown to contain an as yet unidentified factor that causes contraction of all types of vascular smooth muscle (Circ. Res. 19:593, 1966). The current study extends these observations by comparing the activity of this plasma factor with that of other agonists on non-vascular smooth muscle. The method used is based on Vane's multiple organ technique (Brit. J. Pharmacol. 35: 209, 1969). Chick rectum, rat colon, rat stomach and rabbit aorta were subjected to cumulative concentrations of acetylcholine, 5HT, epinephrine, angiotensin, and plasma factor. The following characteristics of the response to plasma factor differentiated it from each of the other agonists: acetylcholine produced strong contraction of all three non-vascular smooth muscle tissues while plasma factor caused relaxation of two of them; 5HT and angiotensin also caused contraction in all tissues; epinephrine produced marked relaxation of the non-vascular smooth muscle tissues which was clearly different from the slight relaxation seen with plasma factor in the rectum and colon and the contraction of the stomach. These results expand earlier findings that there is, in normal plasma, an unknown factor that affects smooth muscle activity.
(Supported by NIH HL-03756 and HL-05682.)

ENDOGENOUS INSULIN SENSITIZATION TO ENDOTOXIN SHOCK. B. J. Buchenan* and J. P. Filkins. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153

Profound hypoglycemia incident to impaired hepatic gluconeogenesis is a common terminal event in lethal endotoxin shock. Since insulin is the dominant physiologic regulator of carbohydrate homeostasis, the role of endogenous insulin secretion in determining endotoxin shock lethality was investigated in 300 ± 20g male rats of the Holtzman strain. Overnight fasting, which depresses insulin secretion, provided significant protection against lethal endotoxin shock induced by 2 mg. Salm. enteritidis lipopolysaccaride administered iv.; lethality was reduced from 69% in fed rats (N=65) to 37% in fasted rats (N=55). Mannoheptulose, a specific inhibitor of insulin secretion, provided protection in endotoxin shock; in fed rats given mannoheptulose (N=50) lethality was reduced from 69% to 48%, and in fasted rats given mannoheptulose (N=84), lethality was reduced from 37% to 6%. Insulin treatment (250mU sc) as well as the insulinogenic sulfonylurea agents tolbutamide and tolazamide sensitized rats to endotoxin shock. Treatment of fed rats with 400 mg of glucose ip., an insulinogenic dose, at either 0, 1, or 2 hrs after 1mg endotoxin iv. increased lethality from 22% in the controls (N=45) to a weighted mean of 45% in the combined experimental groups (N=80); glucose treatment of fasted rats increased shock lethality from 12.5% in controls (N=40) to 42% in the glucose treated animals (N=88). Glucose tolerance testing of overnight fasted rats 2 hrs after 1mg endotoxin iv. indicated no impairment of glucose clearance or insulin release. These data support an intimate role for insulin in the development of the altered carbohydrate homeostasis which is a characteristic and potentially contributive factor to lethality in endotoxin shock. *(Supported by NIH Grants HL 08682 and HL 14540 and NSF Grant GZ-2686)*

EFFECTS OF PROLONGED CARBON MONOXIDE EXPOSURE ON RAT RIGHT VENTRICLE. Lawrence B. Bugaisky and David G. Penney (intr. by W. Weathers). Univ. of Illinois at Chicago Circle, Chicago, Illinois.

Right ventricular (RV) enlargement following certain cardiovascular stresses (e.g. altitude, anemia, and pulmonary artery ligation) is reported to be accompanied by altered in vitro physiological performance (anoxic tolerance, aerobic recovery, and tension development). 500 p.p.m. CO-poisoning (carboxyhemoglobin = 38%) for 30 days also produces RV enlargement. The present study using young adult rats was designed to determine if this enlargement (35 - 40%) also produces such alterations. RV tension development and anoxic tolerance were determined in an apparatus similiar to that of Blinks (J. Appl. Physiol. 20:755, 1965) in a medium lacking glucose. Increased anoxic tolerance was demonstrated by a significant increase in the time taken to reach 50% pre-anoxic tension as compared with controls (12.6 ± 0.9 vs. 9.3 ± 0.6 min.). Additionally, RV anoxic tolerance expressed as a percentage of pre-anoxic tension was greater than controls throughout 15 minutes of anoxia. However, when contractile tension was normalized on the basis of RV wet weight (g/g), CO-exposed animals were significantly lower (30%) than controls. In addition, RV of CO-exposed rats showed an increased ability to recover contractility upon the resumption of aeration. No differences in RV glycogen content either prior to or following 15 minutes of anoxia testing was seen between controls and CO-exposed animals. It appears that CO-exposure increases tolerance during anoxia and ability to recover contractility following anoxia. However, it also appears to decrease the capacity to develop isometric tension. This may be related to observations of others that prolonged CO-exposure results in ultrastructural changes in heart muscle.

DIFFUSING CAPACITY IN LAMBS: POSTNATAL DEVELOPMENT OF FACILITATED PULMONARY CO TRANSPORT. B. Burns and G. Gurtner. Dept. of Environmental Medicine, Johns Hopkins University, Baltimore, Maryland 21205.

Evidence has been presented that the transfer of CO and O_2 may be partially carrier-mediated in the lung and placenta, respectively (Drug Metabolism and Disp. 1(1);374-379,1973). Substances which bind to the mixed function oxidase Cytochrome P-450, which is present in the lung and placenta, reduce the diffusional transport of both CO and O_2. Since drug metabolizing enzyme systems are not fully developed in the newborn fetal lung we investigated the possibility that the carrier may be absent at birth by measuring DL_{CO} using a rebreathing method. Intravenous Heroin, or SKF-525A (extrapolated from a completely blocking dose in a 200g rat on the basis of surface area) showed no difference from control DL_{CO} in the newborn lambs. The DL_{CO} for 9-day old lambs was 50% greater than for newborns and decreased after I.V. SKF-525A. In addition we pretreated 4 ewes for 5-days prior to term deliveries with morphine or SKF-525A to induce precocious maturation of the fetal drug metabolizing enzyme systems. The mean DL_{CO} of these newborn lambs from pre-treated ewes was greater than the DL_{CO} for either normal newborns or 9-day old lambs ($P<.001$). In addition, intravenous SKF-525A was able to reduce the DL_{CO} by 45% in the drug-induced newborns ($P<.025$). As another test for a CO-carrier in the newborn lung, the DL_{CO} was measured at two different normoxic alveolar CO concentrations (0.0065% and 0.06%). The DL_{CO} was identical at both levels in the normal newborn lambs, where is it decreased with increasing alveolar CO% in adult animals which demonstrate facilitation (Fed.Proc.33 421,1974). These data indicate that the pulmonary CO-carrier in lambs is absent at birth but is at least partly developed by the age of 9 days; however,pretreatment of the mother with drugs which induce formation of liver cytochrome P-450 in rats, results in the appearance of a pulmonary CO-carrier at birth. Supported by Amer.Heart Assoc.& PHS grant ES0454.

CONDITIONING OF SEDENTARY YOUNG MALES BY WEARING ANKLE WEIGHTS ON THE JOB. R.L. Burse*, K.B. Pandolf*, and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760.

Nine sedentary Army weather observers [age 25.6 yr (range 19-32); predicted maximum aerobic power (MAP) 30.5 ml/min·kg (range 23.2-38.9)] wore weighted spats (3.0 kg/ankle) for a continuous 20-day conditioning period; 4 of the group continued wearing the spats an additional 20 days. Spats were worn for 7.7 hr/day (range 4.7-9.3), while subjects performed normal job activities in which they walked 2.9 km/day (range 1.8-4.2). Oxygen uptake ($\dot{V}O_2$) and heart rate (HR) responses before and after conditioning were determined at 6 submaximal workloads: level walking at 4.0 and 5.6 km/hr, with and without ankle weights, and ergometer cycling at 2 workloads chosen to elicit HR in the 140-160 and 160-180 ranges. Although not reaching statistical significance, average submaximal HR was reduced and MAP increased for the 9 subjects after 3 weeks' conditioning. Although only 4 subjects continued wearing the weights for an additional 3 weeks, the final reduction in HR while walking with ankle weights and while cycling (overall average: 19 beats/min) and the increase in MAP (10 ml/min-kg) were significantly different from the pretest values ($p < .05$). $\dot{V}O_2$ and minute ventilatory volumes were unchanged, consonant with unchanged body weights. $\dot{V}O_2$ and HR were obtained on-the-job from 3 of the 4 subjects who trained for 6 weeks. HR was increased 3-9 beats/min when spats were worn on the job, except for a 6-19 beats/min increase during stair-climbing, suggesting that the training stimulus averaged less than 10 beats/min. We conclude that the physical condition of sedentary young men can be improved by wearing ankle weights throughout a non-strenuous work day. However, the conditioning process is slow in jobs requiring little more than climbing a flight of stairs every hour, even with weights as great as 3.0 kg/ankle.

WHOLE BODY COOLING WITH PROTECTIVE CLOTHING DURING COLD WATER IMMERSION. G.D. Bynum* and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760.

Heat losses during water immersion have been evaluated for nude and clothed heated copper manikins (Goldman et al., 1966), and for nude men (Gee and Goldman, 1973). Data is now presented for subjects immersed in still, cold water (28°C and 20°C), nude (.14 clo) and in 1/4" vinyl (.43 clo), 3/8" polyurethane (.61 clo), and 1/4" neoprene (.76 clo) wet suits. Metabolic rates (M.R.), EKGs, heat flow (discs at 5 sites), rectal (T_{re}) and 10 skin temperatures ($\bar{T}_s$) were obtained in air, then during a 60 min immersion period, and for 20 min after. For nude men, skin to water temperature gradients and heat flow are comparable to those of Gee and Goldman. Average shifts in $\bar{T}_s$, T_{re} and M.R. relative to the pre-immersion baseline at 15 and 60 min are:

	TW	Nude		Vinyl		Polyurethane		Neoprene	
		15'	60'	15'	60'	15'	60'	15'	60'
$\Delta\bar{T}_s$,°C	28°	-5	-15	-2	-2	-1	-1	-1	-2
	20°	-11	-11	-5	-7	-4	-6	-3	-5
ΔT_{re},°C	28°	-.5	-2.7	-.8	-3.2	-.9	-2.6	-.6	-2.3
	20°	-.5	-3.1	-.6	-2.3	-.6	-2.6	-.4	-1.7
ΔMR,w/m^2	28°	19	39	0	5	5	-1	-6	0
	20°	95	128	10	41	10	41	7	17

The similar responses in the vinyl (0.43 clo) and polyurethane (0.61 clo) suits can be attributed to a poorer fit of the polyurethane wet suit. The T_{re} at 60 min for the nude, and all clothed conditions, taken together with the decreases in M.R. associated with increased insulation, suggest that the effect of insulation is to conserve the metabolic energy cost associated with maintaining a given level of T_{re}.

RECEPTIVE FIELD ORGANIZATION AND RESPONSE PROPERTIES OF MECHANORECEPTOR NEURONS INNERVATING THE SIPHON AND MANTLE SHELF SKIN IN APLYSIA. John Byrne (intr. by E.R. Kandel), Coll. of Physicians and Surgeons of Columbia Univ. and N.Y. State Psychiatric Inst.

Intracellular recordings were obtained from mechanoreceptor neurons mediating the defensive withdrawal reflex of the gill and siphon of Aplysia californica (Castellucci, et al., 1970). The receptive field of the reflex is innervated by two symmetric clusters (LE and RE) of cells located in the abdominal ganglion. These cells seem to be first-order sensory neurons which directly innervate the siphon and mantle shelf respectively. A mechanical stimulus to the skin or an electrical stimulus to the afferent nerve produces an all-or-none action potential without preceding EPSPs in the cell bodies of the mechanoreceptors. These responses can still be elicited after bathing the preparation in solutions of high magnesium for periods greater than 12 hours. The LE (siphon) cells have a mean threshold to vertical surface forces of 0.25 ± 0.16 grams. They are normally silent but respond with a slowly-adapting discharge whose frequency is proportional to the intensity of the stimulus. Receptive field areas vary between 21 and 378 mm^2 and there is extensive receptive field overlap. Five receptive fields can be repeatedly identified according to their size, shape and location on the skin. The RE (mantle shelf) cluster was less thoroughly investigated but appears similar to the LE cells; their field areas vary between 6 and 278 mm^2 and as with the siphon skin there is considerable overlap of receptive fields. Thus the receptive fields of the LE and RE cells provide the central nervous system with a multiple representation of the siphon and mantle shelf skin. The functional significance of these representations has yet to be analyzed.

INHIBITION OF INSULIN SECRETION BY PHYSIOLOGICAL CONCENTRATIONS OF EPINEPHRINE AND NOREPINEPHRINE. L.A. Campfield (Intr. G.A. Bray), Sch. of Med., UCLA, L.A., Calif.

It has been suggested that the sympathetic nervous system controls insulin secretion under normal physiological conditions; therefore, the effects of physiological concentrations of epinephrine (E) and norepinephrine (NE) on the insulin secretion rate (ISR) from perifused, isolated rat islets in response to glucose (G) step inputs were studied. Islets were isolated by collagenase digestion and 30 were placed in each of three chambers. Following a 45 min control period with 5 mM G, the [G] of test perifusate ranged from 5 to 40 mM and reported human fasting concentrations of E (4×10^{-10}M) or NE (2×10^{-9}M) or 10 times those concentrations were added. In the presence of 20 mM G, the change in ISR from control was decreased throughout the experimental period by approximately 40% and 20% in the presence of 4×10^{-9} and 4×10^{-10}M E and 40% in the presence of 2×10^{-9}M NE, as measured by the total insulin secreted (IS). For example, IS was less than control in the presence of 2×10^{-9}M NE ($19.1 \pm 2.74 < 33.2 \pm 2.35$ $P < .05$). At any time during the experiment, ISR is a sigmoidal function of [G]. This function can be described for G alone as follows: threshold - 5 mM, 1/2 max ISR - 10 mM, ISR max - 20 mM. Physiological concentrations of E and NE displaced this curve downward without translation. In conclusion, physiological concentrations of E and NE inhibit insulin secretion from perifused rat islets suggesting that the sympathetic nervous system can modify insulin secretion in the normal resting state.

EFFECT OF POST-OPERATIVE (OP.) RECOVERY ON CARDIOVASCULAR DYNAMICS IN CHRONICALLY INSTRUMENTED DOGS. E.L. Carlson, E.P. McCutcheon*, R.M. Gordon*, H. Sandler. Stanford University, Palo Alto, CA and NASA-Ames Research Center, Moffett Field CA 94035.

Left ventricular function (LVF) was followed in 6 chronically instrumented animals (CIA) by multiple observations almost daily during the first month post op. and weekly thereafter (mean period 64±19sd days). LVF was assessed by heart rate (HR), LV and aortic pressures, LV flow (EMF) and derived variables. Dose response curves were recorded with incremental IV infusions of 3 levels (0.01, 0.02, 0.04 mg/Kg) of isoproterenol (ISO) and norepinephrine. LVF declined slightly during the first post op. week, declined significantly during second and third week (16± 8sd days) and abruptly increased thereafter to a stable level. The variables most indicative of altered LVF were HR, cardiac output (CO), stroke volume (SV) and LVdp/dt. The % change (%Δ) of CO due to 0.04 mg/Kg ISO decreased significantly during the second and third week, as did the %Δ of LV dp/dt (Table below). The data indicate the LVF response to drug induced stress varies during the initial recovery period; it appears that about 21 days post op. are needed to obtain optimal response characteristics. These results also suggest that great care is required in choosing the time LVF is studied in CIA.

*Means with SEM	First week	16	8 sd days	Subsequent Days
CO liters/min. control	2.85 ± .17	3.09 ± .13		2.72 ± .12
CO %Δ 0.04 mg/Kg ISO	56 ± 5.4%	49 ± 5.0%		72 ± 5.2%
LV dp/dt mmHg sec^{-1}cont.	2069 ± 107	2176 ± 58		2059 ± 63
LV dp/dt %Δ 0.04 mg/Kg ISO	42 ± 4.8%	24 ± 3.7		47 ± 3.2%
n	21	37		46

SLOW OSCILLATIONS IN APLYSIA BURSTING NEURONS ARE PRODUCED BY THE INTERACTION OF TWO CURRENTS. N.T. Carnevale* and H. Wachtel. Dept. of Physiology and Dept. of Biomedical Eng., Duke Univ., Durham, N. C. 27706

An endogenous slow oscillation of membrane potential (Vm) is known to underlie the burst firing pattern in certain Aplysia (abdominal ganglion) neurons (L_2-L_6 and R_{15}), but the mechanism of this cyclic activity is not well understood. In order to study this activity, we have devised a track and hold (T/H) voltage clamping technique whereby the cycle can be interrupted at any point and V_m held (clamped) at a fixed potential while the resulting holding current (I_h) is recorded. Applying this technique we have found that no matter where the cycle is broken a maintained inward current (I_{in}) slowly develops. However, if the clamp is applied at, (or shortly after) the depolarized peak (V_{DP}) of the cycle a transient outward current preceeds the development of (I_{in}). Combining these results with previous studies (Wilson and Wachtel, 1974) we conclude that the oscillation is based on the interplay of two current components: (1) a regenerative inward current which underlies the essential instability (negative resistance) of V_m in the range of the oscillation and inexorably drives V_m toward a potential well beyond V_{DP}, and (2) an outward current which is activated by the regenerative depolarization and in turn temporarily overwhelms the negative resistance and thus drives V_m in the hyperpolarized direction. Subsequent experiments employing step command voltage clampinghave confirmed, and further delineated, these two current sources and have also provided a basis upon which to identify the ionic conductance mechanisms underlying them. (Supported in part by NIH grant NS-08476)

REGULATION OF ARTERIAL P_{CO_2} DURING INTRAVENOUS CO_2 LOADING. R. Casaburi, K. Wasserman, D.J. Huntsman*, J. Castagna*, R. Lugliani*, B.J. Whipp, Div. of Respiratory Physiology and Medicine, Harbor General Hospital, UCLA School of Med., Torrance, Calif.

We have previously demonstrated (J. Appl. Physiol. 36:457, 1974) that increased CO_2 flow to the lung produced by increasing cardiac output (without increasing mixed venous P_{CO_2}) results in hyperpnea with arterial P_{CO_2} maintained at its control value. To study if arterial P_{CO_2} could be similarly regulated when CO_2 flow was elevated by increasing mixed venous P_{CO_2} (without changing cardiac output), we produced graded increases of $P\bar{v}CO_2$ using an extracorporeal gas exchanger in five chloralose-urethane anesthetized dogs. Control arterial blood gases and pH differed little from those reported in unanesthetized dogs and showed no significant changes over the course of the experiment. Blood flowed at a rate of 250-300 ml per min. from a femoral artery to the exchanger, where it was equilibrated with high P_{CO_2} gas, before returning to a femoral vein. CO_2 output increased up to fourfold and mixed venous P_{CO_2} increased to an average of 69 mm Hg. Ventilation increased in proportion to the additional CO_2 flow to the lung. Arterial P_{CO_2} was consequently regulated at its control value. In contrast, comparable increases in minute ventilation produced by "conventional" airway loading resulted in arterial hypercapnia with the resulting CO_2 response curve being similar to that found in unanesthetized dogs. We conclude that intravenous delivery of CO_2 to the lungs results in infinite "sensitivity" when computed by conventional techniques (i.e. $\Delta V_E/\Delta PaCO_2$). This suggests a CO_2-linked hyperpnea which is not mediated by measurable increases in mean arterial P_{CO_2}.

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EFFECTS OF EXERCISE ON THE AIRWAYS OF NORMAL MEN. W. Y. Chen* and J.F. Souhrada. Pulmonary Function Lab., Natl. Jewish Hosp. & Res. Center, Denver, CO 80206.

Effects of a submaximal exercise (E) on the pulmonary function were studied in ten healthy male subjects of ages 24 to 40. E consisted of walking on a treadmill at a speed of 6.4 km/hr and an elevation of 20% for a period of ten minutes. The heart rate and oxygen consumption were determined before and during the exercise. The pulmonary functions were tested with the Stead-Wells spirometer, the body plethysmograph, and the Wedge spirometer for the following measurement: forced vital capacity (FVC), forced expiratory volume (FEV_1), maximum mid-expiratory flow rate (MMEF), airway resistance (Raw), thoracic gas volume (Vtg), specific airway conductance (SGaw), and flow-volume loop parameters. The measurements were made twice before the E (baseline values), and 5 and 25 minutes post-E. It was found that in four subjects the MMEF increased 18 to 48% with no appreciable changes in SGaw after the E. In another two subjects the SGaw increased 20% and 42% after the E, without significant changes in the MMEF. The remaining four subjects showed no obvious changes in either parameter. It is concluded that (1) the prominent change in healthy men after a submaximal E is an increase in MMEF or SGaw, (2) in some normal subjects the pulmonary function after exercise remains unchanged, (3) the flow-volume loops showed no differences between the pre- and post-E period, and (4) changes in MMEF were found to be correlated with the changes in the heart rate ($r = 0.71$), whereas SGaw correlated with the oxygen consumption ($r = 0.66$).

EFFECTS OF VARIOUS MORPHINE TREATMENT SCHEDULES ON ACETYLCHOLINE TURNOVER RATE IN RAT BRAIN PARTS: D. L. Cheney*, M. Trabucchi*, G. Racagni*, and E. Costa, Laboratory of Preclinical Pharmacology, NIMH St. Elizabeths Hospital, Washington, D. C. 20032

The turnover rate for acetylcholine (ACh) was determined in the striatum and occipital cortex of rats under the following experimental conditions: 1) acute morphine (20, 40, or 80 μmole/kg, i.p., 45 min); 2) naloxone (24 μmole/kg, i.p., 15 min); 3) naloxone and acute morphine; 4) chronic morphine (300 μmole morphine pellet implant, 3.5 days) 5) naloxone and chronic morphine. Rats were infused intravenously at a constant rate (0.2 ml/min) with phosphoryl(Me-^{14}C)choline (30 μci/kg/min). After 6 min of infusion the animals were killed by focussed microwave radiation and the specific radioactivities of ACh and choline (Ch) in the two brain parts were used to calculate the ACh turnover rate. None of the experimental conditions affected the steady-state concentrations of ACh or Ch. Acute morphine reduced the ACh turnover rate in the occipital cortex but not the striatum. Naloxone alone had no effect but reversed the effect of acute morphine in the occipital cortex. Chronic morphine decreased the ACh turnover rate in the striatum but not the cortex while naloxone immediately reversed this effect in the striatum. Modulation of the cholinergic system by dopaminergic neurons which are affected by morphine (Costa, Carenzi, Guidotti and Revuelta, In: Frontiers in Catecholamine Research) might explain the differences in ACh turnover rate that we found in the two brain areas after acute and chronic morphine.

BIPLANE VIDEOROENTGENOGRAPHIC ANALYSIS OF DYNAMIC REGIONAL LUNG STRAINS IN DOGS. P. A. Chevalier*, J. F. Greenleaf*, R. A. Robb*, and E. H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55901.

Spatial distribution of pulmonary parenchymal strains and changes in regional volumes in the intact thorax are determined from measurements of displacements of metallic (1-mm diameter) markers implanted percutaneously throughout the parenchyma of the right lung (JAP 34:544, 1973). Tracking of these markers is accomplished by means of biplane videoroentgenographic recordings which allow high temporal (60/sec) and spatial resolution (±1.5 mm) measurements of the "tagged" lungs during various respiratory maneuvers simultaneously with intrathoracic pressures, ventilation and ECG on the same videotape (Sturm, JAP, in press). The biplane images plus multichannel analog recordings are transferred from videotape to stop-action video disc, and the tracking of the geometric positions of the metallic markers is performed with the aid of an operator-interactive computer program. A video scan converter produces a computer-generated cursor which is superimposed on the stop-action display of the biplane thoracic image. This cursor is positioned to coincide with the metallic markers, one at a time, until geometric coordinates of all identifiable markers on both projections of the lungs for a single video frame are input into the computer. The true spatial coordinates of each marker corrected for pin-cushion and magnification distortions are then determined. The spatial and temporal distributions of regional parenchymal strains are obtained by determining the distance between markers on a frame-by-frame basis over the extent of the respiratory cycle. Data indicate non-uniformity in regional lung behavior. (Supported in part by NIH grants HE-3532, HL-4664, and RR-7; AF-44620 NASA-NGR-24-003-001, AHA CI-10)

INTERACTION OF OCTAPEPTIDE-CHOLECYSTOKININ, SECRETIN, AND GASTRIN ON CAT GALL-BLADDER IN VITRO. J. Roy Chowdhury*, John W. Fara and Jesse M. Berkowitz. Nassau County Medical Center, East Meadow, N.Y. and State University of New York at Stony Brook, N.Y.

The effects of the three major gastro-intestinal hormones on isometric tension development in strips of cat gall-bladder were studied. Dose response curves were determined for the octapeptide of cholecystokinin (OPCCK) (0.25 to 6.0 ng/ml), gastrin (G) (0.5 to 4 μg/ml) and secretin (S) (0.04 to 0.16 units/ml). G and OPCCK were stimulatory and their effects were not blocked by atropine. The observed maximal response to G averaged 65% that to OPCCK. S was weakly stimulatory in some preparations. Maximally effective doses (MED) of G and OPCCK tested together elicited a response equal to that produced by OPCCK alone. But when an MED of G was first tested for 5 minutes, subsequent addition of a MED of OPCCK failed to produce any further response, whereas the addition of acetylcholine produced a further increment of tension. Likewise, an MED of G did not produce any further effect when an MED of OPCCK was tested first. When G was added in a dose required for one half maximal response (D50) prior to the addition of OPCCK, the subsequent dose-response curve of OPCCK was shifted to the right, but neither the slope nor the calculated maximal response (CMR) were significantly changed. Thus G competitively inhibits OPCCK action on the cat gall-bladder. On the other hand 0.08 units/ml of S shifted the dose-response curves for both OPCCK and G to the left and increased the slopes significantly ($P<0.01$) with increase in the respective CMR's. The combined action of OPCCK (or G) and S are supra-additive. These experiments suggest that OPCCK and G act at a common receptor site, which is different from the S receptor site. Supported by U.S.P.H.S. Grant HL 15422.

FETAL METABOLIC RESPONSE TO SURGICAL STRESS. J.F.Clapp,III*, N. Patel* and R. M. Abrams, Depts. of Obstetrics & Gynecology, Universities of Vermont (Burlington), Dundee (Scotland), and Florida (Gainesville).

Polyvinyl catheters were placed in the descending aorta (via femoral artery) and common umbilical vein (by direct puncture at the umbilicus) of ten lamb fetuses (110-145 days gestation). Ewes had spinal anesthesia. The uterus and its contents were removed from the abdominal cavity for this 1 hr procedure. Fetal metabolic response to this surgical stress was evaluated two hours, two and four days postoperatively. The parameters measured were umbilical blood flow, fetal oxygen consumption, fetal excess lactate accumulation or production, fetal glucose uptake, and fetal amino acid uptake. Twenty-one experiments were completed. The data revealed no significant changes in umbilical blood flow (269 ±12 SEM ml/kg-min) and fetal oxygen consumption (10.4 ± 0.3 SEM ml/kg-min) related to the surgical stress. There was no excess lactate production by the fetuses; rather, there was evidence of lactate accumulation suggesting that lactate itself was utilized as energy substrate by the fetus in utero. A mobilization of glucose and an increased glucose uptake by the fetuses occurred in response to the stress of surgery. An initially negative fetal α-amino nitrogen uptake (-0.74 ± 0.9 SEM mg/kg-min) became strongly positive by two and four days postoperatively (1.99 ± 0.5 and 2.81 ± 1 mg/kg-min, respectively).

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SHIFTS IN CARBON MONOXIDE STORES DURING EXERCISE AT MAXIMAL O_2 UPTAKE B.J. Clark* and R.F. Coburn, Dept. of Physiology, U. of PA Phila. PA

Aerobic capacity during maximal exercise has been postulated to be limited by delivery of O_2 to skeletal muscle tissue, while other views present evidence that O_2 consumption is limited by another process, i.e. effects of ↓ pH on aerobic metabolism. With the first possibility intracellular P_{O_2} (ICP_{O_2}) must drop to a very low level; with the latter, ICP_{O_2} should be normal or greater. We have attempted to determine ICP_{O_2} changes during exercise, from measurements of binding of CO to myoglobin (Mgb). It has been shown in resting skeletal muscle and in cardiac muscle that COMgb % Sat. increases 2-3 fold with tissue hypoxia. This is thought to be due to competitive binding of CO and O_2 to Mgb. There is evidence that for practical purposes, all body CO stores are bound either to Hemoglobin or Mgb, so changes in muscle CO can be determined from measurements of blood CO. We studied normal, non-trained human subjects, 21-41 yrs old, Max$\dot{V}O_2$ 26.6-48.0 ml/kg/min. Subjects, exercised for 6 min on a bicycle ergometer while breathing 21% O_2, with the subjects at Max$\dot{V}O_2$, showed that an average of 6.7±SE 1.2% of CO in blood at the start of exercise shifted out of circulating blood. In identical exps with the subjects breathing 13-14% O_2, Max$\dot{V}O_2$ fell significantly in 5/6 subjs. In these, CO shifts out of blood increased in every exp averaging 11.3±SE 1.9% ($P<.05$). Experiments on anesthetized dogs indicated that arterial pH as low as 6.90 or 2-3 C^{o} increases in body temp did not cause significant shifts of CO. We conclude that the ICP_{O_2} in Max$\dot{V}O_2$ exercising red muscle has fallen. Considering the relative sizes of body Mgb and Hgb pools, the shifts seen at 13-14% O_2 are those expected with a mean $MgbP_{O_2}$ in exercising red muscle <1 mm Hg, and it is likely that ICP_{O_2} limited $\dot{V}O_2$. The smaller CO shifts seen breathing 21% O_2 may be due to a fall in ICP_{O_2} in only a portion of exercising red muscle or to decreases in ICP_{O_2}, less than that occurring with 13-14% O_2.

OVARIAN FUNCTION IN CYCLIC RHESUS MONKEYS AS VIEWED BY LAPAROSCOPY. J. R. Clark*, D. J. Dierschke and R. C. Wolf. Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin.

The technique of laparoscopy (LS) was evaluated as a possible means of studying the dynamic aspects of ovarian function throughout the menstrual cycle in 5 rhesus monkeys. Nine individual intermenstrual intervals were studied and daily blood samples were drawn for hormonal validation of the gross observations made by LS in 7 of these. LS was performed 3 to 10 times during each cycle at 1 to 8 day intervals. The serum concentrations of progesterone (P) and LH were determined by radioimmunoassay. The duration of each intermenstrual interval during which LS was performed was 24 to 32 days in 8 of the 9 cycles and was similar to those which occurred before and after LS in the same animal. Ovulation was confirmed by LS in 7 of these cycles, while 2 of them involved menstrual bleeding without follicular development or luteal function. In those cases where serum samples were available for assay, an LH surge was seen to precede ovulation and P secretion during the 12 to 15 days of the luteal phase was within the normal range. Developing follicles, which subsequently ovulated, were distinguishable by LS as early as day 2 of the menstrual cycle. These data indicate that, based on morphological and hormonal criteria, LS does not significantly influence follicular growth, ovulation and luteal function or cycle length. In consequence, utilization of this method for repeated observations of ovarian morphology during the menstrual cycle in rhesus monkeys appears to be justified.

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DIGESTA FLOW AND ORGANIC ACID CONCENTRATIONS IN THE GASTROINTESTINAL TRACT OF THE PIG. E. T. Clemens* and C. E. Stevens. New York State Vet. Col. Cornell Univ. Ithaca, N.Y.

Twelve mature swine were used to assess the movement of fluid and particulate digesta through their gastrointestinal tract and to determine the diurnal variations in organic acid levels for various segments of the tract. Animals were fed twice daily at 12 hr intervals. Fluid (PEG and ^{51}Cr-EDTA) and particulate markers 2mm O.D. and 2mm, 1cm and 2cm long were administered with the meal. Animals were sacrificed at given intervals following the administration of markers. The gastrointestinal tract was divided into 12 segments for measurements of markers, pH, volatile fatty acids (VFA) and lactic acid (LA) content. The data indicated a rapid evacuation of the fluid and the smaller particles from the stomach and their relatively rapid passage through the small intestine and cecum. There was, however, prolonged retention of both fluid and particulate markers in first the descending and then the ascending colon. Larger particles (2cm) were retained in the stomach throughout much of the 60-hour experimental period. LA concentrations were greatest in the stomach and small intestine. Highest concentrations, averaging 170 mmoles/l, were observed 8 hours post-feeding. The highest levels of VFA in gastric contents averaged 20 mmoles/l. Gastrointestinal pH values showed significant changes with time post-feeding only within the stomach, where they did not reflect the changes in LA concentrations. VFA constituted 92% of the organic acids present in the large intestine. The concentrations of VFA varied markedly with time (150-230 mmoles/l), but at all times constituted the major anions in the large intestinal contents. The study indicated that digesta can be retained for prolonged periods of time in the swine stomach and colon. The high concentrations of organic acids also showed that substantial degrees of microbial digestion of carbohydrates occurred at both sites.

PHYSIOLOGY OF THE NEUROMUSCULAR SYSTEM OF BUCCAL MUSCLE OF APLYSIA. J. Cohen*, K. Weiss* and I. Kupfermann, Dept. Physiol., N.Y.U. Medical School and Dept. Psychiatry, Columbia Univ. and N.Y. State Psychiatric Institute; and Pub. Health Research Inst. City of N.Y.

In order to study the motor organization of the biting reflex of Aplysia, we have recorded intracellularly from a variety of muscles of the buccal mass. Fibers exhibited stable resting potentials of 55-80 mV. Excitatory junction potentials (EJPs) occurred spontaneously if the buccal ganglion was attached and could also be evoked by stimulation of nerves or motor neurons in the buccal ganglion. All muscles studied were polyneuronally innervated, receiving three to six distinct EJPs. It was possible to distinguish characteristic EJPs within identified muscles on the basis of EJP size, time course, and rate and extent of facilitation. We have studied in detail, a large internal strap muscle that inserts along the side of the odontophore. The EJPs in this muscle were chemically mediated, perhaps by acetylcholine. They were increased in high (Ca^{++}) sea water and decreased in high (Mg^{++}) sea water. Bathing the muscle in acetylcholine caused it to contract; cholinergic blocking agents reduced both evoked contraction and EJP size. Action potentials were not observed during contraction of this muscle. Motor neurons producing two of the characteristic EJPs seen in the strap muscle have been identified in the buccal ganglion. Because, as in arthropods, the buccal muscles in Aplysia are organized into anatomically distinct units from which EJPs can be readily recorded, identification of motor neurons is greatly facilitated and it should be possible to characterize in detail the motor organization of the biting reflex in this species. Supported by NIH Training Grants, GMO 1668-10, MH 10315-09 and NIH Grant NS 10757.

DIMINISHED ADRENOCORTICAL RESPONSIVENESS TO ACTH AFTER HYPOPHYSECTOMY: ROLE OF ADRENAL 5α-REDUCTASE. H.D. Colby, J.L. Caffrey*, L.K. Malendowicz* and J.I. Kitay. West Virginia Univ., Morgantown, W.V. and Univ. of Virginia, Charlottesville, Va.

Previous studies have shown that adrenocortical secretion in response to acute ACTH stimulation diminishes with time after hypophysectomy and is restored by ACTH replacement. Studies were conducted to determine the mechanism(s) responsible for the effects of ACTH on adrenal "sensitivity". Rats hypophysectomized for one week secreted little corticosterone (B) (2.1 µg/kg/hr) acutely after ACTH. 5α-dihydrocorticosterone (DHB) was secreted in greater quantity (3.7*) (*$p < 0.05$) and 3β, 5α-tetrahydrocorticosterone (R) at the same rate (2.4). Adrenal mitochondrial cytochrome P-450 concentration (0.71 vs. 1.41 nmoles/mg prot) and cholesterol sidechain cleavage (SCC) activity (0.36 vs. 1.13 µg pregnenolone/10 mg adrenal/hr) were significantly reduced and 5α-reductase activity (38.5 vs. 1.2 µg B reduced/10 mg adrenal/hr) was elevated at that time. Treatment with ACTH for 2 days restored unit SCC activity (1.05) to control levels. B secretion, however, remained low (4.6). Reductase activity (25.4) was still high, causing DHB (10.1*) and R (6.1*) secretion to further increase. Cytochrome P-450 levels increased slightly (0.93). Only after 7 days of ACTH was B secretion (29.5) greater than DHB (15.2) and R (8.1) output. At this time reductase activity was substantially lower (8.4) and cytochrome P-450 levels (1.32) were restored to control values. The results establish the functional significance of adrenal 5α-reductase activity and cytochrome P-450 concentrations in determining adrenal "responsiveness" to ACTH. (Supported by NIH Grant AM03370 and NSF Grant GB41215)

METABOLISM OF EXOGENOUS ATP IN DOG BLOOD, PLASMA, LUNGS AND GRACILIS MUSCLE. A. Collingsworth*, B. Selleck*, and C.C. Chou. Dept. of Physiology, Mich. State Univ., East Lansing, Michigan

The breakdown products of ^{14}C-ATP added to dog whole blood and plasma in vitro were studied using gradient elution ion exchange chromatography. 50% of the ATP added to whole blood and plasma was degraded in about 1½ and 7 minutes respectively. In plasma AMP was the major product of ATP metabolism; whereas in whole blood the exogenous ATP breakdown products were rapidly (in 15 minutes) being resynthesized to intracellular ATP. In four experiments to study uptake and degradation of ATP during passage through the lungs, ^{14}C-ATP was injected into the thoracic vena cava and blood from the aortic arch collected in perchloric acid. 83±3% (mean±SE) of the injected ^{14}C was taken up by the lung. About 3% of the injected ATP survived passage through the lungs undegraded. In seven experiments performed on the in situ constant flow Ringers perfused gracilis muscle, both stable (100 µg/ml) and ^{14}C labeled ATP (500 ng/ml) were almost completely degraded with very little (<10%) uptake of the degradation products on a single pass through the muscle vasculature. AMP was by far the major breakdown product of exogenous ATP metabolism during passage through the vasculature of the gracilis muscle. These studies indicate 1) that only a very small fraction (<8%) of the ATP proposed to be released by skeletal muscle during active hyperemia would appear in venous plasma, and 2) recirculation of plasma ATP would not occur. (Supported by Michigan Heart Association)

CADMIUM ACETATE AND ENDOTOXIN INTERACTION: EFFECT ON HEPATIC PARENCHYMAL AND KUPFFER CELL FUNCTION AND MORPHOLOGY. J. A. Cook*, E. O. Hoffmann* and N. R. Di Luzio. Dept. Physiology, Tulane University School of Medicine and Dept. Pathology, L.S.U. Medical Center, New Orleans, Louisiana 70112

Previous studies have demonstrated that intravenous administration of cadmium acetate (2.25 µmoles/100 g) markedly enhances the susceptibility of rats to low doses of Salmonella enteritidis endotoxin. Three hours following combined cadmium and endotoxin administration abnormal hepatic parenchymal function tests were noted. In contrast, Kupffer cell phagocytic activity was not impaired. In an effort to correlate functional alteration with morphological changes, light microscopic studies of the liver were subsequently conducted in rats at 8 and 16 hr following injection of cadmium and endotoxin alone or in combination. Very mild hepatic lesions occurred after 8 and 16 hr in animals administered endotoxin alone and mild to moderate hepatic alterations were present in the group administered cadmium alone. The livers of rats receiving cadmium and endotoxin, however, were typified by focal areas of necrosis at 8 hr which progressed to massive hepatic necrosis by 16 hrs. Ultrastructural changes at 8 hrs were predominant in parenchymal cells in the livers of rats administered cadmium or cadmium in combination with endotoxin. Although the parenchymal cell alterations were generally similar in nature in both groups, the lesions were considerably more extensive in rats injected with cadmium and endotoxin. Mild vacuolization and desquammation of Kupffer cells were also more prevalent following combined cadmium and endotoxin administration. These hepatic morphological changes support our functional studies which suggest that early parenchymal cell alterations play a role in the pathogenesis of the shock state induced by cadmium and endotoxin interaction.

INTRAVASCULAR BUBBLES ASSOCIATED WITH I.V. INJECTIONS AND ALTITUDE

Julian P. Cooke, Robert M. Olson* and Ronald D. Holden*
Environmental Sciences Division, USAF School of Aerospace Medicine
Brooks Air Force Base, Texas 78235

This study was designed to determine if an intravenous injection of saline would predispose animals to the development of intravascular bubbles during altitude exposure. Ten ml of sterile physiologic saline, free of visible bubbles, were injected into the cephalic vein of anesthetized dogs and after 10 minutes, they were decompressed within one minute to 10,000 ft (523 torr) in air. Ascent was then made to either 20,000 ft (350 torr) or 40,000 ft (141 torr) within either 1, 10, 30, or 60 seconds for exposures lasting 2 minutes. The passage of intravascular bubbles was detected with a chronically-implanted ultrasonic sensor around the main pulmonary artery that was connected to an external flowmeter, together with a magnetic recorder and rapid response oscillograph. Also, a continuous intravenous infusion (20 drops/minute) was given to other animals to evaluate bubble production at 10,000 and 20,000 ft. At ground level pressure, bubbles were detected only in injected animals. At altitude, two to five times as many bubbles (as many as 25/minute) were detected in injected animals as in controls. Also, bubbles were more rapidly evolved after the more rapid ascents. Although the significance of such intravascular bubbles is not completely understood, this study has additionally shown that a delay of 60 minutes following an intravenous injection of 10 ml before ascent to 10,000 or 20,000 ft altitude will insure the absence of any appreciable number of intravascular bubbles.

DEPRESSION OF HEPATIC GLUCONEOGENESIS BY ACUTE LEAD POISONING IN RATS.

Robert P. Cornell, Division of Science, Northeast Missouri State University, Kirksville, Missouri, 63501.

The liver is known to be a primary site of toxicity following acute lead poisoning. Until recently lead was considered to have no significant effect on the liver's vital physiological role in regulating blood glucose levels. Therefore, the present study investigated the possibility that lead alters glucoregulation by inhibiting hepatic gluconeogenesis. Male rats of the Holtzman strain (300 ± 10g) were administered either lead acetate or sodium acetate iv and then fasted overnight. Hepatic gluconeogenesis was assessed both in vivo employing radiotracer as well as chemical conversion of pyruvate (0.3 mmole) or alanine (1.0 mmole) to blood glucose and in vitro using isolated hepatocytes. Hepatocytes were prepared by perfusing the isolated rat livers with an enzyme medium. Lead-treated rats demonstrated a 17.0 to 26.0 percent depression in ^{14}C-pyruvate and ^{14}C-alanine incorporation into blood glucose as well as the absence of a hyperglycemic response to pyruvate or alanine loads. Similarly, isolated hepatocyte gluconeogenesis from either 10mM pyruvate, lactate, or alanine was depressed from 40 to 60 percent for lead-treated rats compared to controls; the addition of lead acetate to normal hepatocytes in vitro, however, had no effect. In addition, isolated hepatocyte incorporation of ^{14}C-pyruvate and ^{14}C-alanine into both glucose and carbon dioxide was significantly decreased following lead treatment. Glucose synthesis from three precursors which do not require a mitochondrial step for conversion to glucose, i.e., fructose, glycerol, and oxaloacetate, was not markedly depressed in hepatocytes of lead-treated rats. These data on hepatic gluconeogenesis support a mitochondrial locus of lead action and suggest that defects in hepatic glucoregulation may play a role in the toxicity of acute lead poisoning.

MUSCLE METABOLISM DURING EXERCISE IN THE HEAT AND COLD. D.L. Costill, W. Fink and P. Van Handel. Human Performance Laboratory, Ball State Univ., Muncie, Indiana.

In an effort to assess the effects of environmental heat stress on muscle metabolism during exercise, six men performed work in the heat (D.B.= 41°C,R.H.= 15%) and cold (D.B.. 9°C,R.H.= 55%). Exercise consisted of three,15 min cycling bouts at 80-85% Vo_2max, with 10 min rest between each. Muscle biopsies obtained from the vastus lateralis before and after each work bout were analyzed for glycogen concentrations. Respiratory exchange, heart rates and rectal temperatures were monitored throughout the exercise. Venous blood samples drawn before and after exercise were assayed for lactic acid, glucose, hemoglobin and hematocrit. Oxygen consumption, heart rates and rectal temperatures were all significantly higher during exercise in the heat. Blood lactic acid averaged 41.1 and 23.3 mg/100 ml in the heat and cold, respectively. The depletion of glycogen was 72.9 mmoles/kg of muscle after cycling in the heat, but only 34.7 mmoles/kg following exercise in the cold. Calculations of the change in plasma volume demonstrate no significant difference between the thermal conditions. Results indicate that mechanical efficiency is reduced in the heat. The findings of an enhanced glycolysis during exercise in the heat is compatible with earlier studies which demonstrated a decreased availability of oxygen due to a reduction in muscle blood flow.

EFFECTS OF CHRONIC INFUSION OF SMALL DOSES OF ANGIOTENSIN II ON ALDOSTERONE SECRETION. Allen W. Cowley, Jr. and Robert E. McCaa. Dept. of Physiol. and Biophys., Univ. of Miss. Sch. of Med., Jackson, Miss. 39216

The role of angiotensin II (A-II) in the long-term control of aldosterone secretion was studied in 6 intact conscious dogs. Blood was analyzed for plasma aldosterone concentration (PAC) and plasma renin activity (PRA) by radioimmunoassay. Blood samples were collected for 2 days before infusion of A-II (5 ng/kg/min; in saline) at 0.28 ml/min. Blood was then collected at 10, 30, 60, 120, 360 min and then daily for 2 weeks during chronic A-II infusion. Arterial pressure (AP) was measured 24 hr/day throughout the experimental period. Control PAC averaged 3.9 ± 0.9 ng% (Mean ± SEM); 10 min, 21.4 ± 4.4; 30 min. 13.5 ± 4.5, 60 min, 17.2 ± 4.3. By 6 hrs PAC decreased to 9.0 ± 2.2 and by 24 hrs to 7.9 ± 1.8 ng%. During the next 2 weeks PAC averaged 5.5 ± 2.8 ng%. AP averaged 101 ± 4.3 mm Hg during the control period, increased to 112 ± 2 mm Hg during the first 12 hrs of A-II infusion, then gradually increased to an average steady-state level of 135 ± 8 mm Hg by the 7th day of A-II infusion. In the control samples plasma Na^+ averaged 141.4 ± 1.1 mEq/L and plasma K^+ averaged 4.0 ± 0.1 mEq/L. Plasma Na^+ remained unchanged throughout A-II infusion while plasma K^+ decreased to an average of 3.70 ± .05 mEq/L. PRA averaged 0.87 ± .02 $ngA_I/ml/hr$ in the control samples and decreased by more than 50% by 6 hrs after A-II infusion. By 24 hrs PRA could not be detected by radioimmunoassay. These data demonstrate that continuous A-II administration at a level capable of producing hypertension causes only a marginal change in PAC which was not significant in these experiments. Decreased plasma K^+ which occurred during the A-II infusion may have contributed to normalization of PAC. (Supported by USPHS Grants HL 14206, HL 11678, and HL 09921)

RELATIONSHIPS OF VELOCITY, STROKE RATE, AND STROKE DISTANCE DURING "FREESTYLE" SWIMMING. Albert B. Craig, Jr. and David R. Pendergast*, Departments of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, N.Y. and School of Medicine and Dentistry, SUNY at Buffalo, Buffalo, N. Y.

Experienced competitive freestyle swimmers made repetitive short (8-10 m) swims at different velocities. Instantaneous velocity and distance were recorded and the tracing was marked at each stroke. Maximal distance traveled per stroke was observed at an average stroke rate of 28/min and velocity of 1.1 m/sec. Maximal velocity was achieved by approximately doubling the stroke rate. At the slower speeds (.5-1.2 m/sec) the distance traveled per stroke was relatively constant for each swimmer, and velocity was increased by incrementing the stroke rate. Further gains in velocity were made by increasing stroke rate and by decreasing the stroke length. The fastest swimmers (1.9-2.01 m/sec) were characterized by having a long distance per stroke (3.0-3.2 m/stroke) at the slower velocities. Their peak velocity occurred at greater stroke rates and with a relatively greater shortening of the stroke than observed in the slower swimmers. Velocity measured by these techniques correlated well with the swimmer's best performance during a 50 yard race.

DIFFUSION CAPACITY, PULMONARY BLOOD FLOW AND LUNG VOLUMES IN A TERRESTRIAL AND AN AQUATIC TURTLE. Eugene C. Crawford Jr., Randall N. Gatz, Helgo Magnussen+ and Johannes Piiper+. School of Biological Sciences, University of Kentucky, Lexington, Ky. and Department of Physiology, Max-Planck-Institute of Experimental Medicine, 34 Göttingen, West Germany.

Resting lung volume, pulmonary blood flow and CO diffusion capacity of the lung were measured in two turtle species, Pseudemys scripta elegans (mean wt.1550g) and Testudo graeca (mean wt.840g). The mean lung volumes, determined by argon dilution, were 160 and 170 ml/kg respectively. Mean respiratory dead space of P. s. elegans (0.6 ml/kg) was smaller than that of T. graeca (2.8 ml/kg). $\dot{V}_{O_2}$ was 0.9 ml/kg·min and 1.5 ml/kg·min respectively. Pulmonary blood flows, determined by N_2O uptake, were 52 and 34 ml/kg·min and the O_2 content difference between pulmonary venous and pulmonary arterial blood was 2 and 5 vol.% respectively. $D_{L_{CO}}$ was about 0.07 ml/min·torr in both species. $D_{L_{O_2}}$ estimated from $D_{L_{CO}}$ (based on diffusion coefficient and solubility ratio O_2/CO) was 0.086 ml/min·torr. The estimated mean gas to blood O_2 pressure difference was 11 torr for P. s. elegans and 16 torr for T. graeca. Comparative values for the chicken and man are about 20 and 10 torr respectively. The $D_{L_{O_2}}$ per unit O_2 uptake for the turtles (0.066) was somewhat higher than that of birds (0.049), but one-half that of man (0.123). (Values for the bird and man calculated from Piiper et al. (1969) Respir. Physiol., 6: 309-317.)

THE EFFECT OF THE MENTAL STRESS OF EXAMINATION WRITING ON PLASMA ENZYME ACTIVITY. Jerry B. Critz. South Bend Center for Medical Education, South Bend, Indiana.

This study investigated the effect of mental stress on the plasma activities of glutamic-oxalacetic transaminase (PGOT) and creatine phosphokinase (PCPK). Ten male first year medical or dental students volunteered for the study. Venous blood samples were obtained one week before and immediately after writing the final examination in "Gross Anatomy and Human Development". There was a statistically significant increase in PGOT (12.5 ± 0.7 and 14.2 ± 0.7 IU/L; P=0.014), while PCPK was unchanged (39.6 ± 4.9 and 41.6 ± 4.9 IU/L; P=0.539) after writing the examination. The subjects might have been under considerable mental stress during the week prior to final examinations; however, data from an independent study on first year medical and dental students had yielded control data essentially identical to that observed in the current study (PGOT=12.9 ± 0.3; PCPK=41.9 ± 1.5 IU/L). The change in PGOT activity may be due to increased glucocorticoid (GCT) secretion which has been reported to occur under similar circumstances. GCTs induce intracellular enzyme synthesis and the resultant elevated tissue levels of GOT could account for the increased PGOT activity if the rate of release and rate of clearance of the enzyme were unchanged. Alternatively, in some species GCTs depress the reticuloendothelial system (RES). Since GOT is cleared from the plasma by the RES the increased PGOT could be due to decreased clearance of the enzyme from the blood. (Supported in part by the Medical Research Council of Canada and the Defence Research Board.)

COMPARATIVE SENSITIVITY OF PULMONARY FUNCTION TESTS IN THE EVALUATION OF EXERCISE-INDUCED ASTHMA (EIA) OR OTHER FORMS OF LARGE AIRWAY OBSTRUCTION (LAO). Gerd J.A. Cropp. National Asthma Center, Denver, Colorado.

Many asthmatics develop acute, reversible, primarily LAO after strenuous exercise. Since there continues to be disagreement which tests are best suited to detect the development and severity of EIA and other forms of LAO, we exercised 60 asthmatic children on a bicycle ergometer and measured exercise-induced changes in Specific Airway Conductance (SG), Functional Residual Capacity (FRC), Forced Vital Capacity (FVC), Peak Expiratory Flow Rates (PEFR), Maximum Mid-Expiratory Flow Rates (MMEF) and Forced Expired Volume in 1 sec (FEV_1). Post-exercise reductions in SG were predictably related to reductions in PEFR, MMEF, FVC and FEV_1 and to increases in FRC, however, small exercise-induced reductions in SG (20-60%) were related only to reductions in PEFR and MMEF. Increases in FRC and reductions in FVC and FEV_1 were usually observed only when SG fell to less than 60% of resting values. Although decreases in PEFR and MMEF were linearly related to decreases in SG, SG had to decrease by 20% before decreases in MMEF and PEFR were consistently observed. We conclude that EIA and acute LAO were detected earliest and most effectively by decreases in the SG and next best by decreases in MMEF and PEFR. Increases in FRC and decreases in FVC and FEV_1 were not useful for the detection of mild LAO or EIA. The FEV_1 test can, therefore, no longer be recommended as the test of choice for the diagnosis of mild LAO.

EVIDENCE THAT LEFT ATRIAL RECEPTORS ARE INVOLVED IN THE ADRENOCORTICAL RESPONSE TO SMALL HEMORRHAGE. George L. Cryer*; Mitchell Grayson* and Donald S. Gann, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

Previous experiments demonstrated that right atrial receptors participate in mediation of secretion of cortisol after small hemorrhage. Inflation of a small right atrial balloon simultaneous with a 5 ml/kg bleed resulted in a 75% decrease in the adrenocortical response to this level hemorrhage. The present experiments were undertaken to study the possibility that left atrial receptors may also be involved. 22 dogs were studied one day after adrenal vein cannulation and placement of a small inflatable balloon inside the left atrium. Timed adrenal venous blood samples were collected before and after hemorrhage with and without simultaneous balloon inflation and were analyzed for cortisol (RIA). 5 ml/kg hemorrhage without balloon inflation leads to increased secretion of cortisol (Δ=3.96 $\pm$ 0.87; P<0.001); whereas 5 ml/kg hemorrhage with simultaneous balloon inflation leads to an insignificant response (Δ=0.32 $\pm$ 0.63; P>0.3). The difference in the two responses was highly significant (P<0.005). The fall in mean arterial pressure was larger in animals with left atrial balloons than in intact animals, excluding mediation by arterial baroreceptors. The fall in right atrial pressure was significantly greater than that seen with a right atrial balloon despite greater inhibition of the response, excluding mediation by right atrial receptors. The results indicate that left atrial stretch can prevent the adrenal response to 5 ml/kg hemorrhage. Thus both right and left atria are implicated in the adrenocortical response to small hemorrhage.

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URINARY AND PLASMA LEVELS OF CYCLIC ADENOSINE 3'5' - MONOPHOSPHATE (AMP) IN MOLONEY SARCOMA VIRUS (MSV)-INDUCED TUMORS. John J. Cupo, Jr.,* John L. Humes,* and Helen R. Strausser. Rutgers University, Newark, New Jersey 07102

The urinary and plasma levels of cyclic AMP of male BALB/c mice injected im into the right hind leg with MSV at 20 days of age were measured by radioimmunoassay. Right leg tumors averaging 11.2 $\pm$ 0.6 mm in diameter developed at the peak of tumor size (day 13) while the diameters of the left legs remained unchanged at 4 mm. Urine samples from 23 uninjected mice averaged 10.3 $\pm$ 1.8 umoles/ml cyclic AMP on the same day that the urine of the virus injected mice averaged 1.6 $\pm$ 0.4 umoles/ml. Plasma values of the controls averaged 1.1 $\pm$ 0.01 pmoles/ml while those of the tumor treated animals at the peak of the tumor growth were 22.1 $\pm$ 1.8 pmoles/ml. Cyclic AMP levels of this type of tumor tissue had previously been shown to be high as compared with normal muscle tissue. The cyclic AMP is hypothesized to be a mediator for prostaglandin E_2 which has been shown to be high in these tumors (Humes, Cupo, and Strausser, Effects of Indomethacin on Moloney Sarcoma Virus Induced Tumors, Prostaglandins, in press). However, the cause of the decrease in urinary cyclic AMP remains unknown.

Supported by the Busch Memorial Fund (Rutgers University).

THE EFFECT OF SLOW INFUSION OF E. coli ON RENAL HEMODYNAMICS. J. E. Dale*, R. D. Bell, J. T. Price* and M. J. Keyl. Univ. of Oklahoma Health Sciences Center and V. A. Hospital, Oklahoma City, Okla.

The effects of a six hour infusion of living E. coli organisms (LD_{100}) were studied in anesthetized dogs. Special emphasis was placed on renal function and hemodynamics. Experimental animals were found to vary greatly in their ability to remove and/or detoxify living E. coli from circulating blood. The magnitude of adverse changes associated with septic shock vary inversely with this ability to clear organisms. In dogs exhibiting a steadily increasing concentration of organisms in blood, it was found that renal blood flow (RBF) initially increased then, after 3 hours, decreased about 50% of control values. Femoral arterial pressure (AP) steadily decreased throughout the experiment. Urine flow changes in proportion to RBF. The renal extraction of para-aminohippurate (E_{PAH}) appears to be relatively stable during the first two hours of E. coli infusion but then declines steadily; ultimately reaching a negative value in all dogs. In contrast, marked changes as noted above were not observed in those animals in which rapid uptake of organisms by liver and spleen prevented a marked septicemia.

RIGHT VENTRICULAR EFFECTS OF LEFT VENTRICULAR UNLOADING WITH AN ABDOMINAL LEFT VENTRICULAR ASSIST DEVICE (ALVAD) IN THE CALF. B.D.T. Daly,* C.H. Edmonds,* S.R. Igo,* D.A. Hughes,* J.J. Migliore,* J.C. Norman. Texas Heart Institute, Houston, Texas.

Experiments were designed to determine possible effects of left ventricular unloading on right ventricular hemodynamics with an abdominal left ventricular assist device (ALVAD). This implantable, pneumatically-driven blood pump is interposed between the left ventricular apex and infrarenal abdominal aorta. With actuation, all indices of left ventricular work are markedly decreased and systemic perfusion is maintained. Catheters were placed in the right and left ventricles for pressure monitoring and a flow probe was placed around the pulmonary artery for determination of stroke volume. In control states, left ventricular peak systolic pressures (LVPSP) were 127±6.1 mmHg and left ventricular end-diastolic pressures (LVEDP) were 8.7±1.8 mmHg. Right ventricular peak systolic pressures (RVPSP) were 36.7±2.1 mmHg, right ventricular end-diastolic pressures (RVEDP) were 7.2±.9 mmHg and stroke volumes were 66.5±3.5 ml. With ALVAD actuation, the entire cardiac output was assumed by the ALVAD. LVPSP decreased to 29.9±6.7 mmHg and LVEDP decreased to 3.3±2.1 mmHg. RVPSD decreased to 36.1±.9 mmHg, RVEDP decreased to 6.6±.6 mmHg and stroke volumes increased significantly to 77.8±3.7 ml. These results indicate that marked left ventricular unloading produced by ALVAD assistance results in increased right ventricular outputs at lower right ventricular end-diastolic pressures. These effects result from reduced right ventricular ejection impedance; improved right ventricular compliance or increased contractility are possible additional factors.

EFFECT OF INSPIRATORY DEPTH ON RELATIVE RIB-CAGE AND ABDOMINAL MOTION DURING VARIOUS BREATHING MANEUVERS. Joseph Danon*, Walter S. Druz* and John T. Sharp. Dept. of Medicine, Hines V.A.H., Chicago, Illinois.

The respiratory magnetometer was used in a way which allows independent measurement of changes with time of the rib-cage and abdomen-diaphragmatic volumes. The output of the magnetometer was calibrated to represent volume by the use of the isovolume maneuver as described by Konno and Mead. The output of the thoracic and abdominal pairs of electrodes were summed, and the sum was calibrated against a spirometer. Normal individuals were instructed to breathe, varying their tidal volumes over wide range. They were studied while breathing slowly and rapidly, this was repeated with resistive loads. These maneuvers were done both sitting and supine. In the supine position the effect of changing FRC by positive pressure breathing was studied as well. Even though the individuals varied from each other considerably, the preliminary observations indicated several characteristic features in all subjects: 1) For each breathing maneuver in both body positions the lung volume at the peak of each inspiration is linearly related to the maximal rib cage volume for the corresponding breath, and poorly related to the abdominal volume. 2) In slow unloaded breathing the rib-cage and the abdominal motion are in phase; with fast breathing or marked resistive loading the rib-cage leads. With marked resistive loading and fast breathing the abdominal motion is almost completely out of phase with rib-cage motion, the latter coinciding with the volume recorded by external spirometer. Under these conditions the abdomen seems to be passively carried by the rib-cage. Similar patterns were seen during resting breathing in patients with severe COPD. 3) The fact that the rib-cage leads during fast breathing, and the rate of change of rib-cage volume is almost always higher than that of the abdomen suggests that the rib-cage muscles are faster than the diaphragm. Supported by NHLI Grant #08789-07.

EFFECT OF HIGH $[K^+]$ ON PARA-AMINOHIPPURATE (PAH) TRANSPORT BY ISOLATED PERFUSED SNAKE PROXIMAL RENAL TUBULES. William H. Dantzler and Sherril K. Bentley*. Dept. Physiol., Col. of Med., Univ. of Ariz., Tucson, Ariz.

Previous work indicated that net PAH transport in distal part of isolated perfused snake proximal renal tubules occurs from bath to lumen against concentration gradient by active uptake into cells on peritubular side and passive diffusion into lumen. Removal of K^+ from bathing medium depressed net PAH transport from bath to lumen apparently by depressing active uptake into cells. In present studies, increasing $[K^+]$ in bath from 3 mM to 40 mM depressed net PAH transport from bath to lumen more than 50% within 10 min, but transport still occurred against a concentration gradient. Despite depression of net transepithelial PAH transport, cell water [PAH] during transport in 40 mM K^+ was about 2X that during transport in 3 mM K^+. No evidence for tissue binding of PAH was found during passive efflux from lumen to bath in 40 mM K^+. Apparent luminal membrane permeability calculated from perfusion studies was about 0.5×10^{-5} cm·sec^{-1} in 40 mM K^+ and about 3.5×10^{-5} cm·sec^{-1} in 3 mM K^+. Apparent peritubular membrane permeability determined from PAH efflux from tubules with oil-filled lumens was about 0.24×10^{-5} cm·sec^{-1} in 40 mM K^+ and about 0.5×10^{-5} cm·sec^{-1} in 3 mM K^+. Measured passive efflux of PAH from lumen to bath in 40 mM K^+ (8.8×10^{-15} moles·mm^{-1}·min^{-1}) during perfusion with 7×10^{-5} M PAH was nearly identical with that predicted from luminal and peritubular membrane permeabilities (8.7×10^{-15} moles·mm^{-1}·min^{-1}). When bath $[K^+]$ was reduced to 3 mM K^+ after 50 min perfusion in 40 mM K^+, net PAH transport returned to control level in 20 min. 10 mM K^+ had effects similar to, but less marked than, 40 mM K^+. Data suggest that increasing $[K^+]$ may depress net PAH transport primarily by reducing luminal and peritubular membrane permeabilities and that this effect is readily reversible. (Supported by NSF GB 38033).

MEASUREMENT OF CSF pH AND Pco_2. D. G. Davies. Dept. of Physiology. Texas Tech University School of Medicine, Lubbock, Texas 79409.

The pH values of CSF sampled by an "in vivo" technique were compared to the pH values of CSF sampled by the more conventional syringe technique. With the in vivo technique, cisternal CSF is drawn directly into the pH electrode (Radiometer-Astrup) by placing the polyethylene capillary of the electrode directly into the shaft of a Riley needle. With the syringe technique, CSF is drawn into a syringe through a stopcock, the dead space filled and the excess CSF flushed into a second syringe which is also connected to the stopcock. A bubble free 1 ml sample of CSF is then withdrawn and immediately capped. The pH is measured within 10 seconds in both methods and the value is recorded when two consecutive readings agree within .005 pH units. In 65 pairs of measurements in 9 anesthetized dogs, it was found that the syringe method always overestimated the CSF pH value as compared to the in vivo method, pH (syringe)= .9946 pH (in vivo) + 0.0835. The ΔpH (pH(syringe) - pH (in vivo) = .041, .042, .043, .044 and .045 U at pH (in vivo) = 7.8, 7.6, 7.4, 7.2 and 7.0. In addition, CSF Pco_2 was measured by 3 methods : 1) in vivo-Astrup(IA), 2) syringe-Astrup(SA) & 3) Pco_2 electrode (Radiometer-BMS-3). In all measurements, the Pco_2 value was higher when the (IA) technique was used, Pco_2(SA) = .8725 Pco_2(IA) + .6 (r = .99). ΔPco_2 (Pco_2(IA) - Pco_2(SA)) = 2.4, 4.9, 7.5 and 10.0 at Pco_2(IA) = 20, 40, 60 and 80 mm Hg. Pco_2 (BMS-3) = .5575 Pco_2(IA) + 7.93 (r = .94). ΔPco_2 (Pco_2(IA) - Pco_2(BMS-3)) = 0.9, 9.8, 18.6 and 27.5 at Pco_2(IA) = 20, 40, 60 and 80 mmHg. The larger deviation in Pco_2 between the IA method and both SA and BMS-3 methods at higher Pco_2 values is consistent with the loss of molecular Pco_2 from the sampling syringe by diffusion. This study suggests that the more conventional methods of measurement underestimate both the acidity and Pco_2 of CSF and that the error increases at higher Pco_2 values.
(Supported by the American Heart Association, Texas Affiliate)

LONGITUDINAL LENGTH AND TENSION CHANGES IN SMALL ARTERIES DURING VASOCONSTRICTION. Darrell L. Davis. Univ. of S. Fla., Tampa, Fla. 33620

Longitudinal tension and length changes have been recorded from hydraulically isolated, in situ, normally innervated segments of anterior tibial arteries of dogs during vasoconstrictor responses. Arterial segments of 1-2 cm in length were isolated between inflow and outflow catheters and perfused with autologous blood. Blood flow and inflow and outflow pressures were recorded to provide pressure-flow data to calculate segment resistance. Longitudinal tension changes were recorded with a Grass force-displacement transducer FT03C. Vasoconstrictor responses were obtained under constant-pressure and constant-inflow perfusion in response to sympathetic stimulation and levarterenol infusion. Longitudinal tension changes during vasoconstrictor responses were minimal when inflow and outflow catheters were tied to the surrounding tissue. When the outflow catheter ties and the connective tissue tethering the vessels were removed, decreases in longitudinal tension, indicative of increases in length, usually occurred. Decreases in longitudinal tensions during vasoconstrictor responses were smaller under constant pressure perfusion than under constant-inflow perfusion. Increases in outflow resistance increased vessel segment intraluminal pressure, and produced increases in length with decreases in longitudinal tension. Changes in length in non-tethered preparations appeared to be predominantly effected by changes in intraluminal pressures. Changes in length during vasoconstrictions were of the order of 25-75 microns, and thus produced negligible errors in calculations of vessel resistance or internal radius under either constant-pressure or constant-inflow perfusion. Supported in part by grants from the Florida Heart and Suncoast Heart Associations.

ELECTRICAL UNCOUPLING IN HEART FIBERS PRODUCED BY INTRACELLULAR INJECTION OF Na OR Ca. W.C. De Mello. Department of Pharmacology, Medical Sciences Campus, G.P.O. Box 5067, San Juan, Puerto Rico 00936.

The effect of Na or Ca ions on junctional conductance of mammalian heart fibers was investigated by injecting the ions electrophoretically into the cell. The electrical coupling was measured by injecting current pulses into the cell and recording the voltage change from an adjacent cell. Input resistance of the injected cell was measured with a single microelectrode connected to a balance bridge circuit. Ca injection produced gradual decline of cell communication and total uncoupling was observed in many experiments. Uncoupling was spontaneously reversed after interruption of Ca injection. The rate of recoupling was, in part, depended on the uptake of Ca by sarcoplasmic reticulum, and was depressed at low temperature. Intracellular Na injection also produced uncoupling which was probably due to the increase in Ca influx secondary to Na injection. Ouabain (5×10^{-6} g/ml) reduced the rate of recoupling after Na injection. The results suggest that failure of Na pump in a cell on group of cells could lead to partial or total uncoupling. (Supported by Grant No. HL-10897 from the National Heart and Lung Institute, Bethesda, Md.)

INNERVATION OF DOG CORONARY ARTERIES. M.J. Denn* and H.L. Stone, Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

The present studies were designed to investigate the possible neural elements in the control of the coronary vascular system by determining the autonomic innervation of major coronary arteries. The methods used consisted of a modification of the Falck and Owman technique for demonstrating in situ catecholamines and a modification of the Krnjevic and Silver technique for the demonstration of cholinesterase in nerve fibers present in the adventitial layer of coronary vessels. The experimental protocol included an examination of the neural innervation of the major coronary arteries in the dog. The arteries examined were the circumflex coronary (CC), left anterior descending (LAD) and right coronary artery (RCA). Adrenergic innervation of the major vessels was found to be relatively dense and consistent in density from one vessel to another. A gradient in the degree of cholinergic innervation was noted, with the CC being the most heavily innervated, while the LAD showed a consistent sparse innervation. The RCA received a more moderate cholinergic neural supply intermediate to that of the CC and LAD. Few small intermeshing neurons were present, the majority forming large, longitudinally running nerve bundles. Light microscopic examination of the hearts of dogs subjected to either cervical vagotomy or total extrinsic cardiac denervation was performed. These studies demonstrated the intrinsic nature of parasympathetic coronary innervation. Following both cervical vagotomy and total extrinsic denervation, no variations in density of cholinergic innervation were noted, indicating that these fibers are probably postganglionic parasympathetic fibers arising from intrinsic ganglia within the ventricles. At the present time it has not been determined whether these fibers traverse the coronaries to innervate the ventricles directly. (Supported, in part, by NIH grant NS 11255.)

REGULATION OF BREATHING UNDER ANESTHESIA. J.Ph. Derenne*, J. Couture*, S. Iscoe*, W.A. Whitelaw* and J. Milic-Emili. Dept. of Physiology McGill University, Montreal, Quebec, Canada.

It is well known that the ventilatory response to CO_2 is depressed during anesthesia. This is generally attributed to depression of the respiratory centres, but recent work has shown that under these conditions the mechanical properties of the respiratory system may be altered. To study it we subjected 5 normal volunteers to CO_2 rebreathing and intermittent occlusion of the airways at FRC under methoxyflurane anesthesia. Inspiratory time (T_i) and total breath duration (T_{tot}) of unloaded breaths remained essentially constant as tidal volume increased. T_i and T_{tot} of the occluded breaths were similar to the corresponding values of the unloaded breaths. Peak occlusion pressure increased linearly with CO_2 and the shape of the occlusion pressure wave remained essentially the same at all levels of CO_2 as shown by the fact that the pressure measured at any time after the onset of the occluded inspiration remained a constant fraction of peak pressure. Although the V_T vs P_{ACO_2} and $\dot{V}_E$ vs P_{ACO_2} relationships were very different from subject to subject, there was much less difference when comparing the occlusion pressure vs P_{ACO_2} relationship indicating that the differences in V_T and $\dot{V}_E$ response to CO_2 were due chiefly to differences in resistance and/or elastance of the respiratory system. We conclude that under methoxyflurane anesthesia peak occlusion pressure or occlusion pressure measured at any fixed time after onset of inspiration is a better index of the sensitivity of the respiratory centres than tidal volume or ventilation and that changes in respiratory system mechanics may be responsible for part of the decrease in ventilatory response to CO_2 under anesthesia.

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POTASSIUM, OXYGEN AND VASCULAR TONE. Reed Detar and Miklos Gellai*. Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire.

PO_2-contractility relationships for helical strips cut from rabbit cardiac and skeletal muscle arteries, 200-400μ o.d., were studied at 3 extracellular potassium concentrations ($[K]_o$): 1.18, 3.18 and 9.18 mM. Contractile responses (50-70% of maximum at 100 mm Hg PO_2) were produced using acetylcholine or histamine for artery strips from heart muscle, and epinephrine or norepinephrine or histamine for artery strips from adductor magnus (white) and soleus (red) muscles. At the intermediate concentration, 3.18 mM$[K]_o$, agonist-induced contractile responses were not changed when PO_2 was reduced from 100 to 60 mm Hg. Contractile responses were, however, depressed progressively as PO_2 was reduced stepwise from 60 to zero mm Hg. In the presence of ouabain, 10^{-5} M, or when lithium was substituted for sodium in the physiological salt solution, variations in PO_2 between 100 and zero mm Hg produced little or no change in contractile responsiveness. At either 1.18 or 9.18 mM $[K]_o$, agonist-induced contractile responses were also minimally affected by variations in PO_2 within this same range. It is concluded that changes in vascular tone associated with variations in PO_2 in the physiological range may be 1). independent of the role of oxygen in oxidative metabolism, and 2). dependent upon Na-K ATPase activity in the vascular smooth muscle cell membrane.

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ANATOMICAL, PHYSIOLOGICAL, AND HEMATOLOGICAL EFFECTS OF TRAINING AND COMPETITION ON FEMALE INTERCOLLEGIATE BASKETBALL PLAYERS. P.S. Diehl*, L.D. Morris*, and E.L. Fox: The O.S.U., Columbus, Ohio.

Nine volunteers from the 1973-74 O.S.U. women's basketball team were tested pre-training (I), pre-competition (II), and post-competition (III), on the following parameters: body composition (ht.,wt., skinfold measures); strength (dynamometer-grip; tensiometer--hip flexion, shoulder flexion, ankle plantar flexion); power (vertical jump); and submaximal and maximal work-effort response ($\dot{V}O_2$,HR,$\dot{V}_E$,$\dot{V}O_2/\dot{V}_E$,O_2 pulse). Monthly hematological determinations involving a CBC,SeFe, TIBC, serum cholesterol, and serum triglycerides were made throughout the study for several subjects. Practices were held 5 da/wk, 2 hrs/da throughout the study (10/23-3/7); in addition the training period (10/23-12/12) included a weight training program 3 da/wk. There were 12 regular season and 8 post-season tournament games. Significant changes in body composition ($P<.05$) reflecting a greater lean body mass to fat ratio were evidenced with no concommitant weight change. Hip flexion and shoulder flexion tensiometer tests indicated a significant ($P<.05$) increase in strength during the pre-season training, which was maintained during the season. Actual vertical jump distances and derived power scores were significantly ($P<.05$) greater in tests II and III than in test I, with no significant difference between tests II and III. A significant ($P<.05$) improvement in cardiorespiratory response to a submaximal work effort as reflected by HR,$\dot{V}O_2$ (ml/kg and l/min), $\dot{V}_E$, and $\dot{V}O_2/\dot{V}_E$, was evidenced between tests I and III. Maximal $\dot{V}O_2$ (l/min and ml/kg) did not significantly change during the study period. Although the number of hematological determinations obtained did not warrant statistical analysis, no adverse trends in the parameters assessed were revealed during training and competition. (Supp. in part by O.S.U. College of Education)

MECHANISTIC BASIS FOR THROMBIN-INDUCED VASODILATION IN THE DOG. J. DiSalvo, C. Schmidt-Huff,* G. Newman,* and G.Grupp. Depts. of Physiol. & Med., Coll. of Med. Univ. of Cinn, OH. 45229.

Recently we found that indomethacin, a compound that inhibits platelet release reactions, significantly reduced hindlimb vasodilation by thrombin (T) in the dog. We suggested that increases in femoral blood flow (FBF) produced with T were partly due to interactions between T and circulating platelets. To explore this hypothesis further we compared the effects of T and T-like enzymes extracted from snake venoms on FBF in dogs anesthetized with pentobarbital. T, reptilase (R, Bothrops atrox), and venacil (V, Agkistrodon rhodostoma) all convert fibrinogen to fibrin, but only T and R appear to cause release of platelet contents. Bovine T and R (1-8 NIH units,ia) produced dose-dependent increases in FBF that were rapid in onset, attained maximal levels in about 15 sec, and occurred without changes in arterial pressure. Responses to ADP (25 µg,ia) T, and R, were sigficantly reduced by apyrase (2 mg/Kg,ia) an ADP-ATPase, but responses to isoproterenol were unaltered. V did not influence FBF. These findings suggest that hindlimb vasodilation produced with either T or R in the intact dog may involve interactions with platelets resulting in release of vasoactive nucleotides. (Supported by grants from the Amer. Heart Assoc., S.W. Ohio Chapter, and Eli Lilly Co. Reptilase and Venacil were donated by Abbott Labs.)

EFFECTS OF HISTAMINE AND INCREASED VENOUS PRESSURE ON LYMPH FLOW AND PROTEIN CONCENTRATION. David E. Dobbins*, Jerry B. Scott, Francis J. Haddy, and George J. Grega. Department of Physiology, Michigan State University, East Lansing, Michigan 48824.

The effects of increased venous pressure (Pv) on lymph flow (LF) and lymph protein concentration (LPC) was studied singly and during the local infusion of histamine (4 μg base/min) (H) or acetylcholine (10 μg base/min) (A) in the forelimb of mongrel dogs anesthetized with pentobarbital. A constrictor band was tightened around the forelimb above the elbow to raise and maintain skin small vein pressure at 45 mm Hg for 90 min (N=7). This caused a sustained increase in LF, whereas LPC remained largely unchanged for 30 min but then decreased falling well below control by min 90. When Pv was increased similarily at min 30 for one hour during a 90 min local infusion of H (N=7) or A (N=7), LF was still further increased. However, with H but not A, LF then waned despite the continued infusion of H and the maintained increase in Pv. Also, Subsequent to the increased Pv, LPC slowly fell either returning to control (H) or falling well below control (A). It is interesting to note that increasing Pv during H initially markedly increased LPC (4.1 to 5.3 g % in 10 min), but that this did not occur when Pv was increased alone or during A infusion. Local infusion of H alone (N=7) for 90 min increased both LF and LPC markedly initially; however, with time both LF and LPC waned with LPC falling almost to control. Visable marked edema was detected only during the local infusion of H subsequent to the increase in Pv. These data suggest that regardless of the mechanism (vesicular transport, enlarged pores) the direct effects of low doses of H on protein efflux in the canine forelimb decrease as both LF and LPC wane with time, and that increasing Pv either singly or during the local infusion of H or A increases water efflux proportionately more than protein efflux, at least in the steady-state.

EFFECT OF RUMINAL OSMOTIC PRESSURE ON ABSORPTION OF A "NON-ABSORBABLE" MARKER, 51-CR-EDTA, FROM THE RUMEN OF THE COW. A. Dobson, A.F. Sellers and V. H. Gatewood*. N.Y.S. Veterinary Col, Cornell Univ., Ithaca,N.Y.

While using the 51-chromium complex of ethylenediaminetetra-acetate [51-Cr-EDTA] as a volume marker in the temporarily isolated ventral sac of the rumen, we found that a high osmotic pressure [O.P.] of the ruminal solution apparently favored its absorption. The following method proved sufficiently sensitive to investigate this possibility. The relation between the time course of the fall of 51-Cr-EDTA activity in the plasma and the amount of a single injection was established. This allowed the prediction of the decline in plasma activity following a period when 51-Cr-EDTA was added to the blood at a constant rate. The absorption rate from a solution in the rumen for a similar period could thereby be inferred from the plasma activity in a sample taken at a known time after the solution was removed. Similar results were observed when the O.P. of the 3 liters of ruminal solution was altered with either NaCl or mannitol. The clearance of 51-Cr-EDTA was low, <0.5 ml/min, and independent of the O.P., when the O.P. was 100-320 m-Osm/kg. When the O.P. was 320-420 m-Osm/kg, the clearance rose sharply with the O.P. reaching about 5 ml/min at 420 m-Osm/kg. Because the enhanced permeability was readily reversed by a return to iso-osmolality, and because our observations fall within the range of osmolality reported after feeding, we assume the increased permeability is a normal phenomenon.

(Supported by NIH Grant AM 04679)

FUNCTIONAL EVALUATION OF THE RAT HEART IN SITU. R.T. Dowell, P.C. Sodt and A.F. Cutilletta (Intro. by H. L. Stone), Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas and Department of Pediatrics, University of Chicago, Chicago, Ill.

In the past, rat heart muscle function evaluation has been limited to isolated in vitro preparations. We have developed methods for obtaining these measurements in the intact rat heart in situ. Female rats (220-250 gm) were anesthetized and positive pressure respiration initiated with room air through a tracheostomy. A cannula was placed in the jugular vein for administrating isoproterenol (0.15 ug) and propranolol (1 mg/kg). Mid-line thoracotomy was performed and an electromagnetic flow probe (6 mm circ.) positioned on the ascending aorta. Pacing electrodes were placed on the right atrium. Left ventricle pressure (LVP) was obtained by puncturing the LV with a 22 ga. needle attached directly to a Statham P37 transducer. This system has a resonant frequency of 140 Hz and flat amplitude to 70 Hz. LVP derivatives (dP/dt) were taken with an analog circuit having a linear response to 100 Hz. LVdP/dt-LVP loop plots were recorded on a storage oscilloscope. The slope of the linear isovolumic contraction portion of the loop was used to calculate an index of contractility. The preparation remained functionally stable and within physiological blood gas and pH limits for at least 30 minutes following surgical procedures. The contractility index was not influenced by increased heart rate, increased afterload or decreased preload. Appropriate changes were observed following isoproterenol and propranolol administration. These studies demonstrate that the in situ rat heart is a stable physiological experimental preparation. It should be useful for evaluating myocardial function since a contractility index derived from pressure-velocity relationships and measurements necessary for pump function analysis can be obtained simultaneously.
(Supported, in part, by the Moody Foundation of Galveston, Texas.)

CORONARY HEMODYNAMICS IN REPERFUSED CANINE MYOCARDIUM. H. F. Downey, P. E. Parker*, F. A. Bashour and A. G. Williams*. Cardiopulm. Inst., and Depts. of Physiology and Medicine, Univ. of Texas Health Sci. Center at Dallas, Tx.

The left anterior descending coronary artery (LAD) of anesthetized, open-chest dogs was occluded for 2 hrs. Blood flow in the left circumflex (LC) and LAD were measured with electromagnetic flowmeters before and for 4 hrs after release of occlusion. Resistances during reactive hyperemia were calculated from peak flows after 10 sec (R_{RH}) and 90 sec (R_M) arterial occlusions. Regional transmural distributions of myocardial blood flow were measured using radioactive microspheres (8-10μ) after 5 min, 2 hrs and 4 hrs of reperfusion. Coronary resistance in LAD increased 56% (5.9 to 8.9) after 4 hrs of reperfusion but was unchanged in LC. In LAD, R_{RH} increased 153% (1.7 to 4.4) and R_M increased 139% (1.0 to 2.4). Myocardial flow in reperfused tissue declined with time and by 2 hrs was non-uniformly distributed (Table). These studies demonstrate continued hemodynamic deterioration in canine myocardium reperfused after 2 hrs of ischemia. (Supported by American Heart Assoc. Texas Affiliate, Inc.)

	Myocardial Blood Flow Control (ml/min/g n=7)			Reperfused		
Time	Epi	Mid	Endo	Epi	Mid	Endo
5 min	.98	1.19	1.07	1.13	.92	1.17
2 hrs	.92	1.13	1.05	.59	.30	.34
4 hrs	.81	.89	.95	.54	.20	.23

TISSUE SPECIFIC VASOMOTOR EFFECTS OF POTASSIUM ION. Brian R. Duling, Dept. of Physiology, Univ. of Virginia, Charlottesville, Va. 22901

Potassium ion has been proposed as a possible mediator of hyperemia in striated muscle and brain. Small elevations of potassium concentration cause vasodilation in vivo, whereas high doses of potassium cause constriction. In many in vitro preparations dilations cannot be induced by potassium. The reasons for these differences are not clear. In the present experiments the vasoactive properties of potassium were assesed in the microcirculation of the hamster cremaster muscle and in muscular and epithelial portions of the cheek pouch. Tissues were transilluminated and suffused with a physiological salt solution whose potassium concentration was varied from 0 to 15 mM (K^+ changes were balanced with Na^+ changes). Diameters of the vessels were measured with a Vickers image-shearing eyepiece and expressed as percent (± 1 SEM) of the control diameter observed during exposure to 4.7 mM K^+. Vascular diameters of the cremaster arterioles were found to vary directly with the suffusion solution potassium concentration from 78 ± 3% in 0 mM K^+ to 155 ± 15% in 15 mM K^+. These responses were sustained for the full 5 min test period only in 15 mM K^+. Responses in muscular portions of the cheek pouch were very similar to the cremaster for both the high and the low potassium concentrations; in the non-muscular portions of the pouch only the constrictor phase was observed. These data indicate that potassium could participate in the initial functional hyperemia in striated muscle. Since the dilation induced by this agent is transient, sustained hyperemia must involve other mechanisms. Also, the findings highlight the potential variability in response to K^+ among various tissues. The differences may reflect smooth muscle individualities or interactions between other tissue elements such as nerves or parenchymal cells. Supported by PHS Grant #12792.

SECRETION OF INSULIN AND OF GLUCAGON IN NORMAL (obOb AND SWISS), OBESE-HYPERGLYCEMIC (obob), AND KK MICE. Joseph C. Dunbar* and Piero P. Foà. Sinai Hospital of Detroit, Detroit, Michigan 48235.

We measured serum insulin and glucagon and the secretion of these hormones by isolated islets of obob and KK mice and of their appropriate controls. When islets of normal mice were incubated or perifused in a recirculating system, they secreted less insulin than when the system was open, suggesting that when endogenous insulin was allowed to accumulate, it inhibited further insulin secretion. This autoinhibition was less marked in obob and KK mice which, perhaps for this reason, secreted more insulin. Similarly, high serum glucagon levels and increased glucagon secretion were noted in obob mice. In these mice, glucagon secretion seemed to have been adjusted at a higher level. No glucagon abnormalities were noted in KK mice. See table.

Mice	Serum	Incubation	Perifusion	
			Open	Recirculating
		Immunoreactive Insulin		
	uU/ml	mU per islet per 2 hours		
obOb	29± 6 (3)	.19±.07 (6)	.85± .11 (10)	.26±.04 (7)
obob	479±98 (4)	.78±.1 (12)[b]	2.04± .23 (15)[b]	.88±.12 (9)[b]
Swiss	35± 8 (11)	.26±.02 (19)	.83± .19 (5)[a]	.24±.06 (4)
KK	47± 9 (12)	.62±.14 (11)[b]	.96± .16 (7)	.58±.06 (4)
		Immunoreactive Glucagon		
	pg/ml	ng per islet per 2 hours		
obOb	66±18 (8)	1.61±.47 (13)	2.72± .56 (9)[a]	1.67±.28 (9)
obob	103±19 (26)	2.67±.52 (12)[b]	5.81± .90 (10)[ab]	3.14±.55 (15)[b]
Swiss	173±25 (8)	3.63±.80 (14)	5.40±1.20 (8)	3.30±.76 (8)
KK	137±20 (11)	3.68±.75 (16)	3.50± .78 (14)	3.60±.55 (13)

a=p <.025 or better vs recirculating; b=p <.05 or better vs control

EFFECT OF EXERCISE ON SPONTANEOUSLY HYPERTENSIVE RATS (SHR). A.P.Dunne*, M.W.Untermeyer*, W.M.Manger, M.Wolff*, H.Wolinsky*, I.von Estorff*, J.Birkner* and S.Dufton*. Dept. of Med. and Rehab. Med., N.Y.Univ.Med. Ctr., N.Y. 10016.

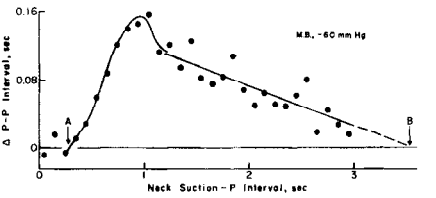
SHR (originally developed by Okamoto) were studied primarily to determine whether any alteration in blood pressure (BP) could be induced by exercise. 18 rats, 2 to 2½ months old, were divided into 3 groups of 3 females and 3 males each. Group I did not exercise; Group II exercised in a rotating wheel ad libitum, and Group III were forced to walk rapidly (.42 miles/hr. for 2 hrs.) 5 days each week. BP, heart rate (HR), weight and distance exercised were recorded weekly for 6 months and the rats were then sacrificed. Blood obtained at this time revealed no significant difference in cholesterol and triglyceride concentrations in the three groups. Pathological studies of various organs (heart, aorta, kidney, brain, liver, lung, stomach and gastrocnemius muscle) revealed minimal arteriolar narrowing in all groups; however, there was no remarkable difference between vascular lesions in the groups. Collagen, elastin and scleroprotein were determined in 2 female rats of each group and found to be greatest in the aortas of Group II. These changes in aorta composition suggest that ad libitum exercise in SHR may have a deleterious rather than beneficial effect. Group II had the greatest weight gain and a pronounced body length increase (perhaps related to increased food consumption and/or conceivably an increased growth hormone release). BP increased progressively in all 3 groups; but appeared slightly more elevated in Group II. HR tended to become slower in Group II than in Groups I and III. Females in Group II invariably ran farther than males. BP lowering was temporarily induced by dehydration or by prolonging the forced exercise. Such BP lowering probably resulted from a decreased blood volume related to dehydration.

INFLUENCE OF SYMPATHETIC NORADRENERGIC NERVES ON OXYGEN UPTAKE ($\dot{V}O_2$) AND CAPILLARY TRANSPORT CAPACITY (PS) IN SKELETAL MUSCLE. Walter N. Durán (intr. by Eugene M. Renkin). Dept. of Physiol. & Pharmacol., Duke Univ. Med. Ctr., Durham, N. C. 27710.

A previous report from this laboratory (Fed. Proc. 30: 211, 1971) indicated that sympathetic nerves may exert a direct stimulatory action on skeletal muscle cell metabolism. To explore this problem we measured simultaneously the changes in $\dot{V}O_2$ and PS for sodium-22 produced by stimulation of sympathetic nerves (L3-L4) in the isolated, blood-perfused dog gracilis muscle. $\dot{V}O_2$ was measured by the Fick principle. PS-Na was estimated from measurements of fractional extraction with the single-injection multiple indicator method. PS-Na decreased during 15 periods of sympathetic stimulation and remained unchanged during one. $\dot{V}O_2$ increased in 6 periods of stimulation, decreased in 7 and remained unchanged in 3. Assuming that capillary permeability (P) remains unaltered, the decrease in capillary transport capacity indicates a reduction in capillary surface area (S) available for exchange. The diffusion distance for O_2 must increase, since a decreased S signifies a reduced number of open capillaries and an increased distance between them. Therefore, the increased $\dot{V}O_2$ observed in 6 out of 16 trials is interpreted as due to a direct stimulatory effect of sympathetic noradrenergic nerves on muscle cell metabolism. In the other trials this effect may have been masked by the vasoconstrictor effect. (Supported by NIH Grant HL-12749.)

TIME CONSTANTS OF THE BARORECEPTOR REFLEX ARC IN NORMAL MAN. D.L. Eckberg*, M.S. Cavanaugh* and F.M. Abboud. Department of Medicine, VA and University Hospitals, University of Iowa, Iowa City, Iowa.

The latency between the onset of baroreceptor stimulation and the occurrence of cardiac slowing, and the duration of the chronotropic effects of baroreceptor activation have been measured in experimental animals but not in normal man. Carotid arterial baroreceptors were activated in six healthy volunteers, using multiple applications of neck suction, -30 or -60 mmHg, for 0.6 sec, timed to sweep the cardiac cycle. The delay of each P wave subsequent to stimulation was plotted as a function of the interval between the onset of neck suction and that particular P wave.



Baroreceptor reflex arc latency (intercept A) averaged 0.35±0.01(SE) sec, and the duration of the chronotropic effects of baroreceptor activation (intercept B) averaged 3.0±0.2 sec. Reflex arc latency was not influenced by the intensity of neck suction, control heart rate or β-adrenergic blockade with intravenous propranolol, 0.2 mg/kg. Atropine, 0.04 mg/kg abolished heart rate responses to neck suction.

These findings suggest that in normal man, cardioinhibition from baroreceptor activation has a short latency, and that the degree of pulse prolongation is critically dependent upon timing of the baroreceptor stimulus within the cardiac cycle. The intensity of sinus node suppression produced by discrete baroreceptor stimuli declines linearly, with a total duration lasting several cardiac cycles.

DIETARY AND EXERCISE INDUCED ALTERATIONS IN PLASMA METABOLIC SUBSTRATES IN YOUNG WOMEN. Duane O. Eddy, Susan M. Anderson, Peggy L. Mahoney, Thomas C. Perrin (intr. by David L. Costill). Ball State University Center For Medical Education, Muncie, Indiana.

It has been noted that starvation results in a decline in blood glucose levels, an elevation in free fatty acids(FFA) and a decline in the basal metabolic rate (BMR) in man. Our objective was to discern which of these physiological events would be reflected in young (17-23 years) obese women (n=20) subjected to a diet of 1000 k.cal./day and a mild exercise regimen for a period of eight weeks. Upon completion of the 8 week program the subjects were divided into two groups according to weight loss, in order to facilitate data analysis. Group A (n=10) experienced a weight loss in excess of 4kg (mean 6.7kg) whereas the Group B weight loss was less than 4kg (mean 1.9kg). During the first 3 weeks, Group A responded with a significant decline in blood glucose levels which returned to the prediet levels by the fifth week of the project. An elevation of equal magnitude of FFA was noted for A and B as prediet levels 0.65μ Eq/ml approached 1.60μ Eq/ml by the fifth week. Cholesterol and triglyceride levels were noted to decline for both groups with a significant reduction occurring in Group A only ($P<0.05$). Plasma glycerol paralleled the elevation of FFA initially with a subsequent decline achieving prediet levels for Group A by the fifth week. The BMR was significantly higher for Group A ($P<0.05$). Group B exhibited a BMR 7% lower than A with 4 subjects exhibiting a decline during the project. In conclusion, it appears that severe dieting produces an initial decline in blood glucose thus imposing an additional physiological stress of borderline hypoglycemia. Compensation occurs by the fifth week with glycerol being one of the potential glyconeogenic precursors. Some obese individuals have lower metabolic rates with a subgroup of that population exhibiting a decline in BMR as dieting is initiated.

ASYMMETRICAL EXCHANGE OF SODIUM IN THE PULMONARY VASCULATURE. Richard M. Effros, New Jersey Medical School, Newark, N.J. 07103

Isolated lungs obtained from 3 kg rabbits were ventilated, and perfused at 1.5 ml/sec with a solution of 10% bovine serum albumin (to prevent edema) in Ringer's lactate solution at pH 7.4 and 35°C. A vascular dye (T-1824 or indocyanine green) and a sodium label (^{22}Na or ^{24}Na) were incorporated in the perfusion solution. After 30 minutes of perfusion, the first solution was suddenly replaced with a second solution containing the alternative vascular and sodium indicators and the entire venous output of the lung was collected sequentially in 60 collection tubes at 3/4 second intervals. Sample indicator concentrations were divided by the corresponding concentration in the perfusion solution containing the indicator to obtain fractional concentrations. The fractional concentrations of indicators in the first solution were subtracted from 1.0 to yield "loading" values comparable to those of the second solution. In each of 5 studies, the loading fractional concentrations of sodium isotope of the first solution were less than those of the second solution by an average of 6.0 $\pm$ 3.2% (S.D.) during the initial interval in which solutions were changing. No consistent asymmetry was found in the vascular dye data. Calculated values of the tracer permeability of sodium from tissue to blood exceeded the permeability from blood to tissues by 8.4 $\pm$ 4.1%. These observations suggest that under steady state conditions, the accumulation of sodium in some cellular and/or interstitial compartment of the lungs is inhibited by asymmetrical sodium transport into the blood. It is likely that the endothelial cells play a role in this process. (Supported by NIH Grants HE12879 and HL15490.)

MOTOR UNIT ACTIVITY RESPONSIBLE FOR THE 9-12 HZ COMPONENT OF HUMAN PHYSIOLOGICAL TREMOR. Rodger J. Elble* and James E. Randall. Dept. Anatomy and Physiology. Indiana University, Bloomington.

Skin and bipolar electromyograms of the right extensor digitorum were obtained from six healthy subjects for the purpose of elucidating the motor unit (MU) activity responsible for the 9-12 Hz component of physiological tremor. Of the thirty-five MU spike trains analyzed, all had mean firing frequencies ranging from 13 to 21 spikes per second. To varying degrees in different subjects, these MU's exhibited a type of frequency modulation, the extent of which waxed and waned with time. The stress of mass added to the extended third digit resulted in a greater extent of modulation, with some MU's exhibiting transient doublet patterns of firing in which interspike intervals (ISI's) of 10 to 30 msec alternated with ISI's of 60 to 90 msec. Adjacent ISI's were correlated as highly as -0.9, and spectral analysis of these spike trains revealed peaks at 9-12 Hz as well as at the mean firing frequencies. Cross-correlation and cross-spectral analyses demonstrated that simultaneously recorded neighboring MU's were coherent ("synchronized") at 9-12 Hz but negligibly so at the mean firing frequencies. Moreover, cross-spectral and coherency analysis of simultaneously recorded MU spike trains and integrated surface EMG's established that the above MU activity was correlated with the "10 Hz bursts" in the surface EMG which in turn were correlated with the 9-12 Hz components of physiological hand and finger tremors. In contrast, there was neglibile coherent activity in the surface EMG and tremor at the mean MU firing frequencies. (Supported by training grant GM-02099 and research grant HL-11985.)

CEREBRAL HEMODYNAMIC EFFECTS OF PROSTAGLANDIN (PG) F_{2a} IN THE DOG. T.E. Emerson, Jr., D. Radawski*, M. Veenendaal*, and R.M. Daugherty, Jr., Depts. of Physiol. and Med., Mich. State Univ., East Lansing, Mich.

The current study was completed to test the hypotheses that PGF_{2a} is: 1) involved in local regulation of cerebral blood flow, and 2) responsible for cerebral vascular spasm and decreased cerebral blood flow frequently observed in traumatic head injury and/or subdural hemorrhage. The effects of PGF_{2a} on cerebral blood flow, cerebral vascular resistance, and cerebrospinal fluid and cerebral perfusion (aortic) pressures were determined in anesthetized dogs. Flow was measured from the cannulated sinus confluens after occluding the transverse canals. Perfusing the cerebral ventricular system with artificial cerebrospinal fluid containing concentrations of PGF_{2a} from 1-100 ug/ml did not affect cerebral blood flow but increased cerebral vascular resistance (7%), aortic blood pressure (12%), and cerebrospinal fluid pressure (24%) at the higher doses. Systemic, intra-aortic arch infusion of PGF_{2a} from 50 to 200 ug/min decreased cerebral blood flow (10%) and increased cerebral vascular resistance (14%) at the highest infusion rate, but did not effect arterial or cerebrospinal fluid pressures. Bilateral, intra-carotid artery infusion of PGF_{2a} at 20 to 80 ug/min produced effects similar in magnitude and direction to systemic, intra-aortic infusion. In summary, our study demonstrates that PGF_{2a} is capable of increasing cerebral vascular resistance and decreasing cerebral blood flow, depending upon the route of administration. However, this effect is small in magnitude, even at high plasma concentration of PGF_{2a}. Furthermore, increasing cerebrospinal fluid concentration of PGF_{2a} to high levels has no effect on cerebral blood flow, suggesting that this agent is probably not directly involved to a major extent in local regulation of cerebral blood flow, or in acute cerebral vascular spasm associated with traumatic head injury or subdural hemorrhage. (Research supported by grants from NIH and the Mich. Heart Assoc.)

BILIRUBIN CLEARANCE AND HEPATIC EXCRETION IN THE PONY. L.R. Engelking*, R. Gronwall, M.S. Anwer*. Dept. of Physiological Sciences, College of Veterinary Medicine, Kansas State Univ., Manhattan, Kansas.

Bilirubin clearance and hepatic excretion were studied in normal ponies with chronic external biliary fistulas. Bile was continuously collected from a flow-through T-tube cannula by gravity drainage. During the first hour of continuous drainage, bile flow decreased to a base level which was subsequently sustained (1.5 ml/min). At that minimal flow, endogenous bilirubin excretion varied directly with bile flow. A tracer dose of ^{14}C-bilirubin was injected into a jugular vein, and its rate of disappearance from plasma and rate of appearance in bile were followed for 24 hours. Plasma bilirubin clearance was calculated from the plasma disappearance of labeled bilirubin and also from the ratio of endogenous bilirubin excretion to plasma bilirubin concentration. The difference between those two calculations gave an index of the amount of bilirubin being stored in the liver during continuous drainage. Bile acids (taurocholic or chenodeoxycholic), infused at 8 µmole/min to increase bile flow, also increased bilirubin excretion. The additional bilirubin excreted was equivalent to the stored bilirubin, as calculated from the clearance discrepancy during minimal flow. During continuous bile acid infusion, bilirubin clearance (based on biliary excretion) increased and approximated the clearance calculated from the labeled bilirubin disappearance.

SUPPRESSION OF ADH BY WATER IMMERSION IN NORMAL MAN. Murray Epstein, David Pins.* and Myron Miller. Depts. of Med., Univ. of Miami Sch. Med., and VA Hospital, Miami, Fla., and SUNY Upstate Med. Ctr. and VA Hospital, Syracuse, New York.

Since previous studies from this laboratory have demonstrated that the redistribution of blood volume and concomitant relative central hypervolemia induced by water immersion to the neck (NI) cause a profound natriuresis and a suppression of the renin-aldosterone system, it was of interest to assess whether the diuresis induced by NI was mediated by an analogous inhibition of ADH. The effects of NI on renal water handling and urinary ADH excretion were assessed in ten normal male subjects, studied following 14 hours of overnight dehydration on 2 occasions, control (C) and NI during which conditions of seated posture and time of day were identical. During C, ADH persisted at or above pre-study values. NI resulted in a progressive ↓ in ADH excretion from 80.1±10.7 (SEM) to 37.3±6.3 μU/min ($p<0.025$). Cessation of NI was associated with a marked increase in ADH from 37.3±6.3 μU/min to 176.6±72.6μU/min during the Recovery hour ($p<0.05$). Concomitantly, with these changes, urine osmolality decreased significantly beginning as early as the initial hour of NI from 1044±36 to 542±66 mOsm/Kg H_2O during the final hour of NI ($p<0.001$). Recovery was associated with a significant mean ↑ in U_{Osm} of 190±40 mOsm/Kg water over the final hour of NI ($p<0.001$).

Since the suppression of ADH occurred without concomitant changes in plasma tonicity, the present observations provide evidence that the inhibitory action of blood volume expansion predominates over the stimulatory action of hypertonicity in regulating ADH release in normal man. Furthermore, these studies are consistent with the suggestion that in hydrated subjects undergoing NI, suppression of ADH release mediates the enhanced free water clearance which has been previously documented.

FETAL ACCUMULATION OF INERT TRACERS IN GUINEA PIG FETUSES WITH AND WITHOUT YOLK SAC PLACENTAS. J. Job Faber, Thomas J. Green* & Kent L. Thornburg. Dept. Physiology, Univ. of Oregon Medical School, Portland 97201 ORE.

Tracers of M.W.'s from 60 to ~ 3.10^6 were injected into the circulation of pregnant sows (urea, mannitol, polyethylene glycol, inulin, human plasma albumin and PVP). The experiments were terminated before the fetal concentrations approached the maternal concentrations, and placental permeability was calculated from the fetal accumulation and the maternal plasma concentrations. In one of the fetuses of each sow the yolk sac circulation was ligated a few days before the experiment. Its littermates served as controls. One operated fetus and three controls did not survive the experiment and were eliminated.

Placental permeability, expressed per gram placental weight, did not vary with fetal weight between 5 and 115 grams. It depended linearly on the coefficient of free diffusion of the tracer over the entire range of M.W.'s investigated (in contrast to findings on the rabbit) and the relation could be shown not to deviate significantly from a true proportionality. In the fetuses with ligated yolk sac circulations, mean placental permeability was somewhat higher than in the controls (n.s.).

It is concluded that the selected tracers diffused through the extracellular spaces of the chorio allantoic placenta of the guinea pig and that these spaces are wide even in comparison to the largest tracers used. The contribution of the yolk sac placenta appears negligible. We calculated from published values for γ globulin concentrations and half lives in adult and fetal guinea pigs, that if the permeability of the placenta for γ globulin may be interpolated on the present data, diffusion through the (chorio allantoic) placenta can approximately account for the entire fetal supply with this protein.

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REDISTRIBUTION OF LOCAL INTESTINAL BLOOD FLOW BY SECRETIN. J.W. Fara and K. Madden*. Dept. of Physiology and Biophysics, SUNY, Stony Brook, New York.

The blood flow distribution within the small intestine of anesthetized cats was investigated during resting conditions and when superior mesenteric blood flow was increased 20-100% by the intravenous infusion of secretin. Radioactive microspheres of 15μ diameter, suspended in 0.1-0.3 ml saline or dextran, were injected into the superior mesenteric artery. Shortly thereafter segments of jejunum and ileum were removed and dissected into mucosal, submucosal, and muscularis fractions. Tissue weight and the radioactivity of each (as a measure of fractional blood flow) was determined. Experiments were done on two groups of cats: 1. those which served as either a control or a secretin infused animal; and 2. those from which segments were removed during both control and hormone infusion periods. For fasted jejunum, blood flow to mucosa, submucosa, and muscularis averaged 24.2, 40.3, and 35.5 percent respectively, and in ileum 34.9, 43.5, and 21.6. During secretin infusion, percentage values for mucosa, submucosa, and muscularis averaged 14.7, 53.0, and 32.3, while ileal fractions averaged 13.2, 68.2, and 18.6 respectively. The results indicate that during a secretin-induced mesenteric vasodilatation there is a significant redistribution of blood away from the jejunal and ileal mucosa to the submucosa. (Supported by USPHS grant HL 15422).

The Hering-Breuer Inflation Reflex and Pattern of Breathing in Suckling Opossums. J.P. Farber and T.A. Marlow. (Intr. by C. Wunder). Department of Physiology, University of Iowa, Iowa City, Iowa 52242.

Relationships between the Hering-Breuer inflation reflex (H.B. reflex) and pattern of breathing during ventilatory chemostimulation with hypercapnic and asphyxiant gases were examined in unanesthetized suckling opossums (Didelphis virginiana). Ventilation was measured using pressure plethysmography, and the H.B. reflex was obtained by inflating the lungs to volumes above FRC using positive pressure. At each inflation volume, the H.B. reflex was measured as an inhibitory ratio (Widdicombe, J., Clin. Sci. 21:163-170, 1961). In rhythmically breathing animals up to ~40 days of age, a constant positive pressure could effectively maintain the lungs at constant volume for the duration of inflation apnea. Ventilatory responses to inspiration of hypercapnic or asphyxiant gas mixtures in these animals usually consisted of increases in tidal volume with little change in breathing frequency from room air controls. Inhibitory ratio per unit volume of lung inflation was reduced during hypercapnia and asphyxia as spontaneous tidal volume increased above room air controls. Inspiration of hypoxic gases often produced irregular breathing and/or depression of breathing rate, therefore responses during hypoxia were not obtained. In older animals (40-60 days of age) air could be pushed out of the lung by expiratory muscles during the Hering-Breuer reflex, and this behavior is similar to that shown by the adult. However, the increased breathing rate associated with ventilatory chemostimulation in the adult was still undeveloped in the 40-60 day old animals. These data suggest that during ventilatory chemostimulation in the suckling opossum the H.B. reflex may be related to neural activity which influences tidal volume.
(Supported by NIH Grant HL-15311 and Iowa Heart Grant 72-G-10)

ISOBARIC COUNTERCURRENT DIFFUSION -- MATHEMATICAL AND PHYSICAL MODELS. L. E. Farhi and J. L. Plewes*. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, NY 14214.

In order to assess the relative importance of the various factors involved in subcutaneous bubble formation during isobaric countercurrent diffusion (Lambertsen and Idicula, Fed. Proc. 33: 455, 1974), we have developed a series of equations based on the physical characteristics of the exchanging gases and of the diffusion layers. Before a bubble appears, the total gas pressure at any point of the diffusion pathway can vary on either side of ambient and a relatively simple relationship describes the pressure profile. Analysis of events after a bubble has developed is somewhat more complex because of the constraint that the total pressure in the bubble must be essentially equal to ambient. Whereas in the no-bubble situation, gases move independently of one another, this is not the case as soon as a gas space develops. To test the validity of our calculations and underlying assumptions, we have constructed a physical model in which the thickness of the various diffusing layers and the two gas species can be varied and in which either pressure at the interface or rate of growth of bubble can be measured. (Supported in part by ONR Contract #N00014-68-A-0216, NIH Grant HL 14414-02 and a fellowship from MRC, Canada.)

FUNCTIONAL LOCALIZATION OF INTRAPULMONARY CO_2 RECEPTORS IN THE DUCK. M.R. Fedde, R.N. Gatz, H. Slama+ and P. Scheid.+ Dept. of Physiol. Sci., Kansas State Univ., Manhattan, Kans. and Dept. of Physiol., Max-Planck-Institut für exper. Med. Göttingen, Germany.

Single unit vagal activity was recorded from 60 intrapulmonary CO_2 receptors in the right lung of anesthetized ducks. The right post-thoracic air sac was cannulated and the mesobronchus was blocked between the ventrobronchi (Vb) and dorsobronchi (Db) with a balloon catheter, permitting unidirectional ventilation of parabronchi (Pb) in either direction. Differences in discharge frequency upon reversal of flow direction permitted localization of 5% of the receptors to cranial, 95% to caudal parts of the lung. Receptors were more precisely located by adding CO_2 to the main gas stream, either proximal or distal to the blocking balloon, during gas flow in both directions. All receptors in the cranial part of the lung were located either in Vb or in ventrobronchial ends of Pb; none were in extrapulmonary airways. Most receptors in the caudal part of the lung were in Db or in dorsobronchial ends of paleopulmonic Pb; some were in neopulmonic Pb. Most CO_2 receptors thus encounter wide fluctuations in CO_2 concentration during the respiratory cycle suggesting that they monitor breath-by breath changes in intrapulmonary CO_2 concentration and thereby provide information on the quantity of CO_2 evolved from blood.

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SPINAL PROJECTIONS TO BRAINSTEM RETICULAR FORMATION. H.L. Fields, G.M. Wagner, S.D. Anderson, and S.A. Raymond (intr. by B. Libet). Univ. of Calif. San Francisco, San Francisco, California 94143

In cats anesthetized with sodium pentobarbital or decerebrated by mid-collicular electrolytic lesions, lumbosacral laminectomy was carried out. A transverse array of 2 or 3 concentric bipolar electrodes were stereotaxically implanted in the nucleus reticularis gigantocellularis (NGC) of the rostral medulla. Square wave 3mA, 0.2 msec stimuli were delivered through NGC electrodes at 1 Hz while the lumbosacral cord was explored with glass micropipettes (5-20 megohm). Thirty neurone projecting to NGC were identified by collision. Twenty responded antidromically to ipsilateral and ten to contralateral NGC stimulation. The average conduction velocity in this sample was 48.3 m/sec. Receptive field (RF) mapping of twenty two projecting cells revealed that RFs were large and relative to the cell under study were ipsilateral (14), contralateral (4) or bilateral (4). Most cells required intense stimuli to produce maximum firing rates and some could only be activated by high intensity mechanical stimuli. Cells were located by recording depth from cord surface and cutting the electrode tip off in situ. Although many cells in superficial layers of the dorsal horn were recorded from, none were found to project to NGC. In contrast, although fewer cells were encountered in the deep layers of the dorsal horn, pars intermedia and ventral horn these regions contained all cells projecting to NGC. In several cells a marked inhibition of spontaneous discharge lasting 100-200 msec, could be produced by single stimuli to either ipsilateral or contralateral NGC. This inhibition was produced by stimuli below threshold for antidromic invasion of the cell under study.

BLOOD ENDOTOXIN DETOXIFICATION AFTER TRAUMA AND ENDOTOXEMIA. James P. Filkins. Loyola University, Stritch School of Medicine, Dept. of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

The ability of the stressed-host to effectively prevent rampant endotoxemia and the resultant shock syndrome is generally considered a key event in survival incident to gram-negative bacteremia, hemorrhage, trauma and organ ischemia. While the hepatic mechanism of endotoxemia prevention - especially those aspects involving sinusoidal macrophage phagocytosis and inactivation - have often been emphasized, the ability of blood to directly inactivate endotoxin is less substantiated. The current study evaluated the ability of whole, heparinized rat blood to detoxify endotoxin after trauma (Noble-Collip tumbling stress) and endotoxemia (iv. Salm. enteritidis lipopolysaccharide). Detoxification was bioassayed using lethality in the lead-sensitized rat. Blood test samples were obtained by cardiac puncture of heparinized rats and then incubated at 37°C for 180 min with 5µg/ml endotoxin. Assay rats received 1 ml of the test blood sample plus 5 mg of lead acetate iv. Control rat blood was negative for detoxifying activity; however, 24 hr. post-trauma or post-endotoxemia blood manifested marked detoxifying activity. The time course of development of post-trauma detoxifying activity revealed little to no activity at 1-2 hrs. post-trauma, but marked detoxifying capability by 4 hrs. Characterization of the detoxifying system in 24 hr. post-endotoxin blood revealed that (1) formed elements were negative while plasma was positive, (2) plasma detoxification was inactivated by either heat or barium sulfate deproteinization, (3) detoxification activity was thermolabile (>65°C) and pH-labile (<3.0). These data are consistent with the notion that a detoxifying protein is elaborated incident to trauma or endotoxemia; it may play an important role in host-defense against shock pathogenesis. *(Supported by NIH Grant HL 08682 and HL 14540)*

INTERACTION OF HUMORAL AND VAGAL STIMULI ON AIRWAY SMOOTH MUSCLE (ASM) OF THE GUINEA PIG TRACHEA *IN VITRO*. P.J.P. Finch*, J.S. Douglas *, and A. Bouhuys. Yale University Lung Research Center and John B. Pierce Foundation, New Haven, Connecticut.

ASM is subject to several regulatory inputs *in vivo*. Study of some of these *in vitro* should provide more understanding of the local mechanism of interaction and their relationship to central regulation of ASM tone. We use an isolated, isovolumetric guinea-pig tracheal tube preparation with the vagi attached. Pressure increments at optimal volume are recorded with varied frequency of stimulation at maximal voltage of the efferent nerves. Spinal afferent and reflex functions are abolished by the surgical removal. We find a rapid, ill-sustained response (10-30 cm water) to high frequency stimulation (10-60 c/s). There is a graded response to low frequency stimulation (0.1-6.4 c/s) yielding a "cumulative frequency/response curve" analogous to a conventional log-dose/response relationship. Examination of this relationship in the presence of different agents in the organ bath shows: (i) Indomethacin (2-6 μg/ml) potentiates high frequencies, by preventing the elaboration and release of bronchodilator prostaglandin (PGE_2) which modulates local responses of ASM. (ii) Sub-threshold and barely active concentrations of agonists (e.g., histamine $5x10^{-7}$ - $5x10^{-6}$M, $PGF_{2\alpha}$ 10-100 ng/ml) or of antigen in actively immunized animals potentiate responses to low frequency (0.1-3.2 c/s) vagal stimulation. They probably alter intracellular calcium ion levels by effects upon membrane potential or upon cyclic nucleotide metabolism or on both. This complexity of the local response to stimuli must be borne in mind in interpreting effects of autonomic transmitters and their antagonists upon ASM responses *in vivo* and *in vitro*. Supported by USPHS grants (HL-14179: SCOR Program, and HL-14534).

REDOX CHANGES OF ISOLATED PERFUSED RAT LUNG WITH METABOLIC INHIBITORS. Aron B. Fisher and Linda Furia*. Depts. of Physiol. and Med., Univ. of Penna. School of Med. and Phila. VA Hospital, Philadelphia, Penna.

Isolated lungs from 200 g rats were perfused at 8 ml/min with Krebs Ringer bicarbonate solution, pH 7.4 and 37°, containing 5 mM glucose and ventilated with 95% O_2:5% CO_2 at 2 ml tidal volume, 80 breaths/min and 2 cm H_2O end-expiratory pressure. The perfusion was terminated by rapidly freezing the lung with clamps pre-cooled at the temperature of liquid N_2. Tissue concentrations of NAD^+, NADH, $NADP^+$, NADPH, lactate (L), pyruvate (P), ∝glycerophosphate (∝GP), dihydroxyacetone phosphate (DHAP), glutamate (glut), and ∝ketoglutarate (∝KG) were assayed by enzymatic methods. L/P and glut/∝KG reflect cytoplasmic and mitochondrial compartmented dehydrogenases, respectively, while ∝GP/DHAP may be displaced from equilibrium by flavin-linked oxidation of ∝GP. In 17 control experiments, ratios of redox couples were L/P 17±1.5 (SEM), ∝GP/DHAP 3.3±0.32 and glut/∝KG 29±23. Maximal change in redox couples was achieved by ventilating the lung with 95% CO: 5% CO_2; L/P increased to 48, ∝GP/DHAP to 14.7 and glut/∝KG to 135. Changes were less marked during perfusion with 2 mM amobarbital or 2 mM KCN and during ventilation with 95% N_2:5% CO_2 (alveolar P_{O_2} = 2 - 4 mm Hg). Control NADH/NAD^+ ratio was 0.01 and NADPH/$NADP^+$ ratio was 0.44. During amobarbital perfusion, the tissue concentration of NADH increased 101% and NADPH increased 63%. The data indicate that changes in lung redox state in response to metabolic inhibitors can be evaluated by measurement of redox couples. Lung redox couples remained partially oxidized when the alveolar P_{O_2} was lowered to 2 - 4 mm Hg. Supported by HL 15013, HL 15061 (SCOR) and the Veterans Administration Research Service.

SINGLE FIBER CHEMORECEPTOR RESPONSE TO HYPERCAPNIA-HYPOXIA
Robert S. Fitzgerald, The Johns Hopkins University, Baltimore MD 21205

Nielsen and Smith (Acta Physiol. Scand. 24:293-313, 1951) showed that hypercapnia and hypoxia interact multiplicatively when stimulating V_E. This raised the question: What is the source of the multiplication? Fitzgerald and Parks (Resp. Physiol. 12:218-229, 1971) showed a multiplicative interaction in whole carotid nerve recording (baroreceptor influence removed). The present study was undertaken to determine the characteristics of the unit at the end of a single chemoreceptive fiber. Six cats were anesthetized with chloralose-urethane; the right carotid nerve was dissected free and repeatedly split until a single or few-fiber recording of chemoreceptor activity could be made. The animals were exposed to increasing levels of CO_2 ($F_{ET}CO_2$=3-12%) at each of four different levels of O_2 (F_IO_2=100,20,15,12%). Counts per second were recorded at several different levels of CO_2 and O_2, and plotted as a percent of the response to the severest stimulus. The single fiber response is qualitatively identical to that of the whole nerve, exhibiting an increase in the slope of the response to increasing F_ICO_2 as F_IO_2 decreases and a plateauing of the slopes of the moderate and severe hypoxia curves at $F_{ET}CO_2$ 7-8%. If $F_{ET}CO_2$ increases from 8 to 12% at an F_IO_2 of 15%, there is little increase in the fiber's response; there may even be a decrease. If, however, at a $F_{ET}CO_2$ between 8 and 12% the F_IO_2 is decreased from 15 to 12%, the fiber increases its activity by about 30% of its maximum response. These results suggest: (1) that the chemoreceptive unit at the end of a single fiber is one source of the multiplicative effect; (2) that the unit has a dual mechanism for chemoreception; and (3) the results observed in the whole nerve cannot be attributed solely to the recruitment of new fibers at a lower F_IO_2. Supported by PHS Grant HL 10342.

PHASIC CORONARY BLOOD FLOW CHANGES WITH PARTIAL CORONARY ARTERY OBSTRUCTION.
John D. Folts, Kim P. Gallagher* and George G. Rowe. Cardiovascular Research Laboratory, Department of Medicine, University of Wisconsin, Madison, Wisconsin 53706.

Coronary blood flow (CBF), aortic and distal coronary artery blood pressure were measured in 15 open chest anesthetized dogs, with electromagnetic flowmeters and pressure gauges. The dogs were given increasing amounts of known fixed partial coronary artery obstruction, using concentric plastic cylinders, 2 mm in length and with varying internal diameters. At necropsy the amount of obstruction was checked by perfusing the obstructed coronary with fixative, under physiologic pressure and examining a stained frozen section. The reactive hyperemia (RH) to a 20 second complete occlusion was recorded with amounts of partial obstruction ranging from 0 to 95%. The RH response began to decrease from control levels with as little as 25% obstruction, and was abolished by an average of 72% of partial obstruction. CBF began to decrease from control levels with 75% partial obstruction, and was directly related to aortic blood pressure with greater than 75% obstruction. A mean pressure gradient across the obstruction of greater than 10 mm Hg. occurred with an average of 52% obstruction, and increased with increasing amounts of partial obstruction. The normal coronary phasic flow pattern, with high diastolic/systolic flow (D/S = 2.7) was decreased by increasing amounts of fixed partial obstruction, and the normal diastolic to systolic flow variations were abolished by an average of 78% obstruction. D/S = 1.0 Thus, at least in the dog, we have evidence that minor degrees of stenosis may be physiologically significant.

CHANGES IN AEROBIC POWER BY INTERVAL TRAINING: EFFECTS OF FREQUENCY AND DURATION. E. L. Fox, R. L. Bartels*, C. E. Billings, R. O'Brien*, R. Bason, D. K. Mathews. Exercise Physiology and Aviation Medical Research Laboratories, The Ohio State University, Columbus 43210.

This study was designed to ascertain whether 7 and 13 week interval training programs with training frequencies of 2 days per week would produce improvement in maximal aerobic power (maxVO2) comparable to that obtained from 7 and 13 week programs of the same intensity consisting of 4 training sessions per week. Sixty-nine, young, healthy, college males were used as subjects. After training, all groups improved significantly in maxVO2 (bicycle ergometer, open-circuit spirometry). This improvement was independent of both training frequency and duration, however, there was a trend for greater gains after 13 weeks. Maximal heart rate was significantly decreased in all groups following training, being independent of both training frequency and duration. Submaximal heart rate also decreased significantly in all groups after training with greater decreases the more frequent and longer the training. It was suggested that: 1) maximal stroke volume and/or maximal a - $\bar{v}$ O2 difference, principle determinants of maxVO2, are less dependent on training frequency and duration, being more dependent on training intensity; and 2) one benefit of more frequent and longer duration interval training is less circulatory stress during and more rapid recovery from submaximal exercise. (Supported by Medical Sciences Branch, Research Division, U. S. Army Medical Research and Development Command, Contract DA-49-193-md-2741).

TRAPPED AIR WITH OPEN AIRWAYS IN THE INTACT ISOLATED RAT LUNG. D. G. Frazer* and K. C. Weber. ALFORD, NIOSH, USPHS, DHEW, and Dept. Physiol. and Biophys., WVU Med. Ctr., Morgantown, W. Va.

Rat lungs were ventilated in a water filled plethysmograph with the level of the carina taken as the zero pressure reference. The plethysmograph was placed in a chamber whose internal pressure was equal to tracheal pressure, P_{ao}. Preceding studies showed that the normalized minimum volume of the lung, the amount of trapped air in the lung at -5 cm H_2O (V_m), divided by the maximum volume for that cycle (V_{max}) increased as the inflation-deflation rate decreased (Fed. Proc. 33:303, 1974), and air was trapped during inflation (Fed. Proc. 33:1494, 1974). In this study, lungs were inflated-deflated from the atelectatic state for 10 continuous cycles at 3.82 cc/min with P_{ao} equal to ambient pressure (P_{amb}) or P_{amb} +350 mm Hg. There was no significant difference between V_m/V_{max} after 10 cycles. In the case where P_{ao} was P_{amb} +350 mm Hg, the lungs were inflated for an 11th cycle and held at V_{max} for 10 minutes. P_{ao} was then allowed to assume P_{amb}, and the lung was held at V_{max} for an additional 10 minutes. When P_{ao} had been P_{amb} -350 mm Hg, V_m/V_{max} decreased from 0.68 to 0.60 between the 10th and 11th cycles, and the area enclosed by the 11th cycle compared to the 10th cycle increased by 150% indicating that the trapped air spaces increased in size. When P_{ao} was P_{amb} +350 mm Hg, V_m/V_{max} increased from 0.66 to 0.91, and the area enclosed by the curve was reduced by 75% indicating an increase in the trapped air space volume. Since P_{ao} changes were made at V_{max}, this study indicated that there was trapped air in the lung when all airways were open. The results of these three studies support the hypothesis that bubbles and/or foam are present within the air spaces of the intact isolated lung and implies that bubbles and/or foam contain much of the trapped air. Supported in part by grants, NASA NGR 49-001-048 and NIH 1F03 OH55262-01.

MAINTENANCE OF ARTERIAL PRESSURE DURING HEMORRHAGE: ROLE OF ANGIOTENSIN II. R.H. Freeman*, J.O. Davis, J.A. Johnson, and W.S. Spielman*. Univ. Missouri at Columbia, Columbia, Missouri 65201.

The role of the renin-angiotensin system in the maintenance of arterial pressure following hemorrhage was studied in conscious dogs. An additional aspect of the study was to investigate the influence of endogenous angiotensin II on the blood level of antidiuretic hormone (ADH). Hemorrhage (20 ml/kg body weight over a 5-20 minute period) decreased the mean arterial pressure from 130±4 mm Hg to 73±13 mm Hg ($P<.005$), but compensatory mechanisms partially restored the mean arterial pressure to 103±7 mm Hg during the 45 minutes following hemorrhage. During this same 45 minute period, plasma renin activity (PRA) increased from the pre-hemorrhage control of 8.8±1.0 ng angiotensin II/ml to 18.8±3.6 ng/ml ($P<.025$) and blood ADH concentration increased from 4.0±1.4 μU/ml to 8.1±2.0 μU/ml ($P<.05$). To evaluate the role of angiotensin II in this compensatory response, a specific competitive antagonist of angiotensin II,]-sar-8-ala-angiotensin II, was infused intravenously at 6.0 μg/kg min^{-1} for 30 minutes; the mean post-hemorrhage arterial pressure decreased from 102±7 mm Hg to 80±6 and 80±6 mm Hg after 15 and 30 minutes of analog infusion ($P<.01$ for both values). During the infusion period, PRA increased from 18.8±3.6 ng/ml to 32.9±6.9 ng/ml ($P<.01$) and ADH concentration in the blood remained unchanged at 7.9±0.6 μU/ml ($P>.25$). After a recovery period of 60 minutes, arterial pressure and PRA returned to pre-infusion levels. These results suggest that angiotensin II plays an important role in the short-term maintenance of arterial pressure following hemorrhage, but the data do not support a role of angiotensin II in the release of ADH during hemorrhage.

CONDITIONS INFLUENCING RELATIONSHIPS OF $P_{0.1}$ AND $\dot{V}_{0.1}$ WITH $\dot{V}_E$ AND RESPIRATORY DRIVE IN MAN. R.A.Gabel* and R.B.Weiskopf. U.S.Army Res.Inst. Environ.Med.,Natick,MA 01760; and Depart.Anes.,Peter Bent Brigham Hosp. and Harvard Med.Sch.,Boston,MA 02115.

Pressure at the totally obstructed airway 0.1 sec after the start of inspiration ($P_{0.1}$) has been proposed as a measure of neural output of the respiratory centers. We are proposing flow 0.1 sec after the start of inspiration ($\dot{V}_{0.1}$) as a convenient alternative to measuring ventilation ($\dot{V}_E$) during studies of ventilatory control. To help define conditions in which $P_{0.1}$ and $\dot{V}_{0.1}$ may not accurately represent respiratory drive and $\dot{V}_E$, respectively, we have measured these variables in two awake normal men during CO_2 rebreathing, with and without resistance and elastance loading (RL and EL). $P_{0.1}$ and $\dot{V}_{0.1}$ were found to be rectilinear with $\dot{V}_E$. $\Delta P_{0.1}/\Delta \dot{V}_E$ was greater with RL than without RL, suggesting increased respiratory drive or decreased functional residual capacity (FRC) during RL. $\Delta V_{0.1}/\Delta \dot{V}_E$ was less with RL than without RL, showing that $V_{0.1}$ is a good substitute for $\dot{V}_E$ only when inspiratory resistance is held constant. With EL causing decrease in FRC but no decrease in $\Delta \dot{V}_E/\Delta P_{ACO_2}$, $\Delta P_{0.1}/\Delta \dot{V}_E$ was less than without this EL, showing that conditions altering FRC change the relationship between $P_{0.1}$ and respiratory drive; $\Delta V_{0.1}/\Delta \dot{V}_E$, however, was the same with and without such EL.

S.A. NODAL ACTIVITY IN RABBIT ATRIA EXPOSED TO TWO IMIDAZOLE ANALOGUES. Clara Garcia-Minor* and Richard S. Tuttle. Masonic Medical Research Laboratory, Utica, N.Y.

The dissociation of chronotropic from inotropic effects of two imidazole analogues was verified in S.A. nodal cells of rabbits. A new inotropic agent 1-(phenylmethyl)-H-imidazole (1-BI) and a steroid analogue without inotropic effects 17-B (1-H-imidazole-5Yl) 5α androstane 3β-11β diol were compared. Microelectrodes, 10-20 megohms, were used to record S.A. nodal transmembrane potentials and basic cycle lengths (BCL). The steroid which was devoid of inotropic activity, produced changes in diastolic depolarization and membrane potential leading to a near doubling of BCL within 10 min. The potent, positive inotropic agent 1-BI produced changes in membrane and depolarative potentials leading to less than an 8% increase in BCL in 10 min. The results suggest that 1-BI is a near pure inotropic agent. The inotropic effects are probably related to improved calcium transport and not to catecholamine release nor to actions upon cyclic 3'5' AMP or the β receptors. The imidazole steroid is remarkable in respect to the pronounced increases in BCL without accompanying changes in inotropic activity. (Supported by Ministerio de Educacion y Ciencia, C.S.I.C., Madrid, Spain and Central N.Y. Heart Assoc. The steroid kindly supplied by J.P. Guthrie, Univ. West. Ontario, Canada.)

GROWTH, SOMATOMEDIN AND METABOLIC RESPONSES TO SOMATOTROPHIN AND THYROXINE. S.T. Gaspard*, R. Wondergem*, and H.M. Klitgaard. Department of Physiology, The Medical College of Wisconsin, Milwaukee, WI.

Somatotrophin treatment of hypophysectomized rats results in increased body weight, however, heart/body weight ratio remains unchanged. Thyroxine increases heart/body weight by affecting heart growth with little or no change in body weight. The combination of thyroxine and growth hormone results in a synergistic effect increasing body weight, heart weight and heart/body weight. In an effort to elucidate the selective actions of these hormones, body weight, heart/body weight and liver/body weight ratios were calculated. In addition the basal metabolic rate, heart and liver succinic dehydrogenase activities and serum somatomedin levels were determined. Daily subcutaneous injections of 20 μg/kg L-thyroxine and/or 25 μg bovine growth hormone were given for 21 days. The thyroxine and thyroxine plus growth hormone treated rats had significantly elevated heart/body weight ratios, heart succinic dehydrogenase and whole animal basal metabolic rates. Liver succinic dehydrogenase showed a similar increase, however, liver/body weight ratios in treated groups were not different from the untreated hypophysectomized rats. Serum somatomedin was stimulated by growth hormone and was further elevated in the thyroxine plus growth hormone treated rats while thyroxine alone appears to have little or no stimulation. These results suggest that stimulation of body growth is related to the somatomedin serum levels, however, the increase in heart weight in thyroxine treated animals may be more directly related to metabolic responses. Supported by Wisconsin Heart Association grant and NIH training grant #5 T01 HL05366.

CENTRAL ORIGIN OF 3 C/SEC PERIODICITY OF SYMPATHETIC NERVOUS DISCHARGE (SND). Gerard L. Gebber and David G. Taylor*. Department of Pharmacology, Michigan State University, East Lansing, Michigan 48824.

A study was made in the anesthetized cat of the synchronized burst of splanchnic or renal SND (recorded as a slow wave) locked in a 1:1 relation with the cardiac cycle (3 c/sec periodicity). The periodic components of SND, and the phase relations between SND and the cardiac cycle were analyzed with autocorrelation and computer summation techniques. Although baroreceptor denervation unlocked the phase relations between SND and the cardiac cycle, the slow wave persisted and the duration of its negative phase (~210 msec) was not changed. This observation contradicts the generally accepted view that the slow wave occurs as the direct result of a waxing and waning of baroreceptor nervous discharge occurring during each cardiac cycle. Rather, it appears that the 3 c/sec periodicity of SND is representative of a vasomotor rhythm of central origin which is entrained to the cardiac cycle by the baroreceptor reflexes. This contention is further supported by the observation that the slow wave was aborted by single shocks delivered to the baroreceptor nerves or paramedian reticular nucleus at appropriate points in the cardiac cycle. This was the case when the stimulus was delivered just before or at the beginning of the slow wave. However, the stimulus was ineffective when applied just after the beginning of the slow wave. These observations suggest that: (1) the slow wave of SND resulted from "avalanche excitation" transmitted through an interconnected population of brain stem neurons; and (2) the baroreceptor-induced sympathoinhibitory effect leading to the entrainment of the slow wave was exerted on interneuronal elements which trigger "avalanche excitation". (Supported by PHS Grant HL-13187).

FATE OF AEROSOLIZED L-α- DIPALMITOYL-LECITHIN IN THE RAT. K. Geiger*, M.L. Gallagher*, J. Hedley-Whyte, S. Warsof*, and E.W. Merrill*. Department of Anaesthesia, Harvard Medical School, Boston, Mass. 02215 and Department of Chemical Engineering, M.I.T., Cambridge, Mass. 02139.

28 Wistar-Lewis rats were anesthetized and their tracheas connected to a 3 MHz nebulizer (LKB), which generated an aerosol containing 250 μCi of L-α-1-palmitoyl-2-palmitoyl-(9-10-^{3}H)-phosphatidyl-choline (^{3}H-DPL) for 3 min each. The fate of ^{3}H-DPL was studied 1 min, 2 hr and 12 hr later. >94% of ^{3}H in lung was always in DPL. Appleton frozen section radioautographs (2μ thick)showed >4x background ^{3}H-DPL in 30% of alveoli. After 1 min 2500±500 (SE) type I cells/mm^3 and 2500±750 type II cells/mm^3 had taken up ^{3}H-DPL (>20 x background). In the first 2 hrs post aerosol grain density in alveoli fell from 3.1±1.0 to 1.1±0.1, while ^{3}H-DPL moved into type II cells and via blood stream into other organs. 2 hrs after exposure only 950±250 type I cells/mm^3 still had levels of >20 x background while 3150±600 type II cells/mm^3 now had this level of ^{3}H-DPL. The corresponding numbers of alveolar macrophages were 450±250 1 min post aerosol and 1100±200 after 2 hrs. Total ^{3}H-DPL in lung decreased from 1110±76 (SE) DPM/mg wet tissue after 1 min to 691±16 after 2 hr and 141±11 after 12 hrs. ^{3}H in liver, spleen, kidney, blood and urine increased with time: liver 5 DPM/mg wet tissue after 1 min to 8 at 2 hr, to 26 at 12 hr post aerosol; spleen 2 to 5 to 15; kidney 2 to 3 to 16; blood 2 to 4 to 13; urine 0 to 6 to 24, respectively. 12±3% of ^{3}H in liver after 2 hrs was in phosphatidyl-ethanolamine (PE), 22±3% in solvent front (SF) and 65±4% in DPL; after 12 hrs 25±3% was in PE, 16±3% in SF and 49±6% in DPL and 7±3% in sphingomyelin and lysolecithin. After 2 hrs 54±8% of ^{3}H in blood was in DPL and 44±8% was in SF. In conclusion (1) intraalveolar deposited DPL is absorbed into lung and transferred to other organs via blood, (2) no degradation of DPL occurs in the lung within 12 hrs, (3) demethylation of DPL occurs in the liver.

RELATIONSHIP BETWEEN PAH ACCUMULATION AND INTRACELLULAR CATION COMPOSITION IN RABBIT KIDNEY SLICES. G.A. Gerencser* and S.K. Hong, Department of Physiology, University of Hawaii School of Medicine, Honolulu, Hawaii 96822.

This investigation was undertaken to test the ionic gradient hypothesis as applied to active solute accumulation using PAH as a model organic acid. Slices were first placed in a 0°C isotonic preincubation medium, transferred to a 25°C isotonic incubation medium and, $[Na]_c$ and $[K]_c$ ("c" for intracellular fluid) were measured as well as S/M PAH. 1) After the slices were transferred from a 10mM $[Na]_m$ ("m" for medium) to one containing 100mM Na and PAH (70μM), both $[Na]_c$ and $[K]_c$ increased; however, only $[K]_c$ increased after transferring to a 10mM $[Na]_m$ containing PAH. 2) Transferring from 10mM $[Na]_m$ to one containing 100mM Na, PAH and 1.5mM ouabain, resulted in no net PAH accumulation, but a net increase in $[Na]_c$ occurred. 3) Transferring from 100mM $[Na]_m$ to one containing 10mM Na, PAH and ouabain resulted in no net PAH accumulation. 4) Transferring from a (10mM Na + 75mM K)$_m$ to ones containing 100 and 10mM Na, the $[K]_c$ in both media remained high, while the $[Na]_c$ only increased in the 100mM $[Na]_m$. PAH accumulation occurred only in slices in 100mM $[Na]_m$. 5) Transferring from a 100mM $[Na]_m$ to a similar one containing PAH, both $[Na]_c$ and $[K]_c$ reached steady state after 10 minutes, after which active PAH accumulation still continued. These results suggest that the Na Gradient Hypothesis is inoperative in the transport of organic acids in rabbit kidney. (Supported by a Grant-in Aid from the American Heart Association and supported in part by the Hawaii Heart Association).

KINETICS OF ATROPINE INHIBITION OF URECHOLINE-STIMULATED ACID AND PEPSIN SECRETION IN DOGS WITH AND WITHOUT VAGOTOMY. R. Gibson*, L. F. Wright* and B. I. Hirschowitz, University of Alabama in Birmingham, Alabama.

Five gastric fistula dogs with intact vagi and three dogs partially recovered (55% with 2-DG), two years after fundic denervation, highly selective vagotomy (HSV), were stimulated with intravenous step-doses of urecholine (20, 40, 80, 120 and 160 µg/kg-hr). Atropine was given as background by intravenous infusion in three different doses (0.2, 0.5 and 2.0 µg/kg-hr). H^+ outputs for each study (225 min) are given below, with the urecholine K_m estimated graphically from normalized curves.

Atropine Dose (µg/kg-hr)	Total H^+ Output (meq)		Urecholine K_m (µg/kg-hr)	
	Intact	HSV	Intact	HSV
0	50.42	63.18 (post-op) 63.48 (pre-op)	65	47
0.2	44.59	55.65	85	70
0.5	27.02	40.60	-	90
2.0	2.57	32.66	-	160
10.0	0	Not done	Not done	

We concluded that the post-vagotomy animals were much less sensitive to atropine than animals with intact vagi. Furthermore, doses greater than 0.5 µg/kg-hr in intact animals appeared to inhibit gastric secretion in a non-competitive manner, while these doses acted competitively in the vagotomized animals.

THE EFFECT OF GLUCOSE, PARA-AMINOHIPPURATE AND HEXANOATE ON RENAL TUBULAR TRANSPORT OF PHOSPHATE IN THE DOG. Jack M. Ginsburg, Medical College of Georgia, Augusta, Ga. 30902.

Renal tubular transport of phosphate (P) has been measured by standard clearance methods in intact and in acutely thyroparathyroidectomized (TPTX) dogs, anesthetized with pentobarbital. Tubular transport maxima for P (TMP) was measured during control clearance periods in which P was infused and again in succeeding periods during which a renal substrate was added to the infusion and finally in the terminal periods of most experiments during which sodium hexanoate was added to the infusion. In intact and in TPTX dogs glucose usually, but not always, inhibited TMP and hexanoate partially or completely reversed the inhibition of TMP. Inhibition of TMP during glucose infusion is not a consequence of the rise in plasma lactate which accompanies glucose infusion. Elevation of plasma lactate to 8 to 12 mM/L by infusion of L(+)lactate did not inhibit TMP. In intact animals a direct relationship between TMP and the sodium to inulin clearance ratio was observed in control periods. In a number of experiments recovery of TMP (following depression by glucose) occurred during hexanoate infusion despite continuing increases in sodium clearance. This observation demonstrates that a significant component of P transport can be dissociated from sodium transport. The inhibition of TMP induced by infusion of para-aminohippurate (PAH) was also reversed by hexanoate. Renal tubular transport of PAH was depressed by hexanoate while transport of N-methylnicotinamide was not. The results of these studies suggest that TMP is, at least in part, independent of sodium transport and may depend on the relative availability of glucose and fatty acid in the plasma or on their interaction in renal metabolism. These studies were supported by NIH grant #AM13415.

EXPIRATORY THRESHOLD LOADING IN STEADY STATE EXERCISE. I. Goldstein*, S. Wotiz*, J. Urbanetti* and N.R. Anthonisen. Respiratory Division, Meakins-Christie Labs., Royal Victoria Hospital and McGill University, Montreal, Canada.

In six young trained adults we examined the effects of expiratory threshold loads (ETL) of 5-40 cm H_2O during steady state exercise at moderate (41-58% $\dot{V}O_2$ max), heavy (74-83% $\dot{V}O_2$ max) and maximum (> 92% $\dot{V}O_2$ max) loads. ETL had no systematic effect on pulse rate, $\dot{V}O_2$ or $\dot{V}CO_2$. Only two subjects were unable to perform at maximum loads with ETL of 30-40 cm H_2O. At moderate work load ventilation and P_{ACO_2} were unaffected by ETL, while at maximum loads P_{ACO_2} regularly increased and ventilation decreased with increasing ETL. Heavy work gave intermediate results. With a single exception ETL induced decreases in ventilation were due to decreases in respiratory frequency with little change in tidal volume. Decreases in breathing frequency were associated with a prolongation of the duration of inspiration; the duration of expiration changed in inconsistent fashion. At moderate work loads inspiratory capacity (IC) decreased with increasing ETL, indicating that functional residual capacity (FRC) increased. At maximum work IC (and FRC) were unchanged by ETL, while at heavy loads FRC increased slightly. Changes in FRC appeared dependent on maintenance of a fixed tidal volume and a maximum end inspiratory volume. At moderate work, end inspiratory volume was 58% IC and increased with ETL to 85-90% IC. At maximum work end inspiratory volume was 82% IC without ETL and did not increase. We also measured mouth pressure 0.1 sec after airway occlusion at FRC ($P_{0.1}$) as an indicator of inspiratory drive. $P_{0.1}$ increased with work load and was further increased by an ETL of 30 cm H_2O.

Effect of submersion in water on expiratory reserve volume (ERV) in man. Sylviane Gontier* and Jean R. Gontier, Université de Montréal, Montréal, P.Q. Canada.

Submersion of the body up to the neck (standing in water) is similar to continuous negative-pressure breathing (NPB). When a subject is head-out immersed, in vertical position, the mean hydrostatic pressure on the thorax is equivalent to 20 cm H_2O. The pressurization of the thorax by water is equivalent to a continuous negative intra-pulmonic pressure of about 20 cm H_2O.

Twenty eight males were used as subjects. ERV was determined for subjects both while immersed upright to the level of the neck in water at neutral temperature (35.5°C) and while seated in air. Submersion experiments were carried out while the subject was seated in water for ten minutes (steady state submersion). The mean of five measurements is reported in air and in water. During submersion the average expiratory reserve volume is reduced from 1684 ml to 670 ml, i.e. from 30% to 7.5% of the vital capacity in air.

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CONTRACTION OF SMOOTH MUSCLE: COMPARISON OF GLYCEROL TREATMENT AND EXPOSURE TO BRIJ-58. A.R. Gordon (intr. by C.W. Urschel). Univ. S. Alabama Coll. Medicine, Mobile, Alabama.

Exposing muscle to 50% glycerol at -20°C for several months renders the muscle permeable to ATP and other ions. This procedure has been used to study tension regulation in smooth muscle but has raised questions concerning the roles of these ions as regards the contractile proteins. To circumvent this long-term and possibly deleterious process, freshly excised segments of rabbit taenia coli were exposed to a 1% solution of a nonionic detergent, Brij-58, containing 5mM EGTA at pH 7 and I=0.1-0.5 M, for 4 hours. The contractile responses of these muscles to Mg++, ATP and Ca++ were very similar to muscle which had been 'glycerinated' for 3-5 months. In the absence of Ca++, the contractile reponse of the smooth muscle to Mg++ and ATP was qualitatively similar to skeletal muscle; as free MgATP concentration was increased, the steady state tension increased then decreased (peak at 1 mM MgATP). The relaxation at high MgATP was more complete at the lower ionic strengths for the Brij treated muscles. Responsiveness to Ca++ (pCa=5) was usually small, occurred at high concentrations of free MgATP, and was easily lost. This labile contractile response to Ca++ may be related to the troponin denaturation found in isolated smooth muscle actomyosin preparations and does not seem to be related to the long-term glycerination procedure. Instead, any alterations in the sensitivity to calcium seem to occur during the first 4 hours of the extraction procedure.

MITRAL VALVE LEAFLET MOTION IN INTACT ANESTHETIZED DOGS.
Douglas A. Gordon,* Yves Mathieu,* Irving Lipton* and Anastasios G. Tsakiris. University of Sherbrooke Medical School, Sherbrooke, Quebec, Canada.

The motion of the mitral valve leaflets during different heart rates was studied in 5 normal anesthetized dogs in which small radiopaque markers were sutured in the atrial surface of both valve cusps and in the endocardial surface of the mitral annulus during cardiopulmonary bypass, one to eleven weeks prior to the studies. The animals were placed in a cineangiographic system and frame-by-frame measurements (100-120 frames/sec) were used to study the changes in position of the mitral cusps during the cardiac cycle under normal sinus rhythm ranging from 42 to 184 beats/min. In addition angiograms were recorded after injections of 6-8ml of radiopaque material either in the left atrium or the left ventricle. It was observed that during heart rates ranging between 78 and 129 beats/min. both mitral valve leaflets opened wide at the beginning of diastole, then closed partially and immediately reopened following atrial systole, whereas when diastole was short (heart rates 130-184 beats/min.) partial closure was not present. In contrast during slower heart rates (42-67 beats/min.) the initial valve opening was followed by partial closure and the leaflets remained practically motionless in this position throughout diastole. Partial valve closure coincided with the appearance of radiopaque material (after left atrial injections) behind the leaflets. These findings support the concept that partial mitral valve closure during diastole is depended on vortex formation behind the mitral leaflets.

IMBIBITION, EXCLUSION AND TRANSPORT PHENOMENA IN THE EXTRACELLULAR MATRIX. H. J. Granger, Univ. Miss. Sch. Med., Jackson, Miss.

Imbibition forces in polyelectrolyte gels include (1) Von't Hoff and (2) Donnan osmotic pressures, (3) electrostatic repulsion between adjacent reticulum subunits, and (4) elastic recoil of the gel matrix. In human umbilical cord (UC) and canine subcutaneous tissue (SC), elastic recoil appears to be the major component of the absorptive force at physiological ionic strength and pH. Thus, under these conditions, the imbibition pressures at normal hydration of -12 (UC) and -5 (SC) mmHg probably reflect a tensile force field generated by the outward recoil of the gel reticulum, thereby producing a negative intragel fluid pressure. A 50-75% increase in hydration reduces the imbibition pressures to 0; a 50% reduction results in an increase in pressure to -60 mmHg (UC). At low ionic strengths, the Donnan and electrostatic repulsion forces become more important. Exclusion of solutes from the matrix is a function of solute size and network hydration. In Tyrode's solution, albumin is excluded from 22 (SC) to 50% (UC) of the available gel volume at normal hydration. The degree of exclusion is an inverse function of matrix hydration. At low ionic strength, albumin exclusion is greater for a given hydration when compared to the Tyrode's experiments, presumably reflecting an electrostatic exclusion component. At normal and high ionic strengths, exclusion appears to result mainly from steric factors. Studies of diffusion (D) and reflection (σ) coefficients for various solutes show that restriction to solute movement is greater than can be accounted for by exclusion alone; hence, frictional interaction of solute and matrix molecules in available spaces may be an important factor. At normal hydration, calculated pore radii were 250 (UC) and 450A (SC). The hydration dependence of matrix properties may provide homeostatic mechanisms for control of transcapillary fluid movement.
(Supported by AHA grant-in-aid 72-947)

FACTORS AFFECTING DIGITAL PULSE CONTOUR AND FOURIER ANALYSIS IN MACACA MULATTA. H. D. Green, G. S. Malindzak, Jr., B. Cook*, J. Taxis*, B. Converse* and R. Buie*. Bowman Gray School of Medicine, Winston-Salem, North Carolina 27103.

Toe digital pulses, detected plethysmographically were recorded on Grass strip charts and digitized on a LINC computer. Cycle length was computed from the ECG using end of QRS as zero time, which approximates onset of LV ejection; cycle lengths were .3 to .95 sec. All data were obtained during maximal cutaneous dilation induced by pentobarbital anesthesia. C = Controls (left leg); S = surgically severely stenosed superficial femoral artery (right leg of controls) (7 Rhesus). L = 8 lesion Rhesus on an atherogenic diet for 19 months. Computations: I. α = zero to foot of pulse; β = foot to peak; $\gamma = \alpha + \beta$. All were expressed seconds (sec) and in fraction of the cycle length (F). II. Fourier analysis: % E = oscillatoryenergy in harmonics (1H to 4H) as per cent of the total in the first 10H. PA = phase angle. Results: In C, S and L α (sec) remained relatively constant; α (F) increased; β (F) remained relatively constant; and β (sec) decreased with decreasing cycle length; % E (all 4H) varied only slightly; PA (F) (all 4H) increased linearly but PA (sec) decreased non-linearly with decreasing cycle length. Pulse data superimposed on slow respiratory waves had to be corrected by subtraction of an appropriate ramp function before Fourier analysis of either % E or PA. S and L prolonged β; increased % E, 1H, and decreased %E 2 - 4H relative to C, but had opposing effects on α. PA for 1H and 2H correlates best with γ. Conclusion: Detection of early atherosclerosis or stenosis will require control data at comparable cycle lengths. (H. D. Green, et al., submitted to Fall meeting, AHA 1974.) Supported by NHLI grants 14164 and 00487.

SPECIFIC BINDING OF ANGIOTENSIN II TO NEUROHYPOPHYSIS NOT CORRELATED WITH STIMULATION OF ADH RELEASE. C.M. Gregg and R.L. Malvin. Depts. of Physiol., Univ. of Rochester Sch. of Med. & Dent., Rochester, N.Y. and Univ. of Michigan Med. Sch., Ann Arbor, Michigan.

It is now established that angiotensin II can stimulate ADH release by a direct action in the CNS. Studies were done on rats to determine whether the locus of stimulation is at the hypothalamic level and/or directly on the neurohypophysis. When isotopically labelled angiotensin was injected into the carotid artery of anesthetized rats, there was a rapid and significant uptake of label by neurohypophysis. No detectable label was found in hypothalamus or other brain areas sampled. This suggested that angiotensin might stimulate ADH release directly from pituitary. In vitro experiments did not confirm this hypothesis. Isolated neural lobes were incubated for 10 minutes in buffer containing angiotensin. Although specific binding of angiotensin to this preparation could still be demonstrated to occur, there was no stimulation of ADH release over control rates. Addition of KCl to the bath produced massive ADH release. However, incubations of intact hypothalamohypophysial systems (containing the supraoptic nuclei) with angiotensin evoked a 500% increase in the rate of ADH release over control. The data support the hypothesis that the known central effect of angiotensin II on ADH release in vivo is at the hypothalamic level.

MEASUREMENT OF RELATIVE CHANGES IN MUSCLE MICROVASCULAR BLOOD VOLUME USING TRANSORGAN PHOTOMETRY. David D. Grewe (intr. by Robert E. Gosselin). Dept. of Pharmacology and Toxicology, Dartmouth Med. School, Hanover, N.H. 03755.

Two dog gracilis muscles were injected intravascularly with a solution of carbon particles and gelatin. Six histological sections were made from each muscle. Photomicrographs taken of each section were examined visually to determine the intravascular distribution of the carbon particles. Other dog gracilis muscles were isolated in vivo and perfused with blood at hematocrits of 5, 15 and 40. A portion of each of the muscles was concomitantly transilluminated at a wavelength of 805 nm. The intensity of the light exiting from the tissue was measured and the tissue light absorbance calculated from the Beer-Lambert law. In other gracilis muscles, alterations in the microvascular blood volume were produced pharmacologically and physiologically in order to effect changes in tissue light absorbance. Results showed that the total quantity of carbon particles contained by the microcirculatory vessels exceeded that of large vessels in all of the 12 sections. For muscles perfused with blood, the light absorbance varied linearly with hematocrit. The drug-induced vasoconstriction and vasodilation of microcirculatory vessels resulted in corresponding decreased and increased light absorbance. It was concluded that the light which exited from the muscle consisted primarily of light which was transmitted by microvascular hemoglobin and also by non-vascular structures including myoglobin, a non-vascular pigment in muscle tissue. A change in the microvascular blood volume which caused a change in the microvascular pigment mass resulted in an inverse change in the intensity of the exiting light and, hence, in the tissue light absorbance. (Supported in part by NIH fellowship PHS 44732 from the NIGMS while the author was at the Department of Physiology and Biophysics, University of Vermont.)

CHANGES IN THE NUMBER OF SODIUM PUMPING SITES AS A MECHANISM FOR THE REGULATION OF THE SODIUM PUMP IN FROG MUSCLE. S. Grinstein* and D. Erlij. Dept. of Physiol. Centro de Investigación I.P.N. México 14, D. F. México.

We have examined the effects of two procedures that increase the rate of Na pumping -Na loading in K-free solutions and NaN_3 (5 mM)- on {^{3}H}ouabain binding by frog skeletal muscle. Both procedures increase markedly {^{3}H}ouabain binding, suggesting that the increased rate of pumping results, at least in part, from an increase in available pumping sites. Since the inhibition of the Na-K pump caused by ouabain is very slowly reversible one can block all the pumping sites in a resting muscle, then transfer it to a ouabain free solution and determine whether NaN_3 will still increase sodium pumping and ouabain binding. When such experiments were performed we found that NaN_3 increased Na pumping and ouabain binding of muscles whose resting pumping sites had been previously blocked by ouabain ($5X10^{-6}M$). These experiments provide further support for the notion that NaN_3 stimulates the Na pump by increasing the number of sodium pumping sites in muscle membrane. Furthermore, there seems to be a limit in the number of the sites available for opening with NaN_3, since after blocking the sites exposed by NaN_3 with ouabain, a second exposure to NaN_3 does not further increase pumping or {^{3}H}ouabain binding.

QUANTITATION OF THE GLUCOSE-ALANINE CYCLE IN PERFUSED RAT HIND LIMB. B. Grubb and J.F. Snarr (Intr. by J. H. Annegers). Dept. of Physiology, Northwestern Univ. Med. Sch., Chicago, Illinois 60611

The release of alanine by muscle has been shown to be greater than can be accounted for by muscle protein catabolism. It has been suggested that part of the alanine is synthesized de novo in the muscle cell by the transamination of glucose-derived pyruvate. After release from the muscle, the alanine is transported to the liver or kidney where it is converted to urea and glucose to complete the cycle. The peripheral phase of this "glucose-alanine cycle" was investigated in isolated fed rat hind limb by perfusing the limb with a solution of bicarbonate buffer containing 2% albumin, 2.4% dextran, 8.3mM glucose, .05μCi/ml glucose-C14 (UL), and 32-34% dog erythrocytes. Total alanine was measured enzymatically. Labelled alanine was separated by ion exchange chromatography and counted on a scintillation counter. Measurement of labelled alanine provided quantitation of the conversion of glucose to alanine. The perfused rat limb produced alanine at an average rate of .26±.03(SD) μmoles/min/4.5g dry leg (n=9) over a 3 hr perfusion period. Thirty Five percent of this alanine, .09±.03 (SD) μmoles/min/4.5g dry leg, was synthesized de novo. Three percent of the glucose taken up by the limb was accounted for by alanine release. Addition of insulin to the perfusate (.7mU/ml) increased the glucose uptake rate by 22%, and the release of de novo-derived alanine by 40%. Since insulin decreased the rate of total alanine released by 6%, a net inhibition of release of alanine derived from muscle protein breakdown is implied. These perfused limb studies support the hypothesis that a significant portion of the alanine released by rat hind limb is synthesized de novo from glucose.

EFFECT OF BARORECEPTOR STIMULATION ON THE REGULATION OF THE DEPTH AND FREQUENCY OF BREATHING IN CATS. M.M. Grunstein*, J.Ph. Derenne*, and J. Milic-Emili. Dept. of Physiology, McGill University, Montreal, Canada.

In 8 spontaneously breathing anesthetized cats subjected to steady-state inhalation of various concentrations of CO_2 and O_2, we have studied the acute effects of baroreceptor stimulation following transient inflation of a balloon catheter in the descending aorta. The latter induced a sudden rise (+80 to +100 mm Hg) in mean blood pressure proximal to the site of aortic obstruction. At all P_{ACO_2} levels above 30 mm Hg, elevation in blood pressure was accompanied by an immediate drop in tidal volume (V_T) and prolongation of the durations of inspiration (T_i) and total breath (T_{tot}). The initial breaths obtained during baroreceptor stimulation fell along the same V_T vs T_i and V_T vs T_{tot} relationships described by breaths obtaining at the normotensive level. Hence, the immediate reduction in V_T upon stimulation of baroreceptors can be attributed to inhibition of the respiratory centers, while the lung volume-related vagal control of T_i and T_{tot} appears to be unaffected. Since, for a given change in blood pressure, a constant reduction in V_T was obtained at all P_{ACO_2} values above 30 mm Hg, it can be concluded that the inhibitory effect exerted by the baroreceptors in additive. At P_{ACO_2} levels below approximately 30 mm Hg, elevations in blood pressure resulted in a variable delay in the onset of inspiration (i.e. apnea), whose duration was found to be dependent on the balance between the prevailing chemical drive (inspiratory-excitatory influence) and the magnitude of baroreceptor stimulation (inspiratory-inhibitory influence).

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GLYCOGEN DYNAMICS IN INFLAMMATORY MACROPHAGES. P. W. Gudewicz* and J. P. Filkins. Loyola University, Stritch School of Medicine, Dept. of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

The ability of inflammatory macrophages to maintain a carbohydrate reserve via glycogen synthesis from glucose as well as by engulfment of exogenous glycogen was investigated in vitro. Rat peritoneal macrophages were harvested 96 hours following the introduction of 1% sodium caseinate ip. Macrophages were incubated at 37°C in the presence or absence of either 10 mM glucose or 10 mg/ml glycogen and intracellular glycogen was isolated by alkaline hydrolysis and alcohol precipitation. The initial glycogen content of 110µg of glycogen/mg of protein was reduced 45% by incubation in a glucose-free Hanks media for 120 min. Addition of either 10 mM glucose or 10mg/ml of exogenous glycogen at the initiation of the incubation period maintained glycogen content at preincubation levels. However, when glucose or glycogen was added to glycogen-depleted macrophages, only glucose restored glycogen content to preincubation levels. The rate of macrophage glycogenesis was measured by the incorporation of glucose-U-^{14}C (0.1uCi/10mM glucose) into intracellular macrophage glycogen. Glycogen-laden macrophages incorporated $27.2 \pm 3.84 \times 10^3$ dpm of glucose into glycogen/30 min/gm protein while glycogenesis was augmented to $71.5 \pm 4.48 \times 10^3$ dpm of glucose/30 min/gm protein in glycogen-depleted macrophages. These studies suggest that macrophages maintain a large glycogen reserve both by glycogenesis from glucose and by phagocytosis of extracellular glycogen at the inflammatory site. Depletion of the macrophage glycogen reserve prohibits further uptake of exogenous glycogen indicating that macrophage glycogen metabolism may function in regulating extracellular uptake of nutrient supply at the inflammatory environment. *(Supported by NIH Grants HL 08682 and HL 14540)*

CONSTRICTION OF CEREBRAL ARTERIES AT HIGH TEMPERATURE. M. Mason Guest, Charles H. Wells and Ted P. Bond*. University of Texas Medical Branch, Galveston, Texas

Anesthetized dogs were subjected to heat stress by immersing them in hot water. The cerebral cortex was exposed and surface blood vessels were observed and photographed. Blood pressure, heart rate and respiratory rate were monitored. Blood samples were obtained and hematocrit, viscosity, leucocyte count, platelet count, coagulation factors and fibrinolytic enzyme factors were measured. As the body temperature rose above 37° both arteries and veins dilated; the dilation became greater in all vessels until a temperature between 41° and 42° was reached. Above 42°, although veins and venules continued to dilate, small arteries and arterioles began to constrict. Constriction of these vessels progressed until the animals expired, usually at a temperature between 45° and 46°. At 44° the diameter of small arteries was usually less than that at 37°. Experiments are in progress in which temperature is raised by other agents. The reaction of blood vessels to high temperatures in other organs will be discussed. We suggest that constriction may help to reduce the rate of temperature rise in the brain, thus helping to protect neural elements from damaging temperatures. (Supported by USPHS NIH Grant HL 16449 and the Shriners Burns Institute.)

A NEW RECEPTIVE FIELD ORGANIZATION IN THE GROUND SQUIRREL RETINA. Moshe Gur* and Richard L. Purple. Lab. of Neurophysiology, Univ. of Minnesota Med. School, Minneapolis, Minn.

Michael (J. Neurophysiol. 31) describes opponent and nonopponent retinal ganglion cells in the ground squirrel retina. His work was done using sodium pentobarbital as the anesthetic agent. We describe here a new class of retinal ganglion cells obtained from the ground squirrel eye while the animal was under light halothane anesthesia (0.5-1%). The cell type was encountered with a frequency indicating at least 15-20% of all retinal units belong to it. It is characterized by a center sensitive to both blue and green photopigments with the same sign, and by a "surround" organization of the opposite sign, but sensitive to only the green photopigment. The "surround" moreover, extends through the center, much as the organization of the X type described by Enroth-Cugell and Robson (J. Physiol. 187). Because of the antagonistic green organization, responses to green light tend to be phasic and on-off in nature, whereas responses due to the blue system are tonic. As a consequence, the cell has no neutral point. For any set of wavelengths equated for equal energy, the pattern of the output discharge, as recorded by post-stimulus histograms, appears to code for hue in that across the blue-green continuum the temporal pattern of output discharge can be easily correlated with specific wavelength of the input light stimulus. (Supported in part by USPHS Grant No. EY-00293 and Grant AF-AFOSR (AFSC)-1221.)

FINE STRUCTURE OF THE SEMINIFEROUS TUBULES AFTER VASECTOMY IN MAN. Johanna P. Hagedoorn and J.E. Davis (intr. by M.J. Freund). Depts. of Anatomy and Urology, New York Medical College, Valhalla, N.Y. 10595.

The extent of changes after vasectomy might influence the restablishment of fertility. To study the morphological effects of vasectomy, testicular biopsies from 3-7 years post-vasectomy individuals were fixed, embedded and stained for light- and electron microscopic examination. Sections of the seminiferous tubules showed: 1) The blood supply to the tubules is intact. 2) The lumen of each tubule examined is patent. 3) The Sertoli cells appear intact, with elongated cell outlines, radially oriented, dense cytoplasm, prominent endoplasmic reticulum, lipid droplets, subsurface cisternae adjacent to Sertoli cell junctions, nuclei with characteristic "cleft" and large tripartite nucleolus. However, a large number of lysosomes are present in the area between nucleus and basement membrane as intact dense bodies and as membrane-coated electron-lucent formations. 4) The germinal epithelium is present and shows normal stages of spermatogenesis, suggesting that sperm formation is not inhibited. Spermatids often occur in the usual clusters of 4-5. However, spermatozoa are not observed in their typical location close to the lumen, enwrapped by digitations of Sertoli cells, but rather they appear abutting the basal part of Sertoli cells, often close to the basement membrane of the tubule. This peculiar location might presage their phagocytic absorption and/or elimination by Sertoli cells.

PHARMACOLOGICALLY RESISTANT, NEURALLY INDUCED CARDIAC TACHYDYSRHYTHMIAS G. R. Hageman* and W. C. Randall. Loyola University, Stritch Sch. of Med., Dept. of Physiology, 2160 S. First Ave., Maywood, Ill. 60153.

Cardiac tachydysrhythmias were induced in 30 anesthetized mongrel dogs during cardiopulmonary bypass by electrical stimulation of the pericardial ventrolateral cardiac nerve (VLCN). Analyses of these tachydysrhythmias with multiple local cardiac electrograms reveal rapid ectopic foci located in or near the internodal pathways, A-V nodal junctional region, and the ventricles. Intravenous administration of atropine, propranolol, and phenoxybenzamine, alone or in combination, failed to prevent the VLCN tachydysrhythmias. In addition, cardiospecific tolamolol and practolol (I.V.) as well as bretylium, guanethidine, reserpine, phentolamine and hexamethonium all fail to prevent VLCN tachydysrhythmias. Furthermore the antiarrhythmic agents quinidine, digoxin, diphenylhydantoin, verapamil, and apridine (I.V.) all failed to prevent VLCN tachydysrhythmias. In order to further concentrate drugs near the ectopic focus, the A-V nodal artery (AVN) of 7 dogs was perfused and verified with acetylcholine induced transient heart block. Administration of the blocking agents and antiarrhythmic drugs via the AVN also failed to prevent the VLCN tachydysrhythmias. Only local neural anesthetic agents, as lidocaine and procaine, were successful in preventing the VLCN tachydysrhythmias. These anesthetics administered via the AVN depressed A-V junctional tachydysrhythmias and often shifted the ectopic focus to a non-perfused area. It is concluded that VLCN stimulation releases an unknown neurotransmitter, or there are cardiac receptors which are resistant to standard autonomic blocking agents and antiarrhythmiac drugs, or the VLCN-myocardial synapse does not involve neurotransmitters. *(Supported by NIH Grants HL 08682 and GM 00999)*

REFLEX BRONCHOCONSTRICTION AFTER SEROTONIN AEROSOLS IN DOGS. H.L. Hahn*, A.G. Wilson*, P.D. Graf*, D. Cotton*, J.A. Nadel. Cardiovascular Research Institute, Univ. of Calif. S.F., San Francisco, Ca. 94143.

We anesthetized 14 dogs with chloralose (100 mg/kg) and urethane (500 mg/kg), paralyzed them with succinylcholine (i.v. drip), and ventilated them artificially. Serotonin aerosol (0.1-1.0%), delivered from a Bird nebulizer, increased total lung resistance in 12 of 14 dogs (mean increase, 569%), but had no significant effect on arterial blood pressure or heart rate. Cooling both cervical vagosympathetic nerves (2-3°C) abolished the bronchoconstriction in 2 dogs and reduced it in 10 (mean reduction, 52%): Bilateral carotid body denervation did not abolish the reflex bronchoconstriction. In each of 6 dogs, the pressure in an isolated segment of trachea increased (mean increase, 12.5 cm H_2O) when the aerosol was delivered only to the lower airways. This tracheal constrictor response was abolished totally by cooling the vagi. Serotonin stimulates lung receptors and this may be the explanation of the present findings. (Supported in part by NHLI grants HL-06285 and HL-14201).

AN OPEN CHEST MODEL FOR CARDIOGENIC SHOCK. B.N. Haicken*, M.S. Gold*, R. Sammartano*, and S.J. Boley. Department of Surgery, Montefiore Hospital and Medical Center of the Albert Einstein College of Medicine, Bronx, N.Y. 10467

Previously described animal models of cardiogenic shock have employed coronary artery embolization with microspheres or mercury, or serial ligation of coronary arteries. These preparations have been limited by a high mortality during preparation and delayed onset of an unpredictable degree of shock. The present model combines embolization and ligation to create a rapid onset of a reproducible level of shock for acute hemodynamic studies. Twenty-four dogs underwent left thoractomy and ligation of the left anterior descending coronary artery 3 cm. from its origin. Proximal to this ligature a polyethylene catheter was inserted into the artery for a distance of 1 cm. and fixed in place. Mercury was injected through this catheter into the left circumflex coronary circulation in increments of 0.025 cc. at 15 minute intervals until the cardiac output fell to 40 percent of preligation values. A 40 percent decrease in cardiac output, maintained for 30 minutes, was defined as cardiogenic shock. Shock was attained in 11 of the 24 dogs (46%). The average time required to develop a shock state was 2 1/2 hrs. Mean decreases of 45 percent in cardiac output and 21 percent in blood pressure were maintained over a six hour observation period. There was no tendency toward spontaneous recovery of cardiac output. Thirteen animals (54%) could not be put into shock: fatal arrhythmias developed in 9, 2 became hypotensive prior to ligation, and in 2 animals catheter misplacement prevented adequate embolization. The technique described creates a reproducible state of cardiogenic shock with rapid onset and an acceptable rate of success.

MEMBRANE FUNCTIONS AND LYMPHOCYTE PHYSIOLOGICAL RESPONSES. Anwar A. Hakim. Univ.Ill. Med. Center. Chicago. Ill.

The present study relates membrane functions to the physiological responses of splenic lymphocytes from normal(NL) and sarcoma-bearing(SL)BALB/c mice.These cells readily take up dextran sulfate(DS).When fixed with glutaraldehyde, DS stains metachromatically with toluidine blue O. NL and SL, (96-98% viable),were purified on nylon columns and cultured for 48hrs in Eagle's medium(MEM) supplemented with 15%calf serum,penicillin(100u/ml),streptomycin(100ug/ml)and DS(10ug/ml).They were washed and aliquots cultured for 72hrs in MEM containing either neuraminidase(Neu),papain(Pa),trypsin(T), hydrocortisone(Hy),cyclic adenosine 3',5'monophosphate(cAMP) histamine(His),isoproterenol(Isop),or theophilline(Th).DS-labelled NL or SL migrated faster than DS-free cells, and NL migrated slower than SL.The cAMP,Hist,Isop,or Th-treated NL migrated faster than the untreated,or Neu,Pa,T,or Hy-treated cells,but slower than the SL or its Neu,Pa,T,or Hy-cells, When exposed to(51)Cr-sarcoma cells(51CrS),SL or DS-SLcaused 85-96%lysis of(51)CrS.Both(51)Cr and DS were found in the cell-free supernatant.Hy,cAMP,Hist,Isop,or Th-treated SL caused 25%lysis,while Neu-treated NL orDS-NLproduced 30-40% lysis of (51)CrS.The untreated NL or DS-NL had no effect.The efficiency of sarcoma cells plating was reduced with Neu-, but increased with cAMP,Hist,Isop,or Th-treated NL.The release of DS from SL or NL varied directly with(51Cr) released from the sarcoma cells.The cytolytic effect of SL is inhibited by membrane stabilizer(Hy)or mediators of cAMP, and is enhanced by altering the structural integrity of the cell membrane with Neuraminidase.

6-AMINONICOTINAMIDE OTOTOXICITY IN THE GUINEA PIG: EFFECTS ON COCHLEAR MICROPHONICS, ENDOCOCHLEAR DC POTENTIAL, AND ENDOLYMPHATIC K^+ LEVELS. Stuart R. Hall and Stanley W. Stadnicki (intr. by Ulrich Schaeppi). Worcester Foundation for Experimental Biology and Mason Research Institute, Worcester, Massachusetts.

The relationship between lesions of the stria vascularis and degeneration of the organ of Corti was examined in 6-aminonicotinamide (6-AN) treated guinea pigs. Animals received a single i.p. injection of 6-AN at a dose of either 10 or 15 mg/kg. Damage to hair cells and the stria was assessed by recording the cochlear microphonic (CM) and endocochlear DC potential (EP) in acute experiments, from 3-23 days after treatment. Additionally, endolymphatic potassium concentration was determined with ion selective microelectrodes. Changes in CM and EP were related to dose and to the interval between treatment and testing. No significant changes in potassium levels were detectable. As early as day 3, EP was reduced, but CM was normal. After day 5, EP continued to decrease, and CM also decreased. After two weeks, CM remained at reduced values, but normal EP values were recorded. The decrease in CM was substantiated by loss of hair cells in the organ of Corti in surface preparations. In summary: 6-AN caused a transient decrease in EP, indicating a reversible lesion of the stria vascularis, and a permanent decrease in CM, indicating an irreversible hair cell loss, without significant changes in K^+ concentration of the endocochlear fluid. (Supported in part by NIH Grant MH-10625, Neurobiology Training Program.)

ARTERIAL, MIXED VENOUS AND CEREBRAL VENOUS BLOOD GASES AND pH IN DOGS SUBJECTED TO HEMORRHAGIC SHOCK. D.F.J. Halmagyi and T.A.Frazer*. Depts. of Surgery, College of P&S, Columbia Univ., New York, N.Y. and Univ. of Sydney, Sydney, Australia.

The role of cerebral hypoxia in the mechanism of irreversible hemorrhagic shock was studied in 14 greyhounds bled to a blood pressure of 45 Torr and reinfused 3 hours later by shed blood, donor blood and dextran. Seven dogs were allowed to die the same day; 7 were made to survive by combined adrenergic receptor blockade (after reinfusion), and were killed next day. These techniques were previously described (J. Appl. Physiol. 30: 186,1971). A teflon catheter was implanted into the sagittal sinus (SS). Multiple blood samples were simultaneously collected from the femoral (FA) and pulmonary (PA) arteries and SS during the control period, during hypovolemia and after reinfusion. At rest blood gases in FA were normal and there was no significant difference between blood gases in PA and SS. During hypovolemia FA pO_2 was normal and pO_2 in SS was higher (30±8 Torr) than in PA (23±7 Torr) the gradient being inversely and linearly related to log blood pressure, suggesting the role of cerebral blood flow autoregulation. In all reinfused dogs pCO_2 in SS was higher (58±10 Torr) than in PA(47±7 Torr). After reinfusion SS pO_2 in the survivors was lower (28±8 Torr) than in the fatally shocked dogs (38±6 Torr). We conclude that these observations do not support the assumption that irreversibility in hemorrhagic shock is related to cerebral hypoxia. (Supported by the National Heart Foundation of Australia).

THE EFFECT OF VARIOUS SALINITIES AND HYPOPHYSECTOMY ON THE ELECTROLYTE METABOLISM OF THE HOLOSTEAN, AMIA CALVA. Robert C. Hanson*, Douglas W. Duff* and Warren R. Fleming. Division of Biological Sciences, Univ. of Missouri, Columbia, Missouri 65201.

Young holostean fish, Amia calva, lived well in environments where the Na^+ concentration ranged from 0.11 µEq/ml to 117 µEq/ml and failed rapidly when transferred to 30% sea water which contained 140 µEq Na^+ per ml. These fish lived for at least a week in distilled-deionized water without food. They retained Na^+ and lost K^+ in this environment. The total-body Na^+/K^+ ratio of juvenile Amia was close to 1.3 when the animals were held in dilute tap water containing 0.11 µEq Na^+/ml. In all other environments tested, the ratio approached or exceeded 2.0, due primarily to K^+ loss. None of the animals lived for more than 10 days in any test environment after hypophysectomy. Hypophysectomy caused a drop in both total-body and serum Na^+ levels. In fresh water (2.2 µEq Na^+/ml) normal Amia were found to have total-body Na^+ levels of 70.33 ±2.16 mEq/Kg and serum Na^+ levels of 119.6 ± 1.9 mEq/l, while hypophysectomy reduced total-body Na^+ levels to 60.79 ± 1.57 mEq/Kg and serum Na^+ levels to 104.9 ± 3.3 mEq/l. Serum and total-body K^+ levels were not affected by hypophysectomy. Hypophysectomized animals had higher Na^+ efflux rates for a 24 hour period after handling than did controls. Neither hypophysectomy nor salinity changes affected serum calcium levels or water permeability.

SMALL VESSEL CONSTRICTION IN RAT SKELETAL MUSCLE DURING HEMORRHAGE WITH TWO DIFFERENT ANESTHETIC COMBINATIONS OF ALPHA-CHLORALOSE AND URETHANE. P.D. Harris, D.L. Wiegman*, F.N. Miller*, and M.J. Devaney*. Depts of Physiol. and Elect. Engr., Univ. of Missouri, Columbia, Mo. 65201.

Small vessel diameters in the cremaster muscle of Sprague-Dawley rats were quantitated by closed-circuit television microscopy. The protocol consisted of a 15-minute control period, a 60-minute period with arterial pressure held at 30 mmHg via hemorrhage from a femoral artery, and a 30-minute recovery period which followed reinfusion of the hemorrhaged volume (HV). Nine rats (174±SEM 21 gm) were anesthetized with 60 mg/kg alpha-chloralose and 800 mg/kg urethane i.p. (group I) and five other rats (172±53 gm) were anesthetized with 120 mg/kg alpha-chloralose and 600 mg/kg urethane i.p. (group II). Average control values for group I were: artery diameter (AD)=125±4.0 µ, vein diameter (VD)=167±7.0 µ, heart rate (HR)=432±17 bpm. Control arterial pressure (MAP) was 99±2.2 mmHg. The maximum HV was 30.5±2.9 ml/kg at 44 minutes of hemorrhage. Average control values for group II were: AD=149±7.2 µ, VD=217±9.9 µ, HR=468±28 bpm, MAP=99±3.9 mmHg. The maximum HV was 32.1±5.4 ml/kg at 52 minutes of hemorrhage. The data ($\bar{x}$±S.E.M.) during hemorrhage were:

	GROUP I		GROUP II	
TIME OF HEMORRHAGE=	15 mins.	50 mins.	15 mins.	50 mins.
AD (% of Control)	73±3.9*	65±5.3*	64±4.4*	54±2.0*
VD (% of Control)	99±1.4	97±2.3	97±3.3	89±7.0
HR (% of Control)	74±5.3*	98±5.9	72±5.6*	101±7.5

*$p<0.05$ for comparison to control values (expressed as 100%)

Hemorrhagic hypotension gave an expected small artery constriction which persisted throughout the hemorrhage period for both anesthetic combinations of alpha-chloralose and urethane. There were no significant changes in small vein diameter during the 60-minute hypotensive period. (Supported by PHS HL13207, HL20422, and HL53252).

ENTEROKINASE SECRETION IN THE DOG. Joseph R. Hassan* and M.H.F. Friedman. Jefferson Medical College, Philadelphia, Pa. 19107.

Secretion of enterokinase by the small intestine was studied in dogs fasted 20-24 hours but water allowed ad lib. In acute experiments under pentobarbital anesthesia two loops of intestine were established between ligatures: one extended from the pylorus to just past the entrance of the pancreatic duct, and the other from this point distally for 20 cm. In some experiments bile or pancreatic secretion or both were excluded from entering the proximal loop either by duct ligation or by duct exteriorization. In other experiments flow of bile and pancreatic juice into the loop was permitted. In all cases gastric juice was excluded from the intestine. The lower loop was constantly perfused with 0.85% NaCl at the rate of 0.5 ml per min for 4 hours. Perfusate samples were collected every 20 minutes. The following were introduced by continuous intravenous infusion for periods of 20 to 80 minutes: secretin, synthetic secretin, pancreozymin, gastrin, caerulein, histamine and serotonin. Determination of enterokinase activity on the supernatant of the centrifuged perfusate samples (pH 6.8 to 7.3) was made by a modified two-stage method based on the methods of Goldblatt and Hummel. Addition of dog bile or bile acids to the perfusing fluid did not increase enterokinase secretion but did accelerate the conversion of trypsinogen to trypsin. Whether or not bile/pancreatic juice entered the upper loop, neither secretin nor synthetic secretin at several dosage levels had a demonstrable effect on enterokinase secretion. Glucagon, pancreozymin, caerulein and serotonin stimulated enterokinase secretion when bile/pancreatic juice had access to the intestine but only pancreozymin and caerulein were effective if the bile and pancreatic secretion were excluded.

LENGTH-TENSION CHARACTERISTICS OF OBSTRUCTED RABBIT URETER. Michael Hausman*, Piero Biancani*, and Robert M. Weiss. Yale Univ. School of Med., New Haven, Ct. 06510.

Obstruction causes changes in the mechanical properties of ureteral smooth muscle. Active and passive length-tension characteristics of the obstructed rabbit ureter were determined. Twenty rabbit ureters, in vivo, were partially obstructed for 10-14 days and segments of the resultant dilated ureters and the contralateral control ureters were excised and placed in a perfusion chamber after measuring in situ dimensions. Muscles were maintained at 37°C with oxygenated Tyrode solution; stimulation rate, 2/min. Active and passive tensions were determined, 15 min. after each length increment. The length of maximum active tension development (L_o) was 20% greater for obstructed than for control ureters. Active longitudinal force (ALF) was 1200 mg. for dilated ureters at L_o. This force was 3.5 times greater than the ALF of control ureters at L_o. Cross sectional muscle area was 10% greater in obstructed ureters than in controls. This small but statistically significant muscular hypertrophy is in itself insufficient to account for the 350% increase in ALF. Thus the obstructed ureter is capable of exerting a larger force per unit cross sectional area of muscle. In addition at any given length, passive tension was lower for obstructed than control ureters, but passive tension increased more rapidly with length change in the obstructed ureter. Thus the elongated and dilated ureter that results from obstruction is able to develop an increased ALF and the peak of this force occurs at a longer length than in normal ureters. (Supported by NIH Grants AM 16021 and AM 13543).

EEG FREQUENCY SPECTRUM CHARACTERISTICS OF SLEEP STATES IN FULL-TERM AND PRETERM INFANTS. V. Havlicek, R. Childiaeva* and V. Chernick. Dept. of Physiology and Pediatrics, Univ. of Manitoba, Winnipeg, Manitoba.

Spectral analysis of the EEG using fast Fourier transform in preterm and full-term infants revealed significant maturational changes in all three stages of sleep. REM sleep in premature infants had significantly higher intensity in delta 1 frequency band (0.1 - 1.5 Hz) but significantly lower intensity in beta 2 band (17.6 - 25 Hz) when compared to full-term infants. The EEG during quiet sleep in premature infants compared to full-term infants had significantly lower intensity in delta 2 (1.6 - 3.5 Hz), theta 1 (3.6 - 5.5 Hz) and theta 2 (5.6 - 7.5 Hz) frequency bands. During indeterminate sleep premature infants showed significantly higher intensity in delta 1, while delta 2, theta 1 and theta 2 had significantly lower intensity. During quiet sleep full-term infants showed significantly higher intensity in delta, theta and alpha frequency bands (0.1 - 12.5 Hz) than during the REM sleep. In premature infants there was significantly lower intensity during the REM sleep only in theta 2 frequency band. The quiet sleep - REM sleep frequency spectrum difference could be readily computed in individual infants. All normal healthy full-term infants (38 - 42 weeks gestational age) showed significant differences as described above, while premature infants (32 - 36 weeks gestational age) and the transitional group (37 weeks gestational age) did not have large differences between quiet sleep and REM sleep. Evaluation of the quiet sleep - REM sleep difference in frequency spectrum of neonatal electroencephalograms may be valuable in assessing normal EEG maturation since this analysis shows typical and significant changes during maturation in the individual infant.

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EFFECTS OF INCREASED CEREBROSPINAL FLUID ADENOSINE CONCENTRATION OR P_{CO_2} ALTERATIONS ON CEREBRAL HEMODYNAMICS IN THE DOG. JoAnn C. Havran* and Thomas E. Emerson, Jr., Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

It has been suggested that adenosine and/or CO_2 may be involved in local regulation of cerebral blood flow. This study was designed to determine whether increasing the cerebrospinal fluid (CSF) concentration of adenosine or increasing or decreasing the CSF P_{CO_2}, influences cerebral hemodynamics (N=8). Cerebral venous outflow was measured from the cannulated sinus confluens after occluding the transverse canals with bone wax. The CSF system was perfused with artificial CSF via a needle inserted into the right lateral ventricle; outflow was via a needle in the cisterna magna. CSF infusion rate was 4 ml/min, which produced adequate CSF pressure to force the perfusate around the entire brain surface, as demonstrated by India ink added to the perfusate, and permitted rapid saturation of the CSF system with the test solution. CSF solutions containing: 1) no adenosine (control soln.); 2) 10 or 100 ug/ml adenosine; 3) high or low P_{CO_2} with no adenosine were perfused for 10-12 minutes. Inflow and outflow CSF P_{CO_2}, P_{O_2} and pH were determined systematically. Cerebral arterial P_{CO_2} was increased by ventilating the animal with 10% CO_2-21% O_2-69% N_2 for 5 min to test the reactivity of the cerebral vasculature. Results indicate that increasing the CSF concentration of adenosine or increasing or decreasing CSF P_{CO_2} does not appreciably influence cerebral vascular resistance or cerebral blood flow. However, comparable increases in cerebral arterial P_{CO_2} resulted in a 104% increase in cerebral blood flow and a 45% decrease in cerebral vascular resistance. Our data do not support the hypotheses that adenosine or CO_2 are involved to a major extent in local cerebral blood flow regulation. (Supported by grants from NIH and the Mich. Heart Assoc.)

THE EFFECT OF CATECHOLAMINES ON THE DYNAMICS OF A-V SHUNTS IN THE LEG OF THE DOG Yuji Hazeyama*, E.L. Dobson, E.R. Lewis*
Lawrence Berkeley Laboratory, University of California

Regional distribution of femoral artery flow was studied in Beagle dogs using the infusion technique developed by C.T. Schmidt of this laboratory (LBL-1518). Radioactive plastic microspheres, 15 μm diam. were infused into the femoral artery. The extent of trapping in the lung, ankle, thigh, and paw were recorded. During the infusion of microspheres, graded doses of norepinephrine were infused intravenously. In general, when a relatively high dose (1 μg/kg/min) was infused, the rate of microsphere accumulation in the lung and paw decreased. The skin temperature of the paw decreased also. After stopping the norepinephrine infusion, both accumulation and the temperature returned toward the control. At lower doses, these effects became less and with 0.1 μg/kg/min, the norepinephrine produced almost no change in the rate of accumulation in the lung, while producing a decrease in the rate of accumulation in the paw, suggesting that capillary flow and shunt flow are independently controllable. Considerable variability was observed from dog to dog in the magnitude of the response to norepinephrine so that the response to graded doses was followed in a single dog. Similar experiments were performed using epinephrine. Although there were significant differences in the response, both norepinephrine and epinephrine produced essentially similar types of changes in the microsphere accumulation rates. The most significant difference between the response to norepinephrine and epinephrine was that epinephrine produced greater changes in the rate of microsphere accumulation than did norepinephrine. This may be due in part to the differential effects of epinephrine and norepinephrine on skeletal muscle arterioles. (Supported in part by U.S. Atomic Energy Commission)

ON-LINE MEASUREMENTS OF MEMBRANE PERMEABILITY WITH A PARTICLE SIZE ANALYZER AND DESK-TYPE HYBRID COMPUTER. H. G. Hempling, Dept. Physiology, Med. Univ. of South Carolina, Charleston, S. C., U. S. A.

Membrane permeability may be measured in hyperosmotic media of permeable and impermeable solutes from changes in cell volume. Methods which detect changes in light transmission in cell suspensions have been used before. We used a Particle Size Analyzer and a desk-type hybrid computer to record rapid changes in cell volume at concentrations as low as 50,000 cells/ml and volumes as low as 4 ml. Pulses from the particle analyzer are integrated for 0.1 second. Each pulse represents the volume of a cell. Total collected voltage is the product of pulse height X number of pulses. The hybrid computer is programmed to track the collected voltage at the end of an operate cycle and to store the voltage for recording during the next operate cycle. The output becomes a direct measure of mean corpuscular volume of the cells analyzed in each period. The method has been applied to ascites tumor cells, erythroblastic leukemic cells, and to lymphocytes with results comparable to those obtained by densimeter methods. Since so few cells are required, a spectrum of permeability measurements is now possible on lymphoid and myeloid cells isolated from 15 ml of peripheral blood or from bone marrow aspirates. This method makes possible large scale screening for the detection of abnormal membrane function associated with myeloid leukemias. Supported by USHPS Grant #CA-12956-03 and American Cancer Society #IN101.

EFFECTS OF ADENOSINE ON THE cAMP LEVELS AND THE Ca^{++}-K^{+} DOSE-RESPONSE CURVES OF VASCULAR SMOOTH MUSCLE (VSM). J.T. HERLIHY, E.L. BOCKMAN, R.M. BERNE, R. RUBIO AND H.C. BAXTER.* Dept. of Physiology, University of Virginia School of Medicine, Charlottesville, Virginia, 22901.

The mechanism whereby adenosine relaxes VSM is not known. It is possible that adenosine acts by increasing the cAMP concentration in VSM as shown for other agents (e.g. ß-adrenergic agents). This possibility was tested in dog coronary and hog carotid arterial strips which had been cleaned, slit longitudinally and incubated for 15 minutes with various agents. Adenosine ($1x10^{-4}$M)-treated strips in both species showed no significant increase in cAMP over controls. For the dog coronary strips cAMP levels were 1.14± 0.17 and 1.08±0.20 pmol/mg protein for control and adenosine treatment, respectively. In the hog carotid strips the corresponding values were 1.49±0.07 and 2.26±0.33 pmol/mg protein. In both species aminophylline ($1x10^{-3}$M) caused a threefold ($p<0.01$) increase in cAMP concentration. No significant interaction was observed when both agents were added simultaneously. Adenosine could relax VSM by inhibiting the excitation-contraction coupling process, either by decreasing the Ca^{++} permeability or by stabilizing the membrane. Adenosine ($3x10^{-6}$M) had no effect on the Ca^{++} dose-response curves of potassium-depolarized vascular strips (complete substitution of NaCl by KCl) from the hog carotid artery, indicating that adenosine does not inhibit external Ca^{++} movement into depolarized cells. Under conditions of 20 mM K^{+}, however, the same dose of adenosine resulted in a profound shift in the Ca^{++} dose response curve down and to the right. The present results indicate that cAMP is not involved in adenosine-induced relaxation of VSM and suggest that it may act by stabilization of the VSM membrane either by hyperpolarization and/or inhibition of some ion movement during sub-maximal excitation. Supported by NIH grants HL05815 and HL10384.

THE ATHEROSCLEROTIC MONKEY: CEREBRAL BLOOD FLOW RESPONSES TO HYPERCAPNIA AND HYPOXIA.
Hernández-Peŕez,M.J.*, H.H.Erickson and J.D.Toft* Division of Neurology, Hershey Medical Center, Hershey, PA, and USAF School of Aerospace Medicine, San Antonio, Texas.

Five adult monkeys (Macaca fascicularis)were fed an atherogenic diet which included 2% cholesterol, 6% coconut oil,and 14% butter. Six control monkeys received a normal laboratory diet. After 23 months, all animals were implanted with Doppler ultrasonic flow transducers to determine internal carotid artery blood flow velocity(ICBFV). Following a two-week recovery period, arterial blood pressure and ICBFV were measured while the monkeys were lightly sedated with phencyclidine. Cerebral blood flow autoregulation(CBFA) was monitored during exsanguination and infusion of metaraminol through a femoral vein while the animals breathed room air,9% CO_2 in air, or after three hours of breathing 100ppm carbon monoxide(CO) in air. The monkeys were then kept in a 100ppm CO environment for seven days and CBFA determined again. AlthoughICBFV was slightly elevated in the diet-fed monkeys while breathing room air,9% CO_2, or after three hours of mild hypoxia, the differences between the two groups were not statistically significant. The time required to achieve 66% of maximal cerebral vasodilatation in response to hypercapnia ($T_{66\%}$)was significantly higher in the diet-fed group: 157± 29 seconds versus 61± 15 seconds in the control group. The vasodilatory response present in the control monkeys after seven days of CO exposure was attenuated in the diet-fed group. At necropsy, gross and microscopic atherosclerotic lesions were observed in the aorta, coronary and peripheral arteries, but the intracranial arteries were relatively free of lesions. The results suggest that in the atherosclerotic primate, when moderate-to-severe systemic lesions appear, CBFA is intact, but the CBF response to hypercapnia or hypoxia may be impaired.

ENVIRONMENTAL FACTORS INVOLVED IN AROUSAL FROM DORMANCY IN SNAILS. Clyde F. Herreid II and Mary Anne Rokitka*. Dept. of Biology, State Univ. of New York, Buffalo, 14214.

Dormant snails from Moracco, Otala lactea, are characterized by a low metabolic rate, low water loss and the presence of one or more calcareous epiphragms across the shell aperature. Arousal from dormancy involves a striking increase in oxygen consumption. As the snail becomes active it pushes the epiphragms aside and may consume them. Water loss increases. Arousal may be stimulated by increasing the vapor pressure: e.g. at 25°C, relative humidities higher than 75% promoted arousal: the higher the RH, the greater was the percent arousal. The speed of arousal after stimulus varied from 20 min. to several hours and was inversely related to the number of epiphragms present. Arousal may be stimulated by lowering the ambient temperature (holding vapor pressure constant): e.g. at 8 mm Hg, no arousals occur at 27°C, 5% of the snails aroused at 18°C, 18% aroused at 15°C and 100% aroused at 5°C. Arousal frequency is affected by light conditions. The highest arousal frequency occurs in continuous darkness, and the lowest in continuous light. Thus, arousal is most likely when temperature is low, humidity is high and light reduced. These conditions prevail in the field after rains or in the evening.

Reflex Effects of sympathetic Afferent Stimulation in the Primate. G.L. Hess, D.R. Kostreva, E.J. Zuperku, J. Neumark, and J.P. Kampine. (Intr. by W.J. Stekiel) Med. Col. of Wisc., Milw., Wisconsin 53226

Afferents of cardiac origin which traverse the sympathetic nervous system and enter the spinal cord, are believed to play a role in the regulation of circulation. Previous work by others has shown only modest changes in heart rate, dP/dt, and blood pressure, in response to electrical afferent stimulation. For these reasons the reflex effects of afferent sympathetic nerve stimulation were studied in Macaque monkeys. Anesthesia was induced with phencyclidine bromide (1-2 mg/Kg). The trachea was intubated and anesthesia was maintained with nitrous oxide, oxygen, pancuronium, and low levels of halothane (0.5 to 1.0%) as required. The depth and rate of ventilation was regulated according to arterial blood gas composition. The chest was opened on the left side and a Biotronic flowmeter placed around the descending aorta. The anterior ansa subclavia nerve was isolated distal to the stellate ganglia. The nerve was cut, and stimulation was performed on the central end and on the sectioned central end of the stellate cardiac nerve using a constant current stimulator. Afferent stimulation produced reflex increases in left ventricular pressure, dP/dt, blood pressure, and heart rate of slightly greater magnitude than previously reported. In addition, right ventricular pressure and dP/dt were augmented by left side stimulation. An increase in stroke volume also occurred, which together with the higher heart rate produced an increased cardiac output. Bilateral cervical vagotomy attenuated but did not abolish these responses. Complete section of all the left side sympathetic nerves, followed by stimulation of the entire chain produced variable results, with a slight cardiovascular depression most often observed.

EFFECTS OF ANGIOTENSIN, VASOPRESSIN AND METHOXAMINE ON CARDIAC OUTPUT, RATE AND CONTRACTILITY IN CONSCIOUS DOGS. Guy Heyndrickx*, Robert McRitchie*, Dedo Boettcher* and Stephen Vatner. Dept. of Med., Harvard Med. Sch. and Peter Bent Brigham Hospital. Boston, MA 02115.

Systemic vasoconstrictor and cardiac effects of angiotensin(AN), vasopressin(ADH) and methoxamine(MX), 3 potent vasoconstrictors with different modes of action, were studied in healthy conscious dogs. These drugs were administered in i.v. graded doses (AN 0.01-0.25μg/kg/min, ADH 1.25-25mu/kg/min and MX 2.5-25μg/kg/min) to 7 conscious dogs 2-4 weeks after instrumentation with left ventricular(LV) pressure(P) gauges for LVP, dP/dt and dP/dt/P, ultrasonic LV diameter(D) transducers for LVD and dD/dt, i.e. velocity(V), electromagnetic aortic flow probes for cardiac output(CO) and arterial(A) P catheters. Control values prior to AN, ADH and MX were nearly identical. For an equal rise in mean AP (+35%), CO fell the least with AN (-15%), an intermediate amount with MX and the most with ADH (-38%). The increase in end diastolic D(+2.3±0.1 mm) and end systolic D(+5.6±0.8 mm) were similar for AN, ADH and MX with the greatest pressor response, while peak dP/dt decreased slightly at this point with all 3 agents. For a 40 mmHg rise in mean AP, heart rate(HR) decreased -37 beats/min with ADH and -21 beats/min with MX and only -4 beats/min with AN. Several weeks after recovery from bilateral cervical section of the carotid sinus and aortic baroreceptor nerves, a 40 mmHg AP rise with AN increased HR by 16 beats/min, while with ADH HR decreased -22 beats/min and with MX HR did not change significantly. Thus, although angiotensin, vasopressin and methoxamine are potent vasoconstrictors, they exert a differential effect on cardiac output for equivalent pressure increases with vasopressin decreasing cardiac output the most and angiotensin the least. This in part may be due to a differential effect on cardiac rate induced by these drugs, since vasopressin elicits the most and angiotensin the least intense bradycardia.

RESTORATION OF VISION AND EYE MOVEMENTS IN GENETICALLY EYELESS AXOLOTLS. Emerson Hibbard (intr. by W. A. Dunson), Pennsylvania State University, University Park, Pennsylvania, 16802.

Right eyes grafted into eyeless mutants of Ambystoma mexicanum at early tailbud stages can establish orderly functional connections in the optic tectum of the host's brain. Animals with eye grafts follow and snap at moving targets held above the water. Most respond normally to movement of an optokinetic drum but in some cases movement of the animal in the drum is consistently reversed. In the latter cases, the optic nerve from the grafted eye may have projected to the ipsilateral rather than to the contralateral tectal lobe but electrophysiological and histological studies have not been completed on these animals. The oculomotor muscles of the grafted eyes are innervated by the appropriate nerves of the host and show normal vestibular nystagmus reflexes. The oculomotor nerves are also present in the completely eyeless mutant innervating small remnants of oculomotor muscles which develop in spite of the complete absence of eyes. Because the gene which causes eyelessness also affects the gonadotrophic hormone production by the pituitary, the eyeless animals are sterile. In order to increase the proportion of eyeless embryos produced in each mating, ovaries of eyeless animals have been grafted into eyed hosts, grafts of hypothalamic rudiments have been made into eyeless hosts, and heads of eyeless animals have been replaced with eyed ones. (Supported by U.S.P.H.S. grant EY01071-02)

CELL MEMBRANE POTENTIALS IN AMPHIBIAN URINARY BLADDER. J.T. Higgins, Jr. and E. Frömter*. Indiana Univ. School of Med., Indianapolis, and Max Planck Inst. für Biophysik, Frankfurt, West Germany.

Ion transport by toad urinary bladder has been extensively studied, but small cell size in this tissue makes microelectrode work difficult. In bladders from amphibia with larger cells, Necturus and Amphiuma, mounted in a leak-free chamber between identical Cl^- Ringer solutions, we have found a very predictable potential (PD) and resistance (R) profile. Transepithelial PD (E_T) ranged from 15-175 mV, lumen negative, and was inversely related to R which ranged from 60 KΩcm^2 in low-PD bladders to 2 KΩcm^2 in high-PD bladders. Microelectrode study showed the basal membrane PD to be nearly constant with a median value of 75 mV, cell negative referable to serosal bath. Thus the wide variation in E_T was due mainly to differences in luminal membrane PD. When E_T was >95 mV the mucosal solution was more negative than the cell (stairstep profile) and when E_T was <90 mV the mucosal solution was more positive than the cell (trough-like profile). With time in the chamber E_T fell, transepithelial R rose, and a stairstep profile progressed to a trough-like profile. The role of Na^+ conductance in determining luminal membrane PD was revealed by amiloride ($5x10^{-6}$M, mucosal bath) which increased luminal membrane and transepithelial R and made the cell more negative referable to the mucosal bath so that E_T decreased while basal membrane PD was almost unchanged. In Cl^--free $SO_4^=$ Ringer solution, increasing serosal bath $[K^+]$ depolarized the basal membrane by more than 37 mV per 10x increase $[K^+]$, but even at 112 mM K^+ a residual basal membrane PD of >30 mV remained. Thus the main features of Ussing's frog skin model are found in amphibian bladder, with a Na^+ diffusion PD across the luminal membrane and a K^+ diffusion PD across the basal membrane. However, the residual basal membrane PD in high $[K^+]$ solutions indicates a role of other factors in determining that potential.

LOWER ESOPHAGEAL SPHINCTER RESPONSE TO CHOLINERGIC STIMULATION: GASTRIN RELATED BY NOT GASTRIN RELEASING. R.H.Higgs*, D.O.Castell, and J.E.McGuigan*, U.S.Naval Hospital, Philadelphia, Pa. and Univ. of Florida College of Medicine, Gainesville, Florida.

Lower esophageal sphincter (LES) pressure has been shown to increase after bethanechol (B) injection, and this response has been at least partially attributed to endogenous gastrin release. We have measured LES pressures and serum gastrin concentrations before and after B (0.08 mg/kg subcutaneously) in controls, patients having vagotomy and antrectomy (V&A), and patients having vagotomy and pyloroplasty (V&P). Results are indicated below:

	Controls		V&A		V&P	
	LES (mmHg)	Gastrin (pg/ml)	LES (mmHg)	Gastrin (pg/ml)	LES (mmHg)	Gastrin (pg/ml)
Basal:	13.0±1.6*	78.8±13.0*	12.7±1.7	49.4±10.0	12.0±1.7	147.0±36.4
Maximal:	25.0±3.5	73.8±12.0	28.9±2.4	58.6± 9.0	38.5±5.0	141.0±72.0

*Mean ± SE

No significant changes in serum gastrin concentrations occurred after B in any of the patient groups. LES pressure increases were significant ($p<0.01$) in all groups, with the response for V&P patients being significantly greater ($p<0.05$) than for controls or V&A patients. In addition, V&P patients had significantly higher ($p<0.05$) serum gastrin values than controls or V&A patients.

Conclusion: The response of LES to B is not dependent on endogenous gastrin release, but does appear to be related to background circulating gastrin levels.

PREVENTION OF DEATH IN ENDOTOXIN SHOCK BY GLUCOSE ADMINISTRATION.
L. B. Hinshaw, R. T. Brantley*, M. D. Peyton*, L. T. Archer*, M. R. Black*, L. J. Greenfield, and J. J. Coalson*. V.A. Hospital and Univ. Okla. Health Sci. Ctr., Oklahoma City, Oklahoma.

Current interest has centered around the role of glucose metabolism in shock and trauma. The purpose of the present study was to determine the relationships of blood glucose levels to hemodynamics, acid-base parameters and survival in anesthetized dogs administered an LD_{70} *E. coli* endotoxin (1.0-1.5 mg/kg). Systemic arterial pressure, blood gases and pH were monitored during a 5-hr period and all surviving animals were observed for 30 hr post-endotoxin. Experimental animals received continuous intravenous infusions of 50% dextrose begun during the early phase of shock. Hematocrits of all animals were maintained constant with 6% dextran. Eight of 11 control animals given endotoxin alone died in a mean time of 13 hr with marked hypoglycemia (12 mg% in 5 hr). Nine additional dogs administered endotoxin received 50% glucose at rates sufficient to maintain blood glucose levels constant (12 cc/kg/5 hr), and all survived. Heart rate, rectal temperature and pH were notably elevated ($p<0.05$) within 5 hr in animals receiving glucose. A second series was studied in which glucose treatment was begun during the intermediate phase of shock when animals became severely hypoglycemic (40 mg%) and infusion was continued up to 7 hr post-endotoxin. A total of 5 animals thus treated survived while 10 untreated control animals died (LD_{100}). These findings clearly document progressively developing hypoglycemia in lethal endotoxin shock. Glucose infusion at rates which maintained normal blood levels of glucose improved certain hemodynamic-metabolic parameters and prevented death in all animals. (Research supported by the V.A. Hospital, U.S. Navy Project N00014-68-A-0496, and NIH Grant HL 15037.)

EFFECT OF FEEDBACK REGULATOR ON cAMP PHOSPHODIESTERASE ACTIVITY.
Ren-jye Ho. E.W. Sutherland Research Laboratories, Dept. of Biochemistry, Univ. of Miami School of Medicine, Miami, Florida 33136.

The cAMP-mediated formation of a feedback regulator (FR) from adipocytes inhibited adenylate cyclase (AC) activity. This action of FR may be associated with the post-peak drop of cAMP levels in adipocytes during hormone action. The possibility of FR increasing the phosphodiesterase (PDE) activity has not been systematically studied. In results obtained from adipocyte whole homogenate assays, the post-peak drop of cAMP in cells did not correlate with the activity of PDE. It was, however, consistent with a decrease in AC activity. In the present study, using partially purified FR as the testing principle, PDE from adipocyte plasma membrane was inhibited. The inhibition of bovine heart PDE (high K_m PDE) by FR was much greater as compared to PDE of adipocyte plasma membrane. Using soluble PDE from rat epididymal adipose tissue, the degree of inhibition by FR was greater when cAMP 100 μM vs. 1 μM was used. The % inhibition of PDE activity by FR was greater at 2 mM Mg^{2+} than at 10 mM. The inhibitory action of FR on PDE appeared to increase K_m for cAMP and decrease V_{max}. The concentration of FR required for 50% inhibition of high K_m PDE was approximately 5-10 times higher than that for membrane bound AC. The possibility of using this assay as a means to determine FR is considered. The physiological meaning of this action remains to be studied. It seems consistent with the thought that a reinforcement of the hormone action by stabilization of cellular cAMP levels through inhibition of PDE is in concert with the inhibition of cAMP synthesis by FR.
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MAGNITUDE, DIRECTION, AND LOCATION OF THE PIG HEART VECTOR. Brian C. Hodgkin*, Ronald W. Millard*, and Clifford V. Nelson, Maine Medical Center, Portland, Maine.

Vectorcardiograms of 41 young anesthetized domestic pigs (7.5-18.0 Kg) were calculated from thoracic potentials obtained using the Nelson lead system. Four of these pigs were studied over a period of 5 weeks to determine the effect of growth on the vector. Location of the vector in two of the growth study pigs was calculated directly from 26 surface potentials using the Gabor-Nelson equations. For all pigs one to three peaks occurred in the spatial magnitude (M) curve. Defining the interval between 5% of maximum M as 100% QRS duration, the first peak (M_1) had a magnitude of 37 $\pm$ 16 k mA-cm and occurred at 13 $\pm$ 5%, M_2 was 149 $\pm$ 60 k mA-cm at 37 $\pm$ 8%, and M_3 was 266 $\pm$ 74 k mA-cm at 53 $\pm$ 6%. M_1 was present 66%, M_2 51%, and M_3 100% of the time. M_1 was oriented to the right, craniad, and ventrad. The vector then swept toward the left, caudally, and ventrally, beginning its subsequent craniad sweep near the midline. M_2 occurred at this time. At the transition between caudad and craniad orientation of the vector, M decreased then increased in magnitude as it continued its craniad sweep to the left and dorsally. The vector attained maximum magnitude (M_3) oriented leftward, craniad and dorsad, then decreased in magnitude with little change in direction. During the five week period that 4 pigs were observed, vector directions did not change but M_3 increased an average of 92% and body weight, 91%. As growth progressed the locus of the vector moved toward the left, caudad, and ventrad during free wall depolarization. For 10 pigs the relationship between M_3 and heart weight (HW) was M_3 = 3.85 HW (gm) + 79.4 k mA-cm, R = 0.905. Since the vector magnitude reflects heart size it is potentially useful in studying progression and regression of hypertrophy.

EFFECTS OF MANGANESE ON POTASSIUM CONDUCTANCE IN CANINE PURKINJE FIBERS. P. M. Hogan and K. W. Spitzer.* Dept. Physiology, State University of New York at Buffalo, Buffalo, N.Y. 14214

In recent years manganese (Mn) has been used as a selective calcium blocking agent in the study of cardiac electrogenesis. The present findings suggest that Mn may also influence potassium conductance (gK). Membrane potential (Vm) was recorded from canine Purkinje fibers to assess the effects of Mn on those aspects of Vm most dependent on potassium current. Superfusion with 2.5 mM Mn in Tyrode solution decreased the rate of terminal repolarization of the action potential and increased the rate of diastolic depolarization, implying an effect of Mn on iK_2 kinetics. Further effects on the potassium system were reflected by changes in maximum diastolic potential (Vmax) during a 2-min period of rapid stimulation. In normal Tyrode solution rapid stimulation resulted in an initial decrease followed by an increase in Vmax. In the presence of Mn the initial depolarization was reduced and the late hyperpolarization increased, suggesting reduced accumulation of $[K]_o$ during overdrive. In higher concentrations Mn caused generalized depolarization. Under these circumstances, rapid stimulation resulted in a marked increase in Vmax within the first few beats. This result could occur if the shortened cycle length increased gK, thus reversing the reduced gK caused by Mn. This idea is further supported by the observation that elevation of $[K]_o$ following Mn depolarization resulted in hyperpolarization. These findings are consistent with the hypothesis that manganese blocks potassium conductance. (Supported in part by USPH Grant HL 16135-01CVA and ONR Contract N00014-68-A-0216 (NR 101-722).)

TRANSMURAL DISTRIBUTION OF ATP AND GLYCOLYTIC INTERMEDIATES AFTER CORONARY ARTERY LIGATION IN DOGS. J.W. Holsinger, Jr., T.B. Allison and R.S. Eliot (intr. by Nina Himwich). Cardiovascular Center, University of Nebraska Medical Center, Omaha, Nebraska.

The shift to anerobic metabolism in skeletal muscle during stress provides sufficient ATP to maintain muscle function. The possibility that subendocardial levels of ATP were maintained by increased glycolysis during ischemia was examined. Ischemic periods (5 min.→4 hr. n=20) were produced by left circumflex artery ligation. Transmural tissue samples were obtained from the center of the ischemic zone and frozen in liquid N_2. The frozen plug was divided into outer (EPI), MID, and inner (ENDO) portions. Metabolites were determined in each portion; values are μmol/g dry wt. In controls (n=14), ATP decreased EPI→ENDO (27.1±0.8→22.9±0.9); glucose-6-phosphate (G6P) increased slightly (0.30±0.07→0.55±0.10) and the lactate/pyruvate (L/P) ratio increased (3.9±0.4→6.4±1.5). Pyruvate levels did not change at any time. After 4 hrs. of ligation (n=5), the subendocardium demonstrated the most significant metabolic changes. ATP: EPI↓72.5% (27.1±0.8±7.5±0.5); ENDO↓86.3% (22.9±0.9→3.13±0.3); G6P: EPI↑3.9-fold (0.30±0.07→1.16±0.43); ENDO↑21.2-fold (0.55±0.10→11.64±1.1); L/P ratio: EPI↑6.6-fold (3.9±0.4→25.6±5.7); ENDO↑10.2-fold (6.4±1.5→65.1±9.1); $p < 0.001$. Elevated levels of G6P and the L/P ratio are indicative of increased glycolysis (via increased glycogenolysis and glucose transport) and decreased pyruvate utilization in oxidative metabolism. The magnitude of ATP depletion in all layers of the ischemic zone indicate that glycolytic production of ATP cannot protect the myocardium from ischemic insult for even short periods of time.

THE EFFECT OF ADENOSINE INFUSION ON OXYGEN CONSUMPTION OF CONTRACTING IN SITU GRACILIS MUSCLE. Donald H. Horstman*, Malcolm Gleser* and James C. Delehunt*, (intr. by Sumner M. Robinson). U.S. Army Research Institute of Environmental Medicine, Natick, MA.

Muscle blood flow ($\dot{Q}$) and oxygen consumption ($\dot{V}O_2$) were determined at submaximal and maximal stimulation rates in the contracting gracilis muscle of the dog. Comparisons (n=6) were made between adenosine (0.4 mg/ml) and isotonic saline, infused into the gracilis artery at a rate of 0.3 ml/min. Blood flow was measured by timed collections of gracilis venous outflow. $\dot{V}O_2$ was calculated from $\dot{Q}$ and measurements of arterial and gracilis venous blood oxygen content ($avDO_2$). Vasodilatation resulted from adenosine infusion as $\dot{Q}$ was, on the average, about 25% greater at submaximal stimulation rates and about 10% greater at maximal stimulation rates than with saline infusion. At submaximal stimulation rates (resulting in $\dot{V}O_2$ between 60 and 90% of maximal $\dot{V}O_2$), $\dot{V}O_2$ was consistently about 5% greater with adenosine infusion than with saline infusion. In experiments in which maximal stimulation rates were achieved (as evidenced by plateauing of $\dot{V}O_2$), no significant difference in maximal $\dot{V}O_2$ was observed between the adenosine and saline infusions. From these data it was concluded that the increased oxygen delivery resulting from increased $\dot{Q}$ at high, yet submaximal work rates, resulted in significant increases in oxygen utilization by the working muscle. It is speculated that this increased aerobic metabolism was accomplished in lieu of anerobic metabolism.

LEFT VENTRICULAR DYNAMICS DURING RECOVERY FROM EXERCISE. Lawrence D. Horwitz, James M. Atkins* and Stanley A. Dunbar*. The University of Texas Medical School at San Antonio, San Antonio, Texas.

Left ventricular dynamics during recovery were measured in 10 dogs, 3 minutes after brief periods of mild, moderate and severe treadmill exercise. Compared with resting values, postexercise heart rates were moderately elevated, stroke volume was unchanged, and the maximum first derivative of the left ventricular pressure was either unchanged or slightly elevated. With moderate and severe exercise, left ventricular end-diastolic diameter increased and continued to be elevated during recovery ($p < 0.05$ after both moderate and severe effort). End-systolic diameter decreased during exercise but was elevated above resting values during recovery from moderate ($p < 0.01$) and severe ($p < 0.05$) exercise. It is concluded that, with strenuous exercise, a sympathetic discharge results in an increase in contractility which recedes promptly during the postexercise period but the Frank-Starling mechanism continues to be a factor. As a result cardiac output exceeds resting values but, since myocardial oxygen consumption is probably low, there is prompt restoration of depleted oxygen stores.

STRYCHNINE ACTION ON SINGLE NEURONS OF THE PERICRUCIATE CORTEX. Chuong C. Huang* and Amedeo S. Marrazzi. Univ. Mo. Inst. Psychiat., St. Louis, Mo.

Although strychnine is now generally regarded as a blocker of inhibitory synapses with observed excitation interpreted as a release phenomenon, some questions still persist as to a direct component in increased EPSPs. In most such cortical studies some form of topical strychnine application has been utilized. Due to the ease of continuous monitoring of gradual onset, plateauing and gradual offset of action following close-arterial (intracarotid) injection, we have applied this method to extra- and intracellular recording from glass micropipets in the pericruciate cortex of the flaxedilized cat. In 122 units in 32 exp. the doses of strychnine sulfate used were from 30 to 300 μg/Kg with 75-150 μg/Kg optimal. Our results show that the primary action which occurs within 20 seconds is inhibitory (81 ū) instead of excitatory (6 ū). Excitation occurred in minutes always following inhibition as a post-inhibitory rebound. In intracellular records, the reduced spike rate is accompanied by hyperpolarization and increased membrane resistance. Thus our results indicate that strychnine's excitation is a release phenomenon. In agreement, we have found that strychnine blocks cortical synaptic inhibition as by indole and catechol amines, which increase membrane resistance, as well as by GABA and glycine, which decrease it. Because of these opposite resistance changes we have had to conclude that strychnine is a non-specific blocker or, possibly, a weak specific blocker for 5HT, NE and LSD and a weak non-specific blocker for GABA and glycine. Unlike the parallel slopes of the dose-response curves for 5HT and its specific blocker CPZ, the strychnine curve is very different with a small slope. Our preliminary equilibrium potential studies do not suggest competitive inhibition between 5HT and strychnine. It is hoped that further equil. pot. and PSP studies along with changing the ionic environment will clarify the respective roles of ionic and metabolic processes involved.

Phospholipid fatty acid synthesis: Relative importance of preformed versus endogenously synthesized fatty acids in the perfused rat lung. P. L. Huffman*, R. A. Rhoades, The Pennsylvania State University, University Park, Pa. 16802

The lung has the ability to esterify exogenous free fatty acid into phospholipids as well as to synthesize phospholipid fatty acid (PLFA) endogenously from glucose. The relative contribution of preformed fatty acid versus endogenous synthesis of PLFA was assessed by comparing the ratio of 9,10-H^3-palmitate to U-^{14}C-glucose incorporated into PLFA. Rat lungs were perfused for 1.5 hr. with a medium containing washed bovine red blood cells resuspended to a 15% Hct with Krebs-Henseleit bicarbonate buffer - 5g% Pentex bovine serum albumin. Glucose and palmitate concentrations were 6mM and 1mM, respectively. Twenty μCi of U-^{14}C - glucose (specific activity 15 mCi/mMole) and 25 μCi of 9, 10 -^3H-palmitate (specific activity 421.5 mCi/mMole) were added as a single pulse into the perfusion medium. Palmitate incorporated into PLFA averaged 3562 ± 225 nmoles/g dry lung/hr (±S.E.) compared to 408.3 ± 48.3 nmoles/g dry lung/hr for glucose yielding a palmitate:glucose ratio of 8.47 ±0.84; indicating 8 moles of fatty acids are converted into PLFA for every mole of glucose. Hypoxia (lungs ventilated with 5% O_2- 5% CO_2 compared to lungs ventilated with 21% O_2 - 5% CO_2) did not alter the relative contribution of palmitate and glucose incorporation into PLFA (ratio = 8.71 ±0.47). Corticosterone (10^{-5}M in the perfusion medium) did not significantly ($P<0.05$) change the ratio (9.34 ±0.8). These data indicate that 1) lung PLFA are synthesized primarily from esterification of preformed fatty acids and endogenous synthesis, either de novo or by chain elongation, is of minor significance; thus emphasizing the importance of fatty acid uptake by lung 2) PLFA synthesis is not immediately affected by hypoxia and corticosterone. (Supported in part by U.S. Air Force Grant #2559.)

EFFECTS OF SODIUM PENTOBARBITAL AND KETAMINE HCL ON THERMOREGULATION IN RHESUS MONKEY. William S. Hunter, Kenneth R. Holmes*, S. Gregory Hipskind*, and Edgar J. Mueller*. St. Louis University School of Medicine, St. Louis, Mo. 63104, and Southern Illinois University--Edwardsville, School of Dental Medicine, Edwardsville, Ill. 62025.

Studies in body temperature regulation are preferably designed to use unanesthetized subjects because drugs commonly used for restraint or anesthesia also compromise homeothermy. Preliminary data indicate that ketamine HCl (dl (2-o-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride) affects thermoregulation less than most other centrally acting restraint or anesthetic agents. While under mild cold stress, adult male or female monkeys (Macaca mulatta, 5-7 kg body wt.) were administered ketamine ranging from low doses (18.2 $mg \cdot kg^{-1}$) suitable for restraining the animal, to high doses (49.8 $mg \cdot kg^{-1}$) producing surgical levels of analgesia. Ambient temperature was maintained constant at 23°C, as was relative humidity (30%). As a steady state thermoregulatory response, the ketamine HCl sedated or anesthetized animals maintained rectal temperature (T_{re}) within $\pm$ 0.5°C of T_{re} at the beginning of exposure, retained peripheral vasoconstrictor tone as indicated by reduced extremity (ear, hand, and foot) temperatures, and maintained metabolic heat production (M) by intermittant bouts of shivering. Sodium pentobarbital anesthetization (52-98 $mg \cdot kg^{-1}$) at the same cold exposure produced immediate increases in extremity temperatures (e.g., 7°C increase in ear skin temperature within 30 min.), reductions in M (29.8 Watts/m^2) and precipitous falls in T_{re} (3-4°C in 2.5 hours). These data indicate that ketamine HCl is effective in quieting or anesthetizing Rhesus monkeys for handling and experimentation without affecting thermoregulatory reflexes as profoundly as conventionally used anesthetics.

DETERMINANTS OF INDUCED SUBENDOCARDIAL ISCHEMIA AS REFLECTED BY DPTI/TTI RATIOS, IN OCCLUDED AND NON-OCCLUDED ZONES OF BOVINE LEFT VENTRICLE. S. Igo,* C. Edmonds,* B. Daly,* D. Hughes,* and J. Norman, Texas Heart Institute, Houston, Texas.

Experiments were designed to compare the effects of transient coronary artery occlusion on myocardial oxygen supply:demand ratios as indirect determinates of subendocardial perfusion in occluded and non-occluded areas of the bovine left ventricle. Ratios less than 0.7 are associated with subendocardial ischemia. Diastolic pressure time index (DPTI) was used as an index of myocardial oxygen supply; tension time index (TTI) was used to quantitate myocardial oxygen demand. Transient (2 minute) focal ischemia was produced by circumflex (Cx) artery occlusion. Mean left ventricular systolic pressure ($\bar{LVP}_S$), mean $\bar{LV}$ end-diastolic pressure ($\bar{EDP}$) and mean coronary artery pressure ($\bar{CAP}$) in the occluded and non-occluded zones were measured. Following Cx occlusion, $\bar{LVP}_S$ and TTI decreased from control levels of 128±12 and 3346±265 to 119±2 mmHg and 3020±363 mmHg sec/min in both zones. The $\bar{EDP}$ increased from 8.7±1.8 to 24±2 mmHg. $\bar{CAP}$ decreased from 118±7 to 107±2 mmHg in the non-occluded zone and from 118±7 to 28±3 mmHg in the occluded zone. DPTI decreased from 3634±267 to 110±122 mmHg sec/min in the occluded zone. The DPTI/TTI ratios decreased insignificantly from 1.09±.12 to 0.98±.21 in the non-occluded zone; they decreased markedly from 1.09±.12 to .04±.05 in the occluded zone. These findings indicate that profound degrees of subendocardial ischemia can be induced in focal areas of the bovine left ventricle in the presence of essentially normal adjacent subendocardial perfusion and that the major determinant is a decrease in $\bar{CAP}$; simultaneously, in the adjacent non-occluded zone a minor decrease in subendocardial perfusion occurs and is due to increased LV end-diastolic pressure.

EFFECT OF POTASSIUM ON SLOW CHANNEL-DEPENDENT AUTOMATICITY IN GUINEA PIG VENTRICULAR MYOCARDIUM. Sunao Imanishi* and Borys Surawicz, UNIVERSITY OF KENTUCKY MEDICAL CENTER, LEXINGTON, KENTUCKY.

Membrane potential was changed uniformly in guinea pig papillary muscle (< 1 mm long, < 0.6 mm diameter) using extracellular depolarizing current pulses (3-7 sec) applied across two electrically insulated chamber compartments. Rhythmic automatic depolarizations (AD) occurred spontaneously in 62 of 69 fibers (89.8%) at membrane potential ranging from -35.2 ± 7.5 (threshold) to + 4.0 ± 9.2 mV (n=62). The rates, maximum dV/dt and overshoots of AD were not dependent on the level of depolarization, and ranged from 2.3 to 2.6 c/sec, 16.2-20.0 V/sec and 48-59 mV respectively. Raising extracellular Ca^{++} concentration (Ca_e^{++}) from 1.8 to 6.8 mM/L or application of Isoproterenol (10^{-6} g/ml) enhanced the rate of AD while lowering Ca_e^{++} to 0.4 mM/L or application of 6 mM $MnCl_2$ solution suppressed AD.

AD were enhanced by lowering extracellular K^+ concentration (K_e^+) from 5.4 to 1.5 mM/L. AD were abolished in 60% of fibers by raising K_e^+ to 15.4 mM/L, and in all fibers by raising K_e^+ to 40 mM/L. This abolition was due to increased K_e^+ and not due to K^+ - induced depolarization because it persisted when membrane potential was held by means of a conditioning hyperpolarizing pulse at the level of control resting potential. The slope resistance increased gradually during slow diastolic depolarization preceding AD.

These results suggest that spontaneous rhythmic AD in fibers with inactivated rapid inward i_{Na} results from the interaction between the time-dependent decrease in outward current (probably i_K) and the background inward current presumably flowing through the "slow channel" carrying Ca^{++} and/or Na^+ ions.

VISION IN SQUIRREL MONKEYS: PHYSIOLOGICAL AND PSYCHOPHYSICAL EVIDENCE OF SEX-RELATED DIFFERENCES. Gerald H. Jacobs. Dept. of Psychology, Univ. of California, Santa Barbara.

Two kinds of evidence have been obtained that strongly implies that male and female squirrel monkeys (Saimiri sciureus) differ systematically with respect to at least some features of visual capacity and visual physiology. First, behavioral measurements of spectral sensitivity have been made in an increment-threshold test situation. Results obtained from a modest sample of squirrel monkeys show the females to have substantially higher sensitivity than males to wavelengths from the 640 nm region of the spectrum. There do not appear to be significant between-sex differences in sensitivity for test lights having shorter wavelength composition. Second, an analysis of unit recordings taken from the lateral geniculate nucleus of this species reveals a clear difference between the two sexes--males and females show significant differences in the relative proportions of the various varieties of chromatic-opponent cells. Although the reasons for these sex-related differences remain obscure, some possible relationships between the physiological and behavioral results can be discerned. (Supported by NSF Grant GB-23551x2)

RESPONSES OF THE PARASYMPATHECTOMIZED CANINE HEART TO NEUROHUMORAL STIMULATION. H. K. Jacobs*, W. C. Randall and M. P. Kaye. Loyola Univ., Stritch Sch. of Med.,Dept. of Physiology,2160 S.First Ave.,Maywood,Ill.

A technique of selective cardiac parasympathectomy and verification testing has been described. This report describes the responsiveness of the model to acetylcholine (ACh), norepinephrine (NE), nitroglycerin (NTG) and methoxamine (MX). Dose response curves to systemic injections of these drugs were established in tranquilized (Sparine, 5 mg/kg) dogs while recording electrocardiograms and systemic blood pressure (BP) before and after parasympathectomy. The absence of supraventricular dysrhythmia along with insignificant atropine induced cardiac acceleration was considered evidence for complete denervation. For a given decrease in BP in response to injected ACh, a greater reflex increase in heart rate (HR) was realized in normal animals than in parasympathectomized animals. In several of the parasympathectomized dogs, an initial decrease in HR was seen upon ACh injection; a phenomenon not observed in the control animals at the low doses used. NE increased BP and reflexly slowed the heart in controls. An identical increase of BP in the parasympathectomized dogs resulted in an increase in HR in response to NE. Preliminary data indicates that MX sensitivity did not differ between controls and experimental animals. NTG caused a greater increase of HR in control dogs than in parasympathectomized dogs. Atropine resulted in a severalfold increase in HR with a concurrent increase in BP in controls. An increase in HR in response to atropine injection was interpreted as incomplete parasympathectomy in the model. The procedures described adequately test the completeness of the parasympathectomy. The possibility exists that an ACh caused bradycardia at very low doses develops as a function of parasympathectomy. The data can be explained in terms of removal of the baroreceptor parasympathetic link to the heart in the model described. *(Supported by NIH Grant HL 08682)*

VENTILATION IN CONSCIOUS DOGS DURING ACUTE AND CHRONIC HYPERCAPNIA.
D. B. Jennings and C. C. Chen*. Dept. of Physiology, Queen's University, Kingston, Ontario.

Dogs were prepared with chronic tracheostomies for placement of an endotracheal tube with 2-way valve for measurement of minute ventilation. Arterial blood samples were obtained from a catheter placed in an exteriorized carotid artery. Six dogs were studied at rest while breathing 5% CO_2 in air acutely and during chronic hypercapnia after 2, 4, 7 and 14 days exposure to 5% CO_2 in air in a chamber. Appropriate control studies with the dogs breathing air were carried out for both the acute and chronic hypercapnia experiments. A triphasic ventilatory response was observed over the 14 days of hypercapnia. After an initial increase in ventilation during acute hypercapnia, ventilation returned to the control level at two days of hypercapnia. Although a reduction in ventilatory drive might be anticipated secondary to readjustments of cerebrospinal fluid acid-base balance at 2 days, we did not expect to find ventilation within normal limits. Another unexpected finding was that subsequently, from 4 to 14 days of hypercapnia, ventilation increased again, relative to control. This secondary increase in ventilation occurred despite the fact that blood acid-base balance was compensated as predicted from the data of other workers. Surprisingly, there was no hypoventilation during the immediate recovery period from chronic hypercapnia. We interpret these findings to indicate that other factors in addition to acid-base balance may play a role in the regulation of ventilation in the conscious resting dog during chronic hypercapnia and during the recovery period from chronic hypercapnia.
Supported by the Ontario Heart Foundation and the Defence Research Board.

ROLE OF ANGIOTENSIN II IN EXPERIMENTAL RENAL HYPERTENSION IN THE RABBIT.
J. A. Johnson, J. O. Davis and B. Braverman*. Dept. of Physiology, University of Missouri School of Medicine, Columbia, Mo. 65201.

Hypertension was produced in rabbits by constricting the left renal artery; in 9 rabbits the opposite kidney was removed and in 8 rabbits the opposite kidney was left intact. To investigate the role of angiotensin II (A-II), 1-sarcosine-8-alanine-angiotensin II, a competitive antagonist of A-II, was infused at 6 µg/min/kg body wt. for 30 minutes in conscious animals. In a control group of 7 unilaterally nephrectomized rabbits mean arterial pressure averaged 81 mm Hg and infusion of the A-II antagonist did not alter the arterial pressure. In a group of Na-depleted rabbits arterial pressure decreased from 81 mm Hg to 63 mm Hg ($P < 0.01$) in response to the A-II analog. Thirty days after renal artery constriction 7 of the 9 one-kidney hypertensive rabbits had normal values for plasma renin activity (PRA) and during infusion of the A-II antagonist arterial pressure was unchanged. However, two rabbits had elevated PRA and the arterial pressure decreased during infusion of the angiotensin analog. In the two-kidney hypertensive rabbits PRA was normal and the arterial pressure was unchanged by infusion of the A-II antagonist. These studies provide evidence that hypertension developed with either high or normal plasma A-II levels in the one-kidney animals; the two-kidney rabbits developed chronic hypertension in which no role for A-II could be demonstrated.
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ANDROGEN MEDIATED SEX DIFFERENCES IN PLATELET AGGREGATION. Malcolm Johnson* and Peter W. Ramwell. Dept. Physiology and Biophysics, Georgetown University, Washington, D.C. 20007.

Coronary heart disease and related cardiovascular lesions occur predominantly in males. Platelet sensitivity to a primary-aggregating stimulus (ADP) was ten times greater in male rats than in females. A similar trend (x 3) was observed in a small population (n=12) of humans. Castration resulted in a decline (x 4) and an increase (x 5) in aggregability, and the same final responsiveness, in male and female animals respectively. Pre-treatment with testosterone (1mg/Kg S.C.) or with estradiol (1mg/Kg S.C.) led to an enhanced (x 3) or a depressed platelet response to ADP. In vitro incubation with physiological concentrations (1 - 10ng/ml) of testosterone potentiated (18.0 ± 1.5 - 40.0 ± 5.0%) rat, guinea pig and human platelet aggregability over that in control (untreated) or estrogen, progestogen or corticosteroid-treated plasma. Irreversible secondary aggregation (collagen or arachidonic acid) was significantly more enhanced (97.0 ± 4.5%) by testosterone than reversible primary aggregation (ADP or epinephrine), in male and female human or guinea pig platelets. The rank order of effectiveness: dihydrotestosterone, testosterone, nortestosterone, methyltestosterone, androstendione and androsterone correlates with the androgenic potency. The effect of the androgens was antagonized in vitro by either an anti-androgen (Flutamide; Schering, U.S.A.) or by a female sex hormone (estradiol). These data suggest a specific role for androgens in vivo in increasing platelet sensitivity to aggregating-stimuli, an established parameter in the development of cardiovascular lesions. Supported by The Education Foundation of America.

REGULATION OF CELL VOLUME BY NA-K AND NA-CA TRANSPORT SYSTEMS IN TAENIA COLI OF THE GUINEA PIG. Allan W. Jones, Dept. of Physiology, U. of Mo. Medical School. Columbia, Mo. 65201.

The maintainence of cell volume in a membrane regulated system is usually thought to result from a balance between Donnan forces, active transport of Na-K, and the differential permeability of the membrane ($P_K > P_{Na}$). However, shifting this balance in various smooth muscles by inhibiting Na-K transport with ouabain or K-free solution has not resulted in the predicted increase in cell volume. This study confirmed that 10^{-5}M ouabain or K-free Krebs resulted in <10% swelling although >90% of cell K had exchanged for Na. Calcium removal under these conditions resulted in uptake of Na and Cl and swelling (>40%). Removal of Ca in the absence of ouabain (Na-K transport operating) caused little change in cell volume, but subsequent addition of ouabain resulted in 40% swelling. Calcium removal acutely decreased ^{24}Na efflux from ouabain treated taenia coli indicating coupling between Na and Ca transport. The counter transport of at least 2 Na for 1 Ca could result in the net movement of solute with an osmotically equivalent shift in water. It is suggested that Na-K and Na-Ca transport systems, operating in parallel, contribute to cell volume regulation in smooth muscle. (Supported in part by USPHS NIH Grant HL 15852 and the American Heart Association).

REFLEX RESPONSES FROM TYPE J PULMONARY RECEPTORS IN THE NEWBORN KITTEN. Madhu Kalia (Intr. by D. Scott, Jr.). Cardiovascular-Pulmonary Div., Dept. of Medicine, Univ. of Pennsylvania, Philadelphia, PA 19104

In recent years considerable interest has centered around reflexes arising from type J pulmonary receptors in adult animals and man. Nothing is known, however, about the existence of the J receptors or the level of function of their reflexes in the newborn. Fifteen kittens ranging from 1 day to 3 weeks of age were studied in the present series. Nembutal, 25 mg/kg I.P. was used as anesthesia. Right atrial and aortic catheters were introduced. Respiration was monitored using a saline-filled esophageal catheter connected to a Statham transducer. EMG of quadriceps and gastrocnemius was also recorded. J receptor stimulation was produced by right atrial injections of phenyl diguanide (pdg) 80 µg/kg. In adult cats within 2 seconds this dose produces reflex apnea followed by rapid shallow breathing, bradycardia, hypotension and skeletal muscular inhibition (Dawes, Mott and Widdicombe, 1959; Deshpande and Devanandan, 1970). In the newborn kitten (1 day to 6 days old) it was not possible to elicit any response with the adult dose of pdg. The dose was increased stepwise from 80 µg/kg (i.e. 8 µg for a 100 gm kitten) to 2 mg/kg at which a short apnea lasting 2 breaths and fall in blood pressure of about 5 mm Hg was observed. In order to produce the full adult responses 8 mg/kg pdg was required. One week old kittens showed fully developed adult respiratory and cardiovascular responses but no effect on motor activity. Three week old kittens show all reflex responses seen in the adult. All these reflexes were abolished after bilateral vagotomy. Similar responses were obtained in two awake kittens with chronic indwelling catheters. The results suggest that J receptor reflexes are poorly developed in newborn kittens and visceral reflexes develop earlier than motor reflexes. (Supported in part by NIH grant HL-08805).

HUMORAL OPSONIC DEFICIENCY IN THE ETIOLOGY OF HEPATIC RETICULOENDOTHELIAL FAILURE FOLLOWING SHOCK. J.E. Kaplan* and T.M. Saba, Department of Physiology, Albany Medical College, Albany, N.Y. 12208

Temporal alterations of the reticuloendothelial system (RES) following sublethal traumatic shock have been previously correlated with changes in circulating opsonic activity (Fed. Proc. 33:298,1974). In the present investigation associated alterations of R.E. function and plasma opsonin levels were investigated following varying degrees of traumatic shock. Male rats (200-350 g) subjected to graded degrees (0-700 rev) of Noble-Collip Drum (NCD) trauma under sodium pentobarbital anesthesia (2 mg/100g) were evaluated 60 min following the initiation of trauma. R.E. function was determined by the phagocytic clearance of systemically injected ^{131}I labelled colloid and plasma opsonin levels were assessed by radio-bioassay. Hepatic R.E. depression was directly correlated with the degree of traumatic shock, being maximally depressed 50.2% at 700 rev. ($p<.001$). In contrast, pulmonary localization of blood-borne particulate matter increased with intensity of traumatization reaching a peak level of 216.7% ($p<.01$) of normal at 700 rev. Splenic phagocytosis increased following sublethal trauma (<300 rev) but manifested progressive failure with further increments in traumatic injury. Opsonin levels declined in direct relationship to the degee of trauma as well as the severity of hepatic R.E. failure with a decline of 73.3% at 700 rev. ($p<.001$). In contrast, at extremely mild traumatization, at a level utilized to develop shock tolerance, an elevation in circulating opsonic activity was observed. These data support the hypothesis that a humoral opsonic deficiency may be mediating the RES depression following traumatic shock. The relationship of this observation to the development of irreversible circulatory failure during shock warrants consideration.

(USPHS - CA-16011 and AM-14382)

PATHWAY SPECIFICITY OF REFLEX HEART RATE CONTROL DUE TO AORTIC NERVE STIMULATION IN THE RABBIT. M.B. Kardon*, D.F. Peterson and V.S. Bishop. Univ. Tex. Health Sci. Ctr., San Antonio, Texas 78284.

Reflex bradycardia was elicited in a total of 23 rabbits via repetitive electrical stimulation of the central end of the sectioned left aortic nerve. The evoked potential was monitored in all experiments. Cardiac R-R interval was monitored "on line" using a PDP 8E digital computer. Supramaximal stimulation (all afferent nerve fibers activated) produced a 14.4 + 1.3% SE increase in R-R interval with vagal and sympathetic efferent pathways intact. Reducing stimulation voltage allowed selective stimulation of the myelinated (A) fibers. Placement of a pair of polarizing electrodes central to the stimulus site permitted A fiber blockade and selective stimulation of the unmyelinated (C) fibers in the aortic nerve. Bilateral vagotomy in 13 animals reduced the peak bradycardia by 45% when all afferents were activated, by 61% when A fibers were activated, and by 48% when C fibers were activated. Stellectomy in 10 animals reduced the peak bradycardia by 26% when all afferents were activated and by 54% when only the A fibers were activated. There was no significant change in reflex bradycardia elicited by stellectomy when only afferent C fibers were stimulated. These findings suggest that reflex bradycardia observed during aortic nerve stimulation in the rabbit is partially mediated by reciprocal changes in vagal and sympathetic efferent activity in response to increased activity of myelinated afferents whereas unmyelinated aortic nerve afferents mediate heart rate primarily by way of vagal efferent pathways. Analysis of the latencies to onset and peak of the reflex bradycardia indicated that those afferent fibers which alter vagal efferent activity cause more rapid reflex heart rate effects than do those which alter sympathetic efferent activity. (Supported in part by NIH Grant #HL 12415-06 and AFOSR Contract #71-2074D).

COMPETITIVE INHIBITION OF PANCREATIC PROTEIN SECRETION BY ISOPROTERENOL. G. A. Kelly*, R. C. Rose and D. L. Nahrwold. The Pennsylvania State University, College of Medicine, Hershey, Pa. 17033.

These experiments were designed to determine the effect of a beta-adrenergic stimulant on pancreatic protein secretion. Four dogs were prepared with gastric and pancreatic fistulae and were studied in the conscious state with the gastric fistula open and the pylorus occluded with an inflated balloon to prevent endogenous secretin release. In one group of experiments the C-terminal octapeptide of cholecystokinin (octa-CCK) was infused intravenously in logarithmically increasing dosages which ranged from 31.5 to 1000 ng/kg-hr. In another group of experiments isoproterenol 7.5 µg/kg-hr was infused intravenously during infusion of octa-CCK in the above dosages. Mean pancreatic protein output in response to octa-CCK progressively increased from 226 mg/15 min at the 31.5 ng/kg-hr dose to 438 mg/15 min at the 1000 ng/kg-hr dose. When isoproterenol was infused with octa-CCK, mean pancreatic protein output at the 31.5 ng/kg-hr dose was 84 mg/15 min, which was significantly lower than the response to octa-CCK alone ($P<0.001$). However, when isoproterenol was infused with octa-CCK at the 1000 ng/kg-hr dose, mean pancreatic protein output was 483 mg/15 min, which was not significantly different than the response to octa-CCK alone. When the data from the dose-response curves for octa-CCK alone and for octa-CCK plus isoproterenol were plotted as response versus response/dose or as the reciprocal of the response versus the reciprocal of the dose, the criteria for competitive inhibition were met. The study shows that isoproterenol competitively inhibits the action of octa-CCK on the output of protein from the canine pancreas.

THE EFFECTS OF EXPERIMENTAL INCREASE IN AIRWAYS RESISTANCE ON THE VENTILATION RESPONSE TO REBREATHING CARBON DIOXIDE. Harold Keltz*, Uma S. Mathur*, and Daniel J. Stone, Veterans Administration Hospital, Bronx, N.Y., and Mount Sinai School of Medicine, New York.

FEV1, MMEF, SGaw were measured prior to and following the infusion of propranolol in twenty healthy, trained male subjects (ages 21-28). In five of these same subjects, 400 micrograms of histamine HCL was administered by nebulization and these studies repeated. In addition, the ventilation response to rebreathing carbon dioxide (modified Read method) was determined in all subjects before and after the infusion of propranolol, 0.15 mg/kilo. The ventilation response was also determined before and after histamine nebulization; oxygen consumption ($\dot{V}_{O2}$) was measured during the several periods of C_{O2} rebreathing. FEV_1, MMEF and SGaw decreased significantly following the administration of both propranolol and histamine. The ventilation response to carbon dioxide rebreathing was significantly decreased by either propranolol or histamine. The oxygen consumption per unit of ventilation measured during C_{O2} rebreathing, significantly rose following propranolol infusion and histamine inhalation. It is concluded that the decrease in ventilation response to carbon dioxide which follows propranolol and histamine administration is due to their constrictive effects on the airways; the determination of the C_{O2} ventilation response curve is another method of detecting airways disease. (Supported in part by grants from the A.M.A. Education and Research Foundation Committee for Research on Tobacco & Health; and Stony Wold Corp.)

A METHOD FOR THE CONTINUOUS DETERMINATION OF LEFT VENTRICULAR COMPLIANCE CHANGES BY THE MEASUREMENT OF PHASIC TRANSMITRAL FLOW IN THE DOG. A. Kennish, E. Yellin, R. Gowda and R.W.Frater (intr. by H.D. Lauson). Albert Einstein College of Medicine, Bronx, New York.

With this report we introduce a method of determining left ventricular diastolic compliance dynamically on a beat-to-beat basis, in the open chest dog. The technique is applicable to monitoring compliance changes during transient and long term (i.e., over many beats) interventions such as changes in: heart rate, contractility, preload, afterload, inflow, outflow, and normal rhythm. During cardiopulmonary bypass an electromagnetic flow probe is sutured supra-annularly to the mitral annulus and the wires brought out the appendage. High fidelity catheter tip transducers measure left ventricular and atrial pressures; a cuff-type electromagnetic flow probe measures ascending aortic flow; and these, along with dP/dt and ECG are recorded on an oscillographic recorder. A sonic digitizer, programmable calculator and X-Y digital plotter are used to analyze the data. Aortic and mitral flow are digitized and integrated to give stroke and filling volume, and a pressure-volume diagram is plotted for any diastolic period of interest, in particular, over any transient sequence of beats. An initial volume is assumed and all subsequent calculations are based on a change in volume. The method's accuracy has been verified by the consistency of results, and the ability to plot a linearly ascending portion of the Frank-Starling curve during volume infusion. Although highly invasive, this method is more accurate than echo- or radiographic means of calculating ventricular volumes, and should prove to be a useful research tool capable of elucidating mechanisms of compliance changes in the intact heart. It should thus prove valuable in the interpretation of data obtained by conventional, non-invasive, but less accurate means.

EFFECTS OF AGING AND SEX ON RAT LIVER AND BRAIN SUBSTRATE, ENZYME, AND COENZYME LEVELS. J.S. Kerr* and H.M. Frankel. Dept. of Physiol. and Bur. Biol. Res., Rutgers Univ., New Brunswick, New Jersey 08903.

Liver and brain tissue substrate, enzyme and coenzyme levels were determined in male and female rats at 3, 6, 12, 18 and 24 months of age. Liver aspartic, citric, glutamic, α-ketoglutaric and malic acids, NAD^+, NADH, $NADP^+$, NADPH, and glutamic, lactic and malic dehydrogenases were determined in tissues removed within 15 seconds, frozen and maintained in liquid N_2. The same procedures and determinations, with the exception of $NADP^+$ and NADPH levels, were used for brain tissue. Liver substrate levels of aspartic, α-ketoglutaric and malic acids were significantly ($P \leq 0.01$) higher in female than in male rats at 3 and 18 months. (Aspartic acid: 0.67 vs 0.46 μmoles/gm tissue at 3 months, and 0.82 vs 0.56 μmoles/gm tissue at 18 months; α-ketoglutaric acid: 0.11 vs 0.05 μmoles/gm tissue at 3 months and 0.27 vs 0.14 μmoles/gm tissue at 18 months; malic acid: 0.29 vs 0.13 μmoles/gm tissue at 3 months and 0.33 vs 0.24 μmoles/gm tissue at 18 months.) In the male, aspartic, glutamic, α-ketoglutaric and malic acids, $NADP^+$ and NADPH levels were highest at 18 months. In the female, aspartic, glutamic, α-ketoglutaric acids, $NADP^+$ and NADPH levels were highest at 18 months. Liver glutamic and malic dehydrogenase activities were significantly ($P \leq 0.01$) higher in female than in male rats at 24 months. (Glutamic dehydrogenase: 78.2 vs 34.2 IU/gm tissue; malic dehydrogenase: 544.4 vs 378.7 IU/gm tissue.) In brain tissue, aspartic, glutamic and malic acid levels decreased significantly ($P \leq 0.05$) from 3 to 24 months in the females, while no significant differences were observed in the males. No significant differences were observed between the sexes in substrate or coenzyme levels in the brain. Age-related dietary alterations may have contributed to the tissue changes observed with aging.

ACUTE PRESSURE CHANGES IN NORMAL AND SURFACTANT DEPLETED DOG LOBES. William R. Kimball*, Edmund E. Faridy, and Robert E. Dutton. Systems Engineering Division, Rensselaer Polytechnic Institute, Troy, New York, Department of Physiology, University of Manitoba, Winnipeg, Canada, and Department of Physiology, Albany Medical College, Albany, New York.

Twelve excised dog lobes were sequentially inflated and deflated with air in constant volume steps lasting 150 seconds, after one previous lobe inflation. Surfactant depletion was accomplished by ventilation at 60% total lobe volume for three hours with humidified nitrogen. Pressure relaxation, the pressure decrease at constant lobe volume during stepwise lobe inflation, was recorded at 1.5, 5.0, and 20.0 seconds after the start of flow, while the pressure rise after a step decrease in lobe volume on the deflation limb, pressure recovery, was recorded at similar time intervals. A statistically significant downward displacement of the depleted lobe volume-pressure curve was noted ($p < 0.01$). Pressure relaxation of normal lobes was greater than that of depleted lobes both shortly after flow ended and at large final pressures. During deflation the pressure recovery of depleted lobes was almost constant at all final lobe pressures, while normal lobes showed decreasing recovery as final pressure approached 2 cm H_2O. The greatest difference occurred between 4 and 7 cm H_2O ($p < 0.01$). Semilogarithmic plots of pressure relaxation vs time demonstrated two significantly different slopes ($p < 0.01$) with time as the logarithmic variable. Absence of time dependent pressure change appears to exist on the deflation limb of the normal curve at a final pressure of approximately 18 cm H_2O. Thus, it appears that alveolar closure occurs at almost all lung volumes in depleted lobes.

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$^{45}Ca^{++}$ EFFLUX FROM RAT LEFT VENTRICULAR MUSCLE. Albert C. Kirby* (introduced by B. D. Lindley), Dept. of Physiology, Case Western Reserve University School of Medicine, Cleveland, Ohio, 44106.

Rat left ventricular papillary muscles or trabeculae carnae, approximately 0.5 mm in diameter and 1 cm long, were loaded with ^{45}Ca for 2-3 hours. Washout samples were collected according to the method of Curtis (J. Gen. Physiol. 55:243, 1970) up to 5 hours and exponential curves fit to the amount of ^{45}Ca remaining in the muscles. ^{45}Ca exchange can be described by the sum of three exponentials. The time constants are approximately 2 1/2 min, 30 min and 3-4 hours. One-half of the exchangeable calcium resides in the slowest exchanging component. The fastest exchanging component is most likely extracellular space and the intermediate one sarcoplasmic reticulum. When rat LVP or TC are stimulated to contract in 0 Ca^{++} medium tension decline can be described with the sum of 2 exponentials with approximate time constants of 2 1/2 min and 30 min. Likewise, ^{45}Ca washout in these same muscles washes out with similar time constants. Even though sufficient calcium remains in the slowest exchanging component to saturate troponin, no tension is developed. It therefore appears that Ca in the first and intermediate components is responsible for activating contraction in rat ventricle. Supported by grants NIH NS-10196, HD-0066-9 and the Greater Cleveland Health Fund.

BRAIN TEMPERATURE DURING REVERSIBLE UPPER RESPIRATORY BYPASS IN THE RABBIT. Matthew J. Kluger and Louis G. D'Alecy*. Dept. of Physiology, Univ. of Michigan Medical School, Ann Arbor, Mich.

This study was designed to test the hypothesis that animals lacking a carotid rete can effectively cool their brains by upper respiratory heat exchange. Seven male New Zealand white rabbits were trained to run in an exercise wheel. At least 5 days prior to experimentation, each rabbit had a reversible tracheal bypass cannula and a hypothalamic thermocouple guide tube chronically implanted. The reversible tracheal bypass enabled the rabbit to breathe normally (through its upper respiratory pathways) or to be placed on "bypass" (breathe through its neck). Prior to exercise, rectal temperature in the "normal" rabbits averaged 0.19°C higher than hypothalamic temperature ($P<0.02$, paired t-test). Following a mild heat stress induced by exercise, this difference increasedto an average of 0.31°C ($P<0.001$, paired t-test). The difference between rectal and hypothalamic temperature following exercise (0.31°C) was statistically greater than the difference preceeding exercise (0.19°C) ($P<0.05$, paired t-test). When the rabbits breathed through the bypass, the cooling of arterial blood by upper respiratory heat exchange was eliminated, and therefore there were no differences between hypothalamic and rectal temperature. These data suggest that even in a species such as the rabbit which lacks a carotid rete, hypothalamic temperature is influenced by upper respiratory cooling of venous blood and that the ensuing transfer of heat from the warmer internal carotid artery to the cooler venous sinuses can effectively cool the brain. (Supported by Rackham Fund 360612 and 360145 and NSF GB 42749X)

EFFECT OF PARATHYROID HORMONE ON SEGMENTAL PHOSPHATE REABSORPTION IN THE THYROPARATHYROIDECTOMIZED DOG. Franklyn G. Knox and Claude Lechene, Department of Physiology, Mayo Clinic, Rochester, Minnesota and Department of Physiology, Harvard Medical School, Boston, Massachusetts.

The sites of inhibited phosphate transport following administration of parathyroid hormone (PTH) to thyroparathyroidectomized dogs (TPTX) were investigated using the recollection micropuncture technique and the electron probe methodology. Ten dogs were thyroparathyroidectomized 18 hours before recollection experiments. Samples of proximal tubule fluid, blood, and urine were collected before and one hour after infusion of 3.3 u/kg prime and 0.1 u/kg/min infusion of bovine PTH or in the absence of hormone infusion in control experiments. Three TPTX dogs which did not receive hormone did not have significant changes in segmental phosphate reabsorption. Following infusion of PTH in seven dogs, the TF/UF phosphate concentration ratio was not significantly changed from .56 $\pm$ SE .05 to .58 $\pm$ .06, the TF/P inulin concentration ratio was decreased from 1.47 $\pm$ .04 to 1.28 $\pm$ .06, $p < .01$ and fractional phosphate reabsorption was decreased from 62 $\pm$ 3% to 55 $\pm$ 4%, $p < .025$. Glomerular filtration rate, renal plasma flow and blood pressure were not significantly changed. Urinary phosphate excretion increased from 3.6 $\pm$ 1.1% to 25.7 $\pm$ 3.0% of the filtered load following PTH infusion, $p < .001$. The decrease in proximal phosphate reabsorption accounted for less than ½ of the increased phosphate excretion in the urine. It is concluded that parathyroid hormone inhibits phosphate reabsorption from nephron segments both proximal and distal to the site of micropuncture in the thyroparathyroidectomized dog. (Supported by NIH grants HL-14133, 18518, 15552, AM-16898 and RR-00679).

THE EFFECT OF SALINE LOADING ON GASTRIC SECRETION. Irwin Koplovitz* and Eugene J. Zawoiski. Department of Physiology, Jefferson Medical College, Philadelphia, Pa. 19107.

The effect of intravenous saline loading (0.4 ml/kg/min for 2 hr) on gastric secretory output was studied in 30 chloralose-urethane anesthetized dogs equipped with a gastric fistula, tracheotomy and both femoral arterial and venous catheterizations. Following a one-hour basal period, gastric samples were collected every 15 minutes under a variety of conditions, including i.v. histamine infusion, i.v. saline loading, saline loading following histamine, and histamine following saline loading. Hematocrit values were determined at intervals: saline loading caused a drop of the hematocrit which ranged between 15.7 and 21.7 percent. Gastric secretory volume and acid output during the saline loading period were significantly higher than basal secretory output whenever the gastric glands were previously stimulated with histamine up to one hour prior to the start of the saline loading period. In contrast, there was no significant increase in gastric secretory output during the saline loading period when histamine had not been previously administered. Saline loading, with the accompanying blood dilution, significantly increased ($p<0.01$) the gastric secretory volume, acid, chloride, and pepsin output in response to histamine. The increase due to the saline was blocked by an intravenous injection of atropine (20 mcg/kg base). These responses to the saline loading were dependent on the relative state of activity of the gastric glands. The augmented histamine-induced response following saline loading, and the resultant blockade with atropine, suggest that in addition to hemodilution there may also be a neurohumoral component.

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TRANSIENT AND STEADY-STATE CHANGES IN BLOOD GASES AND RENAL EXCRETION OF BICARBONATE IN RESPONSE TO GRADED STEPS OF HYPOCAPNIA IN DOGS. Esmail Koushanpour and J. W. McAuley*. Department of Physiology, Northwestern University Medical School, Chicago, Illinois 60611.

This study was designed to determine whether, in respiratory alkalosis, the renal excretion of bicarbonate, $\dot{E}\text{-}HCO_3$, is a direct consequence of changes in the arterial CO_2 tension, pCO_2. If so, we would expect $\dot{E}\text{-}HCO_3$ to closely follow transient changes in pCO_2. Experimental protocol consisted of measuring, in five female dogs, two-hour transient changes in arterial pCO_2, pH and bicarbonate concentration, as well as $\dot{E}\text{-}HCO_3$ after a single step hypocapnia. In five other female dogs, steady-state changes in the same variables were measured after successive stepwise increase in hypocapnia. In all dogs, hypocapnia was induced by hyperventilating the animal at a constant frequency of 15/min with a stepwise increase in the tidal volume by a Harvard positive pressure respirator. Analysis of transient data showed that $\dot{E}\text{-}HCO_3$ reached 90% of its steady-state value (T_{90}) an average of 5.6 min after that for either pH or pCO_2. This time-delay exceeded the blood transport tion lag of 1-1.5 min. The difference in T_{90} between $\dot{E}\text{-}HCO_3$ and pH and between $\dot{E}\text{-}HCO_3$ and pCO_2 averaged 17.0 and 9.8 min, respectively. The transient data is consistent with the view that renal excretion rate of bicarbonate is mediated via cellular-controlled mechanisms rather than as a direct consequence of changes in pCO_2. Results of the steady-state experiments revealed an initial progressive rise in $\dot{E}\text{-}HCO_3$ with increasing step hypocapnia, which declined as hypocapnia was continued. This latter finding corroborates the cellular-controlled mechanisms and suggests the possibility of intracellular potassium concentration as the key factor modulating renal response to prolonged hypocapnia. (Supported in part by a NHLI Grant No. 5-R01-HE09735-08.)

RELATION OF THE PITUITARY GLAND TO GONADAL HORMONE EFFECTS ON THE RAT ADRENOCORTICAL 11β - HYDROXYLASE SYSTEM. R. Kramer*, J. Greiner*, and H.D. Colby, West Virginia Univ., Sch. of Medicine, Morgantown, WV 26506

Previous investigations have demonstrated that testosterone inhibits and estradiol stimulates adrenocortical 11β-hydroxylase activity in rats. Studies were initially carried out to determine if gonadal hormone effects on 11β-hydroxylation were manifested as sex differences in enzyme activity. Adrenal mitochondria from adult female Holtzman rats contained significantly higher concentrations of cytochrome P-450 (0.90 ηmoles/mg prot), the terminal oxidase for 11β-hydroxylation, than those from adult males (0.76). Nonetheless the rates of conversion of 11-deoxycorticosterone (DOC) to corticosterone (B) did not differ (4.6 vs. 5.0 ηmoles/min/mg prot). Moreover, the magnitude of the DOC-induced spectral change in adrenal mitochondria was similar in males (0.023 Δ OD/mg prot) and females (0.022). The concentration of high spin cholesterol sidechain cleavage cytochrome P-450, as reflected by the pregnenolone - induced difference spectrum, was also not sex-dependent (0.015 vs. 0.014). Additional studies were conducted to determine whether the effects of testosterone and estradiol on the 11β-hydroxylase system were demonstrable in hypophysectomized rats. Administration of either hormone did not affect enzyme activity or mitochondrial cytochrome P-450 concentration in the absence of the pituitary gland. ACTH administration, however, increased both 11β-hydroxylase activity (9.4 vs. 4.9) and mitochondrial cytochrome P-450 content (0.93 vs. 0.42). The results indicate that no sex difference in 11β-hydroxylation exists in rats and that gonadal hormone effects on the enzyme are mediated by the pituitary gland, perhaps via their known effects on ACTH secretion. (Supported by NSF Grant GB41215)

MORPHOLOGICAL CHANGES CORRELATED WITH STEADY STATE RESPONSES OF A MECHANORECEPTOR. J. Krauhs* and M. Mirolli. Dpt. Physiology, Indiana University, Bloomington, In.

The S neurons of the crustacean coxal receptors respond with a sustained generator potential lasting for at least 20 min. when a thin muscle, to which they are attached, is stretched by the rotation of the coxa about its hinge on the thorax. The S neurons terminate with two long dendrites (1-1.3mm long) oriented parallel to the long axis of the receptor muscle. Secondary branches arise from the main trunk of the dendrites; these branches are oriented perpendicular to the longitudinal axis of the muscle and in their turn terminate with a great number of thin tubular processes, oriented parallel to the longitudinal axis of the muscle. The processes are embedded in amorphous connective tissue which also contains bundles of collagen fibrils. S neurons were fixed in glutaraldehyde in phosphate buffer with and without stretch being applied to the muscle. Some specimens were perfused with 5mM lanthanum chloride before fixation, and in both stretched and relaxed specimens, the extracellular space around the sensory terminals was open to the large particles of colloidal lanthanum. In both cases one cannot observe, by transmission electron microscopy, any specialized region of attachment between the sensory endings and the collagen fibrils. The secondary branches were more stunted in the receptors fixed when stretched than they were in the relaxed ones. By contrast the diameters of the tubular processes were considerably smaller in the stretched (0.08μm) than in the relaxed (0.11μm) receptors.

TETANIC STIMULATION REDUCES EVOKED POTENTIALS TO SMALL MODE MINIATURE ENDPLATE POTENTIALS (MEPPs). M. E. Kriebel and C. E. Gross (intro. by O. H. Muller). Upstate Medical Center, Syracuse, New York.

Amplitude histograms of spontaneous MEPPs from the frog myoneural junction show a multimodality with a distinct mode of small MEPPs. After successive short periods of nerve stimulation the small mode MEPPs progressively dominate the histograms (Kriebel and Gross, 1974, J. Gen. Physiol. 64, in press). We determined amplitude histograms from edge fibers of the sartorius muscle establishing the position of the small mode MEPPs. After withdrawing the electrode, the sartorius nerve was stimulated at 40 Hz until fatigue at which time the fiber was repenetrated and stimulated at 10 Hz. We then measured the amplitudes of spontaneous MEPPs and endplate potentials (EPPs) until 90% failures occurred. Sequential MEPP and EPP histograms were plotted. After fatigue there were no failures and the EPP histogram was a flat distribution over an amplitude spread several times the mean of the control plot of spontaneous MEPPs. When we experienced 10% failures the EPPs appeared fairly equally distributed among multiple modes covering an amplitude spread about that encountered in the control MEPP plot. At 50% failures most of the EPPs were concentrated below the mean MEPP amplitude of the control plot. With increasing proportion of failures the EPPs were comparable in amplitude to the small mode MEPPs and the spontaneous potentials were also reduced to small mode MEPPs. We also determined MEPP amplitude histograms after sequential periods of stimulation until only small mode MEPPs remained. These small mode MEPPs showed a progressive decrease in amplitude suggesting partial filling. These experiments suggest that small mode MEPPs represent single quanta.

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COMPARISON OF LIMITS OF PRESCRIPTIVE ZONES FOR HEART RATE AND RECTAL TEMPERATURE. K. V. Kuhlemeier and J. C. Petersen (Introduced by Gordan M. Schoepfle) University of Alabama Medical Center, Birmingham, Ala.

Fully clothed healthy men aged 20-50 years walked on a treadmill at a low (122 Kcal/hr/m^2) or a high (235 Kcal/hr/m^2) metabolic rate (MR) at Corrected Effective Temperatures (CET) ranging from 11-35°C. Wet Bulb Globe Temperatures (WBGT) ranged from 8-37°C. Rectal temperatures (RT) and heart rates (HR) after one hour of work were determined. A total of 224 work bouts were performed at CET's selected to fall distinctly above or below the projected limit of the prescriptive zone (LPZ) as defined by A. Lind (J. Appl. Physiol. 18:51-56, 1963). For each metabolic rate pairs of simple linear regression equations based on these data were developed for the regions above and below the projected LPZ. Regression analyses were carried out on the four possible combinations of dependent variables, HR and RT, and independent variables, CET and WBGT. The point of intersection for each pair of regression lines was determined and considered to be the LPZ. The LPZ's for both CET and WBGT of HR and RT at each MR were:

	CET, °C		WBGT, °C	
	HR	RT	HR	RT
Low MR	27.9	28.3	26.5	29.7
High MR	22.7	24.4	23.3	23.9

These data indicate that the LPZ for HR is lower than the LPZ for RT when the environmental heat stress is expressed in terms of CET or WBGT for both high and low metabolic loads. We conclude that HR should be given as much or more attention than RT in determining limits of heat tolerance. (Supported by National Institute for Occupational Safety and Health Contract No. HSM 99-72-45)

ELECTROPHYSIOLOGICAL EFFECTS OF PROSTAGLANDINS E_1 AND $F_{2\alpha}$ ON RAT PREGNANT UTERINE MUSCLE. M. Kumamoto*, A. Nakajima*, H. Niu* and L. Horn, Kyoto and Yamaguchi Universities, Japan and New Jersey Medical School, Newark, N.J., U.S.A.

Intracellular recording from pregnant rat uterine muscle revealed dual, concentration dependent, effects of prostaglandins (PG) E_1 and $F_{2\alpha}$. At low concentrations (10^{-9} to 10^{-8} g/ml) spike amplitude and duration of trains of spikes increased initially, followed by an increasing number of abortive spikes. High concentrations (10^{-6} g/ml) reduced the spike amplitude, followed by cessation of spike activity and membrane oscillations associated with sustained contraction. Using double sucrose gap voltage clamping techniques, it was shown that PG in high concentration depress the early inward current and also shifts the reversal potential to the left (more negative). PG also increases steady state outward current. These effects were reversible. It is remarkable further that PG produced contraction of strips soaked in Ca^{++}-free EDTA containing Krebs solution and in the presence of transition metals (i.e. Mn^{++}). PG also increased force development of preparations depolarized by high $[K^+]_o$. The action of PG will be discussed in terms of its effects on ion permeability and in terms of a possible "direct" effect on force development of uterine smooth muscle. (This study was supported by funds from the Japanese Ministry of Education and the Upjohn Company.)

COMPARTMENTAL ANALYSIS OF VENTILATION-PERFUSION RATIOS IN MAN. T. Kunieda*, A. C. Young and C. J. Martin. Virginia Mason Res. Ctr. and Univ. of Wash., Seattle, Wash.

From an 18-breath nitrogen washout, lung compartments with specific ventilation-to-volume ratios ($\Delta V/Vo$), known N_2 concentrations, and a variable contribution to the expirate were measured (JAP 32: 644, 1972). By estimating O_2 and CO_2 concentrations in the compartments, their ventilation-perfusion ratios ($\dot{V}_A/\dot{Q}$) can be calculated. A compartment with a $\dot{V}_A/\dot{Q} = 0$ was included. Mixing equations for O_2 and CO_2 used the relationship between a change in concentration of gas at mouth level and that estimated in the compartment, corrected for CO_2 production and O_2 uptake during expiration. We assumed a linear relationship with time: $F_{oE}co_2 = \sum_{i=1} \beta_i F_{oCO_2}^{(i)}$; $F_{oE}O_2 = \sum_{i=1} \beta_i F_{O_2}^{(i)}$ where F_{oE} is the corrected concentration of gas at mouth level, $F_o^{(i)}$ is the gas concentration at the beginning of expiration in compartment i and βi is the fraction of gas flow from compartment i. Solutions of simultaneous equations derived from the original equation gave compartmental O_2 and CO_2 concentrations. Applied to a Dill nomogram, the variables related to $\dot{V}_A/\dot{Q}$ were obtained. A mass spectrometer analyzed expired gas (N_2, O_2, CO_2) during air breathing. $\Delta\dot{V}$ was proportional to time as the subjects followed a moving line on a CRT having a sawtooth pattern. This was followed by a N_2 wash, analyzed in the usual fashion and an estimation of virtual venous CO_2 (rebreathing method). Four normal subjects and one with severe obstructive syndrome were studied. The $\dot{V}_A/\dot{Q}$ was ordered in the same manner as $\Delta V/Vo$, i.e., the compartment with lowest $\Delta V/Vo$ had the lowest $\dot{V}_A/\dot{Q}$. There was no relationship between $\dot{Q}/Vo$ and $\dot{V}_A/\dot{Q}$. The subject with obstructive syndrome had a compartment with lowest $\dot{V}_A/\dot{Q}$ and the most shunt (10%).

EFFECT OF HYPEROXIA ON AVIAN REGULATION OF CO_2. A. Kunz and J. King, Dept. of Physiology, Ohio State Univ. College of Med., Columbus, Ohio 43210.

These experiments were carried out on an awake, unidirectionally-ventilated chicken preparation. Air forced thru the bird at 5 L/min. (10 x resting min. vent.) assures that the bird's respiratory movements will not change the CO_2 concentration in its lungs. This opens the CO_2 regulator loop. The loop is then reclosed externally by using a computer to set $\% CO_2 = \int(Q - C \dot{V}_I)\, dt$; where Q is the analog of rate of metabolic CO_2 production, $\dot{V}_I$ is inspiratory ventilation, and a and c scaling constants. This forms a stable system for the regulation of CO_2. Pulses of high $\dot{Q}$ produce fluctuations of CO_2 typical of responses of a linear second order system. The damping ratio of the response reflects the sensitivity of the receptor. When the normoxia (20% O_2) is changed to hyperoxia (50-70% O_2) the CO_2 rises to a higher level. After about 2 to 5 min. the bird brings its CO_2 level back down (usually accompanied by a momentary shift of posture). The response to a Q pulse now shows a decreased damping ratio. Our model interprets this as an increase in receptor sensitivity and/or increased feedback delay. (Supported in part by O.N.R. Grant 101-733 and N.H.L.I. Grant HL 14870-02).

FURTHER STUDIES OF GASEOUS NITROGEN EXCHANGE IN MAN. I. Kupprat*, B. A. Hertig, R. E. Johnson and D. Pierce*.

Since publication of earlier observations from our laboratory (J. Appl. Physiol. 32:155, 1972; Aerospace Med. 43:1, 1972) challenging the long-held tenet that atmospheric gaseous nitrogen (N_2) plays no active part in human respiration, other investigators have studied the phenomenon of N_2 evolved/retained. For the most part, they have reported either no inequality in minute volumes of N_2 ($\dot{V}N_2$) inspired versus expired ($\Delta\dot{V}N_2$) or an N_2 inequality ($\Delta\dot{V}N_2$) such that the quantities of N_2 evolved or retained were insignificant to effect use of the Haldane transformation. We have extended our earlier studies to cover a longer period of observation (3 hrs/test period) in which respiratory data were collected at more frequent intervals (20 min), and inspired and expired air were analyzed for N_2 content. As before, dietary intake was controlled with equivalent amounts of protein (5 kcal pro/kg body wt) fed to 9 male subjects 1 1/2 hrs prior to the observation period. They either rested or walked at 4.8 km/hr. The data from these studies are consistent with those reported previously from this laboratory as to N_2 inequality. However, in plots of $\Delta\dot{V}N_2$ versus time, reversal of sign in $\Delta\dot{V}N_2$ was observed in some tests. For example, in a fast-rest exposure, N_2 retention during the first 1/2 hr was followed by N_2 evolvement for the remainder of the test. N_2 exchange in general was variable among subjects. These findings may offer an explanation for the lack of confirmation of the $\Delta\dot{V}N_2$ phenomenon from other laboratories.

FUNCTIONAL CHANGES WITH XENOGENIC PERFUSION OF ISOLATED LUNGS
K. Kusajima*, S.D. Wax*, W.R. Webb, and J.C. Aust*, SUNY Upstate Medical Center, Syracuse, New York 13210.

To evaluate functional changes in xenografts, isolated, ventilated cat lungs were perfused at physiologic pressures with heparinized venous blood from dogs. Pulmonary blood flow diminished to 41% of control at five minutes ($p < .02$) and to 14% at 15 minutes ($p < .005$). Pulmonary vascular resistance increased four fold at five minutes and seven fold at fifteen minutes ($p < .005$). Dynamic pulmonary compliance with constant volume ventilation diminished only slightly to 83% of control value at 15 minutes. Pulmonary venous blood had normal pH, pCO2 and pO2 even at 15 minutes. By cinemicroscopy, pulmonary xenografts (cat to dog) show capillary sludging within two minutes and almost complete cessation of flow within 15 minutes. The lungs showed cellular aggregation, congestion, perivascular infiltration, and severe interstitial and alveolar edema. These observations show that the explosive hyperacute xenograft rejection has as its early manifestation the irreversible plugging of arteriolar and capillary circulation which would totally destroy function regardless of other alterations.

DEVELOPMENT OF SUGAR TRANSPORT SYSTEMS IN EMBRYONIC CHICK HEART. Howard Kutchai and Susan L. King*, Dept. of Physiology, University of Virginia, Charlottesville, Virginia 22901.

We are attempting to characterize the systems for sugar transport in chick embryo heart at 5-6, 10, 15, and 20 days (just before hatching) of incubation. Sorbitol, a sugar to which adult heart cells are impermeable, is taken up by embryonic chick heart at each stage of development. The permeability of the cell membrane to sorbitol decreases as development proceeds. The sorbitol transport system is distinct from the glucose carrier since glucose at concentrations in excess of the K_m for glucose transport does not inhibit sorbitol uptake. The sorbitol system, in common with sorbitol transport in adipose tissue, has very high K_m ($\sim$50 mM). Phloretin (0.2 mM) and metabolic inhibitors do not decrease the rate of sorbitol uptake. The rate of glucose uptake also decreases as development proceeds. This occurs by means of a progressive increase in the K_m and a decrease in the V_{max} of glucose transport. It had previously been reported that glucose transport in 5-day hearts is unsaturable, but we find that at 5-6 days of incubation the K_m for glucose uptake is about 10 mM. We are unable to demonstrate a response of glucose transport to insulin in 5-6 day hearts. However, the transport of 2-deoxyglucose is stimulated by insulin at 5-6 days as well as thereafter. This is consistent with a recent report that amino acid transport in 5-day hearts is stimulated by insulin.

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EFFECTS OF DIFFERENT CONCENTRATIONS OF FOOD IN THE CANINE JEJUNAL LUMEN ON LOCAL BLOOD FLOW, VENOUS OSMOLALITY, LUMEN VOLUME, AND MOTILITY. P. Kvietys*, R. Pittman* and C.C. Chou. Depts. of Physiology and Medicine, Michigan State University, E. Lansing, MI.

Placement of undiluted, digested food in the jejunal lumen increases local blood flow(Physiologist 16:494, 1973). We compared the effects of luminal placement of undiluted and diluted (1:2, 1:4, and 1:9) digested food on blood flow (BF), venous osmolality (Vosm), lumen pressure (LP) and volume (LV) in double jejunal segments (J. Lab. Clin. Med. 75:729, 1970). One segment (control mean BF, 0.52 ml/min/gm) contained 10 ml of normal saline and the other (control mean BF, 0.45 ml/min/gm) 10 ml of a food solution for 15 min. Normal saline was used as the control for food solutions. As compared to the changes occurring in the saline segments the changes occurring in the segments containing food solutions were:

	N	BF(%)	Vosm(mOsm/kg)	LV(ml)	LP
Food 1:0	6	+43.2*	+10.6*	+3.3*	Increased
Food 1:2	7	+27.0*	+3.0	+0.8	No change
Food 1:4	7	+21.0*	+2.2	-0.4	No change
Food 1:9	6	+18.9*	-0.7	-1.3*	No change

*Statistically significant, p 0.05.

The systemic arterial pressure remained unchanged. The changes in venous osmolality and lumen volume suggest that undiluted food is hypertonic, 1:2 or 1:4 food is nearly isotonic and 1:9 food is hypotonic to plasma. All of these solutions caused an increase in blood flow,but only undiluted food increased jejunal motility. Thus, the increase in local blood flow following luminal placement of food into a jejunal segment is not entirely dependent upon its motility or the tonicity of its contents. Also, the increase in blood flow caused by the 1:4 food solution was much greater than isotonic glucose and comparable to 50% glucose solutions studied earlier(Surgery 71:380, 1972). (Supported by NIH Grant HL15231)

ALTERATIONS IN SICKLE BLOOD P_{50} AND BOHR EFFECT. L.H. Laasberg*, M.B. Laver, J. Hedley-Whyte and Y-F. Teng*. Department of Anaesthesia, Harvard Medical School, Boston, Mass. 02215.

Oxygen affinity for normal hemoglobin can be manipulated by benzoic acid derivatives (Laver et al., Fed. Proc. 33:735, 1974). We have determined the effect of orthoiodosodium benzoate (OISB) on oxygen affinity of sickle blood, hemoglobin S and S cell suspensions in Krebs-Henseleit (K-H) solutions at known 2,3-diphosphoglycerate(2,3-DPG) concentrations. Alterations of O_2-affinity and sickle hemoglobin conformation due to halothane (2-bromo, 2-chloro-1,1, 1-trifluoro ethane) were also evaluated. At pH 7.40 the partial pressure (P_{50}) required for half saturation of control sickle blood with O_2 was 30.8 mm Hg (Hb9.5). Bohr effect (Δ log P_{50}/Δ pH) between pH 6.91 and 7.56(PO_2 23.8 - 40.4, and PCO_2 = 37 mm Hg) was -0.53. The 2,3-DPG concentration in these specimens was 0.87± 0.015 M/M Hb. In presence of 0.05 M OISB in sickle blood, red cell suspension and hemoglobin solution the P_{50} was increased by 4.2, 6.5 and 7.5 mm Hg respectively at 37°C. The effect of halothane on P_{50} in sickle blood is complex. Exposing sickle blood to halothane (13 mg/100ml equilibrating gas) for 30 mins. the P_{50} is 29.5 mm Hg. After 100 mins. exposure to halothane at 37°C the P_{50} is 31.9 mm Hg. These changes in O_2-affinity are small but significant by paired t-test ($P<0.02$). The 2,3-DPG concentration did not change significantly during exposure to halothane for 2 hrs. at 37°C. Optical rotatory dispersion (ORD) and circular dichroism (CD) measurements indicate that halothane causes conformational changes in sickle hemoglobin molecules. These results indicate that O_2-affinity of sickle blood is affected by various chemicals in a most complex manner.

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HYPOXIC DEPRESSION OF VENTILATION. S. Lahiri and R.G. DeLaney*, Cardiovascular-Pulmonary Div., Dept. of Med. and Physiol., University of Pennsylvania, Philadelphia, Pa. 19104

The natives of high altitude with blunted ventilatory sensitivity to hypoxia hyperventilate on breathing 100% O_2 during rest unlike normal sojourners at high altitude. It has been suggested (e.g. Lahiri and Edelman, Respir. Physiol. 6:375, 1969) that relief of hypoxic depression after breathing 100% O_2 at high altitude might have contributed to the increased ventilation in the absence of a normal peripheral chemoreflex. This idea led us to investigate the role of hypoxic depression in the regulation of ventilation. We used cats anesthetized with pentobarbital. Ventilation, arterial blood pressure, end-tidal P_{O_2} and P_{CO_2} were recorded continuously. Arterial P_{O_2}, P_{CO_2} and pH were measured in spot samples. After recording the steady state effects of several levels of PaO_2 ranging from hypoxia to hyperoxia on ventilation and on arterial PCO_2 and pH, the carotid sinus nerves of the animal were cut. One of the central ends of the cut sinus nerves was stimulated electrically (2-6 V, 0.5 msec duration, 5-20 cps) to produce the same previously established ventilation at a given level of hypoxia mimicking the effect of hypoxia on ventilation in the intact animal. On breathing 100% O_2, while the stimulation was continued, the steady state ventilation increased invariably. At the same level of electrical stimulation, the effects of several levels of PaO_2 were investigated. The ventilation was consistently greater at a higher PaO_2 for a given stimulation of the sinus nerve. These results showed that changes in PaO_2 produced an effect on ventilation independent of and opposite to that elicited through peripheral chemoreflexes. It is suggested that a part of this effect is due to hypoxic central depression. (Supported in part by NIH grant HL-08805).

AUTOREGULATION OF SKELETAL MUSCLE BLOOD FLOW DURING HEMORRHAGE. B. LaLone*, J. Schwinghamer, and J. Hall*, Dept. of Physiol., Mich. State Univ., E. Lansing, Mich.

A number of investigators have demonstrated that skeletal muscle blood flow is autoregulated so that relatively small changes in flow occur despite large changes in arterial perfusion pressure. In this study we examined blood flow autoregulation in the surgically isolated, naturally perfused, innervated gracilis muscles of 10 anesthetized dogs when sympathetically mediated vascular tone was elevated by hemorrhage. While the animals were normovolemic and normotensive, gracilis artery perfusion pressure was reduced by compression of the upstream femoral artery with a screw clamp. When gracilis artery pressure was reduced in steps from a control value of 131±3.9 to 112±3.4, 97±3.5, 86±4.3, and 70±3.9 mm Hg gracilis muscle blood flow decreased from 12.6±1.9 to 9.9 ±1.3, 8.8±1.1, 8.6±1.2, and 8.3±1.1 ml/min·100 gms^{-1}, respectively. The clamp was then released and after a brief stabilization period, the animals were rapidly hemorrhaged into a pressurized reservoir so that mean systemic arterial pressure fell from 135±3.8 to 119±2.6. While the animals were maintained hypovolemic and hypotensive, the femoral artery clamp was again adjusted so that gracilis arterial pressure fell from 117±2.7 to 104±2.4, 90±3.7, 78±2.3, and 65±3.2 mm Hg causing gracilis muscle blood flow to decrease from 6.9±0.7 to 6.2±0.6, 5.7±0.6, 5.6±0.7, and 5.2±0.7 ml/min·100 gms^{-1}, respectively. These data indicate that autoregulation of blood flow in the gracilis muscle vasculature was not attenuated by the sympathetically mediated increase in vascular tone accompanying hemorrhage.

DIFFERENTIAL EFFECTS OF VENTROMEDIAL HYPOTHALAMIC LESIONS ON REPRODUCTIVE ACTIVITY IN THE FEMALE RAT. T.J. La Vaque* and C.H. Rodgers. West Side V.A. Hospital , and Biological Laboratories, Dept. of Psychiatry, U. of Illinois Medical School, Chicago, Ill. 60612

A series of experiments investigated the effect of lesions aimed at either the anterior or posterior aspect of the ventromedial hypothalamic nucleus (VMN). Subsequent to lesioning, sexual behavior estrous cycles and ovulation were evaluated. All lesions were performed under ether anesthesia on the morning of proestrus in females showing at least two 4-day or 5-day estrous cycles preceding surgery. Lesions in the anterior VMN region resulted in a high incidence of attacks directed toward the male. Several females died as the result of fights initiated with stimulus males. Coitus and ovulation were blocked and estrus cycles showed variable lengths.

More posteriorly placed lesions in the VMN did not result in high incidences of attack behavior precipitated by male sexual attempts, and the females showed lordosis responding. Estrous cycles tended to be prolonged with a high incidence of consecutive days of vaginal cornification. Receptivity in females with posterior VMN lesions was similar to that observed in females with retrochiasmatic knife cuts in that receptivity occurred on consecutive days. Coitus did not result in reflexive ovulation. The differentiation of reproductive activity on the basis of anterior vs. posterior VMN lesions is of interest in light of reports of differential accumulation of labeled estrogen in the anterior and posterior regions of the VMN.

MICROPUNCTURE STUDY OF SULFATE REABSORPTION IN THE RAT KIDNEY.
C. Lechene (intr. by A. C. Barger), Department of Physiology, Harvard Medical School, Boston, Massachusetts.

The pattern of sulfate reabsorption along the nephron was defined using micropuncture technique and electron probe microanalysis. Sulfate reabsorption was compared to phosphate reabsorption measured in the same samples. Proximal and distal tubular fluid, urine and blood samples were collected in 8 rats during moderate saline diuresis (infusion of isotonic NaCl at 96.6 µl/min). Mean GFR was 1.18 ± .22 SD ml/min; single nephron GFR = 27.5 ± 11.2 nl/min (N = 46); plasma ultrafiltrate sulfate concentration = 2.05 ± .4 mM/l. The concentration of sulfate in samples from the earliest accessible proximal tubule (PT) was less than that in plasma. For all PT collections the mean TF/P sulfate ratio was .76 ± .24 (N = 46) and while the mean percentage of filtered water remaining was 57% [TF/P_{In} = 1.76 ± .51 (N = 46)], the fraction of filtered sulfate remaining was 47% ± 23 (N = 41); this fraction decreased to 22% ± 4 (N = 9) in the late accessible PT (TF/P_{In} = 2.62 ± .27). In four distal tubules TF/P_{In} was 2.59 and it remained 13% of the filtered sulfate. In the urine U/P sulfate ratio was variable (7.44 ± 5.20) while the fraction of filtered sulfate excreted was nearly constant (5.34% ± 1.89). The results indicate that the bulk of sulfate reabsorption occurs in the early proximal tubule. The comparison between fractional sulfate excretion in the superficial distal tubules and the urine may indicate some reabsorption in the collecting ducts. Lastly, the pattern of sulfate reabsorption in the proximal tubule is similar to that of phosphate.

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CENTRAL VENTILATORY INTERACTION OF HYPOXIA AND HYPERCAPNIA. Lu-yuan Lee*, Howard T. Milhorn, Jr., and John A. Lerch*. Dept. Physiology, Univ. Miss. Med. Center, Jackson, MS

The response of the central respiratory mechanisms to CO_2 in anesthetized dogs was investigated with a cross-perfusion technique. The recipient dog was vagotomized to abolish the stimuli from the aortic chemoreceptors. The circulation of the carotid chemoreceptors was isolated from the systemic circulation and perfused continuously with blood from the donor dog. To control the carotid chemoreceptor CO_2-H^+ drive, the donor was artifically ventilated after complete peripheral chemoreceptor denervation. Arterial blood pressures of both recipient and donor dogs were controlled by the height of a common blood reservoir. The peripheral chemoreceptor drives were set at three different levels by ventilating the donor dog with different O_2 concentration gas mixtures(10, 21 and 100%). For each concentration of O_2 used to ventilate the donor, $\dot{V}$-Pa_{CO_2} lines were obtained while the recipient breathed either normal air or low oxygen. Arterial blood samples were taken at the end of a 6 min on-transient. A 6 min recovery period was allowed between stimulus periods. Results in 6 experiments suggest that the interaction between hypoxia and the $\dot{V}$-Pa_{CO_2} response occurs not only at the peripheral chemoreceptors but also in the central nervous system. With the carotid chemoreceptor drives maintained at normal level, the slope of the $\dot{V}$-Pa_{CO_2} line of the central respiratory mechanism decreased from 0.52 (liter/min/mm Hg) while breathing room air to 0.45 during hypoxia($P<0.05$). The central respiratory response to a given rise in arterial P_{CO_2} is depressed by hypoxia and is not significantly affected by the variation of peripheral chemoreceptor drives.

EFFECT OF GASTRIN AND RELATED PEPTIDES ON H SECRETION BY NECTURUS GASTRIC MUCOSA. Marian LeFevre, Jesse M. Berkowitz, and Melvin Praissman. Nassau County Medical Center, Brookhaven National Laboratory and School of Medicine, SUNY.

The effects of synthetic human gastrin I (G), the C-terminal tetrapeptide of gastrin (TP) and the C-terminal octapeptide of cholecystokinin (OP) on acid secretion by the Necturus gastric mucosa were determined in a chambered preparation. All three peptides caused H secretion but the stimulation was less with the (OP) than with (G) or (TP). Single doses of (G)(concentrations of $5x10^{-9}$ to $5x10^{-7}$M; 15 experiments) or (OP) ($3x10^{-8}$M) stimulated H secretion for at least three hours while the response to single doses of (TP) ($5x10^{-7}$ to $1x10^{-5}$M; 26 experiments) lasted only 1.5 hours. (TP) solutions that had already been used to cause secretion were unable to stimulate a new mucosa, but fresh (TP) solutions were able to stimulate the mucosa. A steady high secretory level could be obtained by renewing the (TP) solution every 30-50 minutes. These findings indicate that (TP) is rapidly inactivated and suggests a protective role for the N-terminal 1-13 peptide fragment of gastrin. Paired mucosa from single animals were treated with repeated doses of (TP) ($5x10^{-6}$M) and (OP) ($3x10^{-8}$M) together. (TP) induced H secretion was reduced 64% in the presence of (OP) during a three hour period ($p<.001$, 10 experiments). (G) induced stimulation was also reduced 45% in the presence of (OP) ($5x10^{-8}$M) and this was significant ($p<0.02$). These studies show that the gastric mucosa of Necturus is more responsive to (G) and (TP) than to (OP). We have further shown that a weak agonist of H secretion, (OP), can inhibit stronger agonists. These results indicate that the Necturus gastric mucosa maybe used as an in vitro tool to assess structure-function relationships of G.I. hormones.

GLYCOGENOLYSIS AND MYOCARDIAL DEVELOPED TENSION. Eugene A. Lentini and Clare Johann*. Albany College of Pharmacy, Union University, Albany, N.Y. 12208.

The quantitative relationship between glycogenolysis and the myocardial developed tension during prolonged substrate depletion was investigated. Anterior and posterior trabeculae carneae from the rat's left ventricle were bathed in an appropriate Ringer's solution. The developed tension was measured by standard techniques. The developed experimental model allowed for the accurate determination of changes (Δ) in the concentration of endogenous glycogen due solely to the experimental conditions. The rates of stimulation were 1/sec, 4/sec or 6/sec for a 2 hour period. Muscles were stimulated only at one frequency. The Δ glycogens of muscles stimulated at 1/sec vs 6/sec were significantly different. The cumulative developed tensions at 6/sec vs 1/sec were also significantly different. From a Lineweaver-Burk graph, it was calculated that 1σ glucose produced $3X10^6$ mg cumulative developed tension. The Δ glycogens and developed tensions of stimulated muscles treated with iodoacetate (IAA) were less than that of untreated muscles. Even though lipids contribute to the myocardial energy pool, inhibition of glycolysis with IAA significantly suppressed the contractility of the columnar preparations. The results indicate that in the absence of exogenous substrate glycolysis influences the myocardial developed tension.

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A UNIFYING MEASURE FOR ELECTRICAL MYOCARDIAL STIMULATION AND DAMAGE THRESHOLDS--COMPARISON BETWEEN IN-VIVO AND IN-VITRO DATA. Eugene Lepeschkin, Stanley Rush*, Janice Jones* and Ronald Jones*. University of Vermont, Depts. of Medicine and Electrical Engineering, Burlington, Vermont.

Stimulation (pacing), defibrillation or damage (standstill, rapid arrhythmia or fibrillation) thresholds in myocardial cell cultures (sheets, clumps and aggregates), using currents with uniform density distribution, are compared with similar criteria published in the literature for other preparations using transthoracic electrodes, distant electrodes with isolated hearts in conducting medium, direct epicardial or endocardial electrodes and intracellular electrodes.

The results, when expressed as total current or voltage, vary widely, but can be brought into closer conformity with each other when expressed in terms of current density or electric intensity in the myocardium or the voltage gradient across the cell membrane. The basic principles by which these comparisons have been made are discussed. (Supported by USPHS Grants RO1 HL 15346, RO1 HL 01486 and 5 K6 HL 440.)

STEADY-STATE PRESSURE-FLOW CURVES OF RESTING DOG GRACILIS MUSCLE BY TWO TECHNIQUES. T.A. Lesh, R.F. Bond and H.D. Green. Indiana Univ./Muncie Center for Med. Educ. at Ball State Univ., Muncie, IN 47306 and Bowman Gray Sch. Med., Winston-Salem, NC 27103.

Peripheral circulatory pressure-flow studies under basal conditions require selective alteration of local arterial pressure by invasive techniques that may cause distortion of the data; it is infeasible to evaluate this distortion by the standard of control data from a completely undisturbed preparation, but some useful information is yielded by cross-comparison of results obtained by different methods of pressure control. Accordingly, we made plots of steady-state outflow vs. perfusion pressure (15 mm Hg increments; range 30-150 mm Hg) from 2 series of 6 isolated, acutely denervated, resting gracilis muscles in anesthetized mongrel dogs: Series 1, nonpulsatile perfusion via a roller pump and gracilis-arterial catheter with a Starling-resistance shunt circuit acting as a pressure controller; Series 2, local arterial supply surgically undisturbed, and hindquarters perfusion pressure manually regulated by oscillatory inflation of a balloon in the abdominal aorta distal to the renal artery. No statistically significant difference could be shown between the 2 plots, except marginally at pressures near 150 mm Hg. The generally comparable results with these 2 techniques indicate that catheterization of the gracilis artery, per se, does not greatly alter the shape of the gracilis pressure-flow curve. (Supported by NIH Grants HE-05392 and -00487, plus grants-in-aid from N.C. Heart Assoc. and Ball State Univ.)

NON-CHEMORECEPTOR STIMULUS TO VENTILATION INDUCED BY SODIUM CYANIDE. Sanford Levine (intr. by A. P. Fishman). Cardiovascular-Pulmonary Division, Dept. of Medicine, University of Pennsylvania and VA Hospital Philadelphia, Pa. 19104.

It is well known that an increase in minute ventilation ($\dot{V}E$) follows intra-aortic infusion of sodium cyanide. Previous investigators have attributed this increase in $\dot{V}E$ to cyanide stimulation of peripheral arterial chemoreceptors. The present study seeks to determine the ventilatory response of peripheral chemodenervated (CD) dogs to intra-aortic cyanide infusion. Accordingly, denervation of the carotid and aortic chemoreceptors was carried out in chloralose anesthetized dogs. Completeness of the denervation was tested by having such animals inspire low O_2 gas mixtures; no increase in $\dot{V}E$ was observed. Sodium cyanide (1.2 mg/kg) was administered to CD dogs via a catheter which was positioned in the upper abdominal aorta; a ten-minute infusion period was used in all experiments. Maximum carotid arterial cyanide concentration did not exceed 10^{-5}M. Following cyanide infusion, oxygen consumption decreased and arterial lactate, lactate/pyruvate ratio increased; $S\bar{a}O_2$ and art. [H+] remained constant. $\dot{V}E$ increased 146 $\pm$ 61% and $P\bar{a}CO_2$ decreased 21 $\pm$ 3 mm Hg. These data demonstrate that intra-aortic cyanide infusions, which induce tissue hypoxia, evoke a stimulus to $\dot{V}E$ which arises in tissues other than peripheral arterial chemoreceptors.

THE EFFECTS OF SYSTEMIC HYPOXEMIA ON THE PARTITION OF PULMONARY BLOOD FLOW DURING UNILATERAL HYPOXIC VENTILATION. M.G.Levitzky*, J.C.Newell*, J.A.Krasney and R.E.Dutton. Albany Medical College, Albany, NY 12208

We have recently suggested (Fed. Proc. 33:447,'74) that arterial hypoxemia may interfere with the mechanism attenuating blood flow to the unilaterally atelectatic lung. The present study was undertaken to determine if a similar interaction between the systemic and pulmonary circulations exists during unilateral ventilation with 6% O_2. Mongrel dogs, anesthetized with pentobarbital (30mg/Kg), were artificially respired after differential cannulation of the main stem bronchi with a Carlens catheter. Following median sternotomy, blood flow was monitored by electromagnetic flow probes placed on the left pulmonary artery (Q_L) and on the pulmonary trunk or aorta (Q_T). Blood gases were analyzed by standard electrodes. Following 10 min. of bilateral 100% O_2, 6% O_2 was substituted as the gas mixture inspired by the left lung. PaO_2 was maintained above 70 mm Hg when the right lung was ventilated with 100% O_2. In this situation, $Q_S(=Q_L/Q_T)$ fell to 54$\pm$7%(SEM) of the control value. The right lung was then ventilated with room air (while the left lung still received 6%O_2) causing PaO_2 to fall to 42$\pm$3 mm Hg. This was accompanied by a rise in Q_S to 94$\pm$9% of the control value. Restoration of 100% O_2 ventilation to the right lung restored PaO_2 to levels above 70 mm Hg and Q_S fell to 53$\pm$8% of control. This increase in pulmonary blood flow to the unilaterally hypoxic lung during arterial hypoxemia was also seen in dogs in which the right lung received the 6%O_2, but in contrast, these responses did not occur after peripheral chemoreceptor denervation. These experiments indicate that the attenuation of blood flow to hypoxic lung is not well maintained when arterial hypoxemia is allowed to develop. The peripheral chemoreceptors may mediate this phenomenon.

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OXYGEN CONSUMPTION DURING APNEA IN THE DOG. Y.C. Lin, T.O. Moore* and S.K. Hong, Dept. of Physiol. Univ. Hawaii Sch. Med. Hon. HI 96822.

The existence, in diving mammals, of O_2 conserving mechanisms during apneic diving is convincing, although the evidence is circumstantial. However, it is doubtful that O_2 conserving mechanisms operate during apnea in the "non-naturally" diving mammals, including man, though bradycardia and/or vasoconstriction are present during apnea. Dogs of either sex were anesthetized with 30 mg/kg Nembutal. The trachea was intubated with a cuff endotracheal tube, and apnea was initiated at the end of inspiration by clamping the trachael tube for a total of 80 sec. Bradycardia, reduction in cardiac output and peripheral vasoconstriction developed gradually throughout the entire apneic period. O_2 consumption during apnea was measured by summing the rate of O_2 removal from the lung, from the arterial blood, and from the venous blood. The rate of O_2 removal from the lung was estimated by measuring arterio-venous O_2 difference and cardiac output, and was calculated according to Fick's principle. O_2 disappearance from the blood was estimated by measuring arterial and venous O_2 content at 20 sec. intervals and by assuming a constant blood volume throughout the apneic period of 86 ml/kg, 20% of which is in the arterial tree. Rate of O_2 disappearance from the lung decreased continuously during apnea. The rate of O_2 removal from the lung was one-fifth of the pre-apneic rate, 4.72 $\pm$ 0.20 (7 dogs) ml/min/kg at the end of 60 sec. However, there was no difference in O_2 consumption during apnea up to 60 sec because of depletion of O_2 stores in blood. At 80 sec of apnea, however, the rate of O_2 disappearance from the circulatory system is reduced. This cannot be regarded as O_2 conservation, but rather indicates failure of the organ systems under extreme hypoxia. (Supported in part by ONR contract N00014-67-A-0387-0014, and NOAA 04-3-158-29).

SYSTEMIC HYPOOPSONEMIA AND RETICULOENDOTHELIAL FAILURE DURING HEMORRHAGIC HYPOTENSION IN DOGS. Daniel J. Loegering* and Thomas M. Saba, Department of Physiology, Albany Medical College, Albany, N.Y. 12208

While depression of the reticuloendothelial system (RES) during hemorrhagic shock has been demonstrated, the etiologic mechanism responsible for this RES failure has not been determined. This investigation evaluated the concept that changes in circulating opsonin levels could be involved in the etiology of RES host-defense failure during hemorrhagic hypotension. Male dogs (10-20 kg) anesthetized with sodium pentobarbital (25 mg/kg) and artificially ventilated were hemorrhaged into a pressurized reservoir to a mean arterial blood pressure of 40 mm Hg. Plasma opsonin levels were determined prior to hemorrhage and at 60 min post-initiation of hemorrhage; at 5% uptake; at 15% uptake; and at 30% uptake of the maximum shed blood volume. Opsonin levels were maximally decreased by 40% at 5% uptake as compared to sham hemorrhaged control dogs. RES function was determined by the clearance rate of injected gelatininzed ^{131}I labeled R.E. test lipid emulsion (700 mg/kg). In contrast to control dogs ($t/2$ = 15.6±1.1 min; K = 0.019), there was pronounced R.E. failure in the hemorrhaged dogs ($t/2$ = 45.0±4.5; K= 0.007) primarily due to a significant ($p<.001$) 45% depression in hepatic Kupffer cell phagocytosis. Thus, RES depression associated with hemorrhagic hypotension, especially during the early stages, may be due to a depletion of circulating opsonin protein. Furthermore, these findings suggest that opsonic protein administration (opsonin therapy) may provide a means to circumvent RE failure during shock.

EFFECT OF PROLONGED HEMORRHAGIC HYPOTENSION ON VASCULAR TISSUE CATECHOLAMINE CONCENTRATIONS IN THE RAT. J.H. Lombard,* S. Contney,* and W.J. Stekiel. Dept. of Physiol. Med. Coll. of Wis., Milw. Wis. 53233.

Male rats, averaging 280 g, were anesthetized with sodium pentabarbital and subjected to periods of prolonged hemorrhagic hypotension (MABP = 35 mm Hg). Catecholamines were determined fluorometrically and expressed as μg/g wet wt. (uncorrected for recovery) in tissue samples from the superior mesenteric artery (SMA) and small mesenteric arteries (250 μ) and veins (400 μ). Recovery averaged 65 ± 2% (SEM) for norepinephrine (NE) and 74 ± 5% for epinephrine (E). Measurements were grouped according to the level of compensatory response during the period of hypotensive stress: 1) early and 2) maximum compensation (30 and 70 min. respectively) and 3) early and 4) severe decompensation (90 min. and 30% uptake of maximum bled volume, respectively). In nonhemorrhaged controls, NE concentrations in small arteries averaged 2.1 ± .17 (SEM), which was significantly higher than the mean NE concentrations of small veins (1.0 ± .19) and SMA (0.3 ± .04). This agrees with the greater density of adrenergic innervation of the small arteries. The mean NE concentrations in small arteries during both early and severe decompensation were significantly lower than that of nonhemorrhaged controls. No significant differences were observed in tissue NE concentrations of small veins or SMA between controls and experimental groups. Small artery E concentrations in both decompensatory groups tended to be lower than those of control or early hemorrhage groups. These findings agree with our earlier data reported for dogs and suggest that depletion of adrenergic transmitter, resulting from the hypoxia and ischemia of severe hemorrhagic stress, is an initial step in the failure of compensation in peripheral vascular beds. (Supported by a grant from the Wisconsin Heart Association).

COMPARISON OF CASTOR OIL (CO) TO OLIVE OIL (OO) AS INHIBITORS OF GASTRIC SECRETION. James F. Long and Antoni Wojtowicz*. Schering Corporation, Bloomfield, N. J. 07003

The intestinal hormones, GIP and VIP, have been implicated in certain diarrheal diseases. These same hormones have been shown to inhibit gastric secretion in the dog. The present study was performed to determine if the diarrheagenic lipid, CO, was a more potent inhibitor of gastric secretion than the non-diarrheagenic OO. If so, it would implicate these hormones in the mechanism of CO-induced diarrhea. Inhibition of feeding stimulated gastric secretion with 2 gm/kg and 1 gm/kg of CO or OO was tested in dogs equipped with either Pavlov (PP) or Heidenhain (HP) gastric pouches. These lipids were given p.o. 30 minutes after the meat meal, suspended in a vehicle containing 1% PF68 and 2.4% lecithin. The vehicle itself served as the control. Dose related inhibition was observed in both PP and HP dogs. Maximum inhibition was 80% with OO and 60% with CO in the PP dogs at 2 gms/kg and 75% and 40%, respectively, in the HP dogs. The duration of the inhibition was longer in the PP dogs when CO was given than with OO. In the HP dogs, a marked "rebound" in gastric secretion occurred with the CO which was not present in the PP dog. Diarrhea was consistently observed in those dogs which received 2 gm/kg CO. These results indicate that the diarrhea seen after CO does not involve increased release of intestinal hormones which have gastric inhibitory activity.

SIZE OF ARTERIOVENOUS ANASTOMOSIS IN THE FEMORAL CIRCULATION. V. Lopez-Majano, S. C. Lin and J. K. Lee, Chicago Med. School and Gottlieb Memorial Hospital, Chicago, Il.

Plastic carbonized microspheres 50 and 200 micra in diameter labeled with Yterbium^{169} were injected in the common femoral artery of living dogs under general anaesthesia to study arteriovenous shunting in the femoral circulation. Shunting was demonstrated when the 50 micra particles were injected because radioactivity corresponding to between 5 and 50% of the injected dose was detected in the lungs. When the size of the microspheres was 200 micra, no radioactivity was detected over the lungs. This indicates that the arteriovenous anastomosis in the femoral circulation are smaller than 200 micra. The distribution of the femoral circulation in the whole limb was studied by injecting the same particles into the femoral artery and sacrificing the animals. The skin, muscle and bone were isolated and counted separately. There was less radioactivity in the skin when the 50 micra size particles were injected which indicates that most of the arteriovenous anastomoses are located in the skin.

OPSONIN MEDIATED ALTERATIONS IN HEPATIC AND SPLENIC MACROPHAGE FUNCTION DURING DEVELOPMENT. Janice Lorenzen* and T.M. Saba, Dept. of Physiology, Albany Medical College, Albany, New York 12208

The importance of the reticuloendothelial system (RES) in non-specific defense, coupled with observed age dependent variations in non-specific resistance, suggest the existence of variation in phagocytic activity during development. In the present investigation, phagocytic and opsonic parameters were studied as a function of age in Holtzman rats (7-90 days of age). Phagocytic activity was assessed by the vascular clearance and tissue localization of ^{131}I-labeled colloid and the opsonic or phagocytosis supporting capacity of serum was evaluated by radio-bioassay. Opsonin levels were maximal at 10-14 days of age; declined significantly ($p<.01$) by 21 days; and slowly increased to adult levels by 90 days. Phagocytic activity was maximal over the 10-14 day interval ($t/2 = 5.6$min; $K = .056$) and decreased ($p<.02$) progressively until 21 days of age ($t/2 = 14.7$ min; $K = .026$). The liver, lung and spleen manifested a progressive decline in relative per gram tissue phagocytic capacity with organ growth. The humoral factor (opsonic protein) which mediated, in part, these phagocytic adjustments, can be isolated by ammonium sulfate fractionation and high-voltage electrophoresis (J. RES 13: 410, 1973). It is a heat-labile (60°C-20min), heparin dependent, alpha-2-glycoprotein capable of directly stimulating phagocytosis. Thus, age dependent variations in R.E. function may be due to both opsonic alterations as well as the decreasing ratio of RE cells to non-phagocytic tissue elements with growth. The relationship of these findings to age dependent variations in resistance to traumatic shock and tumor growth are presently under investigation.
(USPHS - CA-16011)

IN VITRO TESTS OF A PRESUMED CIRCADIAN RHYTHM IN A MOLLUSCAN NEURON. C.M.Lukowiak* and J.W.Jacklet, State Univ.of N.Y.at Albany, Albany, N.Y.

A single neuron, R15, in the abdominal ganglion of Aplysia californica is reported to have a circadian rhythm in the rate of action potential (AP) discharge (Strumwasser, 1965). We have devised culture conditions which allow the continuous monitoring of intracellular activity for up to eight days. It does not appear that the cell is degenerating in culture since AP amplitude, membrane potential, burst pattern, and synaptic contacts are maintained. Under these conditions a reproducible 24-hour rhythm is not seen, although transient increases in the AP rate lasting several hours commonly occur within 30 hours after dissection. The timing of the maximum AP rate within this 30 hour period for animals dissected during the light part of the LD cycle can be predicted on the basis of the time of both dissection and the dark-light transition. Attempts were made to entrain spiking in R15 in vitro. Light, temperature, and synaptic input, which are all effective in modulating R15's activity, were used in various combinations in a cyclic regimen. The temperature and synaptic input cycles resulted in 2-100 fold variations in the AP rate and concommitant changes in the burst pattern. Since there are no transients in R15's activity when these cycles are phase-shifted and the driven rhythm does not persist for even one cycle when the cell is returned to constant conditions, the AP rate appears simply to be driven by the temperature or synaptic input cycle and not entrained. Since variations in the AP rate in R15 are not periodic in constant culture conditions and stimuli effective in modulating the activity do not entrain a rhythm, it is proposed that the transient peaks in AP rate observed on the first day in culture represent delayed expression of perturbations in R15's activity produced by dissection and the last experienced dark-light transition and are not activity peaks of a typical circadian rhythm.

EFFECT OF OUABAIN ON RENIN SECRETION FROM RENAL CORTICAL CELL SUSPENSIONS. H. Jay Lyons* and Paul C. Churchill. Wayne State Med. Sch. Detroit, Mich., 48201.

Renin secretion is hypothesized to be inversely related to tubular fluid sodium concentration or load in the vicinity of the macula densa. However, renin secretion from tissue slices has been directly related to sodium concentration of the medium. Recent evidence indicates that this relationship can be both inhibited and reversed by ouabain (10^{-3}M). We have monitored renin secretion from renal cortical cell suspensions while varying media sodium concentration to compare with these tissue slice results. Rat kidneys were removed under barbiturate anesthesia, the capsule and medulla excised, and the cortex minced. The cells were separated with collagenase (2mg/ml) and collected by centrifugation. They were evenly distributed into reaction vials and incubated in Krebs-ringer bicarbonate solution of varying sodium concentration (50-144 mM). Renin was assayed by radioimmunoassay. Increasing the media sodium concentration resulted in a linear decrease in the rate of renin secretion. This inverse relationship was not affected by addition of ouabain (10^{-3}M) to the media. The differences between these results and those obtained previously with tissue slices may be due to either a collagenase induced alteration in membrane properties or the loss of structural integrity of the renal cortex. (Supported in part by grants from the Kidney Foundation of Michigan and from the National Science Foundation (GB 35263).

THE BLOOD PRESSURE RESPONSE TO PERFUSING THE CAROTID BODY WITH HYPOXIC BLOOD IN THE CHICKEN. Michael Magno, Dept. of Physiology, Albany Medical College, Albany, New York 12208

During systemic hypoxia in both anesthetized and unanesthetized chickens, there is a progressive fall in blood pressure. This hypotension is in contrast to the maintenance or increase in blood pressure reported for most other species. This study was conducted in order to determine whether the chicken has a mechanism that could produce an increase in blood pressure when stimulated by hypoxia. In seven adult White Leghorn females anesthetized with phenobarbital (180 mg/Kg, I.V.), the left carotid body was perfused with tonometered blood (P_{O_2}: 18-39 mm Hg). As an expediency, the hypoxic blood was allowed to flow to the vascular beds supplied by the left vertebral and cranial arteries. Systemic blood gases were maintained normal by unidirectional ventilation. Respiratory movements were monitored with a pneumograph and an increase in the frequency and amplitude of respiration was used to verify that the carotid body had been stimulated. The perfusions lasted 90 to 120 seconds and produced increases of 4.2±0.8 mm Hg (mean±S.E.) in systolic pressure and 6.5±1.4 mm Hg in diastolic pressure ($P<0.01$ for both). Inspection of the data revealed that the tendency for diastolic pressure to rise more than systolic pressure occurred at the more severe degrees of hypoxia ($P_{O_2}<25$ mm Hg). These data show that the chicken does possess a mechanism by which hypoxia can produce an increase in blood pressure. Although such a mechanism apparently exists in the chicken, it does not dominate the blood pressure response to systemic hypoxia as is the case for the chemoreceptor-induced vasoconstriction in mammalian species. (Supported by the Heart Association of Eastern New York and USPHS Grant #FR5394).

MYOCARDIAL BLOOD FLOW AND FUNCTION IN HYPERTROPHY INDUCED BY VOLUME OVERLOADING. A.B. Malik and A.S. Geha, Washington University School of Medicine, St. Louis, Mo., 63110 and Albany Medical College of Union University, Albany, N.Y. 12208

Hypertrophy was produced by bilateral femoral arteriovenous fistulas in 6 adult dogs. Biventricular hypertrophy was maximal 7 mo. after the procedure. Left and right ventricular weight-to-body weight ratios (g/kg) of 6.06±.41 and 1.94±.25 respectively in dogs with non-failing hypertrophied hearts (V) were higher ($p<0.01$) than values of 3.82±.16 and 1.26±.070 in 7 normal dogs (N). Cardiac function was compared in the two groups and total and regional coronary flows were measured using labeled microspheres. Measurements in hypertrophied hearts were made 2 hr after closure of fistulas to minimize the effects of volume overloading. Left and right coronary flows (ml/min/100g) of 82.1±.81 and 46.2±.071 in V were lower ($p<0.01$) than values of 167.1±.22 and 91.5±.16 in N. The reduction in flows were due to decrease in perfusion pressure and increase in resistance. The reduction in flows were equally evident in endocardial and epicardial layers of RV and LV. Parameters of cardiac function such as cardiac index, stroke volume, ratio of peak LV dp/dt-to-isovolumic pressure and LV Vmax were greatly reduced ($p<0.01$). LV O_2 consumption of 9.52±1.07 ml/min/100g was lower ($p<0.01$) than mean value of 17.1±2.1 ml/min/100g in normal dogs. Unlike LV hypertrophy of an equal degree induced by pressure overloading (Fed. Proc. 33:1150), LV hypertrophy induced by volume overloading results in more significant depression not only in coronary flow but also in LV O_2 consumption and function. Thus there is a greater loss of coronary vascular and functional reserve in left ventricular hypertrophy produced by volume overloading.

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LONG-TERM SLEEP REDUCTION IN FRONTAL CATS. Robert J. Marcus* and Jaime R. Villablanca. Dept. of Psychiatry, Mental Retardation Ctr., NPI, Univ. of California, Los Angeles, 90024.

This study was performed in five cats in which all frontal areas rostral of A22 (Snider-Niemer stereotaxic coordinates) were removed by aspiration and in three sham-operated cats. Neocortical, hippocampal, pontine, neck muscle, and orbital recording electrodes were implanted. Sleep-wakefulness (S-W) was studied by means of 24-hour polygraphic recording sessions (a total of 11) conducted in a sound-attentuated chamber on the third to fifth postoperative day and every 10-30 days thereafter for up to six months. The time spent by each animal in waking, non-rapid eye movement sleep (NREMs) and REMs was expressed as a percentage of the 24-hour recording period. An average of these percentages for all the animals in each recording session was calculated. An average for each S-W state which included the percentages of all sessions (average cumulative percentages) was also calculated. In the frontal cats, REMs was significantly reduced in five out of 11 sessions and REMs was significantly below control values in three out of 11 sessions; wakefulness was significantly increased in all but three sessions. The average cumulative percentages for both NREMs (40%) and REMs (11%) were significantly ($p<0.001$) below the control values (50.2% and 15.4% respectively) whereas the waking cumulative percentage (49%) was significantly ($p<0.001$) above the control value (34.4%). It is concluded that cats with bilateral frontal cortical ablation exhibit a long-lasting, although moderate, reduction of sleep. It appears, therefore, that frontal cortical areas are part of a forebrain system involved in sleep-wakefulness control (Arch. ital. Biol, 110: 345, 1972).

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THE INFLUENCE OF EXTRACELLULAR Na^+ ON Na^+, K^+, AND Cl^- CONCENTRATIONS WITHIN GALL BLADDER MUCOSAE. Duncan W. Martin. Univ. of Arkansas, Fayetteville, Arkansas.

Intracellular ion distribution (Na^+, K^+, Cl^-) and transport were studied in rabbit gall bladders. In addition, Na^+, K^+, and Cl^- concentrations were determined as a function of extracellular Na^+ in both rabbit and cattle gall bladder mucosae. Ion determinations were performed on mucosal cells scraped from underlying tissues. Rabbit mucosal cells were obtained after treatments done on the whole gall bladder while bovine gall bladder mucosal cells were utilized as suspensions in an appropriate Ringer's solution. Cells of both types were centrifuged and pellets exposed to appropriate volumes of trichloracetic acid after which dilutions were made for analysis by flame photometry for Na^+ and K^+ and electrometric titration for Cl^-. Transport in rabbit gall bladders was measured gravimetrically. The high Na^+ and low K^+ concentrations were unchanged by transport measurement procedure but Cl^- concentrations were significantly elevated. In both the rabbit and cattle cells intracellular Na^+ declined as a function of lowered extracellular Na^+ (tetraethylammonium ion or choline ion was substituted for Na^+). Thus the high intracellular Na^+ is not maintained by the cells. Intracellular K^+ is inversely related to extracellular Na^+ in rabbits while it is independent of Na^+ in bovine tissue. Cl^- within rabbit cells shows an inverse non-linear relationship to extracellular Na^+ while there is no apparent relationship between these ions in bovine cells. Supported by NIH AM12832.

SEROTONIN CONSTRICTION OF THE CEREBRAL EXTRAPARENCHYMAL ARTERIES. J. B. Martin* and C. E. Rapela. Bowman Gray Sch. Med., Winston-Salem, N. C. 27103.

The effect of serotonin (5-HT) on cerebral extraparenchymal arteries (CEA) was estimated by measuring the difference (ΔC-V) between the common carotid and vertebral wedge pressures. The latter were obtained by threading catheters retrograde into both vertebral arteries up to the level of C_2. Validity of ΔC-V as an index of resistance across the CEA is supported by marked decrease in vertebral wedge pressure observed when both common carotids were occluded. Cerebral venous outflow (CBF) was measured with EMF. The mean between the common carotid and vertebral wedge pressures was used as the best index of the perfusion pressure of the brain. NaVB anesthetized, heparinized dogs were used. 5-HT (300-750 μgm) intracarotid produced no change in common carotid pressures, an increase in the ΔC-V of about 25 mmHg, and no change in CBF. During hypercapnia (cerebral autoregulation absent) 5-HT produced no change in common carotid pressures, a 20 mmHg increase in ΔC-V, and a decrease in CBF to 73%. We conclude: 1) the increase in ΔC-V following 5-HT indicates constriction of the CEA; 2) lack of change in CBF during normocapnia indicates autoregulation in response to 5-HT-induced decrease in perfusion pressure; 3) abolition of CBF autoregulation by CO_2 allows that the 5-HT-induced constriction of the CEA be manifested by a decrease in CBF. These data support the hypothesis that the intra- and extraparenchymal cerebral arteries may respond differently to humoral stimuli. (NIH HL-00487, 05392 and N. C. Ht. Assn.)

NITROGEN DILUTION CONSTANT: A METHOD OF COMPENSATING FOR FRC AND Vt ALTERATIONS WHEN COMPARING BASELINE AND SUBSEQUENT N2 CLEARANCE CURVES. J.L. Mauderly, W.C. Nenno and G.A.Morrison (intr. by B.A. Muggenburg) Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico 87108.

Nitrogen clearance curves of human and unsedated canine subjects were constructed by plotting F_{ETN2} against breath number during open circuit measurements of FRC. Curves were analyzed graphically and the slope of the main component was described in terms of $B\frac{1}{2}$, the number of breaths used to lower F_{ETN2} to $\frac{1}{2}$ its original value. The value of $B\frac{1}{2}$ was directly proportional to the quantity (FRC/Vt). The quantity [$B\frac{1}{2}$/(FRC/Vt)] was relatively constant for normal individuals regardless of FRC or Vt, and was called the "nitrogen dilution constant" (NDC). Because NDC is constant, it can be used to predict the $B\frac{1}{2}$ of a subject by multiplying that subject's mean baseline NDC by the (FRC/Vt) measured during a subsequent washout. The difference between predicted and baseline $B\frac{1}{2}$ of subjects with altered clearance curves indicates the portion of the mixing defect due to FRC and Vt changes. The difference between the predicted and measured $B\frac{1}{2}$ of those subjects reflects the portion of the mixing defect due to abnormalities other than changes in breathing pattern. The method permits the comparison of baseline and subsequent curves under conditions of altered FRC/Vt ratios, and the partitioning between effects of breathing pattern and lung pathology. It is simple to use and does not require computer analysis. (Research performed under USAEC Contract AT(29-2)-1013 and in facilities fully accredited by the American Association for Laboratory Animal Care.)

THE EFFECTS OF TIDAL VOLUME ON THE INTERACTION BETWEEN DIFFUSIVE AND CONVECTIVE GAS MIXING. R.W. Mazzone*, H.I. Modell* and L.E. Farhi (intr. by H.D. Van Liew). Dept. Physiol. State Univ. of New York at Buffalo, Buffalo, N.Y.

The efficiency of gas delivery to the alveoli depends upon the interaction between convective and diffusive gas mixing in the lungs. To investigate the possibility that this interaction could be affected by the size of the tidal volume, normal subjects inspired various volumes of an SF_6, Ar, O_2 mixture beginning at FRC. Following inspiration the subject expired at a constant rate to residual volume. Concentrations of SF_6 and Ar were monitored and plotted as functions of expired volume. The data obtained indicate that as the inspired volume is increased from 750 mls to 2 L, convective flow reaches more peripheral regions of the lungs. Comparison of our data with that of Cumming, et al. (Resp. Physiol. 2: 386, 1967) indicates that this phenomenon is dependent upon the volume inspired rather than the end-inspiratory level. These results imply that as tidal volume increases the role of diffusive mixing in the distribution of ventilation may be reduced. It further implies that, at larger tidal volumes, pulmonary gas exchange may be influenced more by the efficiency of gas delivery to parallel units rather than by diffusion within units. (Supported in part by ONR Contract #N00014-68-A-0216 and NIH Grant HL 14414-02.)

ALDOSTERONE RESPONSE TO CHRONIC INFUSION OF POTASSIUM IN INTACT DOGS. Robert E. McCaa, Connie S. McCaa, Thomas J.C. Woods*, Paul J. Lijnen* and Arthur C. Guyton. Dept. of Physiol. and Biophys., Univ. of Miss. Sch. of Med., Jackson, Mississippi 39216

Aldosterone secretion fails to increase in anephric man in response to acute or prolonged infusion of angiotensin II. Yet, marked alterations in aldosterone secretion have been observed in anephric man in response to changes in plasma potassium concentration. Also, there is a positive correlation between the increase in plasma potassium concentration and plasma aldosterone concentration in anephric man during the 4 consecutive days between periods of hemodialysis. The present study was designed to evaluate quantitatively the role of potassium in the long-term regulation of aldosterone secretion. After a 2 day control period, six intact conscious dogs were infused with KCl, 250 mEq/day, for 17 days. Blood samples were collected twice daily for the determination of plasma aldosterone concentration (PAC), plasma cortisol concentration (PCC), plasma renin activity (PRA), serum Na^+ and serum K^+. The data are summarized below: (Mean ± SEM; * = $p < 0.05$)

		CONTROL	EXPERIMENTAL	RECOVERY
serum K^+	(mEq/L)	4.1 ± 0.5	4.9 ± 0.8*	4.2 ± 0.5
serum Na^+	(mEq/L)	140.5 ± 1.0	142.2 ± 1.0	142.2 ± 1.0
PRA	(ng/ml/hr)	1.64 ± 0.3	0.80 ± 0.2*	1.31 ± 0.2
PAC	(ng/100 ml)	6.7 ± 1.8	20.4 ± 4.2*	7.8 ± 2.0
PCC	(μg/100 ml)	1.15 ± 0.2	1.20 ± 0.2	1.00 ± 0.3

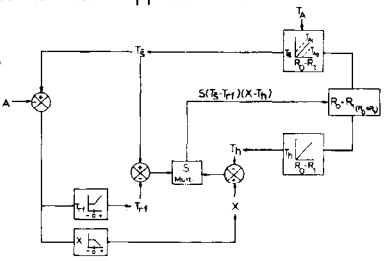
Chronic infusion of potassium ions into conscious intact dogs resulted in suppression of plasma renin activity and sustained increase in plasma aldosterone concentration. These data indicate that potassium may play a primary role in the long-term regulation of aldosterone secretion. (Supported by USPHS Grant HL 09921)

VASOMOTOR INNERVATION OF THE NASAL MUCOSA. T. V. McCaffrey* and R. D. Wurster. Sponsored by R. D. McCook. Loyola University, Stritch Sch. of Medicine, Dept. of Physiology, 2160 S. First Avenue, Maywood, Ill.60153.

Experiments were undertaken to determine the effects of sympathetic nerve stimulation on the resistance and capacitance vessels of the nasal mucosa of the cat. Twenty cats anesthetized with chloralose 60 mg/kg were used in the study. Responses of the resistance vessels of the nasal mucosa were measured by catheterizing the vein of the pterygoid fossa and measuring venous outflow with a photoelectric drop counter. Capacitance vessel response was measured with an intranasal balloon connected to a volumetric pressure transducer. Stimulation of the cervical sympathetic chain produced decreased flow and increased nasal patency on the ipsilateral side without measureable contralateral response. The response of the resistance and capacitance vessels becomes maximal at a stimulus frequency of six to eight Hz. with a reduction in blood flow of 40% of control levels. Transection of the Vidian nerve in the pterygoid fossa produced a marked reduction in the efficacy of sympathetic stimulation indicating that a major part of the sympathetic innervation of the nasal mucosa travels in the Vidian nerve. Resting sympathetic tone is indicated by the increase in blood flow and reduction in nasal patency which accompanies transection of the cervical sympathetic chain. These observations suggest that both the veins and the resistance vessels of the nasal mucosa are very sensitive to small changes in sympathetic tone. Further studies are being conducted to determine the participation of the nasal vessels in general cardiovascular reflexes. *(Supported by NIH Grant HL 08682)*

A MODEL FOR CNS CONTROL OF THERMOREGULATORY EFFECTORS. G.N. McEwen, Jr. and J.E. Heath. Dept. of Physiol. & Biophys., Univ. of Illinois, Urbana

The POAH of unrestrained adult rabbits was heated and cooled by a water perfused thermode at ambient temperatures (T_A) of -8, 0, 10, and 20°C. Metabolism (M), heart rate (HR), breathing rate (BR), rectal (T_{re}), ear (T_e), back (T_b), and POAH (T_h) temperatures, and postural adjustments (PA) were continuously monitored. Responses were modeled by the equation $R_0-R_1=S(T_s-T_{rf})(X-T_h)$. Pa, M, and HR respond most often as if T_{rf} and X are constant, not affected by T_A (central predominant response), CPR. T_e and BR respond as if T_{rf} and X are variable, dependent on T_A (peripheral predominant response), PPR. A preferential sequence was noted for the onset of these effector responses. The difference in response types and sequence can be explained by assuming that each effector is independently controlled. Peripheral temperature input (T_s) is compared with a term for peripheral "state" (T_{rf}), and one for nonthermoregulatory inputs, perhaps "psychological state" (A). The output of the comparison of T_s and A acts on T_{rf} and X, a central "state" term, such that when A is large, it tends to maintain T_{rf} and X at tonic levels, resulting in a CPR from the effector. A small A would result in a PPR where T_{rf} and X change with T_A. We suggest that T_{rf}, X, and A have common multiple inputs for each of the effector responses, and that differential evaluation of these inputs is responsible for the different response types observed, and the sequencing of effector responses. Supported in part by NSF GB 13797.



EFFECTS OF ESTROGEN PRETREATMENT ON ISOPROTERENOL NECROSIS IN THE JAPANESE QUAIL (COTOURNIX COTOURNIX). James J. McGrath and Loren G. Martin.* Peoria School of Med., Peoria, Ill.

Experiments were conducted to assess the influence of estrogen pretreatment on the severity of isoproterenol-induced cardiac necrosis in the Japanese Quail. Male birds were castrated at 4 weeks of age and allowed to recover for 1 week. All birds were injected for 3 weeks with cottonseed oil in which either β-estradiol-3-benzoate (1.0 mg) or testosterone propionate (1.0 mg) had been dissolved. After the treatment period isoproterenol was injected subcutaneously (80 mg/kg body weight) on two consecutive days at 24 hour intervals. The hearts were removed on the third day and damage scored on a 0(least)-4(greatest) scale. The body weights of estrogen-treated castrates (EC) were greater than testosterone-treated castrates (TC), untreated castrates (UC) and sham operated males (SM). Myocardial necrosis was least severe in the EC group, moderately severe in the TC and UC groups and most severe in the SM group. Thus estrogen pretreatment affords some degree of protection against this type of cardiac necrosis in the Japanese Quail despite increasing the rate of body weight gain.

CARDIOPULMONARY FUNCTION IN PRONGHORN ANTELOPE. Tom McKean and Ben Walker* Dept. of Zoology and Physiology, Univ. of Wyoming, Laramie, Wyo. 82071.

Pronghorn are probably the second fastest land mammal with a top speed of about 60 m.p.h. Pronghorn are endurance runners as well as they have been observed running at an average speed of 40 m.p.h. for over 10 min. To determine if the pronghorn has become physiologically adapted for running we measured a number of parameters which are thought to influence the delivery of O_2 to muscle and the removal of respiratory and metabolic acids both in the pronghorn and in its unspecialized control, the domestic goat. Average values obtained are as follows:

	PRONGHORN	GOAT
Heart wgt./body wgt.	0.948	0.495 g/100 g.
Hemoglobin	18.8	11.5 g/100 ml
Blood volume	9.29	6.59% body wgt.
Hematocrit	0.44	0.31
Airway resistance	1.34	2.85 cm H_2O/l/sec.

It is concluded that the pronghorn is physiologically specialized for running compared to goats of equal size.

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CEREBELLAR STIMULATION AND CEREBRAL BLOOD FLOW. J.C. McKee* and H.L. Stone, Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

Electrical stimulation of the fastigial nucleus produces a rapid elevation of arterial pressure (AP). Nothing is known about the effects upon cerebral blood flow (CBF). Five rhesus monkeys were implanted with Doppler flow probes around the left common carotid artery with the external carotid ligated. After a week of recovery, the animals were anesthetized with alpha chloralose, paralyzed and mechanically ventillated. The average arterial Pco_2 was maintained at 28.9 mm Hg. Stimulation was performed with a bipolar electrode at a frequency of 160 Hz, pulse duration of 0.1 msec., and intensities from 0.5 to 3.5 mA. Stimulation produced an increase in CBF and a decrease in cerebral vascular resistance (CVR). The threshold response for AP and CBF was 0.5 mA. The increase in CBF and the decrease in CVR reached a plateau at 1.5 mA while AP continued to increase to the end of the stimulation intensity range, but with a decrease in the slope above 1.5 mA. At 2.5 mA the average change in CBF was 82% $\pm$ 21% above the control and the average change in CVR was 25% $\pm$ 8% below the control. At 3.5 mA the average increase in AP was 30% $\pm$ 11% above the control. The change in CBF in cc/min. was linearly related to the change in AP. The results indicate that the increase in CBF and the decrease in CVR reach a plateau and begin to decline toward control values prior to the maximum increase in AP. Due to a greater increase in CBF than in AP, CVR decreases which indicates a vasodilation of the cerebral vascular bed. Stimulation of the deep cerebellar white matter evokes a physiological mechanism producing a neurogenically mediated vasodilation in the cerebral circulation.

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INHIBITION BY VERAPAMIL OF PULMONARY VASOCONSTRICTIVE RESPONSE TO ALVEOLAR HYPOXIA. I. F. McMurtry*, J. T. Reeves, and R. F. Grover. University of Colorado Medical Center, Denver, Colorado.

The relative roles of electro- and pharmacomechanical coupling in mediation of excitation-contraction coupling in vascular smooth muscle vary according to vessel and agonist. Pulmonary vasoconstriction in response to alveolar hypoxia is mediated either directly by depolarization of the vascular smooth muscle (electromechanical coupling) or indirectly by stimulation with an extravascular, chemical mediator (electro- and pharmacomechanical coupling). If hypoxia-induced pulmonary vasoconstriction is mediated by electromechanical coupling, then it should be susceptible to blockade by verapamil, an inhibitor of transmembraneous Ca^{++} influx and the contraction elicited by membrane depolarization. This hypothesis was tested in isolated, blood-perfused, rat lungs by comparing the inhibitory effects of verapamil (10^{-8} to 10^{-4} g/ml) on pressor responses to alternate stimulation by alveolar hypoxia (2.5% O_2) and 1 ug angiotensin II, an agonist known to be mediated largely by pharmacomechanical coupling. Whereas the inhibitory threshold for the hypoxic pressor response was 10^{-8} g/ml, it was 100 times higher (10^{-6} g/ml) for the response to angiotensin. The response to hypoxia was blocked completely at 10^{-4} g/ml, while that to angiotensin was reduced by only 47%. Inhibition of hypoxia-induced vasoconstriction was persistent, but that of the angiotensin-induced response became less with continued perfusion. Prostaglandin $F_{2\alpha}$ was similar to angiotensin in its resistance to blockade by verapamil. These results suggest that the pulmonary vasoconstrictive response to alveolar hypoxia is mediated primarily by electromechanical coupling and are consistent with the idea that hypoxia acts directly to depolarize the vascular smooth muscle.

CARDIOVASCULAR RESPONSE TO HEMORRHAGE IN CONSCIOUS DOGS BEFORE AND AFTER DENERVATION OF ARTERIAL BARORECEPTORS. Robert J. McRitchie*, Stephen F. Vatner, Guy Heyndrickx* and Eugene Braunwald. Dept. Med., Harvard Med. Sch. and Peter Bent Brigham Hospital. Boston, MA 02115.

It is generally held that arterial baroreceptors play a critical role in the cardiovascular compensation to hemorrhage. Since anesthesia interferes with circulatory control, 10 dogs were studied conscious before and 2-4 weeks following bilateral cervical section of the carotid sinus and aortic nerves. Instrumentation included left ventricular(LV) pressure gauges, ultrasonic LV diameter gauges for LV diameter and dD/dt, i.e. velocity, arterial pressure catheters and electromagnetic flow probes for cardiac output. Adequacy of denervation was confirmed by abolition of reflex heart rate changes in response to nitroglycerin and methoxamine. Hemorrhage, 1 ml/sec up to 25 ml/kg, altered arterial pressure(-15%)(control=91mmHg), LV end-diastolic diameter -7.9 mm, cardiac output -42% and increased total peripheral resistance +49%, heart rate +69 beats/min (control=82beats/min) and indices of cardiac contractility, i.e. dP/dt/P(+11%) and velocity(+10%) in intact dogs. In arterial baroreceptor denervated dogs hemorrhage reduced arterial pressure(-41%)(control=101mmHg), LV end-diastolic diameter -4.6 mm, cardiac output -59% and increased total peripheral resistance +15% and heart rate +17 beats/min (control=114beats/min), but not dP/dt/P and velocity. In dogs with intact arterial baroreceptors anesthetized with pentobarbital, 30mg/kg, hemorrhage 25 ml/kg reduced arterial pressure(-51%). Thus, the normal vasoconstrictor response to hemorrhage was almost abolished by arterial baroreceptor denervation, while cardiac output fell by similar magnitudes in both the intact and denervated dogs. Furthermore, denervation markedly attenuated the normal tachycardia and abolished the normal initial small increases in dP/dt/P and velocity induced by hemorrhage.

FIRST APPARENT DISSOCIATION CONSTANT, pK_1', OF PLASMA AND ERYTHROCYTES IN THE HUMAN. Arthur A. Messier (intr. by Karl E. Schaefer). U.S. Naval Submarine Medical Research Laboratory, Groton, Connecticut 06340

The first apparent dissociation constant of carbonic acid, pK_1' of plasma and red cells was determined on venous blood of ten healthy, adult, male, human subjects. pH and P_{CO_2} of plasma and red cells were analyzed electrometrically and a micromanometric method was used for the determination of total carbon dioxide content. Erythrocyte carbamino hemoglobin levels were estimated and used for the correction of erythrocyte pK_1'. Each blood sample was subjected to the following regimen before centrifugation, 1) As Drawn from the antecubital vein, 2) Oxygenated with a 5% CO_2, O_2 balance gas mixture, and 3) Reduced with a 5% CO_2, N_2 balance gas mixture. pK_1' of plasma and red cells are presented:

		AS DRAWN	OXYGENATED	REDUCED
PLASMA	Mean	6.099	6.125	6.105
(N=10)	SD	.028	.026	.026
RBC	Mean	6.144	6.187	6.157
(N=10)	SD	.039	.040	.032

The consistently larger values for red cell pK_1' than the respective plasma data may be attributed to the greater amount of carbamino hemoglobin concentration present in the erythrocytes. A simplified method for the calculation of erythrocyte bicarbonate concentration using the experimentally determined red cell pK_1' value has been formulated. The method involves the use of a regression equation relating serum and red cell pH, the equivalence of plasma and red cell P_{CO_2}, along with the experimentally determined red cell pK_1'.

ARTERIOLAR REACTIVE HYPEREMIA: MODIFICATION BY INDOMETHACIN. Edward J. Messina*, Richard Weiner and Gabor Kaley. New York Medical College, Department of Physiology, Valhalla, N.Y.

Postocclusive arteriolar responses were studied in the cremaster muscle of anesthetized Wistar strain male rats weighing 90-130 gm. In vivo changes of diameters of single arterioles were quantitated with an image-shearing television microscope and recording system after their occlusion for 15, 30, or 60 seconds. The increase in diameters and the duration of the hyperemic responses varied directly with the period of occlusion. The mean increase in diameter and the mean duration of the response for 15, 30 and 60 second occlusions were $8.7 \pm 0.6\mu$ and 27 ± 5 sec., $11.6 \pm 0.7\mu$ and 40 ± 5 sec., and $14.1 \pm 0.7\mu$ and 64 ± 10.0 sec., respectively. Postocclusive responses were variable between animals, whereas responses of a single arteriole were reproducible over a 3 hr. test period. Repetitive occlusions did not affect arteriolar responsiveness as vasodilator responses to bradykinin and vasoconstrictor responses to norepinephrine remained unaltered. Indomethacin, an inhibitor of prostaglandin synthesis, decreased both the maximum increase in diameter and the duration of the vasodilator response following occlusion. These findings support the conclusion that in this vascular bed reactive hyperemia is at least partially dependent upon the presence of prostaglandins.
(Supported by NIH grant HL12342)

EFFECTS OF PREGNANCY AND EXOGENOUS PROGESTERONE ON PLASMA RENIN ACTIVITY (PRA) IN FEMALE PYGMY GOATS. James Metcalfe, Walter J. McDonald* and Dharam S. Dhindsa. Dept. of Med., Univ. of Oreg. Medical School, Portland, Oregon.

Normal human pregnancy is associated with increases in PRA and renin substrate concentration and high circulating levels of angiotensin II (A II). In 6 nonpregnant adult female Pygmy goats, PRA was measured by radioimmunoassay. Values of 0.39 ± 0.25 (S. D.) ng of angiotensin I/ml plasma/hr were obtained. In mid-pregnancy (50-100 days of the 145-day gestation period) PRA rose to 0.50 ± 0.19 (6 animals) and in late pregnancy (after 100 days), PRA reached 0.95 ± 0.32 (11 animals). Late pregnancy PRA was significantly higher than nonpregnant values ($p < 0.005$) and also significantly higher than mid-pregnancy values ($p < 0.01$). Exogenous progesterone causes increased PRA in human males, and plasma A II concentration rises in the luteal phase of the human menstrual cycle, but conflicting results have been reported concerning the effects of exogenous progesterone on PRA in dogs. Progesterone (in oil), 6 mg/kg body wt/day i.m., was given to 5 nonpregnant adult female Pygmy goats for 1 to 6 weeks and caused no change in PRA. Four other goats were given the same dose of progesterone in late pregnancy and their PRA (1.05 ± 0.49) after 1 to 6 wks of progesterone was unchanged from control animals at the same stage of pregnancy. (Supported in part by USPHS NIH grant #14121 and the Oregon Heart Association.)

COMPARATIVE INHIBITION OF HYPOTHALAMIC UPTAKE OF 5-HYDROXYTRYPTAMINE AND NOREPINEPHRINE BY 5-OH- AND 5-MeO-INDOLE DERIVATIVES. Donald C. Meyer*, W. B. Quay and Yu Heng Ma* Neuroendocrinology Section, Waisman Center on Mental Retardation and Human Development, and Endocrinology-Reproductive Physiology Program, University of Wisconsin, Madison, Wisconsin 53706.

Indole derivatives and tritium-labeled 5-hydroxytryptamine (5-HT) and norepinephrine (NE) were incubated with homogenates of hypothalamic tissue taken from adult male rats maintained on a 12-hour daily photoperiod (LD 12:12). Incubations 1 to 40 minutes in length were with concentrations of indole derivative compounds from 5×10^{-8} to 5×10^{-5} M. Uptake of 5-HT was inhibited by 6-hydroxytetrahydroharman ($P<0.01$) at 5×10^{-6} M, and by 6-methoxytetrahydroharman ($P<0.001$) and 5-hydroxytryptophol ($P<0.01$) at 5×10^{-5} M. Melatonin, 6-hydroxymelatonin and 5-methoxytryptophol lacked significant inhibitory action on uptake of 5-HT at all concentrations tested. None of the tested compounds were inhibitory to hypothalamic uptake of NE. These results support the possibility that some of the indole metabolites found in brain and pineal gland may participate in modulating aminergic mechanisms in the hypothalamus by means of uptake inhibition in 5-HT neurons or binding sites. The lack of effect by melatonin in these experiments suggests that its site(s) of action lie either in other mechanisms or in other structures. Although the natural brain or pineal occurrence of tetrahydroharmans remains to be proven, formation of 6-methoxytetrahydroharman in vitro (McIsaac, W. M. 1961) and by pineal *O*-methylation (Quay, W. B. and L. I. Smart 1967) are known. (Supported in part by Public Health Service Training Grant No. 2-T01-HD-00104-09 from the National Institute of Child Health and Human Development, and by Ford Foundation Grant No. 630-0505A.)

REGIONAL CEREBRAL BLOOD FLOW (r-CBF). M.W. Meyer, M.R. Tripp*, N.F. Paradise*, D.A. Gerasch*, and I.J. Fox. Dept. of Physiology, University of Minnesota, Minneapolis, Minnesota.

This study compares the measurement of CBF by constant-rate infusion of tritiated water (THO) and Ce-141 labeled microspheres (spheres). Tracers were injected into the left atrium of 16 open-chested dogs anesthetized with pentobarbital. Spheres were flushed in during the first 10-13 sec of a 26-28 sec infusion of THO during which blood was sampled from the aortic arch for reference flow. Brains were removed within 10 min of death and frozen in liquid N_2. Multiple 45-170 mg samples taken from various regions on one side of the brain were digested and the THO concentration (Ci) determined for each sample. Sphere γ-activities were determined in 0.23-1.93 gm samples taken from corresponding regions on the other side of the brain for r-CBF calculations. The γ-activity in the remainder of each brain was also determined in order to calculate $\overline{CBF}$. $\overline{CBF}$ averaged 0.30 ml/gm/min for experiments (N=5) using 25 ± 5 μ spheres and 0.39 in those (N=10) using 7-10 μ spheres. The $p\overline{CO_2}$, however, was less in the experiments using 25 μ spheres, 19.2 vs 32.7 mm Hg, which could explain the flow difference. The comparison of relative flow indices, $Ci/\overline{Ci}$ vs $(r\text{-}CBF/\overline{CBF})$ spheres, showed better agreement for 8 μ than for 25 μ spheres. In regions of high flow indices, THO/sphere ratios, while <1.0, were lower than suggested by a linear time-invariant model. The greater variability observed when using the 25 μ compared to 8 μ spheres (least-squares correlation coefficient, 0.69 vs 0.86) could be attributed to lower numbers of 25 μ spheres in the tissue samples. Uptake of THO and spheres indicate the presence of heterogeneity of blood flow in the brain. We cannot conclude which indicator provides the most accurate measure of heterogeneity or r-CBF. (Supported by NIH Grant #'s DE02212, HL08068 and NB03364.)

ELECTROCARDIOGRAPHIC CHANGES AT DIFFERENT CARDIAC VOLUMES PRODUCED BY TACHYCARDIA AND ACUTE HEMORRHAGE. Ronald W. Millard*, Brian C. Hodgkin*, and Clifford V. Nelson, Maine Medical Center, Portland, Maine.

Previous studies have shown that the presence of intracardiac blood distorts potentials due to cardiac vectors (Brody effect). Little is known about the influence of end-diastolic blood volume on these potentials. In 14 anesthetized young domestic pigs (8-12.5 Kg), thoracic surface potentials from the Nelson vectorcardiographic (VCG) lead system were applied to a digital computer for construction of spatial magnitude (M) curves. The effects of acute hemorrhage (H) and tachycardia (HR), both known to reduce end-diastolic blood volume, on the M curves were examined. Three characteristic peaks, M_1, M_2, and M_3, in the curve were examined. Left ventricular end-diastolic pressure (EDP) was measured by catheter. HR was increased by right atrial pacing. Radially oriented cardiac vectors, M_1 and M_2, fell slightly from 15 to 14 k mA-cm and 108 to 101 k mA-cm as HR was raised from 160 to 240 beats/min. Tangentially oriented vectors, M_3, increased significantly from 285 to 330 k mA-cm. EDP fell from 11 to 4 mmHg. Increasing HR from 240 to 300 beats/min caused further decline in M_1 and M_2 while effecting no change in M_3. Rapid stepwise H up to 20 ml/Kg body weight resulted in decreased M_1 and M_2 by 48% while M_3 increased 35% over control values. EDP fell from 16 to 5 mmHg during H. Controlling HR during H did not modify the effects of H on cardiac vectors. Cholinergic and beta-adrenergic blockage failed to prevent effects of HR and H on M curves. EDP fell after increased HR and H under all situations suggesting that changes in end-diastolic blood volume were responsible for the observed effects in the M curve. Thus the VCG may be useful for determining acute end-diastolic volume changes.

EVIDENCE FOR A METABOLICALLY DEPENDENT ELECTROGENIC PROCESS CONTRIBUTING TO THE RESTING POTENTIAL OF A CRUSTACEAN STRETCH RECEPTOR.

M. Mirolli. Dpt. Physiol., Indiana Univ., Bloomington, Ind.

The dendrites of the S neurons of the crustacean coxal receptors respond with a sustained depolarization when stretch is applied to the muscle receptor organ by rotation of the coxa. The membrane potential of these dendrites in fully relaxed receptor organs was studied by recording intracellularly from a point 0.2-0.5mm from the receptor endings. Recording was differential. The receptors were kept in a small perfusion chamber; both the ionic composition of the perfusing fluid (Artificial Sea Water, ASW), and its temperature could be rapidly changed. Measurements of the cable properties of the dendrites indicate an apparent membrane resistance of less than ten Kohms.cm^2. The membrane potential of the relaxed receptors is highly sensitive to temperature changes: cooling from 15 to 4C$^\circ$ results in a depolarization from about -50 to about -35mV. Both increasing and decreasing the extracellular potassium concentration results in a depolarization; however, the response to cooling is preserved in high potassium, but it is abolished in low potassium. Ouabain also abolishes the response to cooling. Substitution of external Sodium with either Lithium or Choline does not have an immediate effect on the temperature response. Exposure for more than a few minutes to solutions which substantially differ from ASW in their ionic composition results in irreversible changes, leading ultimately to the abolition of the membrane potential.

THE EFFECT OF ADDED ELASTIC AND RESISTIVE LOADS ON THE RELATIONSHIP BETWEEN TIDAL VOLUME AND DURATION OF INSPIRATION IN ANESTHETIZED CATS. G. Miserocchi*, J. Milic-Emili and H. Karajian*. Dept. of Physiology, McGill University, Montreal, Quebec, Canada.

In anesthetized tracheotomized cats we have studied the immediate effects of added elastic and resistive loads on the relationship between tidal volume and duration of inspiration at different levels of ventilatory drive. The duration of inspiration was determined both from the spirometric tracings (T_i) and from measurements of the integrated diaphragmatic activity (T_i eq). Volumes corresponding to these times were defined as V_T and V_T eq, respectively. The V_T vs T_i relationship obtained with resistive loads lay to the right of that obtained with elastic loads, i.e., with resistive loads longer T_i's were needed to reach the same V_T. However, the relationship between V_T eq and T_i eq was found to be the same for both elastic and resistive loads. During the unloaded breath, the difference between T_i and T_i eq was small, and it was further reduced by added elastic loads. On the contrary, this difference increased progressively with increasing resistances, dropping to zero when an infinite resistance was applied (occlusion at FRC). The observed difference in the V_T vs T_i relationship between elastic and resistive loads can probably be attributed to differences in time constant (ratio of total flow resistance and elastance). During the control breaths, the time constant is probably short enough for peak volume to be almost in phase with peak diaphragmatic activity and the same is also valid during elastic loading when the time constant was further shortened. On the contrary, added flow resistances prolong the time constant so that peak volume lagged behind peak diaphragmatic activity. As a result, T_i increased progressively with increasing added resistance. Constancy of the V_T eq vs T_i eq relation suggests that the vagal modulation of T_i is similar for both added resistive and elastic loads.

THE DEVELOPMENT OF FUNCTIONAL MOTOR INNERVATION IN THE EMBRYONIC CHICK LIMB. Deborah G. Morris and Lynn Landmesser (intr. by G. Pilar) Yale University, New Haven, Connecticut.

The development of innervation in the hindlimb of the chick was studied from stage 24- hatching by sequentially stimulating, in isolated spinal cord-limb preparations, each spinal nerve contributing to the crural and ischiatic plexus and by observing the movements thus elicited. The contribution of each spinal nerve to the innervation of selected muscles was assessed by visual observation and by tension recording. Throughout development, the pattern of spinal nerve distribution to individual muscles was very constant. The pattern could be detected at early times, even before the division of the primitive muscle masses into their constituent muscles. Similar results were obtained by determining the contribution of each spinal nerve to the compound action potential recorded from each of the major nerves emerging from the ischiatic plexus. This pattern was likewise similar throughout development. Furthermore axon reflexes between different muscle nerves were never obtained. It can be concluded, that individual motorneuron axons do not appear to grow randomly into the limb nor do they send branches into more than one muscle nerve. Rather, within the resolution of our technique, they show a high degree of selectivity in initial outgrowth and synapse formation.
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ELECTROLYTE COMPOSITION AND CONSTRICTION IN DOG HINDLIMB VEINS. Thomas W. Morris*, Margaret L. Swain*, and Lysle H. Peterson. Bockus Research Institute, University of Pennsylvania, Philadelphia, Pa.

The objective of this study was to correlate electrolyte compositions with the ability of the dog lateral saphenous and femoral veins to reduce their diameter. A segment of the vein was catheterized and functionally isolated though not exposed. Pressure in the segment was controlled by a reservoir of adjustable height, and the segment was perfused with physiological saline solution (PSS) at 38°C. At 10 minute intervals the segment was perfused with radiopaque contrast media, and diameters were measured radiographically during a 60 second elevation in segment pressure. This procedure was performed when the segment smooth muscle was relaxed by $NaNO_2$ and when it was maximally constricted by norepinephrine (NE). With smooth muscle relaxed by $NaNO_2$ (.2 mg/cc), the diameter of the lateral saphenous vein was 4.67±.11 mm at a pressure of 40 mmHg. With the smooth muscle activated by NE (.5 µg/cc), the diameter of the lateral saphenous was reduced to 1.61 ±.20mm at 40 mmHg. A much smaller difference has been reported in the diameter of the femoral vein with a maximal dose of NE given systemically and during sympathetic ganglia stimulation. The apparent difference (12:66%) in the ability of the femoral and lateral saphenous veins to reduce their diameters corresponds to a 1:2 ratio in both K^+ and Mg^{++} contents of the two veins. Assuming that K^+ and Mg^{++} contents reflect the amount of smooth muscle, the ability to reduce diameter appears to be closely related to the amount of smooth muscle in the vein wall. A significant amount of creep was observed in constricted veins, but, not in relaxed veins. This supports the hypothesis that creep is a property of "active" venous smooth muscle.

COMPLIANCE CHARACTERISTICS OF EXCISED MOUSE LUNGS. Catherine E. Morstatter*, Roger M. Glaser*, Eric R. Jurrus*, and Harold S. Weiss. Dept. of Physiology, College of Medicine, The Ohio State University, 333 W. 10th Ave., Columbus, Ohio 43210.

Pressure-volume (P-V) curves were obtained on an X-Y plotter from lungs filled and emptied with air or saline. The lung, connected via tracheal cannula to an infusion pump, was suspended vertically inside a sealed jar. Transpulmonary pressure and displaced volume were measured by Statham pressure transducers. With air, an initial filling and emptying cycle up to 30 cm H_2O was used to ensure opened alveoli. Total lung compliance (C_{tot}) was evaluated primarily on a following P-V curve, beginning at 5 and going to 15 cm H_2O and back. For the initial cycle, continuous filling (5 ml/min) was compared to stepwise filling (1 min pauses at each 5 cm H_2O increment) and found to have minimal effects on the subsequent 5 to 15 cm H_2O curve. Saline P-V curves were accomplished on degassed lungs. The slope of the straight portion of the filling curve was used to determine tissue compliance (C_{tis}). The first two consecutive saline fillings had identical slopes. Method of killing mice had a marked effect on compliance. C_{tot} was 23.2±2.0(SE)ul/cm H_2O for 22 female white laboratory mice (avg. 27.1 g) killed by cervical dislocation and 35.9±1.3 for 61 mice (28.4 g) killed by Na pentabarbital overdose. Decapitation was similar to cervical dislocation in its effect on C_{tot}. C_{tis} was not affected by method of killing, averaging 206.3±4.9; therefore, the method of killing probably had its primary effect on surface forces. Seven male mice close in weight (33.1 g) to the female Na pentabarbital-killed mice reported above, and killed similarly, had higher lung compliances, with C_{tot}=52.7±1.3ul/cm H_2O. Correlations were not significant between body weight and lung compliance. For the 61 females, body weight 22-34g, b=0.3±0.6ul/cm/g and r = 0.07.

CARBON DIOXIDE TRANSPORT IN THE RED CELL-FREE PRIMATE EMPLOYING A HEMOGLOBIN SOLUTION.

Gerald S. Moss*, Colathur K. Palani*, Richard DeWoskin*, Maryanne Michuda*, Arthur L. Rosen. From the Departments of Surgery, Cook County Hospital, The Abraham Lincoln School of Medicine, University of Illinois at the Medical Center, and the Hektoen Institute for Medical Research, 1825 West Harrison Street, Chicago, Illinois 60612.

Oxygen and carbon dioxide transport by a stroma free hemoglobin (SFH) solution was investigated in red blood cell-free adult baboons. The animals were exchange transfused with SFH (n=9) or Dextran-75 (n=9) in a random sequence. All animals were mechanically ventilated with room air, and kept normothermic. The exchange transfusion continued until death, or until zero hematocrit was achieved. Direct oxygen consumption, carbon dioxide production, cardiac outputs, and blood gases were measured. All dextran treated animals died at hematocrits between 2 and 5%. All SFH treated animals survived at zero hematocrits. Data (means ± S.E.M.) for CO_2 transport in SFH animals are presented.

	CONTROL PERIOD	3 HOURS, 0 Hct.
Total Hb, gm%	13.8 ± .8	6.3 ± 0.4
CO_2 Prod., ml/kg/min	4.41 ± .45	4.26 ± 0.44
R.Q.	.79 ± .04	0.85 ± .07
Venous pCO_2, mm Hg	36.3 ± 1.8	41.1 ± 3.0
Venous pH	7.45 ± .01	7.32 ± .04
Cardiac output L/min	3.43 ± .29	2.94 ± .29

We conclude that SFH supports life in rbc-free primates, breathing room air. SFH solutions permit normal CO_2 transport and excretion.

This study was supported by funds from Army Grant No. C-1106.

EFFECT OF MATERNAL VASCULAR PRESSURE ON FETAL PLACENTAL HEMODYNAMICS IN SHEEP, E.K.Motoyama, H.Goto*, T.Fuchigami*, B.Rao*, Y.Namba* and C.J. Zigas*. Depts. of Anesth. and Ped., Yale Sch. Med., New Haven, Ct.06510

Fetal placental flow (Qfp) and resistance (Rfp) may be affected by the maternal arterial or uterine venous (MUV) pressures (Pma, Pmuv) which exert pressure surrounding collapsible fetal vasculature. We examined such effect in 2 series of experiments in near term Dorset ewes under light pentobarbital anesthesia. Pma, Pmuv, umbilical arterial and venous pressures (Pua, Puv) were measured via indwelling catheters. In the first series of 7 ewes with intact lambs in utero, occlusion of bilateral MUVs raised Pmuv without decreases in Pma. Pua did not change until Pmuv exceeded an average of 47 mmHg above which Pua increased and Qfp decreased as measured with indwelling electromagnetic flow probes on umbilical arteries. Rfp increased by 22.6±3.7 (SEM)% ($p<.001$). Occlusion of the descending aorta decreased Pma by 71 mmHg which was associated with a prompt and transient fall in Pua and frequently with an increase in Qfp. The average Rfp decreased to 91±1.2% of the control ($p<.001$). These changes were due neither to hypoxia nor autonomic neural influence. In the second series in 5 ewes, the entire placenta was perfused in situ with an occlusion pump and extra corporeal circuit (Physiologist,15:222,1972). The results were similar to those from the first series. Occlusion of MUVs and resulting increase in Pmuv above 26.5±3.2 mmHg raised Pua and Rfp to 111±2.8% of controls ($p<.001$). When Puv was increased stepwise Pua did not change until Puv reached an average of 25.4±1.4 mmHg above which Pua increased as Puv increased. Occlusion of the descending aorta and resulting reduction of Pma by 64 mmHg was associated with a decrease in Pua and Rfp (87.4±1.1%, $p<.001$). These findings indicate the presence of Starling resistor effect of maternal vascular pressure upon intact fetal placental circulation. (Supported in part by NIH grants: HD-03119,HL-14179 (SCOR).)

LUNG LAVAGE USING A SINGLE LUMEN ENDOTRACHEAL TUBE IN DOGS. B. A. Muggenburg and J. L. Mauderly*, Lovelace Foundation for Medical Education and Research, 5200 Gibson Blvd., SE, Albuquerque New Mexico, 87108.

The physiologic response of the cardiopulmonary system during and after lung lavage, using a single endotracheal tube was evaluated. Beagle dogs were anesthetized with halothane-oxygen and placed in lateral recumbancy. A single lumen Magill-type endotracheal tube was placed in the trachea and oxygenated saline slowly introduced to a volume approximating the total lung capacity of the dependent lung. The fluid was then drained by gravity and the lungs briefly ventilated. The lavage sequence was repeated until 5 washes were completed. Then the dog was rotated and the washing sequence repeated on the other lung. The heart rate slowed during the procedure but no changes were noted in the pulmonary arterial or systemic arterial mean pressures. The tension of O_2 in the arterial blood decreased but no buildup of CO_2 was found. Pulmonary function at 24 hours after lavage revealed afew mild changes in breathing pattern and gas exchange. By 168 hours after lavage, pulmonary function values were not significantly different from baselines values.

(Research performed under USAEC Contract AT(29-2)-1013 in facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.)

BLOOD PRESSURE CHANGES INDUCED BY ANGIOTENSIN II ANALOGS. H. Munoz-Ramirez*, M.C. Khosla*, and P.A. Khairallah. Cleveland Clinic, Cleveland, Ohio.

Infusion (250 ng/kg/min) of several 1-8 substituted angiotensin II analogs elicited a pressor response in ganglion blocked rats. Such response was of the same magnitude (17 mm Hg) whether a branched [Sar^1, Ile^8] or non-branched aliphatic residue [Sar^1, Ala^8] was substituted for phenylalanine in position 8. With the same dose no pressor effect was seen when alanine or phenylalanine were substituted for tyrosine in position 4. When given 30 min after starting the analog infusion, phentolamine reduced and sometimes reversed the pressor response. However, phenoxybenzamine, injected 30 min prior to the analog infusion, did not completely block the initial pressor response. In adrenalectomized rats, the pressor effect of the octapeptides was reduced approximately 50% during the first 5 min and disappeared completely by 15 min. The rise in blood pressure induced by angiotensin II was effectively blocked by the analogs. Measured at the ED_{20} levels, dose ratios during infusion of [Sar^1, Ile^8], [Gac^1, Ile^8] and [$MeAla^1$, Ile^8] were respectively 24, 19, and 16. For the same peptides, the corresponding values in adrenalectomized rats were 6, 2 and 7. The data indicate that the 1-8 substituted angiotensin II analogs release adrenal catecholamines. These amines may in turn influence the observed antagonistic potency of these peptides. (Supported in part by HL-6835 and in part by a grant from the American Heart Association).

CORRELATED CHANGES OF CONDUCTION VELOCITY AND OF SITES OF SYNAPTIC INPUT ON AXOTOMIZED MOTONEURONS. John B. Munson, John G. Scott*, and Lorne M. Mendell. Univ. of Florida Coll. of Med., Gainesville (JBM) and Duke Univ. Medical Center, Durham, N.C. (JGS and LMM).

Transection of cat motor axons results in a loss of synaptic input onto the soma and proximal dendrites of the axotomized motoneurons. In addition, conduction velocity of the axon proximal to the transection is diminished (Mendell, Munson and Scott, Brain Research, 1974). More specifically, conduction velocity declines progressively from an average of 80 m/s in normal motoneurons to an average of 50-60 m/s at 60-80 days postoperative. Diminished conduction velocities were seen 3 days postoperative; experiments at prolonged postoperative times remain to be conducted.

Integrity of synaptic input onto the motoneuron soma and proximal dendrites may be related to axonal conduction velocity of the axotomized motoneuron, since abnormally increased numbers of failures of Ia afferent input are seen on motoneurons conducting below 60 m/s. Surviving synapses between Ia afferents and these slow conducting axotomized motoneurons are restricted to distal dendrites, as inferred from the slow-rising EPSP's in these motoneurons. Axotomized (and normal) motoneurons conducting at greater than about 60 m/s possess the normal complement of Ia afferent inputs onto their soma and proximal dendrites as well as onto their distal dendrites. Reinnervation of axotomized motoneurons into muscle is accompanied by recovery both of normal conduction velocity and normal distribution of Ia synaptic input. (Research support derived from grants NS 08411, NS 34608, MH 10230 and GM 00929)

REDUCED INFORMATION PROCESSING CAPABILITIES FOLLOWING COMMISSUROTOMY IN THE MONKEY. R.K. Nakamura* and M.S. Gazzaniga. State University of New York, Stony Brook.

The well-known consequences of commissurotomy have suggested the presence of two separate mental systems in the chiasm, callosum, anterior commissure sectioned animal or man. In prior studies, it was suggested that the combined mental efforts of the two hemispheres are superior to those seen in the normal intact callosum animal. These studies left open the possibility that a decrement might be seen in the split if the behavioral task was more complex and involved, in some sense, greater processing capability. In the present study, split-brain monkeys and controls were compared on their ability to do two match-to-sample tasks, one color and one pattern, presented sequentially. The tasks were intermixed such that one (color) was started before and completed after the other (pattern), thus nesting one task inside the other. In such a test sequence, the inner pattern discrimination can be done with relative ease in all animals whereas the ability to remember the color match is severely impaired in the split but not the normal. It is as if the split-brain animal does not have the cortical capacity to put on "hold" one piece of information while processing another. With extensive training there was some evidence in one split out of four that the ability to perform close to the normal range was possible. The experiment showed that in some instances one half-brain was deficient in its overall capacity as compared to a normal intact whole brain. Aided by USPHS Grant #MH 17883-04.

ALTERED THERMOREGULATION IN K DEPLETED RATS. E.E. Nattie*. (intr. by S.M. Tenney). Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire 03755.

Rats with diet-induced K depletion alkalosis have altered CSF HCO_3^- homeostasis and altered control of the ventilatory pattern (f and V_T) in comparison to similarly alkalotic rats without K depletion. These effects can be shown by repletion experiments to be K related (Fed. Proc. 33:454, 1974). The K depleted rats were noted to be hypothermic at T ambient of 22°C. Studies of body temperature, $\dot{V}_{O_2}$ and ventilation during acute (1 hr) exposure to a wide range of ambient temperatures indicated: a). K depleted rats are hypothermic at T_{amb} below the thermoneutral point, b). they have no increase in metabolism in response to cold, and c). they do have a ventilatory response to cold. Further studies using pyrogen injections to mimic cold exposure showed that the response to pyrogen was the same in both controls and K depleted animals but the absolute T_{rat} of the K depleted group remained lower at all times suggesting an altered set-point. The $\dot{V}_E$ and $\dot{V}_{O_2}$ response to pyrogen was similar in both groups. The results indicate that the hypothalamically mediated mechanisms of thermogenesis in K depleted rats differ in response to acute cold stress as compared to pyrogen injections. In addition, the demonstrated dissociation of $\dot{V}_{O_2}$ and $\dot{V}_E$ in cold stressed K depleted rats suggests that the normal close match of these parameters is a centrally controlled process. (Supported by PHS Grant HL 02888-18.)

ABSENCE OF GLOMERULAR CAPILLARY PRESSURE AUTOREGULATION IN NEPHRONS WITH INTERRUPTED DISTAL DELIVERY. L. G. NAVAR, B. CHOMDEJ*, AND P. D. BELL*. Dept. of Physiology. Univ. of Miss. School of Med. Jackson, Miss.

Micropuncture studies in dogs have indicated that interruption of normal volume delivery to the distal nephron may interfere with a distal tubule to afferent arteriole feedback mechanism thus leading to an elevated single nephron filtration rate and an inability to autoregulate in response to a decrease in renal arterial pressure. To evaluate the effect of interrupted distal delivery on glomerular pressure (GP) and its autoregulation, the proximal tubule was blocked with oil and maximal stop flow pressure was measured using a micropressure servo null system. GP was estimated from the sum of the plasma colloid osmotic pressure (measured with a membrane osmometer) and the proximal stopflow pressure. A mild isotonic mannitol diuresis was imposed and free flow proximal tubular pressure, peritubular capillary pressure, renal blood flow and GFR were also measured at control arterial pressure in 18 dogs and during reduction of renal arterial pressure in 7 dogs. At a mean control arterial pressure of 120±4 (SE) mmHg, proximal tubular pressure was 23±1.4 mmHg and GP averaged 69±2.5 mmHg, a value greater than that estimated for nephrons with normal distal delivery. GP varied significantly ranging from 90 mm Hg to 45 mmHg over an arterial pressure range of 150 mmHg to 85 mmHg. In response to decreases in renal arterial pressure, GP failed to demonstrate autoregulatory behavior although autoregulation of renal blood flow, GFR and proximal tubular pressure was observed. Regression analysis indicated a fall in GP of .5 mmHg per mmHg decrease in arterial pressure. These results indicate that interruption of distal delivery interferes with the ability of the nephron to autoregulate GP. They provide further evidence for the existence of a distal tubular feedback mechanism that participates in the control of glomerular dynamics.

FALL IN BLOOD PRESSURE AFTER UNCLIPPING IN CHRONIC ONE-KIDNEY HYPERTENSION. Richard Neubig* and Sibley Hoobler, Univ. of Michigan, Ann Arbor, MI.

The removal of the constricting clamp in one-kidney Goldblatt hypertension (1-KGH) of long standing, causes a prompt reversal of the hypertension. The unclipping is accompanied by a marked natriuresis, leading to the hypothesis that the fall in blood pressure (BP) is due to loss of salt and water. Three groups of 1-KGH rats underwent one of the following procedures: A (n=7) unclipped; B (n=6) sham unclipping; C (n=9) unclipped but infused with 0.9% saline to replace the urine excreted. Direct arterial BP was measured hourly in conscious, unrestrained rats for six hours after the procedure. From the second hour on, Groups A and C had fallen significantly ($p<0.05$) more than Group B which was not significantly down from preoperative levels. Urine excretion was 33.3 ± 11.3, 10.0 ± 3.7, and 49.8 ± 11.3 ml/kg body weight in six hours in Groups A, B, and C, respectively. In Group C, water loss was kept to zero by the saline infusion and salt balance was positive in seven rats and the other two were kept to a loss of less than 5% of total excreted sodium. In these experiments the BP fell after unclipping in spite of the prevention of loss of salt and water. Possible explanations of the fall include release of a vasodilator by the kidney or a shift of internal fluid compartments independent of excretion.

EFFECTS OF EXERCISE ON AORTIC INPUT IMPEDANCE IN THE DOG. Wilmer W. Nichols, William E. Walker*, and William R. Milnor. The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.

The effects of exercise on aortic input impedance and resistance were studied in three dogs. Pulsatile blood flow and pressure were measured with chronically implanted electromagnetic flow probes and miniature pressure transducers. Changes in the standard hemodynamic variables while running on a treadmill, as compared with the resting state, were similar to those reported by others: an increase in mean flow from 37 (SEM ±1.2) ml/sec to 93 ±15 ml/sec, an increase in stroke volume from 22 ±2 ml to 28 ±4 ml, and a decrease in vascular resistance from 3741 ±210 dyne sec cm^{-5} to 1846 ±180 dyne sec cm^{-5}. The characteristic aortic impedance modulus (Zo), calculated from the frequency spectrum of input impedances, increased in all experiments, rising from a resting average of 181 ±26 dyne sec cm^{-5} to 249 ±62 dyne sec cm^{-5} during exercise, and the oscillations of impedance moduli with frequency decreased in amplitude. These changes in aortic impedance are similar to those previously reported from this laboratory for the pulmonary artery. The decreased amplitude of impedance oscillations was presumably due to the decrease in reflections that accompanies peripheral vasodilatation, but the increase in characteristic impedance is more difficult to explain. It was probably not secondary to passive distention of the aorta, for the mean arterial pressure increased significantly with exercise in only 1 of the 3 animals. Moreover, in other experiments in which mean aortic pressure was raised by an average of 63% by infusion of norepinephrine, Zo rose by only 29%. This also argues against an increase in circulating catecholamines as an explanation of the changes observed. The most probable cause of the increase in Zo is increased sympathetic neural stimulation of smooth muscle in the aortic wall during exercise.

INVIVO MICROVASCULAR RESPONSES TO EXTRACELLULAR IONS AND EXCITING AGENTS
P.A.NICOLL Physiology, Ind. Uni. Bloomington, Indiana

The essential nature of $Ca^{++}$for excitation-contraction coupling in various vascular muscle has been clearly established. Recent use(BILKE et al Microvasc.Res.7,181,74.) of Verapamil that blocks Ca^{++}entrance where noradrenaline still gives limited response suggests some Ca^{++}store intracellularly. Nicoll and Speeden (Physiologist 15,227,72.) demonstrate depolarization and very slow action potentials proceed spontaneous contraction in invivo preparations of Bat wings. This response of single muscle cells can be used to evaluate contributions of specific ions and excitants. Solutions of known composition and excitants are infused near selected microvessels through accurately placed micropipetts. The minute volume infused only briefly disturbs interstitial pressure. Responses are observed at 700X optical magnification and recorded on T.V. tapes for analysis. Venules more readily respond but arterioles and lympatics give qualitative similar reactions. Ca^{++}free bicarbonate-CO_2 buffered isotonic NaCl,LiCl,CholineCl and tris buffered solutions with $Ca^{++}$and K^+ cause relaxation and vigorous microcircular blood flow that is gradually replaced by vasomotion and tonic constriction in 5 to 20 minutes. Addition of $Ca^{++}$from 2.5 to 10 mM/L induces vigorous vasomotion at normal rates. K^+ from 5 to 25 mM/L in Ca^{++}free solutions has no action. With adaquate Ca^{++}it initially increases vasomotion rate and later intensifies magnitude. EDTA infusion immediately inhibits all contraction however excited and establishes brisk flow for varying time intervals. Verapamil also blocks all activity for up to an hour or more even of noradrenaline. Therefore these single non-innervated vascular muscle cells appear to be dependent on,and extremely sensitive to, changes in available extracellular calcium. Supported in part by a grant-in-aid from RESEARCH AND ADVANCED STUDIES INDIANA UNIVERSITY BLOOMINGTON

RESPIRATORY REFLEX RESPONSES ELICITED BY STIMULATION OF THE AFFERENT THORACIC VAGUS AND ITS BRANCHES IN THE CHICKEN. T.E. Nightingale*, J.C. Richardi*, USDA Poultry Res. Lab., Georgetown, Del. 19947 and D.F. Peterson, Univ. of Tex. Health Sci. Ctr., San Antonio, Tex. 78284.

Thirteen mature male chickens were anesthetized with I.M. Equithesin. The thoracic cavity was opened, air sacs broken and unidirectional respiration begun. Ventilation was maintained at 4 1/min with 94% air and 6% CO_2. This technique produces normal respiratory movements independent of artificial respiratory gas flow. The left vagus nerve and its branches were identified through the thoracic cavity and, at preselected sites, isolated for electrical stimulation. Supramaximal stimulus parameters were selected (5-10 volts; pulse duration, 0.5-2.0 milliseconds; frequency, 10-20/sec). Responses to electrical stimulation were compared to one minute removal of CO_2 from the respiratory gas. CO_2 removal produced abrupt onset of apnea which was maintained throughout the period of zero CO_2 and persisted up to 60 seconds after re-addition of CO_2. Return to control respiratory amplitude was gradual. Stimulation of the thoracic vagus above the lungs always produced sustained apnea. Normal respiratory pattern resumed immediately after stimulation ended. Left thoracic vagal stimulation below the level of the lungs and heart did not affect respiration. Stimulation of left cardiac branches of the vagus near the heart reduced respiratory amplitude slightly in 50% of the animals. Stimulation of the left vagus above the small middle and posterior pulmonary branches occasionally produced apnea, but always reduced respiratory amplitude. Stimulation of the large anterior pulmonary branch of the left vagus eliminated functional respiratory movements in all birds. These results indicate that reflex regulation of respiration of thoracic origin in the chicken is generated from receptors in the lungs and is primarily carried in the anterior pulmonary vagal branch. (Supported by AFOSR-2525)

Influence of monoamines and pineal gland compounds on ^{3}H-LRF transport by median eminence. Mary F. D. Notter* and K. M. Knigge. Dept. of Anat. Univ. of Rochester, Rochester, New York.

Anatomical and physiological evidence has accrued to suggest that monoamines and pineal gland products influence neuroendocrine processes and that one site of their action may be at the level of the median eminence. In this study, we have examined the effect of these agents on in vitro uptake and efflux of ^{3}H-LRF by median eminence (ME) of mink (Mustela vison). The following substances were examined with regard to their effect on 20 min. uptake from a solution of 50 ng/ml ^{3}H-LRF: norepinephrine (NE), dopamine(DA), serotonin (5-HT), (0.5 and 20 μg/ml); melatonin (Mel), (1 and 10 ng/ml) and arginine vasotocin (AV), (2 and 20 ng/ml). NE, 5-HT, Mel and AV had no notable effect on uptake of ^{3}H-LRF at either high or low dose. Uptake was significantly lowered ($P \geq .01$) by 0.5 μg/ml DA and increased ($P \geq .02$) by 20 μg/ml DA. Efflux of ^{3}H-LRF from ME was examined by first preloading tissue with 50 ng/ml ^{3}H-LRF for a 60 min. period followed by a 30 min. incubation in hormone free media to which the various agents were added. In vitro efflux of ^{3}H-LRF from ME is biphasic, with an initial fast component (0-10 min.) followed by a longer phase of slow release. No substance tested influenced the initial fast component of ^{3}H-LRF efflux. 5-HT (20 μg/ml) decreased ($P \geq .02$) the slow component of ^{3}H-LRF release. These data suggest that DA may have a dose-dependent action in facilitating or inhibiting LRF uptake in the ME and that 5-HT may be involved in influencing release.

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CARDIOPULMONARY EFFECTS OF COMBINED EXERCISE AND +G_z ACCELERATION. S. A. Nunneley* and D. S. Shindell* (intr. by H. Rahn). Dept. Physiol., State Univ. of N.Y. at Buffalo, Buffalo, N.Y. 14214.

In upright man gravity and acceleration cause pooling of blood in dependent veins and a perfusion gradient in the lungs. Leg exercise counteracts these effects through (1) local pump action and (2) systemic responses to increased metabolic demand. Experiments to separate these mechanisms were made on four male subjects on a centrifuge at 1, 2, and 3G directed head-to-seat (+G_z), at rest (R), and pedaling with no load (NL), 20, 50, or 100 Watts. Measurements included steady-state cardiopulmonary function and cardiogenic oscillations. The table gives means for all subjects.

	$\dot{V}_{O_2}$(ml/min)			$\dot{V}_E/\dot{V}_{O_2}$(L/L)			HR(beats/min)		
	R	NL	100	R	NL	100	R	NL	100
1G	310	512	1275	26	26	24	72	79	106
2G	314	658	1420	30	26	24	84	86	110
3G	363	857	1668	42	27	26	103	97	133

Both G and work raise $\dot{V}O_2$, $\dot{V}CO_2$, and $\dot{V}E$. At rest, increased G raised $\dot{V}E/\dot{V}O_2$ and altered end-tidal gas ($\uparrow PO_2, \downarrow PCO_2$); pedaling NL returned these variables toward their R/1 G levels, while adding work produced little further change. HR rose with G and work, but at 3G the NL pulse was lower than at rest. Thus pedaling alone (NL) ameliorated many G-effects. In contrast, pulmonary perfusion is related to added work load. At 1 G, NL eliminates cardiogenic oscillations, but at 2 and 3 G their amplitude decreases progressively as work increases. (Supported in part by ONR Contract N00014-68-A-0216,NIH Grant NL 14414-02,and USPH 5 T01 GM00341.)

EFFECT OF COCAINE ON THE CONTRACTILE RESPONSE TO CATHECHOLAMINES OF NORMAL AND FAILING RIGHT VENTRICLES IN DOGS. Dennis D. O'Keefe*, R. Nathan Grantham*, Edward A. Beierholm*, George Z. Kapellakis*, M. Andre Vasu*, Robert A. Guyton* and Willard M. Daggett. Mass General Hospital, Dept. of Surgery, Harvard Medical School, Boston, MA.

This study was undertaken to evaluate the effect of cocaine on the sensitivity to norepinephrine (NE) and isoproterenol (I) of normal and failing canine myocardium. Measurements of right ventricular contractile force in 7 normal dogs were made with Walton-Brodie strain gauge arches placed on the right ventricle in acute experiments under chloralose-urethan anesthesia. NE (1 mcg) and I (0.5 mcg) were injected into a pulmonary vein in bolus doses before and after cocaine, 5 mg/kg intravenously. Right ventricular failure was produced in a second group of 7 dogs by tricuspid valve avulsion and pulmonary artery banding. After six weeks to six months of chronic failure, measurements of contractile force were made according to the same protocol as in normals. Increments in developed force (ΔDF) and rate of rise of force (ΔdF/dt) in response to NE and I before and after administration of cocaine, 5 mg/kg, were compared by Student's t-test for nonpaired data in each group. Normal hearts showed a significant increase in ΔDF to NE (25.5±5.2 g to 71.9±10.3 g, $p<0.01$) and ΔdF/dt (429±44 g/sec to 1159±259 g/sec, $p<0.05$) after cocaine. Failure hearts showed no significant changes in ΔDF (47.3±11 g to 40.9±16.7 g) or ΔdF/dt (1008±412 g/sec to 1490±543 g/sec) after cocaine. Cocaine did not significantly affect the ΔDF or ΔdF/dt response to I in normal or failing myocardium. These data indicate that cocaine does not increase sensitivity to NE under conditions of right ventricular failure, suggesting that the type of sensitivity produced by cocaine in normal hearts may already be present in the failing myocardium.

IMPROVED TECHNIQUES FOR MEASUREMENT OF RENAL INTERSTITIAL HYDROSTATIC PRESSURE. Cobern E. Ott* and Franklyn G. Knox, Department of Physiology, Mayo Clinic, Rochester, Minnesota.

The chronically implanted hollow perforated capsule technique has been used to measure interstitial fluid pressure in many tissues. While this technique has been used in the kidney, capsules small enough to be easily implanted fill readily with tissue, while larger capsules are difficult to implant, may result in trauma, and may distort the normal physiology of the kidney. In addition, pressures measured from these capsules with passive measuring systems are slow to respond to physiologic changes. Recent improvements minimize these problems. Two 3 x 5 cylindrical capsules made from porous polyethylene (PE) matrix material with 60 micron pores were implanted in the left renal cortex of 19 dogs. Tissue did not grow into the PE matrix and the pores created a permanent fluid filled space in communication with the interstitium. Measured pressures were independent of the length of time implanted and ranged from 3 to 13 mm Hg with an average and standard error = 6.4 $\pm$ 0.6 mm Hg. Responsive pressures have been obtained from capsules implanted for 11 months. Response time of the measured pressures was improved by use of an active servo-null pressure measuring device. Pressure measurements with the active device require only a fraction of the time required by passive pressure measuring systems and permit pressure measurements from more than one capsule to be obtained in the same experiment. In control and experimental conditions, measurements from two capsules in the same kidney differed by less than 1.0 mm Hg ($n = 13$, $\bar{\Delta} = .87 \pm .17$ mm Hg). The results indicate that the combination of the implanted PE matrix capsule and the servo-null pressure measuring device can be used to obtain rapid and reproducible measurements of renal interstitial hydrostatic pressure.

RECOVERY TIME FROM REACTIVE (RD) AND ACTIVE DILATION (AD) AT CONSTANT FLOW AND CONSTANT PRESSURE IN THE CANINE GRACILIS MUSCLE. T. Owen, I. Ehrhart*, F. Haddy, and J. Scott. Mich. St. Univ., E. Lansing, MI. 48824

In order to assess the roles of myogenic and metabolic factors in active and reactive hyperemia we studied recovery times in the denervated, vascularly-isolated canine gracilis muscle, pump-perfused at either constant flow rate (CF) or constant perfusion pressure (CP; pressure maintained constant by an electronic controller and a servo-pump). After each of several time periods during which flow to the gracilis was stopped (from 30 s to 5 min), the time required for return to baseline resistance was measured. Time to recovery was also measured following gracilis nerve stimulation (6;1.6 msec) at various frequencies and time periods. Partial results are given in the table (N=10):

Recovery Time (min)

Reactive dilation				Active dilation					
30 s occl.		5 min occl.		2 s-3 Hz		1 min-0.8 Hz		3 min-3 Hz	
CP	CF	CP	CF	CP	CF	CP	CF	CP	CF
1.8	2.8	7.8	13.4	1.0	1.7	2.7	6.1	13.4	21.8
P<.02		P<.02		P<.30		P<.005		P<.005	

The recovery time from 1 and 3 min occlusions and from 1 min stimulations at 1.6 and 3.0 Hz were also significantly greater at CF. The initial resistance following relief of occlusion decreased as a function of occlusion time. In many experiments, the resistance decrease seen on restoration of flow was transiently interrupted by a rise of resistance, followed by a second, longer-lasting dilation. Since restoration of oxygen and metabolite concentrations should be a function of blood flow, the lengthened recovery time at constant flow indicates that metabolic factors contribute to both active and reactive hyperemia in skeletal muscle.

DEVELOPMENT OF RADIOIMMUNOASSAY FOR URINARY KALLIKREIN. N.B. Oza, A. Piwonska* and O.A. Carretero. Henry Ford Hosp., Detroit, Mi.

Rat urinary kallikrein (Kk) was measured by its ability to release kinins from purified dog plasma kininogen. The kinins were measured by a radioimmunoassay (RIA) which was capable of measuring 10pg of kallidin (Kd). Rabbits were immunized against Kd coupled to ovalbumin. The antiserum was preheated to 60° C for 30 min to denature pre-Kk and Kk inhibitor(s). The resulting antisera was used in a final dilution of 1:18,000 to obtain binding between 35-42%. The antibodies recognized Kd, bradykinin and methionyl-Kd, however had no affinity for angiotensin I. The kininogen interfered in RIA & therefore it was removed by precipitation & chromatography. Trace amounts were subtracted as blanks. Bradykinin (8-Tyrosin)-I^{125}-triacetate & the kinins generated after Kk catalysis, were purified by absorption on Amberlite IRC-50 resin & elution in 50% acetic acid (Talamo et al., 1969). The RIA mixture contained 0.1ml antigen (approx. 3000cpm), 0.1ml diluted antiserum & 0.4ml of 0.1M tris-acetate buffer, pH 7.4, containing 0.2% gelatin & 0.1% neomycin, & was incubated for 24 hrs at 4° C. Free antigen was absorbed on dextran coated charcoal. Synthetic Kd ranging from 25-200pg was used to construct a standard plot. The RIA was performed at pH 7.0, 7.4, & 8.0. Although the displacement was better at pH 8.0, there was greater dispersion within duplicates & therefore a pH of 7.4 was chosen for subsequent experiments. Rat urine gave a volume dependent (1 to 8µl) linear relationship & generated 2.94±0.27 µg/ml/min Kd. Thus the RIA should be applicable to determine normal & altered Kk excretion in a variety of pathophysiological conditions. (Supported by NIH grant HL 15839-02 & MHA)

METABOLIC ENERGY EXPENDITURE AND TERRAIN COEFFICIENTS FOR WALKING ON SNOW. K.B. Pandolf*, F.R. Winsmann*, M.F. Haisman*, and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760.

Terrain coefficients for light and heavy brush, swamp and sandy level terrains were reported (Soule and Goldman, 1972) as empiric coefficients fitting the measured data to a basic treadmill energy cost prediction equation (Givoni and Goldman, 1971). The present study investigated a terrain coefficient for snow of various depths. Ten subjects each walked at two speeds, 0.67 and 1.12 m/s (1.5 and 2.5 mph) on a level treadmill, and on a variety of snow depths. Expired air was sampled, using a Max Planck respirometer, during minutes 4-9 and 10-15 of 15 min walks. Snow profiles (i.e., snow depth, footprint depression, density, temperature and hardness) were constructed for the various walks. The ratio of the energy cost of walking in the snow, to the energy cost of walking on the treadmill at the same speed, increased linearly with increasing depth of footprint up to a 17.0 cm depth of footprint, where the energy cost is roughly tripled. Thus, at this snow depression, energy expenditure at 1.12 m/s with about 9 kg of clothing and respirometer weight had reached the rather high levels of $\sim$ 750 kcal/hr. This is well above the 425 kcal/hr $\pm$ 10% described as self paced "hard work" for various terrains and loads (Hughes and Goldman, 1970). Greater snow depressions (> 17.0 cm) must slow walking speed to below 1.12 m/s; e.g., at an average of $\sim$ 38.0 cm depth of footprint, subjects terminated their snow walks due to exhaustion (at 92% of maximal oxygen uptake with a mean heart rate of 189 bt/min). All except one subject were unable to complete 15 min at 1.12 m/s, and the least fit (and also heaviest) subject could not finish at 0.67 m/s for this footprint depth. In addition to speed, performance for snow walking appears limited by the progressively higher leg lift and added static work with increasing depth of footprint.

EFFECTS OF SODIUM DEPLETION ON RENOVASCULAR HYPERTENSION IN SHEEP. Harold R. Parker, Thomas C. Lee and Sarah D. Gray. Departments of Surgery and Human Physiology, University of California, Davis, California 95616.

Renal hypertension (RHT) was produced in sheep by unilateral renal artery constriction which reduced blood flow 40%. When RHT was well established hyponatremia (HN) was induced by draining parotid gland saliva while withholding dietary salt. This decreased serum sodium concentration from 145 to as low as 125 mEq/L. Serum potassium was simultaneously lowered when the latter cation was secreted in parotid saliva in place of sodium because of HN. Na/K of saliva decreased from 32 to 0.12 in one sheep. Reversal of Na/K was probably due to aldosterone since the sheep were in negative salt balance during HN. Plasma volume increased slightly in some sheep during RHT and did not contract during HN. Body weight decreased progressively in several sheep as HN became severe. RHT was not reduced in sheep which lost weight but returned toward normotensive levels in sheep which maintained body weight. Nephrectomy of the clamped kidney promptly returned blood pressure to the control level. To measure differences in epinephrine sensitivity, log dose response curves were determined for 2 cm long helical strips of renal artery during control and hypertensive periods. The concentration of epinephrine necessary to produce a half-maximal constrictor response was lower for control ($7.4 \times 10^{-4} \pm 2 \times 10^{-4}$ mg/ml) than for hypertensive strips ($2.9 \times 10^{-3} \pm 8 \times 10^{-4}$ mg/ml, mean $\pm$ SEM). Results of these experiments suggest that renal artery constriction increases smooth muscle sensitivity to pressor amines. Although RHT of sheep may regress during negative sodium balance the mechanism is not contraction of extracellular space. Release of a hypotensive mechanism during sodium deprivation is implied. Supported in part by grants from the Sacramento-Yolo-Sierra and Central Mission Trails Heart Associations.

EVIDENCE FOR FACILITATORY TRANSPORT OF MODALINE SULFATE BY INHIBITION OF PERIPHERAL MONOAMINE OXIDASE ON INTRACEREBROVENTRICULAR ADMINISTRATION. Surendra S. Parmar*, Basheer Ali*, Stanley J. Brumleve and Radhey S. Misra*. Dept. Physiol. & Pharmacol., Univ. N. Dak., Med. Sch., Grand Forks, N. Dak., and Dept. Pharmacol. & Therap., K. G. Medical Coll., Lucknow Univ., Lucknow, India.

Mechanisms concerned with the central control of the peripheral cardiovascular functions have not yet been fully explained. Effects of intracerebroventricular administration of modaline sulfate (2mg/kg) were investigated on monoamine oxidase (MAO) activity of rat brain, heart and liver homogenates. MAO activity was determined fluorometrically using kynuramine and manometrically with tyramine and 5-hydroxytryptamine as the substrate. Inhibition of brain and heart MAO was observed after 30 sec of administration of modaline sulfate. MAO inhibition of 56%, 42% and 59% in brain during oxidative deamination of kynuramine, tyramine and 5-hydroxytryptamine respectively was reduced to 40%, 28% and 42% after 15 min and thereafter remained constant up to 8 hr. Similar inhibition of heart MAO was 60%, 44% and 42% after 30 sec which, however, increased to 80%, 64% and 67% after 15 min and remained constant up to 8 hr. Inhibition of liver MAO by 38%, 14% and 26% with kynuramine, tyramine and 5-hydroxytryptamine respectively was observed after 60 sec. No inhibition of liver MAO was observed after 2, 4 and 8 hr indicating biotransformation of modaline sulfate or its active metabolite(s) in liver to inactive metabolite(s). These results have indicated that the spontaneous inhibition of peripheral MAO may in some way reflect the possible mechanism for the neural control of the peripheral cardiovascular functions of drugs affecting central nervous system activity. (Supported in part by USPHS NIH Grant 1 T01 HL 05939-01A1 and the Council of Scientific and Industrial Research, New Delhi, India.)

MECHANISM FOR THE CONCENTRATING OF L-ASCORBIC ACID IN POLYMORPHONUCLEAR CELLS. Kris Parnicky* and Nancy R. Stevenson. CMDNJ-Rutgers Medical School, Piscataway, New Jersey.

L-Ascorbic acid (L-HA) and dehydro-L-ascorbic acid (DHA), the reduced and oxidized form of vitamin C have different mechanisms of transport across some cell membranes. We have studied the uptake of both forms by guinea pig polymorphonuclear (PMN) cells. Peritoneal exudates were obtained 12 to 18 hr. after a peritoneal injection of a buffered solution of Na-caseinate. The washed cell suspension contained a minimum of 94% PMN's. The cells were preincubated in vitamin-free media then incubated in media containing tracer amounts of ^{3}H-D-mannitol and the appropriate form of the vitamin. DHA was not observed to be transported against a concentration gradient when calculations were based on the concentration of the oxidized form. It did appear to be transported against a gradient when calculations were based on total vitamin concentrations (T/M=8). The uptake of DHA was not altered by Na^{+} ion replacement by $Iris^{+}$ ion, or by the presence of 2,4-dinitrophenol (0.1 mM) or ouabain (0.1 mM) in the media. L-HA was not observed to be transported against a gradient when calculations were based on either the reduced form or the total vitamin. Since 10 to 14% of the L-HA in the media oxidized to DHA during incubation it is assumed that the majority of the uptake observed with L-HA was due to the movement of the newly formed DHA. Although the total vitamin concentration in the tissue increased to a greater extent when cells were incubated with DHA than with L-HA, the percentage of L-HA in the tissue total vitamin was the same after incubation with either form (88%). It is concluded from this work that DHA enters the PMN by a non-active mechanism and is rapidly reduced to L-HA. PMN's appear to be relatively impermeable to L-HA, thus this form of the vitamin accumulates within the cells. This work was supported by a NIH Post-doctoral Fellowship FO2 AM37687 and a NIH Grant AM10696.

METABOLISM OF PLASMA GLUCOSE IN NORMAL DOGS DURING PARENTERAL NUTRITION.

P. Paul, G. A. Reichard, Jr.*, R. N. Myers,* M. Mirilov,* and W. L. Holmes,* Div. of Research, Lankenau Hosp., Philadelphia, Pa. 19151

Hyperglycemia frequently occurs during the initial period of parenteral hyperalimentation (HA) in malnourished patients. Furthermore, during HA the nutrient solution is infused directly into the bloodstream thereby circumventing physiologic control processes relating to absorption and assimilation in the gastrointestinal tract, including the liver. Studies were done in normal 5-day fasted unanesthetized dogs receiving HA in the femoral or portal vein for 24 hr. Infusion rates were adjusted such that glucose was given at rates at least equal to normal endogenous production. During the last 3 hr of HA rates of glucose production and oxidation were determined by isotope tracer techniques using ^{14}C-glucose. Blood glucose concentrations, markedly elevated during the initial infusion period, declined to constant but still elevated values during the later HA period. At the same HA infusion rate, portal venous administration consistently produced obtunded hyperglycemic responses. Regardless of infusion site, the calculated rate of glucose production was always equal to the rate of glucose infusion, indicating cessation of endogenous production. At the highest HA infusion rate employed, the administered glucose, if completely oxidized, was theoretically capable of supporting total energy expenditure. However, under these conditions, oxidation of plasma glucose accounted for only 50% of total energy expenditure, suggesting other substrates may be utilized.

RESPONSE OF IMMUNOSYMPATHECTOMIZED RATS TO CHRONIC EXERCISE.

D.E. Paynter,* C.M. Tipton, and R.D. Matthes.* Exercise Physiology Laboratory, University of Iowa, Iowa City, Iowa 52242.

It is unclear whether some of the adaptations associated with training will occur in sympathectomized animals. Using normal (N) and immunosympathectomized (IS) rats, this matter was studied with trained (T) and nontrained (NT) animals assigned to 4 groups (12 rats/group). They were exercised for 4-6 times/week for 12 weeks in a motor driven treadmill at speeds, grades, and durations varying from 8 to 22.8 m/min, 0-9%, and 10-80 min/day. Measurements of urinary catecholamine levels, histological evaluation of adrenergic innervation patterns, and differences in rectal temperatures indicated that the antiserum was effective in producing sympathectomized animals. Unanesthetized final resting heart rates were 267 $\pm$ 5 and 286 $\pm$ 4 ($\bar{X}$, SE) for the normal and the NT groups respectively and 291 $\pm$ 5 and 284 $\pm$ 4 for the IS rats that were assigned to NT and T groups. Anesthetized resting mean blood pressures (MBP) were also measured and for the N animals values of 115 $\pm$ 4 for the NT and 103 $\pm$ 3 mmHg for the T were found. The IS NT rats had pressures of 99 $\pm$ 2 while the T were 95 $\pm$ 3. Blood pressure responsiveness was measured in all groups after infusions of catecholamines and after exposure to lower body negative pressures (LBNP). The IS groups exhibited signs of supersensitivity and an inability to reflexly compensate for the effects of LBNP. There were no significant differences between NT and T animals in these measures regardless of groups. At sacrifice, both T groups had significantly greater muscle cytochrome oxidase activity, smaller adipocyte diameters, and higher ligament wet weight/length ratios than their NT controls. It was concluded that a change in "sympathetic tone" is an important consideration in explaining some but not all the adaptations associated with training. Supported in part by Grant Nos. 5T01GM00225-15 and HL14388-2.

HUMAN VENTILATORY RESPONSES TO VARIOUS LEVELS OF BICYCLE EXERCISE. D.H. Pearce* and H.T. Milhorn, Jr., Univ. Miss. Med. Ctr., Jackson, MS 39216.

The objective of this study was to quantitate the dynamics of pulmonary responses of humans to bicycle exercise initiated without warning. The breath-by-breath ventilatory respones of 10 normal males to bicycle exercise, breathing room air, was determined. A digital computer analyzed signals recorded during the experiment for tidal volume, respiratory frequency, minute ventilation, end-tidal P_{CO_2} and P_{O_2}, oxygen and carbon dioxide transfers, and heart rate on a breath-by-breath basis. Each experiment consisted of 8 min rest or no load pedaling, 8 min of exercise, and 10 min of rest or no load pedaling. Qualitatively, the responses at the initiation and cessation of exercise with regard to the fast(F) or slow(S) component at various work loads was considered. For a ventilatory response to be described as fast (F) it must have had at the ON transition a sharp rise in minute ventilation and a rapid decrease in alveolar CO_2 or a rapid increase in alveolar O_2. The opposite pertained to the OFF transition. We conclude from the following table that the rapid change in ventilation at the transition of exercise load is not a regular response feature, varies with load, and type(ON or OFF).

TYPE	$\dot{V}_E$	P_{CO_2}	P_{O_2}	HR	WORK LOAD (N-M)/MIN
ON	2F/8S	10S	10S	5F/3S	600*
OFF	2F/8S	2F/8S	2F/8S	5F/3S	
ON	6F/1S	2F/8S	2F/8S	8F	0
OFF	3F/3S	1F/9S	1F/9S	3F/4S	
ON	9F/1S	3F/7S	6F/4S	9F	300
OFF	4F/6S	10S	10S	4F/6S	
ON	7F/3S	10S	10S	9F/1S	600
OFF	7F/3S	4F/6S	3F/7S	6F/4S	
ON	7F/3S	2F/8S	3F/7S	8F/2S	800
OFF	7F/3S	4F/6S	4F/6S	3F/7S	

*no load pedaling control periods.

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CONCENTRATION AND BIOASSAY OF A NATRIURETIC ACTIVITY IN THE BLOOD OF VOLUME EXPANDED RATS. J.W. Pearce and A.T. Veress*, Dept. of Physiology Univ. of Toronto, Toronto, Ontario.

Cross-circulation of a volume-expanded rat (following blood infusion and urine-reinfusion) with an isovolemic partner leads to a natriuretic response in the latter due to a humoral activity not of adrenal or renal origin (J.Clin.Invest. 51, 2631). In the present study, plasma from a reservoir containing 13 ml. of donor blood, equilibrated for one hour with the circulating blood of volume expanded (E) or isovolemic (C) rats, has been fractionated using a G-50 Sephadex gel column (100 x 1.5 cm) and 10 mM ammonium acetate eluate. The effluent volume showing absorption at 280 mμ (between 25-190 ml) was divided into four fractions, freeze dried and the residues redissolved in 1 ml saline and assayed for natriuretic activity in hydropenic rats. Only Fraction I (between 25-75 ml. effluent volume and containing the plasma proteins) produced a natriuretic response significantly greater for E than for C plasma ($p<.01$). The difference in natriuretic responses to this fraction, representing an activity superimposed on the volume-expanding effect of the hyperoncotic injection, reached a maximum of 4 μEq/min.g_{KW} between 20-60 min after injection and declined to 2 μEq by 100 min. No significant differences in the responses (E compared to C) to Fractions II-IV were observed. The natriuretic activity of Fraction I (E) can be attributed to a large molecule, probably protein, or to a protein-bound moiety; its action on sodium excretion developed within 30 min and was sustained over at least one hour. (Supported by the J.P. Bickell Foundation).

BIOMECHANICS OF FLOATING IN WATER. David R. Pendergast* and Albert B. Craig, Jr., Departments of Physiology, School of Med. and Dent. SUNY at Buffalo, N.Y. and University of Rochester School of Med. and Dent. Rochester, N. Y.

It has been observed that the energy cost of swimming the overarm crawl stroke per unit of distance (V_{O_2}/d) is significantly less for women than for men (33.4 and 46.8 ml/m respectively) over a wide range of velocities. The V_{O_2}/d was significantly less in women even when corrections were made for surface area. It was also observed that women had a more horizontal attitude than men while swimming. Feet floats were attached to the ankles of men, and this modification decreased the V_{O_2}/d to a value which was similar to that of the women. Buoyancy added to the legs of the women did not decrease the V_{O_2}/d. These findings suggested that women might have a lower body density less than that of men. Treating the fully immersed body as a beam with the fulcrum placed at the center of air, the force with which the feet tended to sink or rise was measured directly. This force ranged from positive to negative values as a function of the body density. For men the force at the feet was significantly greater than women for any given total body density. These observations imply that the energy cost of maintaining a horizontal swimming position would be greater for men than for women and provides a possible explanation for the lower V_{O_2}/d of women.

EFFECT OF SODIUM INTAKE ON RENAL POTASSIUM EXCRETION. Linda Peterson* and Fred S. Wright. Yale Univ. School of Medicine, New Haven, Conn.

An understanding of the relation between dietary sodium intake and potassium excretion is complicated by previous, apparently conflicting, observations that Na deprivation may result in either reduced or increased rates of K excretion. We have examined the extent to which the effects of dietary Na depletion may be modified by other factors that affect distal K secretion. Clearance and free-flow micropuncture experiments were performed in normal or Na depleted rats to examine K transport along the superficial distal tubule and between this segment and the final urine. Animals were infused with electrolyte free solution or with solutions containing NaCl, KCl or both. If given no Na acutely, Na depleted rats had lower rates of K excretion than normal rats. When NaCl was given during the experiment Na depleted rats had higher rates of K excretion than normal rats. When KCl and NaCl were infused together, K excretion increased in both groups but Na depleted rats again excreted K faster than normal rats. Micropuncture results showed that the lower K excretion in Na depleted rats was due to increased K absorption beyond the distal tubule when no Na was infused; increased K secretion along the distal tubule when NaCl was infused; and increased K secretion along the collecting duct when NaCl and KCl were infused. Administration of DOCA for 1 day to rats fed a normal diet before acute infusion of NaCl increased distal K secretion to the rates observed in Na depleted animals. We conclude: 1) Chronic Na depletion results in reduced K excretion if no Na is infused acutely; 2) Na depletion increases the capacity of the distal nephron to secrete K in response to acutely infused Na and K; 3) increased levels of adrenal mineralocorticoids in Na depleted animals contribute to the increased rates of distal secretion.

THE RELATIONSHIP OF BODY-FAT CONTENT TO ISOMETRIC ENDURANCE AND DEEP MUSCLE TEMPERATURE OF THE FOREARM. J.S. Petrofsky* and A.R. Lind. St. Louis Univ. Sch. of Med., St. Louis, Mo.

Previous investigators have reported that the endurance time of fatiguing static effort at any given proportion of maximal strength is independent of the muscle group, of muscle strength, and is unaltered by dynamic or static training. However, we have recently shown that this seemingly unalterable relationship between strength and endurance does not apply to subjects whose body-fat content varies. In contrast, we found an inverse relationship between the endurance time and body-fat content. In the present study this relationship was investigated further in trained subjects before and after either weight loss or weight gain to elicit a mechanism for this response. Deep muscle temperature of the forearm at rest, a variable known to exert a profound influence on isometric endurance, was found to vary directly with the subject's body-fat content. In contrast, when muscle temperature was stabilized by prior immersion of the forearm in a controlled temperature water bath, endurance was no longer influenced by the body-fat content. It can be concluded that the increase in muscle temperature in the overweight can be held solely responsible for their lower endurance.

HYPOGLYCEMIC EFFECTS OF ENDOTOXIN IN EVISCERATED DOGS. Marvin D. Peyton,* Lerner B. Hinshaw, and Lazar J. Greenfield. Univ. of Oklahoma Health Sci. Ctr. and VA Hospital, Okla. City, OK 73190.

Although hyperglycemia usually is noted during clinical shock, recent observations in endotoxin-shocked canines have documented profound hypoglycemia. To investigate the pathophysiology of this hypoglycemia, dogs were eviscerated under pentobarbital by ligation and division of the celiac, superior, and inferior mesenteric arteries and the portal vein with removal of the intestinal tract from distal esophagus to rectum including pancreas. Group I (n=6) consisted of animals administered an LD_{80} of endotoxin following evisceration and Group II (n=5) served as eviscerated controls. Measurements were made of femoral arterial pressure (FAP), pulmonary arterial pressure (PAP), arterial pH, $Pa0_2$, $PaCO_2$, 0_2 content and blood glucose.

There were no survivors in Group I beyond 2½ hours while each of the animals in Group II were viable for 4 hours. Blood glucose values remained stable (mean 100 mg.%) in Group II but decreased precipitously to a mean of 22 mg.% at the end of 2 hours ($p < .005$). FAP decreased significantly in Group I at the end of one hour compared to Group II ($p < .01$). $Pa0_2$ decreased slightly in Group I and arterial pH decreased to 7.28 compared to 7.42 mean for Group II. $PaCO_2$ decreased comparably for each group at the end of 2 hours. Serum insulin assays are pending.

Results indicate enhanced peripheral utilization of glucose following endotoxin in the absence of splanchnic hormones and suggest that stable blood glucose levels may correlate directly with survival.

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CHANGES OF ACETYLCHOLINESTERASE (AChE) AND CHOLINEACETYLTRANSFERASE (ChAc) CORRELATED WITH THE FORMATION OF CHOLINERGIC SYNAPSES IN THE CHICK EMBRYO. G. Pilar, V. Chiappinelli, H. Uchimura* and E. Giacobini*
Biological Sciences Group and Biobehavioral Sciences Dept., Univ. of Ct., Storrs, Ct. 06268.

In the adult ciliary ganglion, 60% of the ChAc is localized in the pre- and 40% in the postsynaptic neural elements. 100% of the iris ChAc occurs in the ciliary nerve terminals. 25% of AChE is present preganglionically and 75% postganglionically. In the iris neuromuscular junctions 15% is in the terminals and 85% is in the muscle (Uchimura, Pilar, Suszkiw and Giacobini unpublished observations). Both enzymes' activities were measured in ganglia: during synapse formation (St 26-30, Hamburger & Hamilton), cell death (St 34-39) and synapse maturation (St 39-hatching), and in the iris prior to and during the period of synapse formation (St 26-33;33 1/2-38), (Landmesser & Pilar, 1974a &b, J.Physiol. in press). AChE: a rapid increase in the iris coincides with the formation of synapses. In ganglia a 10-fold increase starts at St 32, and adult values are reached at St 38. ChAc: in the iris lower activities (0.15×10^{-10} moles/g/hr) are found at St 26-34. Then a gradual 10-fold rise occurs. After St 39, there is a 50-fold increase. In ganglia there is a progressive increase from St 28 ($1.87-6.37 \times 10^{-10}$ moles/g/hr). From St 31 on there is a steady faster increase until St 45. It is inferred that a) at least in the iris muscle the nerve terminals induce the formation of AChE postsynaptically; b) that ganglion cells are biochemically differentiated from the onset of synapse transmission; and c) the formation of the iris muscular junctions triggers the initial increase in synthesis of ChAc in these ganglion cells

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LOCALIZATION OF HYPEREMIA FOLLOWING MEALS. R. Pittman*, P. Kvietys*, and C.C. Chou. Depts. of Physiol. and Med., Mich. State Univ., E. Lansing,MI.

In anesthetized dogs, food in the stomach initially increased blood flow(BF) in the celiac artery, followed 30minutes later by an increase in the superior mesenteric artery (SMA); whereas, infusion of food into the duodenum only increased BF in SMA without a change in BF in the celiac artery (Fed. Proc. 33:338, 1974). In this study BF in SMA (by electromagnetic flowmeter) and an isolated segment of the jejunum (by timed collection of venous outflow) were simultaneously measured before and during 1) infusion of digested food into the duodenum at 4 ml/min for 60 min (N =6) or 2) placement of digested food into the jejunum for 15 min (N=10). BF in percent of controls (SMA=15 ml/min/kg, jejunum=0.48 ml/min/gm) following the infusion or placement of food are shown below:

Food in	BF in	5	15	20	25	35	50	60 min
duodenum	SMA	109	120*	123*	122*	126*	121*	122*
	jejunum	98	98	98	98	103	94	95
		2	6	9	12			15 min
jejunum	SMA	99	97	94	91			89
	jejunum	124*	117*	130*	138*			143*

*$P < 0.05$ as compared to the control.

Systemic pressure was not significantly altered. Similar infusion or placement of normal saline did not significantly alter BF in SMA or jejunum. These studies indicate that infusion of digested food into the duodenum raises BF in SMA, but does not alter BF in an isolated jejunal segment having no contact with food. On the other hand, placement of digested food in the isolated jejunal segment promptly increases local BF but does not alter BF in SMA. These data further support the conclusion that the increased BF in the splanchnic viscera following a meal is localized in the area performing digestive functions, i.e., secretion, absorption, and digestion. (Supported by NIH Grant HL15231)

IN VIVO DETERMINATION OF PERCENT OXYHEMOGLOBIN IN THE MICROVASCULATURE. Roland N. Pittman and Brian R. Duling, Dept. of Physiology, University of Virginia, Charlottesville, Virginia 22901.

Previous studies have indicated that significant quantities of oxygen may diffuse out of vessels other than capillaries (Circ. Res. 27, 669, 1970). This results in a progressive decline in periarteriolar PO_2. The aim of the present experiments was to assess the extent to which there is an accompanying desaturation of hemoglobin. A new spectrophotometric method for measuring percent oxyhemoglobin in blood (S) has been described previously and shown to be valid for microvessels of the hamster cheek pouch (The Physiologist 16, 423, 1973). The cheek pouch was suffused with a bicarbonate-buffered physiological salt solution, with CO_2 held at 5% in control measurements. In the suffused, transilluminated tissue, simultaneous steady-state measurements of perivascular PO_2 (with O_2 microelectrodes) and S were made on vessels ranging in size from 15 to 100 microns I.D. The data agreed well with the oxyhemoglobin (HbO_2) dissociation curve for hamster blood. Associated with the previously reported longitudinal gradient in PO_2 was a corresponding gradient in S which was consistent with predictions from the HbO_2 dissociation curve. Significant shifts in the measured saturation could be produced by varying the CO_2 between 1% and 10% in the suffusion solution. The longitudinal gradients in PO_2 and S persisted under these conditions. Saturation changes were also found to be related to red cell velocity. These studies indicate that the previously reported longitudinal gradient is a manifestation of oxygen unloading from red cell hemoglobin.

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PHYSIOLOGY LABORATORY PROGRAMS IN MEDICAL EDUCATION. James L. Poland, Kenneth E. Guyer, Jr., and Hugo R. Seibel. (intr. by Steven Price). Medical College of Virginia, Richmond, Virginia.

The value of a laboratory program in physiology courses taught to first year medical students has often been questioned. Information collected through questionnaires indicates that the average time devoted to the laboratory has steadily declined in recent years while lecture time has remained unchanged. There also appears to be a shift toward experiments which can be done on humans. There is great reluctance to completely abandon the laboratory program and the majority of physiology departments have retained a lab program centered around student conduction of preassigned experiments and sprinkled with demonstrations, conferences, and seminars. Laboratory attendance is required in most departments, but on the average the student's laboratory performance contributes only 10% of the student's final grade. The two most highly regarded objectives for a laboratory program are "supplementation and reinforcement of didactic material" and an "appreciation of experimental development and methodology". It is difficult to objectively determine whether or not the objectives of any laboratory program are being reached and any subjective evaluation tends to be greatly biased. Although visual aids are considered very advantageous by most, they are used during only a small percentage of the total lab time. There remains great diversity of opinions concerning the significance of a laboratory program and how it should be conducted. Remarks contributed indicate that any laboratory exercise must reflect the convictions of the local staff in order to be a worthwhile learning experience.

ANALYSIS OF A PERIODIC BREATHING PATTERN ASSOCIATED WITH MAYER WAVES. Canio Polosa, George Preiss* and Steve Iscoe*. McGill University, Montreal, Canada.

Cats subjected to common carotid artery occlusion and hemorrhage developed a waxing and waning of respiratory amplitude recurring with a period of 24 seconds (range 10 to 60). Occasionally the wanning phase terminated with an apnea. This respiratory pattern, reminiscent of "periodic" breathing, was associated with an oscillation of sympathetic neural activity. and of systemic arterial pressure, of the same period. A similar pattern of modulation of phrenic nerve activity was observed during neuromuscular block and artificial ventilation, and when, in addition, the associated systemic arterial pressure oscillation was eliminated by alpha-blockade. These findings suggest that this breathing pattern is not the result of an analogous pattern in the discharge of gas tension-sensitive and/or blood flow- and pressure-sensitive receptors which is fed back to the CNS. Hence the pattern must be generated within the CNS with no need of rhythmic sensory information. The pattern can be accounted for by the assumption that the central respiratory drive potentials are riding on top of a slow oscillation of phrenic motoneuron membrane potential with a 24 sec period. (Supported by MRC of Canada).

THE EFFECT OF CERVICAL SYMPATHETECTOMY ON REGIONAL BRAIN BLOOD FLOW DURING HEMORRHAGIC SHOCK. J.T. Ponessa,* P.Sandor,* A.G.B. Kovach* & E. T. Angelakos. Dept. of Physiology, Hahnemann Medical College, Phila., PA. 19102 and Semmelweis Medical University, Budapest, Hungary.

In a series of five cats, regional blood flow in deep thalamic structures was continuously monitored using a thermal washout technique. After severe hemorrhage (MABP=35-40 mmHg) of 50-70 minutes duration, acute bilateral transection of the cervical sympathetics produced a local flow increase in only one of the five cats, and this instance was probably due to a relatively large pressor response which accompanied the transection. The cortical blood flow response to sympathectomy following a milder shock regimen was studied in the dog. Flow in this series was measured by the H_2 washout technique. In 12 electrode placements in 6 dogs, acute bilateral cervical sympathectomy was followed by an increased cortical flow in 6 cases, unchanged in 3 cases and decreased in another 3 cases. It is concluded that, at least in some instances, sympathetic discharge may account for part of the reduction in cortical blood flow in mild shock. However, in severe shock, this effect was not seen, and, if present, was probably obscured by the other powerful factors which impair the general circulation. (Supported in part by a U.S. Navy Themis Contract).

SPLANCHNIC VASCULAR RESPONSES TO PROSTAGLANDIN INFUSIONS IN THE CANINE
Judith A. Post* and Kenneth M. Hanson. Department of Physiology, Ohio State University College of Medicine, Columbus, Ohio. 43210

Pilot studies have been done on effect of 15-30 min. prostaglandin (PG) infusion in denervated dog liver and small intestine preparations. PGA_1 was infused via mesenteric artery 30 min. at rate of 2 μg/kg/hr in 11 gut preparations. Blood flow increased and resistance decreased reaching maximum response (+57% and -38%, respectively, $p<0.01$) after about 1 min. By 10 min. mean values had returned to control level and remained so throughout the infusion. Systemic pressure significantly ($p<0.01$) decreased after 10 min. (-10%) and continued to fall (-14% after 30 min.). Initial dilator response was about 50% less with 1 μg/kg/hr dose. Effect not blocked by Sotalol. Another 11 gut preparations PGB_1 was similarly infused but at 80 μg/kg/hr. Initial dilator response was brief, small (mean -14% resistance change) and not statistically significant. After 1-2 min. flow decreased and resistance increased throughout infusion (at 30 min. -41% and +57%, respectively). PGA_1 was infused (2 μg/kg/hr) via femoral vein in 11 liver experiments. There was initial transient decrease (6%) in hepatic artery resistance after 5 min. with return to control at 10 min. Liver blood flow and systemic pressure decreased. There was little change in portal vein resistance or bile flow. PGB_1 was infused (80 μg/kg/hr) in another 11 preparations first via portal vein and then hepatic artery. There was a slight hepatic artery dilation particularly when given by latter route with little change in other parameters.

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ATP IN RAT LUNG TISSUE. E.M. Postlethwait, S.L. Young, and J.H. Knelson (intr. by G.S. Malindzak) Environmental Protection Agency, Research Triangle Park, N.C.

Krebs has reported a marked reduction of ATP concentration in liver slices when compared to the isolated perfused liver (Adv. Enz. Reg. 8:335, 1970) and concluded that metabolic studies of liver based on tissue slice (TS) techniques may be misleading. We used the isolated perfused rat lung preparation (IPL) as described by O'Neil and Tierney (A.J.P. 226:867, 1974); tissue slices 1.0 mm thick were made with a McIlwain slicer. The perfusate and incubation medium were Krebs phosphate buffer, equilibrated with 95% O_2 and 5% CO_2, pH 7.4, with 5 grams albumin/100ml and 4 mM glucose at 37°C. After rapid freezing in liquid N_2, tissue was extracted in perchloric acid; ATP was measured with a DuPont Luminesence Biometer and DNA by the diphenylamine reaction. We measured ATP concentration in rapidly frozen rat lung tissue: [1] immediately after removal from the animal (control), [2] after isolation and perfusion for 90 minutes, [3] immediately after slicing (TS 0 min.), and [4] after tissue slicing and incubation for 90 minutes.

IPL	TS
Control - .31 (±.02)[n=13]	0 min - .16 (±.01)[n=8]
90 min. - .39 (±.03)[n=6]	90 min - .32 (±.03)[n=16]

Values in the table are μmoles ATP/mg DNA (± S.D.). We conclude there is a 50% reduction in lung tissue ATP immediately upon slicing, and after 90 minutes of organ perfusion or tissue slice incubation, lung tissue ATP concentrations are comparable.

RELATIVE IONIC PERMEABILITIES OF EPITHELIAL CELL MEMBRANES FROM CURRENT-VOLTAGE GRAPHS. A. C. Poutala and R. E. Swanson. Dept. of Physiology, Univ. of Oregon Medical School, Portland, Oregon 97201.

Equivalent electrical analogs of epithelial tissues indicate why classical electrophysiological analysis fails to yield reasonable values for relative permeability coefficients of ions for apical and basilar cell membranes of "low resistance" epithelia. Due to the high ionic conductance of the paracellular shunt pathways in these tissues, the net ionic current traversing the apical and basilar membranes will not be zero under most experimental conditions. Therefore those electrophysiological methods of analysis which depend on net ionic current being zero cannot be applied correctly to these epithelia. We have developed a method of analysis, based on Goldman flux (i.e., ionic current) equations, which allows the determination of relative ionic permeabilities of epithelial cell membranes. In all steady state conditions (i.e., those conditions in which the net ionic current thru each membrane is identical), we propose that for any epithelium there is a unique set of Goldman flux equations which describe the electrophysiological characteristics of the apical membrane. Similarly, a unique set of Goldman flux equations describes the basilar membrane. These two sets of flux equations can be identified in principle on current-voltage graphs by their ability to fit all membrane potential data collected from ionic substitution experiments. We will present the pertinent features of this graphical analysis for obtaining relative ionic permeabilities of epithelial cell membranes.

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CRITICAL LEVELS OF INTERMITTENT MATERNAL HYPOXIA ON FETAL SURVIVAL. Gordon G. Power, Tom Bennett*, Jan W. Kuzma*, and Lawrence D. Longo. Loma Linda Univ. School of Med., Loma Linda, CA 92354.

The fetus may experience periods of intermittent hypoxia during labor. In these experiments we simulated the effects of labor on fetal oxygenation by exposing 36 pregnant rabbits (26 to 28 days gestation) and their 392 fetuses in utero to intermittent hypoxia. A gas mixture containing 3, 4, 5 or 6% O_2 in N_2 was administered to a rabbit for 0.5, 1, 2 or 3 minutes, alternately with a recovery period of air breathing of 0.5, 1, 2 or 3 minutes. A given cyclical pattern was continued for 2 hours and fetal survival recorded 1 hour thereafter. After 2 minute exposures to 6, 5, 4 and 3% O_2 maternal arterial P_{O_2} had fallen to 26, 23, 19 and 16 mm Hg, respectively. Results for a recovery interval of 1 minute showing the percentage of fetuses surviving in each litter is given in the chart below. Fetal survival diminished when the recovery interval was shortened to 0.5 minutes and improved when lengthened to 2 or 3 minutes. Correlation of fetal survival with size and location in the uterine horn and histologic examination of fetal brains is underway. In conclusion, hypoxia results in maternal death when mothers repeatedly breathe less than 4% O_2 for 2 minutes or more. Fetal death is a function of maternal inspired P_{O_2}, duration of exposure and duration of recovery period. Supported by USPHS HD 04394, 03807 and United Cerebral Palsy Foundation.

Percentage of Fetuses Surviving

% O_2	Duration (min) 3	2	1	0.5
3	0+	0+	0	100
4	60	47	100	100
5	25	100	100	100
6	33	100	100	100

+ Maternal death

EXCITATORY CEREBELLAR INFLUENCE ON THE INFERIOR OLIVARY NEURONS. R.J. Preston*, J. Kocsis*, S.T. Kitai. Wayne State University School of Med., Morin Memorial Lab., Detroit, Mich.

Recent anatomical studies find evidence for projections from the cerebellum to inferior olive (IO). To assess the functional character of this circuitry, extra- and intracellular microelectrode recordings from IO neurons were made in surital-chloralose or nembutal anesthetized cats. Brief electrical pulses were delivered through bipolar stimulating electrodes to the nucleus interpositus (IP) of the cerebellum, brachium conjunctivum (BC), its decussation(DBC) and red nucleus (RN). Antidromic field potentials evoked by stimulation of inferior cerebellar peduncle were used to aid localization of IO. Antidromic units showed their typical multiple-spiked discharge. Extracellular unitary recordings demonstrated that two groups of responses, based on latencies, exist following stimulation of IP or BC. Intracellular recordings revealed that the short latency group arose from monosynaptic EPSPs and the longer latency group from polysynaptic EPSPs. RN stimulation also evoked monosynaptic EPSPs and short latency unitary spikes in the IO neurons. These EPSPs were via slow conducting rubro-olivary fibers. Findings indicate that the short latency IP evoked responses may be due to a direct excitatory cerebello-olivary feedback pathway, and the longer latency IP evoked responses to indirect feedback pathway through RN. (Supported by NIH Grant NS 00405 and NSF Grant GB 35532)

ACID-BASE EFFECTS ON KIDNEY SLICE AMMONIAGENESIS (NH_3) IN THE PRESENCE OF PHYSIOLOGIC FUELS. H.Preuss, O.Vavatsi-Manos* and K. Baird*. Georgetown U. Med. School, Washington, D.C.

To determine how substrates alter NH_3 under different acid-base conditions, rat kidney slices from acidotic (A) and control rats (C) were incubated in bicarbonate-buffered medium at pH 7.0, 7.4 and 7.8. Glutamine (G), palmitate (P), lactate (L), and B-OH butyrate (BOH), were added in physiologic blood concentrations. Under every condition studied, slices from A compared to C produced more ammonia. With G alone or G + P + BOH, pH did not alter ammoniagenesis in A or C. However, addition of L to G or G + BOH + P resulted in a significant depression of NH_3 from A and C at pH 7.4 and 7.8, but no change at pH 7.0. NH_3 from G by A incubating in L at pH 7.0 exceeded NH_3 by C at pH 7.4 approximately 3 times (22.1 um/g/90 min to 58.6 um/g/90 min, $p<.01$). Therefore, both external pH and/or HCO_3^- and tissue adaptation to acidosis affect G metabolism in the presence of L. Our results suggest that substrates at physiologic concentration regulate NH_3 differently in slices from control and acidotic rats at varying pH.

Slice Ammoniagenesis (um/g/90 min)

	CONTROL			ACID		
Substrate	7.0	7.4	7.8	7.0	7.4	7.8
G	39.5	36.4	34.8	52.4	53.8	51.0
G+P+BOH	43.4	49.2+	44.6+	60.9*	59.2*	56.2*
G+L	35.4	22.1+	20.2+	58.6	44.2+	42.9+
G+P+BOH+L	49.3+	19.2+	19.5+	67.9+	36.3+	36.0+

+ $p<.01$ * $p<.05$ compared to G at same pH
minimum of 6 rats for each average

UNIDIRECTIONAL ION MOVEMENTS IN THE ISOLATED HINDGUT OF THE BLOWFLY LARVA, SARCOPHAGA BULLATA. Robert D. Prusch. Division of Biomedical Sciences. Brown University. Providence, R.I.

Previous measurements of net ion fluxes and transepithelial potentials across the isolated hindgut of the blowfly larva, Sarcophaga bullata, have indicated that this system is capable of moving K^+, Na^+, NH_4^+, and Cl^- ions against an electrochemical potential gradient from the outside medium into the gut lumen. In the presence of the appropriate medium, the isolated gut is capable of maintaining an electrical potential difference of 15 mV, lumen negative in respect to the outside medium. Preliminary investigation of unidirectional ion movements have been undertaken to further characterize the ionic distribution in this system. The unidirectional influx of Cl^- was 5.46×10^{-8} moles/cm^2.min while Cl^- efflux was 1.92×10^{-8} moles/cm^2.sec. Unidirectional K^+ influx was determined to be 1.43 moles/cm^2.min and K^+ efflux was found to be 0.45×10^{-8} moles/cm^2.min. The unidirectional influx of Na^+ was 1.21 moles/cm^2.min. According to the Ussing flux ratio analysis, K^+ and Cl^- are not distributed passively, i.e., $J^i/J^o \neq C_i/C_o e^{-EF/RT}$ for K^+ or Cl^-. The movement of both K^+ and Cl^- into the isolated gut lumen appears to involve an active process. The effect of the addition of 1 mM NH_4^+ to the outside medium is to increase the unidirectional Cl^- influx and to decrease the unidirectional K^+ influx, indicating that NH_4^+ competes with K^+ secretion, with Cl^- moving actively with both K^+ and NH_4^+.

Isobarbic vs. Isovolumetric Stimulation of Cardiac Sympathetic Afferents R.V. Purtock, R.L. Coon, E.J. Zuperku, S. Peters, and J.P. Kampine (Intr by G.B. Spurr) Med. Col. of Wisc., Milwaukee, Wisc. 53226

Receptors located in the wall of the left ventricle which respond to pressure and/or displacement and whose afferent nerves traverse the thoracic white rami have been described. The purpose of this research was to better define the adequate stimulus for these receptors. Anesthetized dogs were placed on total heart-lung bypass. Systemic arterial perfusion pressure was maintained between 70 and 90 mm Hg. Blood gases were maintained at a PO_2 above 150 mm Hg, PCO_2 between 35 and 45 mm Hg, and pH 7.35 and 7.44. A method of alternate isobaric-isovolumetric contractions of the left ventricle was developed. Isobaric conditions were imposed by placing a balloon in the ventricle which was attached to a pressurized air filled 50 L reservoir. Since the stroke volume represented only a small fraction of the total system volume, the pressure increase in the system, during systole was negligible. The signal from a pneumotachometer placed in the connecting tubing, was electronically integrated to obtain the instantaneous volume changes in the ventricle. Isovolumetric contractions were measured with a second balloon in the left ventricle which could be fluid filled. Nerve activity was obtained from the left thoracic white rami using bipolar electrodes and was recorded with ECG, left ventricular pressure and stroke volume on a strip chart recorder and Tandberg tape recorder. Afferent nerve activity was analyzed with respect to the cardiac cycle using an Ortec histogram computer. This analysis indicated that both displacement and pressure receptors exist in the left ventricle but that receptors which respond to pressure appear to predominate in the nerves studied.

EFFECTS OF LOCAL EXERCISE AND SYSTEMIC BLOOD VOLUME INCREASE ON BLOOD FLOW AND O_2 IN COLLATERALLY PERFUSED CANINE LIMBS. D. Radawski*, R. Underwood*, T. Burns*, and R. Daugherty, Michigan State University Departments of Physiology and Medicine, East Lansing, MI.

This study investigated the above procedures in canine forelimbs in which the brachial artery was chronically versus acutely ligated. In 7 dogs the right (R) brachial artery was completely ligated 4-6 weeks before the experiment while the left (L) brachial artery was completely ligated just prior to the experiment. Arterial and R and L brachial venous O_2 contents, brachial venous (muscle, F_m, ml/min) outflows and brachial artery (P_{BA}) and venous (P_{BV}) pressures were measured during control periods, during active hyperemia (faradic muscle stimulation, 7V, 1.6 m sec, 6/sec) and after systemic volume expansion (30 min Dextran infusion = 2% body weight). R and L skeletal muscle vessel resistances (R_m, mmHg/ml/min) were calculated. In order to estimate skeletal muscle oxygen the O_2 delivery to O_2 utilization ratios (O_2) were computed from arterial O_2 x F_m/arterial-venous O_2. Initially RF_m = 21.3, RO_2 = 142 and RR_m = 4.1 while LF_m = 16.3, LO_2 = 64 and LR_m = 5.7. Local exercise decreased RO_2 to 81 and RR_m to 2.6. Corresponding values for L were 30 and 4.6. Dextran infusion decreased RR_m from 4.4 to 2.9 and increased RO_2 from 48 to 89. Corresponding values for L were 6.5 to 5.0 and 65 to 123. These data indicate that chronically ligating a limb may produce greater initial blood flow and may allow a greater active hyperemic response. However, chronic ligation may not have any significant effect on the magnitude of the response to systemic dextran infusion.

RESPONSE OF TOAD BLADDER APICAL MEMBRANE POTENTIAL TO MUCOSAL Na^+, Cl^- and K^+. A. G. Ramsay, D. L. Gallagher*, G. Sachs and R. L. Shoemaker. M.I. Bassett Hosp., Cooperstown, N.Y. and Univ. Alabama in Birmingham.

In the open circuit state, the epithelial cell of toad bladder is electro-positive to mucosal solution. This suggests that apical membrane Na^+ permeability is $>$ than that of Cl^-, the major mucosal solution anion. Thus apical membrane potential should be a direct function of mucosal $[Na^+]$, but be independent of mucosal $[Cl^-]$ and $[K^+]$. The concept was tested with micro-electrode experiments. Apical membrane P.D. and transepithelial potential increased in a curvilinear manner with progressively increasing mucosal $[Na^+]$. Greatest P.D. response occurred between 10^{-3} M and 10^{-2} M Na^+. Semilogarithmic plot of mucosal $[Na^+]$ and apical P.D. showed a highly significant regression coefficient of 9.41. Apical and transepithelial P.D. was uninfluenced by mucosal $[Cl^-]$ and $[K^+]$. Semilogarithmic plots of mucosal $[Cl^-]$ and $[K^+]$, and apical P.D. showed regression coefficients that were not significantly different from 0. In another approach, change in apical P.D. was measured 5 min. after imposition of a 40 mV apical potential by a clamp of constant direct current. With 10^{-1} M Na^+ present in mucosal solution and the cell electro-negative, apical P.D. decreased 10.7-11.6 mV. Δapical P.D. with cell electro-positive was 0. With cell polarity either + or -, and mucosal solution either 10^{-1} M K^+ or $8.8 \cdot 10^{-2}$ M Cl^-, Δapical P.D. was 0. It is concluded that apical membrane P.D. is dependent on mucosal $[Na^+]$, and independent of mucosal $[Cl^-]$ and $[K^+]$. This suggests permselectivity of the apical membrane favoring Na^+ with consequent separation of charge and electropositivity of cell. Curvilinear response of P.D. to Na^+ suggest finite limitation of permeation sites.

ENDOCRINE RESPONSES TO FOOD IN NORMAL AND DIABETIC INDIVIDUALS. N. Ian Ramus*, Hugo V. Villar*, David D. Reeder, Phillip L. Rayford* and James C. Thompson. The University of Texas Medical Branch, Galveston, Texas.

The major endocrine abnormalities in diabetes mellitus (DM) are ascribed to insulin and glucagon. An increased incidence of several varieties of gastric dysfunction (delayed emptying, mucosal atrophy, diminished parietal cell mass, decreased acid output) suggests there may be a disturbance in the metabolism of other gastrointestinal hormones. Methods: To test this hypothesis, we have measured basal and postprandial levels of insulin, glucose, glucagon, cholecystokinin (CCK), calcium and gastrin in 10 normal individuals and 5 patients with DM (we have measured basal gastrin values in an additional 4 normal and 14 DM patients). Results: Insulin and Glucose: Normal subjects had a typical insulin response to food (2.7 μU/ml basal, 114 μU/ml peak) and a slight and transient increase in blood glucose. In the DM subjects, insulin rose only slightly (13.1 to 36.3 μU/ml), and glucose rose from 120 to 209 mgm% at 2 hrs. Glucagon: Basal levels were 1.18 ng/ml in normals and 1.49 in DM patients; after food, peak levels were 1.45 and 1.70 respectively. Basal and postprandial levels of CCK and calcium in DM patients were not different from controls. Basal gastrin levels were 126 pg/ml in normals and 280 pg/ml in DM patients ($p<0.01$). Although basal values overlapped among the 2 groups, all control levels were <200 pg/ml, whereas 70% of gastrin levels in DM patients were >200 pg/ml. After the meal, gastrin rose to a similar extent in both groups (normal 102%; DM 80%). Conclusions: Typical insulin, glucose and glucagon abnormalities were measured in DM patients. Basal and postprandial levels of gastrin were significantly higher in DM. This may be a reflection of delayed gastric emptying and diminished acid inhibition of gastrin release.

Concurrent Measurement of d(LVP)/dt and Contractile Force in Intact Non-Human Primate. D. C. Randall, O. A. Smith, M. P. Kaye, W. C. Randall & K. H. Martin*. Division of Behavioral Biology, Johns Hopkins Univ., Baltimore; Regional Primate Research Center, Univ. of Washington, Seattle Dept. of Physiology, Loyola Univ., Maywood, Ill.

Eight chair-restrained rhesus monkeys were implanted with left ventricular catheters to measure the rate of rise of ventricular pressure (dP/dt). An isometric force transducer was also sutured onto the left ventricular myocardium to measure contractile force (CF) in 4 of the monkeys. Positive inotropic responses were elicited in these animals by administration of isoproterenol (5 μgm/kg) and by controlled behavioral situations including exercise, eating and "emotional" conditioning. Concurrent changes in CF and the maximum dP/dt were compared during each of the above situations. Both variables typically increased during pharmacologically and behaviorally induced increases in myocardial contractility. Linear correlation coefficients relating changes in dP/dt and CF ranged from 0.8 to greater than 0.9 ($p < .01$) which in turn suggests that each variable responded in a similar manner to a given inotropic intervention over a wide range of physiological conditions. The possible influence of alterations in afterload and preload on dP/dt was investigated in the remaining 4 monkeys after surgical denervation of their hearts to eliminate possible direct neural reflex effects. Arterial pressure and left ventricular filling pressure were increased by infusion of phenylephrine and decreased by nitroglycerine. A quantitative analysis of the resulting changes in dP/dt showed that alterations in loading resulted in only very small effects on dP/dt in intact monkeys with areflexic hearts. (Supported by NIH Grants RR 00166, HL 04741, HL 06945, HE 08682 and HL 05889)

EFFECTS OF 1 HOUR OF RENAL PEDICLE OCCLUSION ON DOG KIDNEY FUNCTION AND O_2 CONSUMPTION. Howard M. Randall, Jr. Department of Physiology, Louisiana State University Medical Center, New Orleans, Louisiana, 70112.

We have reported that renal functional changes occurring after 1 hour of renal arterial (RA) occlusion in the dog are largely due to a decrease in GFR and not to tubular dysfunction. Present studies were designed to determine the effects of occluding both the RA and collateral vessels (RP) on several renal functions and $\dot{Q}O_2$. The left renal pedicle and perirenal fat containing collateral vessels were occluded for 1 hour and then released. $\dot{Q}O_2$ and total renal blood flow (TRBF) were determined in the ischemic left kidney only, while clearance measurements were made in both kidneys before and up to 3 hours after ischemia. After occluding the RP the clearances of inulin, PAH, and osmols, as well as the rate of reabsorption of Na^+ ($\dot{T}Na^+$) and PAH extraction, were significantly lower than values obtained after occluding the RA. Also, the % rejection of Na^+ was increased significantly by RP occlusion but was not changed by RA occlusion. Since the decreases in $\dot{Q}O_2$ and TRBF were comparable in the 2 types of studies, the differences in response did not appear to be due to changes in the rates of tissue perfusion or energy metabolism. Because of the increase in % rejection of Na^+ and a marked decrease in $\dot{T}Na^+/\dot{Q}O_2$ after RP occlusion it would appear that tubular dysfunction does occur. Perhaps a viable collateral circulation is of significance in preventing or at least reducing tubular dysfunction during acute RA occlusion. (Supported by USPHS Grant No. HE 11987).

CARDIAC DYSRHYTHMIAS IN THE CONSCIOUS DOG - A MODEL OF AUTONOMIC IMBALANCE. W. C. Randall, M. P. Kaye, G. R. Hageman*, and H. K. Jacobs*. Loyola University, Stritch School of Medicine, Department of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

Knowledge of the precise projection patterns of both sympathetic and parasympathetic nerves onto the canine heart is now available, and ablation of specific portions of these efferent neural supplies is feasible. Differential denervation of the SA node and atrial tissues, leaving the innervation of the AV node and ventricular tissues via the ventrolateral cardiac nerve essentially intact, involves surgical excision of the tissues around the complete circumference of the superior vena cava (SVC). The dissection is continued medially from the SVC across the superior surfaces of the right and left atria and the adventitia is removed from the complete circumference of the pulmonary artery and between the roots of the pulmonary artery and ascending aorta. At operation, bipolar electrodes are implanted over the SA node, inferior right atrium and right ventricle. The leads are brought through the chest and skin of the neck. Completeness of denervation is tested by electrical stimulation of both right and left vagi and stellate ganglia before closure of the chest with recordings of contractile force and electrical activity from atria and ventricles. All animals are ambulatory on the first post-operative day and are started on treadmill exercise while ECG and direct atrial and ventricular electrograms are recorded. Whereas resting heart rhythms originate in supraventricular locations following operation, AV nodal or junctional rhythms are regularly elicited during direct stimulation of the left sympathetic supply. Stressful stimulation during treadmill exercise or norepinephrine injection also induce definitive cardiac dysrhythmia. *(Supported by NIH Grant HL 08682)*

FETAL CONTROL OF UTERINE BLOOD FLOW. John H. G. Rankin and T. M. Phernetton* University of Wisconsin, Medical School, Madison, WI.

The effect of changes originating in the fetal environment on the uterine placental blood flow was tested in 10 near-term ewes. Catheters were placed in a fetal hind limb artery and vein, a maternal femoral artery and the maternal left ventricle. An electromagnetic flow probe was placed on the largest of the 2 uterine arteries. Each ewe was allowed to recover from surgery for 1 or 2 days. The uterine and umbilical blood flows were measured with radioactive microspheres before and after the injection of norepinephrine (NE) into the fetal venous catheter. Dosage of NE ranged from 50 μg to 200 μg. The infusion of NE produced a profound decrease in the uterine blood flow. The change in the uterine blood flow began less than 1 minute after the injection of NE and its time course approximated that of the fetal pressor response. The uterine flow response was probably secondary to the effects of NE on the fetus, and not due to the direct effect of NE on the maternal vasculature. This conclusion is supported by 2 observations. 1) NE injected into a normal fetus caused a profound decrease in the uterine blood flow and little or no response in the same fetus after the fetus became acidotic. 2) The response of the uterine blood flow was abolished when the alpha receptors of the fetus were blocked with phenoxybenzamine (25 mg/fetus). The uterine vascular bed retained its ability to react to NE administered to the mother following fetal acidosis or phenoxybenzamine block in the fetal circulation even though, under these conditions, it failed to react to NE administered to the fetus. The uterine blood flow in the near-term sheep can respond to changes in the physiologic state of the fetus. These responses can be large, amounting to at least 50% of the uterine blood flow. This suggests that the uterine blood flow is in part controlled by the fetus.
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ENZYME CONFORMATION CHANGES IN THERMAL ACCLIMATION STUDIED WITH IMMUNOLOGICAL TECHNIQUES. Frank S. Ranuska* and Irving Gray. Georgetown University, Department of Biology, Washington, D.C.

In recent publications we have reported that in the case of several enzymes, acclimation to a 10°C decrease in temperature in poikilotherms brought about a stable change in the tertiary or quarternary conformation. These conclusions, based on thermodynamic data, have been confirmed through an immunological study of glyceraldehyde-3-phosphate dehydrogenase (G3PDH). The enzyme was isolated and purified from rainbow trout, Salmo gairdneri, acclimated to 5°C and 15°C. Antibodies to the two were produced in rabbits. Antisera were obtained after 3 weeks (Short Term, ST) and 12 weeks (Long Term, LT) of immunization. It was found that the 15°C G3PDH reacted strongly with both anti-15°C-sera but not with anti-5°C-serum (ST) and only slightly with Anti-5°C-serum (LT). 5°C G3PDH reacted strongly with both anti-5°C-sera but not with anti-15°C-serum (ST) and only slightly with anti-15°C-serum (LT). After incubation of the enzyme with its antiserum, the kinetics of the G3PDH assay were affected. A Lineweaver-Burk analysis of the data was indicative of non-competitive inhibition. There was little or no cross reaction.

ULTRAFILTRABLE ATP AND 2,3-DPG CONCENTRATIONS IN COLD-STORED HUMAN ERYTHROCYTES. Nayer Rassaian*, Wayne E. Marshall*, Linda Greenwald*, and Akira Omachi. University of Illinois at the Medical Center, Chicago, Illinois, 60680.

Free ATP and 2,3-diphosphoglycerate concentrations have been determined in lysates of erythrocytes that had been cold-stored for various periods of time under blood bank conditions. Erythrocytes were washed with cold 0.9% NaCl and lysed by adding 2 volumes of water to each volume of washed cells. Acid extracts were prepared from washed cells, lysates, and ultrafiltrates; the latter were formed by forcing lysate fluid through a PM-10 membrane in an Amicon ultrafiltration device under N_2 pressure. In ACD-stored erythrocytes, total 2,3-DPG and ATP decreased in 2 weeks by 85 and 20%, respectively. The free ATP fraction declined from 50 to 10% of the total ATP, whereas the free 2,3-DPG fraction increased from 20 to 100% of the total 2,3-DPG during this time. In CPD-stored cells, the changes were minimal over the 2 week period. When fresh ACD blood was incubated at 5^{o} in N_2 as well as in air, free 2,3-DPG and ATP were lower under anaerobic conditions by 60 and 25%, respectively. With 2 week-old cells, the corresponding differences were 10 and 85%. These findings correspond in general with the observations of Udkow *et al.* on hemoglobin solutions containing ATP, 2,3-DPG, and Mg^{++} (Nouv. rev. franc. d'Hematol. 13:817, 1973). Our results indicate that free ATP levels in ACD-stored erythrocytes decrease in 2 weeks because ATP binding to hemoglobin increases as competition from 2,3-DPG declines in these hypoxic cells. The reduction in free ATP concentration may be a significant factor in the development of the storage lesion. (Supported by USPHS Grant HL 13567).

ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN REGULATION OF THE LEVEL AND 24-HOUR RHYTHM OF RAT CARDIAC GLYCOGEN. E.E. Rau*, S.B. Jones* and D.K. Meyer, Dept. of Physiology, Univ. of Missouri, Sch. of Med., Columbia, Mo. 65201.

The circadian oscillation of rat myocardial glycogen levels is well documented. It is also well established that i.p. administration of 6-hydroxydopamine (6-OH-DA) results in long lasting, but not permanent, depletion of peripheral tissue catecholamines other than in the adrenal medulla which appears to be refractory to the depleting action. The objective of this study was to determine whether the sympathetic nervous system modulates the regulatory mechanisms controlling heart glycogen levels. Male Wistar rats averaging 125 grams were entrained on an alternating light (0600-1800 hrs.) - dark (1800-0600 hrs.) cycle. Experimental animals received either 30 plus 50 mg/kg of 6-OH-DA (i.p.) separated by 2 hours or received combined adrenal demedullation and 30 plus 50 mg/kg 6-OH-DA. Sham animals received equivalent volumes of the isotonic saline vehicle or combined sham demedullation and the equivalent volumes of vehicle. Demedullated rats were re-entrained for 10 days prior to experimentation. Rats were injected at 4 hour intervals (0000, 0400, 0800, 1200, 1600 and 2000 hrs.) and were terminated at various times after administration of 6-OH-DA (2 hrs., 24 hrs., 6 days and 12 days). Myocardial glycogen and catecholamine content was measured. Chemical sympathectomy significantly elevates cardiac glycogen levels but does not eliminate the glycogen circadian rhythm. Combined chemical sympathectomy and adrenal demedullation may eliminate the rise and peak of the glycogen rhythm. The results support the hypothesis that the mechanisms controlling cardiac glycogen levels may be modulated by the sympathetic nervous system. (Supported in part by NIH Grants HL 05810 and HL 16041)

EFFECT OF GIP AND VIP ON GASTRIN RELEASE AND GASTRIC SECRETION. Phillip L. Rayford*, Hugo V. Villar*, David D. Reeder and James C. Thompson. The University of Texas Medical Branch, Galveston, Texas.

Secretin and glucagon have been shown to suppress gastrin release and gastric secretion. Gastric inhibitory polypeptide (GIP, 2 μg/kg/hr) and vasoactive intestinal polypeptide (VIP, 1 μg/kg/hr), which are both members of the secretin-glucagon family of hormones, were individually administered in 2-hour infusions to 5 Heidenhain pouch dogs in order to test their effects on gastric secretion and on serum values of gastrin, glucose, insulin and calcium in the basal and post-prandial state. Results: Gastrin: Mean basal gastrin values were 62 pg/ml, 47 pg/ml and 50 pg/ml in the control, VIP and GIP studies respectively. VIP and GIP infusions had no effect on basal gastrin. The gastrin response to food was significantly decreased with VIP at 60, 75, 90 and 120 minutes after feeding. GIP infusion also decreased the gastrin response to food; significant differences were found at 120 minutes. Glucose: Blood glucose rose slightly and similarly after food in all 3 groups. Insulin: Serum insulin levels rose only slightly in control groups and were not affected by VIP-GIP. Calcium values did not change throughout the studies. Acid: The 2-hour output after feeding was 6.29 mEq in the control study; this was suppressed by VIP (2.76 mEq) and by GIP (3.21 mEq). Conclusions: Previously reported GIP-induced increases in insulin during glucose infusion were not seen with GIP given after a normal meal. GIP and VIP diminished the gastrin response to food and decreased acid output after food.

RADIOIMMUNOASSAY MEASUREMENT OF THE DISAPPEARANCE HALF-TIME OF EXOGENOUS CHOLECYSTOKININ. David D. Reeder, Hugo V. Villar*, Edward N. Brandt, Jr.*, Phillip L. Rayford* and James C. Thompson. The University of Texas Medical Branch, Galveston, Texas.

The physiologic effects of an injection of cholecystokinin (CCK) are rapid in onset and relatively brief in duration. The disappearance half-time ($T\frac{1}{2}$) of CCK is not precisely known; previous studies of the disappearance of CCK from the circulation have been hampered by the lack of precision of bioassay techniques. We have determined the disappearance pattern and half-time of CCK, measured by radioimmunoassay, after an injection of purified CCK. Methods: Seven fasting mongrel dogs were given an i.v. injection (2 IDU/kg) of purified porcine CCK (Jorpes) over 2 minutes. Serum samples were obtained before, during and at frequent intervals after the injection. Serum concentrations of CCK were measured using a sensitive and specific radioimmunoassay technique for CCK developed in our laboratory. The data were analyzed by linear regression analysis for calculation of the disappearance half-time. Results: The mean basal serum CCK concentration in 7 dogs was 454 pg/ml. At the end of the CCK injection, the level had risen to 728 pg/ml; 4 minutes later, CCK was 542 pg/ml and by 14 minutes after the injection, the levels were back to baseline. Regression analysis indicated that the disappearance curve was best fit by a single exponential. The calculated disappearance half-time was 2.59 minutes. Conclusion: As measured by radioimmunoassay, exogenous porcine CCK disappears rapidly from the circulation of dogs. The short disappearance half-time indicates that the mechanisms for catabolism are potent and efficient.

FLUX-RATIO AND SHORT-CIRCUIT TESTS NOT SUFFICIENT TO CONCLUDE THAT ION TRANSPORT IS PASSIVE. W. S. Rehm, F. M. Hoffman* and S. S. Sanders. Dept. of Physiol. and Biophysics, University of Alabama in Birmingham, The Medical Center, University Station, Birmingham, Alabama 35294.

It is generally accepted that an ion is passive if a) its net transport under Ussing-Zerahn short-circuit conditions is zero and b) its movement obeys the Ussing flux-ratio equation, i.e., $J_{12}/J_{21} = (C_1/C_2)\exp(zF\Delta\psi/RT)$. We will show by means of a conceptual model that unless the ion pathways are conductive or can be represented by equivalent circuit conductive pathways that the above criteria are necessary but not sufficient for deciding that the ion transport is passive. Our model consists of two membranes in series (M_1 and M_2). M_1 has parallel passive conductive pathways for Na^+ and Cl^-; M_2 has parallel passive conductive pathways for K^+ and Cl^- and in addition has an active neutral NaCl mechanism which pumps NaCl from the cytoplasm (between M_1 and M_2) to the other side of M_2. Under steady state open-circuit conditions the rate of Na^+ transport equals that of Cl^-. Under steady state short-circuit conditions a) I_K must be zero and $I'_{Cl} = I_{SC}$ for M_2 (primes refer to M_2), b) $I_{SC} = I_{Na} - I_{Cl}$ (for M_1) and $|E_{Cl}|$ in $M_1 = |E'_{Cl}|$ in M_2 (but with opposite orientation). Hence $I_{SC} = [R_{Cl}/R'_{Cl} + R_{Cl})]$ I_{Na} and $I_{Cl} = R_{Cl}/R_{Cl}I_{SC}$. Now if $R_{Cl} \approx R'_{Cl}$ then $I_{Cl} \neq 0$ but if $R_{Cl} >> R'_{Cl}$ then $I_{SC} \approx I_{Na}$ and the net transport of $Cl^- \approx 0$ and the flux-ratio for $Cl^- \approx 1$. It will be shown that by using appropriate values for the concentrations of the ions in the various compartments, and with $R_{Cl} >> R'_{Cl}$, the ratio of the unilateral fluxes would approximate that predicted by the flux-ratio equation. Therefore, to warrant the conclusion that Cl^- is a passive ion more information is needed than the short-circuit and flux ratio tests (e.g., the magnitude of R_{Cl}/R'_{Cl}). (NSF and NIH support.)

PROTECTIVE EFFECT OF A PROSTAGLANDIN DERIVATIVE ON MORTALITY FOLLOWING CORONARY LIGATION AND VENTRICULAR FIBRILLATION. R.L.Riley,* D. Polis,* & E.T.Angelakos. Hahnemann Medical College, Phila., PA. and Naval Air Development Center, Warminster, PA.

A new, base catalyzed, stable free radical derivative of PGB1 (named PGBx) which has been found to restore oxidative phosphorylation in degenerated non-phosphorylating mitochondria in vitro was studied for its effect on survival of primates subjected to cardiac hypoxia by coronary ligation followed by specific periods of induced ventricular fibrillation (VF). Acute coronary ligation (left descendans) was performed in male rhesus monkeys (5-9 kg) anesthetized with pentobarbital. VF was induced in all animals 20 min. after ligation (unless it occurred spontaneously prior to that) and in intervals of 20-30 min. thereafter and maintained for 4,6,8,12 and 24 minutes in successive periods. Electrical defibrillation (EDF), cardiac massage (CM) and intracardiac norepinephrine (NE) as needed were used to restore cardiac function. Recovery was established by return of blood pressure to pre-VF levels (min. systolic 40 mmHg) without exogenous support. Out of 16 control animals (C) 60% recovered after 4 min. of VF and 20% after 12 min. Experimental animals (E) were pretreated with PGBx and were given CM, NE and/or PGBx as needed following EDF. Of 16 E animals, all (or 100%) recovered after 4 min. of VF and 88% and 80% after 12 and 24 min., respectively. Median recovery time from probit regression was 5 min. and 90 min. for C and E groups, respectively. The extent of cortical EEG recovery was greater and occurred sooner following EDF in the E than C groups. There were no detectable cardiovascular effects nor any obvious anti-arrhythmic effect attributable to PGBx treatment. It is concluded that PGBx significantly enhances recovery from cardiac hypoxia following VF in primates with coronary ligation.

THE INFLUENCE OF INSULIN ON SUCCINIC DEHYDROGENASE ACTIVITY IN RAT LIVER IN VIVO. John S. Rinehart* (SPON: A.R. Lind). St. Louis Univ. Sch. of Med., St. Louis, Mo. 63104.

Previous investigation has demonstrated that if rats are maintained on a feeding schedule which allows only five hours of feeding in each twenty-four hour period, then the enzymatic activity of succinic dehydrogenase (SDH) will vary significantly according to the time of sacrifice. Further investigation implicates insulin as a factor in the regulation of the succinic dehydrogenase activity. If insulin is administered during the postabsorptive state, then the normal rise in SDH activity is inhibited. When animals are made diabetic by the administration of alloxan, the normal pattern of rise and fall in SDH activity is abolished; however, if insulin is administered as a single injection in the diabetic animals immediately after food withdrawal, then the pattern of rise and fall in SDH activity is reestablished. In our experiments to date, none of the gluconeogenic hormones tested when administered in vivo have altered the normal pattern of SDH activity.

FOREARM CUTANEOUS VENOUS CAPACITY DURING BODY TEMPERATURE TRANSIENTS PRODUCED BY LEG EXERCISE. M.F. Roberts*, C.B. Wenger*, and J.A.J. Stolwijk. John B. Pierce Fndn. Lab. and Yale Univ. Sch. Med., New Haven Conn. 06519.

To obtain an understanding of the thermal control of peripheral venous capacity, we have studied forearm venous volume in subjects whose internal temperature was increased by leg exercise.

Four subjects exercised upright on a Monark bicycle ergometer designed to allow measurement during exercise of forearm volume by electrocapacitance plethysmography. The forearm venous capacity was taken as the difference between the volume measured with the veins filled to a congesting pressure of 10 mmHg and with the veins emptied by pneumatic counterpressure on the arm. This technique separates changes in venous volume from volume changes caused by capillary filtration. Internal temperature was measured with an esophageal probe at heart level (T_{es}), and mean skin temperature was computed from a weighted mean of eight skin sites. The subjects exercised at 50% $\dot{V}O_2$ max at an ambient temperature of 25°C.

Subjects exercised for 5 min and rested for 2 min. Between exercise periods counterpressure was applied to the arm and venous volume determined.

During these experiments, T_{es} rose 0.5 to 1.0°C and forearm venous capacity rose by about 2cc/100cc for a 1°C rise in T_{es}. The results indicate that peripheral venous capacity is not maximal at neutral body temperatures. NIH Grants ES-00123, ES-00354, and supported by NASA NGR 07-008-002.

MECHANISMS OF CIRCULATORY ADAPTATION TO ACUTE HEMODYNAMIC OVERLOAD IN CONSCIOUS DOGS. E. Rodriguez-Lopez*, T. Solomon* and W. Ehrlich. Johns Hopkins Univ. Sch. of Medicine and Sch. of Hygiene, Baltimore, Md. 21205.

This study explored the time sequence relationship of mechanisms responding to a sudden increase in aortic outflow resistance. The combined response eventually restored cardiac output (Qao) to near control levels in spite of the sustained rise in aortic pressure (Pao). A balloon inflated (1.5 ml of air) in the descending thoracic aorta of four conscious, standing dogs produced a 10% step increase in Pao from 117 to 128 mm Hg (average of 69 trials with 4 dogs). The response was a 30% decrease of Qao within 2 seconds, with a drop in stroke volume (SV) of 24% and in heart rate (HR) of 7.5%. Right atrial pressure (Pra) rose by 0.7 mm Hg. Within 4 seconds Qao fell by 39% and HR dropped 27% while SV was decreased by only 14%. Pra rose by 2 mm Hg. This indicates that initially Qao was limited mainly by force-velocity effects of the afterload on the myocardium and soon after by the aorto-carotid stretch receptor reflex. The gradual restoration of Qao, which was nearly complete in 18 seconds, is thought to be the result of at least three influences; 1) Starling effect, secondary to increased preload and filling time; 2) Escape from the vagal influence of the aorto-carotid reflex, as indicated by a return of the pulse rate to near control values, possibly due to an overriding vascular reflex from the underperfused beds, shifting the autonomic balance to sympathetic predominance; and 3) The redistribution of flow to beds with shorter time constant of drainage (Caldini, et al, 1974) of the head and forelimbs.

SERUM APOLIPOPROTEIN PROFILE IN SUCROSE INDUCED HYPERLIPOPROTEINEMIA. Paul S. Roheim, Diane Edelstein*, and Gloria L. Vega*, Albert Einstein College of Medicine, Dept. of Physiology and Medicine, Bronx, N.Y. 10461.

The apolipoprotein profile of sucrose induced hyperlipoproteinemic rats was compared to those of controls. The apolipoprotein profile consists of measurement of apolipoprotein concentration in serum, distribution of apolipoproteins within lipoprotein classes, and determination of apolipoprotein composition of the different lipoprotein classes. Serum apolipoprotein concentration and distribution were measured by quantitative immunoelectrophoresis and the apolipoprotein composition of the different lipoprotein classes was determined by polyacrylamide gel electrophoresis. During sucrose induced hyperlipoproteinemia the serum apolipoprotein concentration increased, especially that of apo-C which increased by 60%. Apo-B serum concentration remained unchanged while marked alteration in the distribution of apo-B between VLDL and LDL was observed. The apo-B present in VLDL increased from 25% of the total apo-B to 66%, with a corresponding decrease in the LDL apo-B concentration during sucrose induced hyperlipoproteinemia. This might be the result of a possible defect in the interconversion of VLDL to LDL. The distribution of apolipoprotein C within lipoprotein fractions remained unchanged. Considerable amounts of two apolipoproteins were found in the d>1.21 fraction; these were the 35,000 mol wt protein which has a high arginine content and the 46,000 mol wt protein which is mainly present in HDL. 26% of the serum concentration of the 46,000 mol wt apolipoprotein was found in the d>1.21 fraction in control sera as compared to 11% in the hyperlipidemic sera. This suggests a shift of this apolipoprotein from the d>1.21 fraction to other lipoproteins. These data demonstrate a specific alteration of apolipoprotein profile in sucrose induced hyperlipoproteinemia.

EFFECTS OF CORTISOL AND THYROXINE ON FATTY ACID AND PHOSPHOLIPID BIOSYNTHESIS IN FETAL RABBIT LUNG. S.A. Rooney*, I. Gross*, E.K. Motoyama and J.B. Warshaw*. Yale University School of Medicine, New Haven, Conn.

Cortisol and thyroxine accelerate fetal lung maturation and increase surfactant production. We have examined the effect of these two hormones on some enzymes of fatty acid and phospholipid synthesis in fetal rabbit lung. At 24 days gestation cortisol (1 mg) was injected both into 37 fetuses and their amniotic sacs in one uterine horn of 11 does. Those in the other horn were injected with saline and served as controls. Thyroxine (1µg) was similarly administered to 30 fetuses from 9 does. The fetuses were delivered at 27 days. Cortisol inhibited de novo fatty acid synthesis in the soluble fraction by 51.9±10.3% ($p<0.005$) as measured by the incorporation of acetyl-CoA into pentane extractable fatty acid. This was due to inhibition of both acetyl-CoA carboxylase and fatty acid synthetase activities. There was no effect on mitochondrial or microsomal fatty acid elongation. Choline phosphotransferase activity was not affected (104.0±12.8% of control value), although it has previously been reported to be stimulated by cortisol. The incorporation of radioactivity from [^{14}C]glycerol-3-phosphate in the presence of CDP-diglyceride into lipid, a measurement of phosphatidylglycerol (PG) biosynthesis, was increased 69.5±2.9% ($p<0.005$) by cortisol treatment. Thyroxine had no effect on any of the enzymes examined. As fatty acids are components of cell membranes as well as of surfactant, the inhibition of fatty acid synthesis may be related to the known inhibitory effect of cortisol on growth. It also raises the possibility that a significant portion of surfactant fatty acid is derived from non-pulmonary sources. The stimulation of PG synthesis is of particular interest since this surface active lipid is a known component of surfactant. (Supported by grants from NIH (HL-14179 (SCOR) and HD-8293)and the Connecticut Heart Association (536)

PULMONARY WEDGE CATHETERIZATION DURING POSITIVE END-EXPIRATORY PRESSURE (PEEP) VENTILATION. R.J. Roy*, S.R. Powers, Jr.*, and R.E. Dutton. Departments of Physiology and Surgery, Albany Med. Col., Albany, N.Y.

The effect of PEEP ventilation upon pressure recording from a pulmonary artery wedge catheter as studied by obtaining 39 simultaneous recordings of left atrial (LA) and pulmonary artery wedge (PW) pressures at varying levels of PEEP with the thorax either open or closed. Lateral roentgenograms were taken to determine the relative position of the catheter tips. The following results were obtained:

	End-expiratory Pressure in cm H_2O							
	0		5		10		15	
	LA	PW	LA	PW	LA	PW	LA	PW
	Pulmonary Artery Wedge Tip Anterior to Left Atrial Catheter Tip							
Mean	5.3	5.7	5.7	6.8	6.7	9.9	8.9	15.2
SE±	0.6	0.5	0.7	0.5	0.6	0.5	0.7	0.8
	Pulmonary Artery Wedge Tip Posterior to Left Atrial Catheter Tip							
Mean	3.5	3.0	4.2	3.7	4.2	4.9	5.9	7.8
SE±	0.7	0.6	0.5	0.5	0.6	0.4	0.6	0.5

These results suggest that when the wedge catheter tip is vertically above the left atrial catheter tip, the wedge pressure recording follows airway pressure for PEEP above 5 cm H_2O. For PEEP of 5 cm H_2O and below, and for wedge catheter tip positions vertically below left atrial catheter tip at all levels of PEEP, the wedge catheter pressure follows left atrial pressure. Prediction formulas are derived for the error in measuring pulmonary vascular resistance due to varying wedge catheter tip position. In addition, it was observed that when the balloons are inflated, the tips of all currently available balloon-tipped catheters lie impinged against the enclosing vessel wall.

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EFFECT OF CONSTANT LIGHT (LL) ON FEMALE MICE HOUSED IN THE PRESENCE AND ABSENCE OF MALES. K.D. RYAN AND C.S. CAMPBELL (Intro. by N.B.Schwartz), Northwestern U. Med. Sch., and U. of Ill. Coll. of Med., Chicago, Ill.

Regularity of the mouse estrous cycle is cued to external stimuli, including the light-dark cycle and the presence of a mature male. Exposure to a male mouse results in shorter estrous cycles (Whitten, W.K., 1956, J. Endo. 13:399) and it has been suggested that mice, like rats, show a persistent estrous syndrome when housed in LL (Murthy and Russfield, 1970, Endo. 86:914). The purpose of this experiment was to compare the effects of LL on estrous cycles in mice housed in the presence or absence of males. Female white Swiss mice (CD-1, Charles River) were housed in LD 14:10 or in LL, singly caged or separated from a male by a perforated divider. After 120 days all animals were autopsied. Singly housed LL females showed a 41% incidence of lengthened cycles over controls, compared to a 16% incidence over controls in LL females with males. Persistent vaginal cornification occurred in only 2 of 16 LL mice, in contrast to 21 of 25 rats housed under the same lighting conditions. Regardless of housing, mice in LD autopsied on proestrus had elevated uterine intraluminal water, wet uterine weight and serum estradiol, but low serum progesterone in comparison to metestrus. Both groups of LL mice also had higher uterine weights at proestrus than metestrus. However, singly housed LL mice had low uterine water on both days while LL mice housed with males resembled LD controls. No differences in serum steroids were found between proestrus and metestrus in either group of LL mice. In conclusion, the cycle-lengthening effect of LL in the mouse can be reduced but not prevented by the presence of a male. Presence of a male does not, however, prevent the loss of a detectable steroid pattern in LL mice. (Supported by grants from FFRP to C.S. Campbell and HD 07504 to N.B. Schwartz).

A PASSIVE COMPONENT OF VOLUME REABSORPTION IN PROXIMAL STRAIGHT TUBULES. J. A. Schafer and T. E. Andreoli. Univ. Ala. Med. Ctr., Birmingham, Ala.

We evaluated the characteristics of volume reabsorption in proximal straight tubules isolated from rabbit renal cortex. In tubules perfused and bathed at 37° C with Krebs-Ringer (KR) buffers containing 25 mM HCO_3^- and 114 mM Cl^-, net volume reabsorption (J_v, nl min^{-1} mm^{-1}) and spontaneous transepithelial voltages (V_e, mV, lumen to bath) are, respectively, 0.43 and -1.13. Both values become zero, either at 21° C or with 10^{-4} M ouabain in the bath. The tubules are Cl^--permselective (Abs. Am. Soc. Nephrol. 6:92, 1973). The present experiments assessed J_v and V_e in tubules perfused with fluid resembling that obtained from late proximal convolutions. In paired experiments, tubules were perfused with: either a low Cl^- KR buffer (LoCl, pH 7.4) containing (mM) 114 Cl^-, 25 HCO_3^-, 5 alanine and 8.3 glucose; or, a high Cl^- KR buffer (HiCl, pH 6.6) containing 138 Cl^-, 3.8 HCO_3^- and 13.3 urea. LoCl and HiCl bathing media had the same respective ionic constituents, and uniformly contained 5 alanine, 8.3 glucose and 6% albumin. With HiCl perfusate and LoCl bath at 37° C, J_v and V_e were, respectively, 0.34±0.04 (SEM) and +0.54±0.1. At 21° C, J_v fell to 0.15±0.02 and V_e rose to +1.41±0.09; both the J_v and the V_e values obtained at 21° C differed significantly from control results at 37° C ($p<0.001$) and from zero ($p<0.001$). Moreover, J_v and V_e at 21° C were both reduced to zero when the Cl^- gradient was abolished by changing either the perfusate to LoCl or the bath to HiCl. Results statistically indistinguishable from those at 21° C were obtained at 37° C when 10^{-4} M ouabain was added to the bath. We conclude that, for a HiCl perfusate and LoCl bath: first, the rise in V_e produced by cooling or ouabain may represent loss of an electrogenic component due to active Na^+ transport; second, at 21° C or at 37° C with 10^{-4} M ouabain, V_e is a Cl^- diffusion potential and J_v depends on passive forces generated by the Cl^- gradient.

THE REVERSAL OF THE INHIBITION OF COLLATERAL CIRCULATION DEVELOPMENT INDUCED BY AN AORTIC THROMBUS USING SEROTONIN DEPLETION AND RECEPTOR BLOCKADE. R.G. Schaub and K.M. Meyers (intro. by W.M. Dickson) Washington State University, Pullman, WA 99163.

This study was designed to investigate the relationship of platelet serotonin (5-HT) to inhibition of collateral circulation development induced by an aortic thrombus by investigating the effect of blood 5-HT depletion or 5-HT receptor blockade following thrombolic occlusion. In all cats permanent ligations were placed at the iliac bifurcation and circumflex iliac arteries. A thrombus was produced by injection of 10-20 units of thromboplastin. In 9 cats blood 5-HT was depleted using a single dose of reserpine (0.1 mg/kg i.m.) followed by para-chloro-phenylalanine (p-CPA) (100 mg/kg orally) every 3 days. An additional 8 cats were treated with a potent 5-HT antagonist cinanserin HCl (4 mg/kg i.v.) before surgery. The development of collateral circulation was assessed by aortograms 3 days after occlusion, the presence of paralysis, and measurement of hind limb blood flow by the hydrogen desaturation method immediately before and 3 days after occlusion. In reserpine-p-CPA treated cats blood 5-HT concentration was 10% of pre-treatment controls on the day of surgery. In this group 3 cats completely recovered, 4 cats exhibited partial recovery, and 2 cats were paralyzed. Hindlimb blood flow was 80% of control flow 3 days after occlusion. In cinanserin treated cats, 2 cats exhibited complete recovery, 5 cats exhibited partial recovery, and one cat exhibited paralysis. Blood flow was 60% of control flow 3 days after occlusion. These results suggest that blood platelet serotonin may be an important factor in inhibition of collateral blood flow development following an aortic thrombus. This study was supported by a grant from the Washington State Heart Association. Dr. Schaub is a Washington Heart Association Postdoctoral Fellow.

STUDIES ON THE MECHANISM OF AMYLASE RELEASE IN THE PERFUSED RABBIT PANCREAS. M. Schebalin*, M.J. Siegman and M.H.F. Friedman. Jefferson Medical College, Philadelphia, Pa. 19107.

The amylase secretion from the arterially-perfused rabbit pancreas was measured in response to Ca^{+2}, Ba^{+2}, Mn^{+2}, Cs^{+1}, Acetylcholine (ACH) and Cholecystokinin (CCK). Perfusion fluid was modified Locke (2.2 mM Ca^{+2}). Pancreatic secretion was collected over a period of 3.5 hours. Spontaneous amylase secretion declined exponentially in the presence of 2.2 mM Ca^{+2}. A dose-response relation between secretion and the $[Ca^{+2}]$ perfused was observed. In calcium-free media the decay was more rapid and secretion stopped. While elevated Ca^{+2} the amylase output rose to a peak at about 2 hours and then gradually declined. Ba^{+2}, Mn^{+2} and Cs^{+1} (2.2 and 8.8 mM) evoke secretion, but the effects of these ions differed with regard to concentration and the concomitant presence or absence of 2.2 mM Ca^{+2}. Introduction of 2.2 or 8.8 mM Ca^{+2} or Mn^{+2} in glands perfused with Ca^{+2}-free Locke resulted in proportional increases in amylase output, but with Ba^{+2} an inverse relationship between ion concentration and response was found. Introduction of 2.2 or 8.8 mM Ba^{+2} in the presence of calcium resulted in proportional increments in amylase output, but with Mn^{+2} an inverse relationship held. A high concentration of Cs^{+1} always gave a small secretory response, independent of the presence of Ca^{+2}. 10 mM Mg^{+2} in the presence of 2.2 mM Ca^{+2} stimulated amylase secretion. The responses of 10µg ACH in the presence of Ca^{+2}, Ba^{+2}, Mn^{+2}, Mg^{+2} or Cs^{+1} followed the same dose-response pattern evoked by the cations alone. The secretory responses to ACH and CCK were Ca^{+2}-dependent. The responses to Ca^{+2}, Ba^{+2} and CCK were not blocked by atrophine, suggesting a direct action on the acinar cell. With repeated ganglionic stimulation with DMPP, the first secretory response was smaller than subsequent responses, suggesting a compartmentalization of amylase.

MICROVASCULAR VOLUME CHANGES FOLLOWING PHENYLEPHRINE STIMULATION. Robert E. Schoen* and Carleton H. Baker. Dept. of Physiol., Coll. of Med., Univ. of South Fla., Tampa, Fla. 33620.

Values for changes in microvascular volumes have been extrapolated from total organ plethysmographic recordings, intravascular radioactive tagging, and other macroscopic means. The accuracy of such conclusions has been criticized. The present study was designed to measure by direct visualization microvascular radius and length changes during periods of vasoconstriction. Rat mesentery was exteriorized and irrigated with warmed Ringers solution for microscopic visualization. Rats arterial blood pressure was continuously monitored by a femoral cannula. Vasoconstriction was effected with varying concentrations of phenylephrine introduced into the irrigating solution. Arterioles (15-50μ), venules (15-70μ), and capillaries were observed. Diameter measurements were obtained with a Vickers Image Splitting Eyepiece, while length measurements were obtained with a Grass Force Displacement Transducer attached to the microscope stage. As the concentration of phenylephrine was increased arteriolar constriction produced progressively greater reductions in radius. Arteriolar length also increased over a range of 0 to approximately 10% as the dosage of phenylephrine was increased. Vessel blood volume, calculated on the assumption that the vessel was a cylinder, decreased with increases in the drug dosage. Since arterioles increased in length concurrent with a decrease in radius, it would appear that decreases in vessel volume estimated only on the basis of the radius changes would be excessive. Similar calculations on veins and capillaries are being made. (Supported by the Florida Heart Association, Suncoast Heart Association and NIH Grant HL-14541.)

Effects of Leukocytic Pyrogen and NaAspirin on PO/AH Neurons When Microinjected at Different Sites in the Hypothalamus. Eugene P. Schoener* and S. C. Wang. College of P & S, Columbia University, New York.

Leukocytic pyrogen and NaAspirin were microinjected into the preoptic/anterior hypothalamic (PO/AH) areas of urethane anesthetized cats under thermoneutral conditions. The responses of identified thermoregulatory neurons to leukocytic pyrogen, microinjected into the contralateral PO/AH area, were studied. In addition, the attempt was made to determine whether NaAspirin would alter the activity of pyrogen pretreated neurons when injected into the PO/AH area opposite to that which received the pyrogen. Units were identified as thermoregulatory by their response to either peripheral or peripheral and central thermal stimulation; both "warm" and "cold" responsive neurons were examined. In almost every instance, administration of the pyrogen to the contralateral PO/AH area produced a change in the firing rate of the distal thermoregulatory units. Approximately half of the neurons were excited and half were depressed, independent of their thermoresponsive behavior. When NaAspirin was microinjected into the opposite PO/AH area after pyrogen, it always altered the neuronal discharge and invariably the change was in the direction of the unit's thermal response. It may be proposed that neural pathways exist between the two PO/AH thermoregulatory neuron pools which allow for bilateral excitatory and inhibitory interaction. (Supported by NIH Training Grant NS 05173)

URANYL NITRATE (UN) INHIBITION OF Na^+ TRANSPORT IN A URINARY EPITHELIUM. J. H. Schwartz* and W. Flamenbaum, Walter Reed Army Institute of Research, Washington, D. C. 20012

Previous studies of UN induced acute renal failure suggest that the effect of UN results in abnormalities of ion transport by various nephron segments. To determine whether UN directly alters active Na^+ transport, its effect on the isolated turtle urinary bladder was studied. Bidirectional ^{22}Na-^{24}Na fluxes were measured across short-circuited bladders. The addition of 0.1 mM UN to the mucosal (M) solution resulted in a 61.1±5.1(SE)% (n=12) decrease in the short-circuited current (SCC), without a change in transepithelial resistance. Net Na^+ flux decreased from a mean control of 13.1±2.5 to 5.5±1.2 $\mu Eq/hr/8cm^2$ ($P<0.001$) due primarily to a 58% decrease in M to serosa (S) flux. Thus, the change in SCC results from inhibition of Na^+ transport. In other bladders, removal of UN from M after 15 min did not reverse the effect of UN on the SCC. However, with addition of 2mM dithiothreitol (DTT) to M after UN the SCC returned to control values (n=8). Pre-treatment with 2mM DTT abolished the effect of UN on the SCC (n=8). S addition of 4mM UN did not measurably affect the SCC or unidirectional Na^+ fluxes (n=6). These studies suggest that UN markedly inhibits active Na^+ transport by altering sulfhydryl groups in the M membrane of the epithelium of turtle urinary bladder without altering the integrity of this tissue as a barrier to passive ion flux.

DISTRIBUTION OF KALLIKREIN IN THE KIDNEY. A.G. Scicli*, N.B. Oza* and O.A. Carretero. Henry Ford Hosp., Detroit, Michigan.

It is recognized that both superficial and deep nephrons in the cortex (C) have structural and functional differences. Since renal kallikrein (KK) could play a role in the regulation and distribution of renal blood flow. It seemed of interest, then, to study the distribution of this enzyme in the kidney. For this, dog kidneys were washed out with Ringer through the renal artery to eliminate traces of blood and urine. A segment of the kidney was cut into 5 sections: 3 equal sections from the C, & 1 each of the medulla & papilla. The sections were homogenized & KK solubilized with 0.5% deoxycholic acid. The KK of the homogenate was determined by incubating an aliquot of the sample at pH 8.5 with purified dog substrate in the presence of peptidase inhibitors. The kinins generated were measured by bioassay in the hindleg of the dog. The distribution of the KK is expressed as a percent of the total activity found in the 5 sections. The following results were obtained: outer C 41.8±8.1; middle C 28.2±2.7; inner C 21.2±6.1; medulla 4.3±2.1; & the papilla 4.2±3.5. The difference between the outer & middle C, between the middle & inner C, & between the inner C & medulla were significant at the level of $p<0.01$, $p<0.05$ & $p<0.001$ respectively. In summary, KK is located in the C with a gradual decreasing concentration from the outer C to the juxtamedullary region. The distribution pattern of the KK is similar to that of renin. Further, if KK regulates renal blood flow distribution then its location would suggest that it could facilitate the blood flow to the outer C where the short nephrons are found. (Supported by NIH grant HL 15839-02 and MHA)

STRESS-RELAXATION AND CONTRACTILE ACTIVITY OF ARTERIAL SMOOTH MUSCLE. C.L. Seidel* and R.A. Murphy. U. Virginia Med. Sch., Charlottesville, VA.

In response to a sustained increase in length the isometric tension of arterial strips increases to a maximum and then decays slowly. The purpose of this work was to test the hypothesis that the magnitude of the strain induced increase in tension (Peak) and the amount of isometric tension decay (stress-relaxation, SR) are proportional to the level of activation of the contractile system. Medial-intimal strips from hog carotid arteries were placed at the optimal length for force development (l_o). The contractile system was activated to various levels using physiological salt solutions containing K^+ concentrations (substituted for Na^+) ranging from 4.7 to 140 mM. After the development of a steady-state level of contractile activity, a strain of 2% l_o was applied at a rate of 0.001 or 0.018 l_o/sec. Isometric tension was observed until it reached a constant level and then length was returned to l_o in 4.7 mM K^+. There was a linear relationship between contractile activity and the magnitude of Peak or SR. The lines describing these relationships (i) had slopes that were significantly larger ($p < 0.002$) at the faster strain rate, (ii) had slopes that were not significantly different ($p > 0.1$) from each other at a given strain rate, and (iii) had intercepts (x 10^6 dynes/cm^2) that were not significantly different ($p > 0.1$) than zero.

	Slow Strain (n=7)		Rapid Strain (n=7)	
	Slope	Intercept	Slope	Intercept
Peak	0.24 ± 0.02 (SE)	0.20 ± 0.05	0.44 ± 0.04	0.20 ± 0.05
SR	0.30 ± 0.02	0.04 ± 0.01	0.52 ± 0.03	0.05 ± 0.02

These results suggest that (i) the magnitudes of Peak and SR are directly related to contractile activity, (ii) at zero contractile activity SR is zero, and (iii) "resting" arterial strips may possess tonic contractile activity because SR is observed in strips not activated by increased K^+. This work was supported by USPHS grant # HL14547.

CONTROL OF CALCITONIN RELEASE IN MAN: IN VITRO STUDIES. Helena P. Selawry, Kenneth L. Becker, Leonard E. Bivins, Richard H. Snider, Omega L. Silva (Intr. by J. N. Cohn). Veterans Administration Hospital, George Washington and Georgetown Universities, Washington, D. C.

There is a paucity of data concerning the mechanism of calcitonin (CT) release in normal man. Using a sensitive radioimmunoassay for human CT and a protein kinase binding assay for cyclic AMP (cAMP), we have explored, in vitro, the physiology of CT release in normal man. Fresh pieces of human thyroid (80-100 mg) were incubated in 2 ml Krebs Henseleit buffer at 37° for 15-30 minutes. CT in media and cAMP in tissues were measured following the administration of glucagon (GL), pentagastrin (PG), theophylline, dibutyryl cyclic AMP (d-BcAMP), calcium, phosphate, and magnesium in increasing concentrations. The results showed that PG and GL were the most potent stimuli for the accumulation of both CT and cAMP. Control values for CT and cAMP were 50 picograms per ml of media and 0.67 picoMole/mg tissue weight, respectively. In the presence of 100 μg/ml of PG, these values increased to 2250 picograms per ml of media for CT and 1.85 picoMoles/mg tissue weight for cAMP. Theophylline increased both CT and cAMP.D-BcAMP released CT, but only in the presence of calcium. Calcium alone was often surprisingly ineffective. The results suggest that the gastrointestinal hormones exert their CT releasing effects directly via an increase in cAMP. On the other hand the role of calcium in the release of CT may be primarily permissive.

ACTION OF GLUTAMATE ANALOGS ON MUSCLE FIBERS IN LOBSTER WALKING LIMBS. R.P. Shank* and A.R. Freeman. Institute of Psychiatric Research and Departments of Psychiatry and Physiology, Indiana University Medical Center, Indianapolis, Indiana 46202 and Department of Physiology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140.

Compounds with structural similarities to L-glutamate were tested for pharmacological activity in 5 ways: effects on the membrane potential, effective membrane resistance, amplitude of evoked EPSPs and IPSPs, and on the action of applied L-glutamate. Fifteen compounds possessed excitatory activity which resembled qualitatively that of L-glutamate, but none was as potent as the presumed transmitter. Six L-glutamate analogs exhibited predominantly antagonistic activity: these included kainic acid, D-aspartate, D-glutamate, D,L-homocysteate, D,L-aminoadipate, and D,L-α methyl glutamate. Kainic acid was the most potent antagonist, but a concentration of 1 mM was required for appreciable antagonistic activity. Kainic acid, D-glutamate and D-aspartate antagonized the action of applied L-glutamate or L-glutamate plus L-aspartate applied simultaneously. L-aspartate has previously been reported to enhance the excitatory action of L-glutamate (Kravitz et al., in Excitatory Synaptic Mechanisms, Eds. P. Anderson and J.K.S. Jansen, Universitetsforlaget, Oslo, 1970, and Shank et al., Comp. Biochem. Physiol., 50A, 1974). D-aspartate prevented the potentiative effect of L-aspartate but had only a weak blocking effect on the action of L-glutamate. The present observations are consistent with the concept that L-aspartate plays a role in neuromuscular excitation in lobster walking limbs, and that excitatory synaptic receptors have distinct L-glutamate and L-aspartate binding sites. This research was supported by NSF and NIMH grants.

NEURAL PLASTICITY VS. GENETIC FACTORS IN THE SIAMESE CAT VISUAL SYSTEM. C. J. SHATZ (intr. by D. H. Hubel). Department of Neurobiology, Harvard Medical School, Boston, Mass. 02115.

During the critical period in kittens, the central nervous system (CNS) is susceptible to the effects of visual deprivation. If one eye is closed, cells atrophy in those layers of the lateral geniculate body (LGB) representing the deprived eye; at the cortical level, most cells are driven only by the nondeprived eye. If an artificial squint is induced, although the majority of cortical cells have normal receptive field properties, many fewer cells than usual receive input from both eyes. If kittens are raised in an environment limited to lines of a single orientation, the overall preference of cortical cells is strongly biased in favor of that orientation used during rearing. The existence of this critical period suggests that at least early in life the CNS is capable of a certain degree of plasticity. The visual system of the Siamese cat may provide a further example of plasticity. Due to a genetic mutation, aberrant fibers representing a region of ipsilateral visual field extending up to 20 degrees from the midline cross in the optic chiasm and terminate in the contralateral (wrong) LGB. Further, in the "Boston" Siamese cat, the geniculocortical projection is rearranged so that this abnormal representation of ipsilateral visual field is inserted between the usual contralateral representations in cortical areas 17 and 18. Finally, the sites of origin and termination of visual fibers in the corpus callosum are much more widespread than in the ordinary cat. Either innate genetic factors similar or identical to those responsible for the initial, aberrant decussation; or secondary, plastic readjustments of connections in response to it, could account for these alterations in connections at the cortical and callosal levels. It is difficult at present to distinguish clearly between these two alternatives.

UTERINE PROSTAGLANDINS AND CONVERSION OF ARACHIDONIC ACID TO PROSTAGLANDIN F BY THE BOVINE OVARY. Shemesh, M.* and W. Hansel. Cornell University, Ithaca, N.Y.

Four animals each at days 1-5, 10-14, 15-17 and 20-22 of the estrous cycle were completely anesthetized and the following samples collected: 1) uterine venous blood, 2) ovarian arterial blood, 3) jugular blood and 4) endometrial tissue. PGF, estrogens and progesterone were measured by radioimmunoassay. Uterine vein levels of PGF (ng/ml, M $\pm$ S.E.) were elevated ($P < 0.05$) at days 15-17 of the cycle (2.85 $\pm$ 0.22), when compared to days 1-5 (0.138 $\pm$ 0.03) or days 10-14 (0.187 $\pm$ 0.06). The levels remained high until day 20 (1.47 $\pm$ 0.10), but declined before the onset of estrus. Similar changes in endometrial PGF levels were also observed. Endometrial PGF (ng/g dry tissue, M $\pm$ S.E.) increased from 45 $\pm$ 12 at days 1-14 to 131 $\pm$ 9.5 during days 15 to estrus. However, PGF levels were not significantly elevated in ovarian arterial blood at any time during the estrous cycle. Since large amounts of arachidonic acid (A.A.) are present in luteal phase bovine endometrial tissue (Shemesh, et al., J. Animal Sci., 1974, in press), the effects of AA injected directly into the corpus luteum were studied. AA placed directly into the bovine corpus luteum in vivo caused the following sequence of events: a) a marked and rapid increase in PGF in ovarian venous blood, b) a sharp rise in jugular vein blood estrogen levels and c) a brief, transient rise and then a fall in jugular vein blood progesterone levels. The results suggest that an enzyme system capable of converting AA to PGF is present in the bovine ovary and that PGF caused increased estrogen secretion by the ovary.

COMPARATIVE STUDY OF THE MATCHING OF PRE- AND POSTSYNAPTIC ELEMENTS IN A SINGLY MOTOR INNERVATED CRUSTACEAN MUSCLE. R. G. Sherman, Clark University, Worcester, Mass.

Previously, motor nerve terminals were found to be selectively matched in certain structural and physiological properties to particular muscle fibers in the singly motor innervated stretcher muscle of the spider crab Hyas araneus (R. G. Sherman and H. L. Atwood, J. Gen. Physiol. 59: 586-615). To test how widespread this matching of pre- and postsynaptic elements might be and to compare the neuromuscular properties of the stretcher muscle in different crustaceans, the degree of facilitation (presynaptic property) and the sarcomere length (postsynaptic property) as well as other neuromuscular properties were determined for muscle fibers in four different species of crustacean. Three crab species (Gecarcinus lateralis, Grapsis grapsis, Goniopsis cruentatus) and a species of spiny lobster (Panulirus argus) were examined. Least squares regression analysis showed that, in spite of the presence of a considerable range in values, a significant correlation exists between the extent of facilitation and sarcomere length in all four species. Nerve terminals displaying a high degree of facilitation tend to innervate the longer sarcomere-length muscle fibers, whereas poorly facilitating terminals innervate the shorter sarcomere-length fibers. Furthermore, muscle fibers showing large excitatory postsynaptic potentials at a frequency of 1 Hz are innervated by poorly facilitating terminals and vice versa. These findings agree with those obtained for the spider crab and support the notion that selective matching of pre- and postsynaptic elements is a general property of single motor units in crustaceans.

MECHANISMS OF TWITCH POTENTIATION IN SMOOTH MUSCLE BY NITRATE AND CAFFEINE. Marion Siegman, Jefferson Medical College, Philadelphia, Pa.

The mechanisms whereby isometric twitch tension (P) can be potentiated by nitrate (10-30 mM) and caffeine (1 mM) were studied using strips of the rabbit taenia coli bathed in Krebs-bicarbonate solution at 22°. In the concentrations specified neither agent induced spontaneous activity. By analysis of the first derivative of tension development (dP/dt), the ability of these agents to affect calcium delivery and/or calcium removal could be distinguished. Nitrate (NO_3^{-2}) acts by an intensification of the maximum intensity of the active state, taken as the maximum dP/dt ($\dot{P}$), and is without effect on relaxation processes. NO_3^{-2} lowers the mechanical threshold, estimated from K^+ contractures. Thus the action of nitrate is limited to calcium delivery. In contrast, the dP/dt of caffeine-potentiated twitches showed an increased $\dot{P}$ and negative acceleration as well as prolonged negative deceleration, reflecting increased Ca^{+2} delivery and decreased Ca^{+2} removal, respectively. The "early" effects of caffeine can be explained by a lowering of the mechanical threshold. NO_3^{-2} is more potent than caffeine, and when combined, mechanical activation exceeded that in caffeine alone, the difference being dependent upon the NO_3^{-2} concentration. In 30 mM NO_3^{-2} -caffeine-Krebs, mechanical saturation was reached, because $\dot{P} = \dot{P}$ for a tetanus. NO_3^{-2} shifts the log dose-response curve for P and $\dot{P}$ vs. $[Ca^{+2}]_o$ to the left at calcium concentrations exceeding 0.5 mM. In 0.5 mM Ca^{+2} media neither NO_3^{-2} nor caffeine could elicit responses to single DC shocks, but repetitive stimulation was effective, suggesting that an adequate supply of Ca^{+2} from an intracellular source is essential to evoke a twitch. When NO_3^{-2} and caffeine are combined, the degree of potentiation depends upon the sequence of their administration, suggesting a multiplicity of sites of action, some common to both agents.

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ADRENERGIC AND CARDIOVASCULAR RESPONSES TO ACUTE HEAT STRESS IN THE ANESTHETIZED DOG. M. Singer* & E.T.Angelakos. Hahnemann Medical College, Philadelphia, Pennsylvania

Anesthetized dogs (pentobarbital 30mg/kg i.v.) were heated (hyperthermia blankets) to terminus or to a maintained temperature of 42.5°C. Heart rate increased slowly up to 42.5°C and rapidly thereafter to a peak of 230. Myocardial tension (force gauge) did not change significantly while left ventricular end-diastolic pressure rose only near terminus. Cardiac output and peak ejection velocity rose gradually to a peak of +170% at 42.5°C and then declined rapidly at higher temperatures or slowly if the temperature was kept at 42.5°C. PCO2 rose while pH & pO2 fell but all were stabilized while the temperature was held at 42.5°C. Propranolol (1mg/kg), acute bilateral stellate ganglionectomy or acute bilateral adrenalectomy produced little qualitative difference in the pattern of the cardiovascular responses or the ultimate events although the first two procedures produced a depression in the early phase. Plasma catecholamine levels did not rise significantly in spite of the terminal profound hypotension. However, cardiac responses to exogenous catecholamines were maintained. These results seem to implicate a failure in adrenergic responses as the precipitating cause of death in acute hyperthermia. (Supported by a DoD, ONR Contract)

IDENTIFICATION OF A HUMORAL ALVEOLAR-MACROPHAGE ENHANCEMENT FACTOR. William A. Skornik,* Donald P. Dressler* and Paul Nathan. Harvard Med. School, Boston, Mass. and Shriners Burn Institute, Cincinnati Unit, and University of Cincinnati, Ohio.

In vivo studies from our laboratory have shown that rapid killing of P. aeruginosa delivered by aerosol to the lungs of normal rats is due to alveolar macrophages. Further work described the stimulation of this function of the alveolar macrophage in vitro by factors present in lung lavage fluid. The function of rat alveolar macrophages were studied using lung washings. At a bacteria/macrophage ratio of 10:1 in vitro, alveolar macrophages from normal, unburned rats incubated in control media alone (pooled normal rat serum) phagocytized 7.8×10^3 P.aeruginosa organisms. Of this number phagocytized, 27% were killed in 30 minutes. The addition of lavage fluid from normal rats increased intracellular killing to 58% ($p < .01$). When alveolar macrophages washed from the lungs of burned rats, one day post burn, were incubated with normal lavage fluid, intracellular killing was doubled compared to the control value. This is of great importance because in vivo studies of lung bacterial clearance have demonstrated that a severe defect exists in the clearing mechanism one day post burn. In fact, with P.aeruginosa a 50% mortality due to bacterial pneumonitis occurs following aerosol challenge of rats one day post burn. Rats challenged 5 days later have no mortality and this was confirmed in vitro by the excellent phagocytosis (1.23×10^5) and intracellular killing (33%) exhibited by alveolar macrophages from rats six days post burn incubated in their own lavage fluid. The data further indicates that following burning, pulmonary lavage fluid contains a factor that significantly interferes with intracellular killing of phagocytized bacteria and this factor affects alveolar macrophages from both normal and burned rats.

EFFECTS OF PLACENTAL HORMONES ON GLUCONEOGENESIS IN THE RAT. Celia D. Sladek (intro. by A.A. Hakim) SUNY Brockport, N.Y., 14420.

Alterations in maternal carbohydrate metabolism during pregnancy are well documented. Human chorionic somatomammotropin (HCS) and estradiol (E) have been implicated as factors partially responsible for these alterations. HCS has been shown to possess diabetogenic actions. Elevated gluconeogenesis is characteristic of both diabetes and pregnancy. This study assesses the effects of HCS and E on gluconeogenesis in rats. Virgin ovariectomized rats received subcutaneous injections of HCS (6 mg in saline) and/or E (5µg in corn oil) twice daily for 14 days. Rats not receiving HCS and/or E received sham injections. Gluconeogenesis was evaluated, following a 24 hr fast, by measuring incorporation of intravenously injected U1-C^{14}-alanine (0.75 mmole in 0.5cc) into glucose and hepatic glycogen. Blood samples were obtained at 5,10,20, and 30 min post-injection. Glycogen analyses were performed on liver samples obtained 30 min post-injection. C^{14}-glucose was isolated from C^{14} alanine in the blood samples using ion-exchange resins. Percentage alanine conversion to glucose was calculated as described by Herrera, et al (J. Clin. Invest. 48:2260, 1969). Gluconeogenesis was decreased in animals receiving E ($p < .05$). This occurred coincident with hyperinsulinemia ($p < .05$). In animals receiving HCS, insulin also was elevated, however no inhibition of gluconeogenesis was observed in these animals. Combined treatment with E and HCS resulted in gluconeogenic inhibition which was comparable to that obtanined with E treatment alone ($p < .01$). This occurred in the face of elevations in serum insulin approximately twice that observed with either HCS or E treatment alone. Hepatic glycogen content was increased in the E treated animals ($p < .005$). These observations suggest that HCS opposes the effects of insulin on hepatic metabolism.

USE OF PULSE TRAIN HYPOXIC FORCING FUNCTIONS TO DEFINE NONLINEARITIES OF VENTILATORY CONTROL DURING CAROTID BODY PERFUSIONS. E.J. Smith* and R. E. Dutton. Rensselaer Polytechnic Institute, Troy, N.Y. and Albany Medical College of Union University, Albany, N.Y.

To determine nonlinear elements of a previously developed open loop model of the respiratory control system (J. Appl. Physiol.35:844,1973), 47 pulse train hypoxic forcing functions of 3 sec on-10 sec off and 10 sec on-10 sec off duration were generated at the carotid bodies of 10 anesthetized dogs by means of carotid artery loops and a perfusion system. End-tidal P_{CO_2} was held constant during these experiments by adding CO_2 to the inspired air as needed. Mean control P_{aO_2} was 92.5 ± 1.8 mm Hg, 3 sec on-10 sec off perfusion P_{O_2} was 29.5 ± 1.1 mm Hg, and 10 sec off-10 sec on perfusion P_{O_2} was 29.8 ± 0.8 mm Hg. During both perfusions, tidal volume increased during the first sec accompanied by an increase in breathing frequency. Ventilation ratio ($\dot{V}E_{test}/\dot{V}E_{control}$) rose from 1.0 to a peak of 2.8 ± 0.4 for the 3 sec on-10 sec off perfusions and to a mean peak of 4.2 ± 0.4 for the 10 sec on-10 sec off perfusions. Recovery from the hypoxic pulse was complete within 10 sec. An abrupt increase in ventilation ratio to these same levels was noted for succeeding pulses. The mathematical equivalent to these pulses was used to force a time varying model of the response of ventilation to hypoxic stimuli. This model is characterized by a nonlinear feedback system consisting of two parallel loops, one containing fast linear dynamics and the other, slow linear dynamics. Analysis with phase plane graphical techniques has identified the nonlinearities to be acting in a manner analagous to diodes in the input to both fast and slow loops and also as a linear gain with a nonlinear clamping component in the fast loop.

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FACTORS AFFECTING THE RESPONSE OF HUMAN SUBJECTS TO POSTURAL AND COLD PRESSOR TESTS.

J.J. Smith, D.J. McDermott*, D.G. Kamper*, R.W. Gotshall* and W.J. Stekiel, Medical College of Wisconsin, Milwaukee, Wisc. 53233.

Because of increasing use of non-invasive stress tests for cardiovascular diagnosis, a study was undertaken of factors influencing the response of normal subjects to certain standard stress tests. In the cold pressor test, the young men (YM), 20 to 26 years of age, had a greater increase in heart rate and a lesser increase in systolic pressure than older men (OM), 40 to 49 years. With a 20 min., 70° head-up tilt, YM had greater increases in heart rate and diastolic pressure than OM. A limited number of post coronary occlusion patients (CP), 40 to 49 years old, had heart rate and blood pressure changes in both tests similar to normal subjects of comparable age (OM). During tilt the plasma norepinephrine concentrations were greater and plasma epinephrine concentrations less in CP than in the control OM group. The results suggest that age is an important determinant of the response to tilt and cold pressor tests, and that metabolic as well as hemodynamic factors may be useful in assessing stress test response.

A SHORT METHOD FOR THE ISOLATION OF SOMATOTROPHS FROM THE RAT PITUITARY GLAND. G. Snyder* and W. C. Hymer. Department of Biology, The Pennsylvania State University, University Park, Pa. 16802.

In a previous study (Hymer et al. Proc. Soc. Exp. Biol. Med. 1972) we reported that rat pituitary somatotrophs could be isolated to a purity of 80-90% by the combined techniques of velocity and density centrifugation. However the relatively long time required to prepare the somatotrophs (5-7 hrs) limited, in terms of convenience, the type of experiment that could be carried out on them. Accordingly we have developed a shorter method to isolate somatotrophs: one which is based on the observation that the somatotrophs are the most dense of the 6 cell types contained in the anterior pituitary. The method involves sequential centrifugation of freshly dispersed pituitary cells ($1.5x10^7$) prepared from seven 250 gm male rats through two discontinuous density gradients of 20-28% bovine serum albumin (BSA). The frequency of somatotrophs in the initial cell suspension is 38.6±2.1%. After the first centrifugation the purity of the somatotroph fraction is 74.7±7.1%. After the second centrifugation purity of the final somatotroph fraction is 84.1±5.9%. The entire procedure takes less than 2 hours. The purified somatotrophs incorporate ^{14}C-amino acids into protein in linear fashion for 4 hours. Moreover, they release approximately 20% of their growth hormone content when challenged with 6 mM dibutyryl cyclic AMP during a 1 hr incubation period. Finally, the cells retain their ultrastructural integrity during isolation. Conclusion: The availability of these cells appears to provide an ideal model to study the mechanisms whereby specific growth hormone releasing or inhibiting factors act on the somatotroph to effect their characteristic response. (Supported by NSF Grant No. GB-33686 and PHS Career Development Award No. 1-K04 AM 15808-01 AMK from NIAMD.)

CERTAIN ASPECTS OF ZINC METABOLISM IN MAN. Herta Spencer, Dace Osis*, Emilie Wiatrowski*, and James Coffey*. VA Hospital, Hines, Illinois.

Zinc, an essential trace element, has been shown to be an important growth factor in man and to promote wound healing. In order to delineate the metabolism of zinc in man, metabolic balances of zinc were determined under strictly controlled dietary conditions by analyzing the dietary zinc intake and the excretions in each 6-day metabolic period. Zinc in the diet, urine, stool, and plasma was analyzed by atomic absorption spectroscopy. On a 12-14 mg dietary zinc intake per day, zinc is excreted mainly via the intestine. The urinary zinc excretion is low, about 0.5 mg/day, and the zinc balance is in equilibrium. Raising the dietary zinc intake to 22 mg/day or lowering it to 7 mg/day did not alter the metabolism of zinc. Loss of weight induced by dietary restriction or by total starvation markedly increased the urinary zinc excretion and resulted in a zinc loss of 10-15% of the total body stores of zinc. This marked loss of zinc was not associated with a decrease of the plasma levels of zinc and there was actually an increase of these levels. The studies indicate that during adequate nutrition the zinc balance is in equilibrium while catabolic states are associated with a loss of zinc which is not reflected by the plasma levels of zinc. (Supported in part by AEC Contract AT(11-1)-1231-95 and in part by the National Dairy Council.)

DEFINING THE SIZE AND POSITIONAL RELATIONSHIPS OF THE LIVER BY RADIOCOLLOID SCANNING. Richard P. Spencer, Victor W. Lee*, Mohamed A. Antar*. Sect. Nuclear Medicine, Yale Univ. School of Medicine, New Haven, Conn.

A functional property of the liver, its ability to accumulate radioactive colloids, can be used for external visualization of the organ and hence to measure its size and positional relationships during life. After intravenous administration of approximately 50 microcuries of ^{99m}Tc-sulfur colloid (size ~ 1 μ) per kilogram of body weight in patients, rectilinear scans or gamma camera scintiphotos were obtained and the rib and body margins noted. We had previously shown that in the adults seen here, the vertical length of the liver was 17 ± 2 cm. The commonest causes of a small liver (under 13 cm in adults) were the terminal stages of alcoholic or postnecrotic cirrhosis, and the effects of long term portal vein thrombosis. Enlarged livers were most commonly due to fatty infiltration, tumor involvement, or the result of cirrhosis. In 50 consecutive cases, 17 (34%) showed hepatic extension into the left upper quarter of the abdomen. There was no difference, in the percentage of cases with this extension, between the scans read as normal (6/19 or 32%) and those read as abnormal (11/31 or 35%). In 9 cases of splenectomy, 5 had extension of liver tissue into the left quarter of the abdomen. The portion of the liver lying above the last rib on the right was variable. A principal factor in the extension of the liver below the costal margin was the presence of chronic obstructive pulmonary disease and flattening of the diaphragm. This could be quantified by noting the amount of hepatic tissue above (A) and below (B) the rib and calculating the quantity A/(A+B). As far as the lower extension of the liver is concerned, in approximately 10,000 liver scans, in only 4 did the liver extend as far as the iliac crest. (Supported by USPHS CA 14969 and by DT-34D from the American Cancer Society).

SYSTEMIC AND INTRARENAL ARTERIOLAR ACTION OF ANGIOTENSIN II IN DOGS WITH EXPERIMENTAL HIGH OUTPUT HEART FAILURE. W.S. Spielman*, J.O. Davis, R.H. Freeman*, and T.E. Lohmeier*. Department of Physiology, University of Missouri School of Medicine, Columbia, Mo. 65201

Dogs with experimental high output heart failure (HOF) are known to have an elevated plasma renin activity (PRA); therefore, the present study was undertaken to evaluate the role of angiotensin II (AII) in this pathophysiological state. HOF was induced by placing a large aorta to vena cava fistula midway between the renal vessels and the iliac bifurcation. Following evidence of cardiac failure, dogs were infused with a specific AII antagonist, 1-sar-8-ala-AII (6 μg/kg/min^{-1}) to evaluate the role of AII in the maintenance of arterial pressure (AP); AP was measured in the aorta below the fistula. In five conscious dogs with HOF, infusion of 1-sar-8-ala-AII resulted in a fall in AP from a control mean of 101±7 to 83±7 mmHg ($p<.001$) 45 min after beginning the infusion. PRA increased from a control value of 41±5 to 136±23 ng/ml ($p<.01$) with the antagonist. Following a one hour recovery period AP returned to control levels (106±6 mmHg; $p<.01$) and PRA was significantly lower than during the infusion (51±6 ng/ml; $p<.01$). To evaluate the intrarenal role of angiotensin II in HOF, two dogs were anesthesized and the AII antagonist was infused into the renal artery (0.2 μg/kg min^{-1}). Infusion of the antagonist produced a marked increase in RBF from (160 to 210 and 96 to 165 ml/min). AP in one dog was measured below the fistula and in the other was measured above by placing a catheter in the brachial artery. Infusion resulted in a fall in AP in both dogs. This response in AP was similar to that observed in conscious dogs with HOF. The data demonstrate an important role for angiotensin II in the regulation of AP and RBF in dogs with HOF. (Supported by HL 10612 and HL 05810).

EFFECT OF *E. coli* ENDOTOXIN ON NOREPINEPHRINE-STIMULATED LIPOLYSIS IN SUBHUMAN PRIMATES. J.A. Spitzer and I. Hikawyj* Dept. of Physiology, Louisiana State Univ. Med. Center, New Orleans, La. 70112.

Previous work [Spitzer, Proc. Soc. Exp. Biol. Med. 145, 186 (1974)] demonstrated that exposure of dog fat cells to *E. coli* endotoxin *in vivo* (during endotoxin shock) or *in vitro* results in a higher norepinephrine (NE) stimulated lipolytic response than that obtained from normal cells. Since the hemodynamic response to shock is different in primates than in dogs, it was of interest to study metabolic adjustments due to endotoxin in primates also. Isolated fat cells were prepared and their cell size distribution determined from omental adipose tissue obtained from overnight fasted, male Rhesus monkeys. An aliquot of the washed cells was used as untreated control, the rest was exposed to *E. coli* endotoxin (Difco) in a concentration of 0.2μg/0.5 ml of cell suspension (corresponding to about 100 mg of wet weight of tissue) for 10 min. at 37°C. The cells were then washed again and incubated for 1 hr. at 37°C in Krebs-Ringer bicarbonate buffer, containing 4% bovine serum albumin, 5.5μmoles/ml glucose, 0.2μg/ml NE or 2.0μg/ml NE. At the 2.0μg/ml NE level, cells were also incubated in the presence of 5.0μg/ml Indomethacin (I). Lipolysis was assessed by glycerol (G) release per 10^6 cells. Mean cell diameter was 54.76± 4.58 (S.E). After endotoxin treatment the fat cells released significantly more G at both NE levels than did untreated cells. G release by treated vs. untreated cells incubated in the presence of NE+I was not significantly different. The results indicate that even though subhuman primates and dogs differ considerably in their hemodynamic response to shock, the alterations in NE-stimulated lipolysis elicited by endotoxin administration are similar in both species.

(Supported by ONR contract No. 108-969.)

ELECTRICAL SURVIVABILITY IN THE COLD (5°C) OF THE ISOLATED HEART FROM A HIBERNATOR, THE 13-LINED GROUND SQUIRREL, *CITELLUS TRIDECEMLINEATUS*. W. A. Spurrier* and A. R. Dawe. Loyola University, Stritch School of Medicine, Dept. of Physiology, 2160 South First Avenue, Maywood, Ill. 60153 and Office of Naval Research, Chicago, Ill.

We view hibernation as a unique phenomenon in which the entire animal participates, that is, each organ may be capable of hibernating alone. During hibernation, tissues manifest a unique cold survivability at T_B of 5°C. Two years of experimentation demonstrated that a circannual adaptation was occuring in the heart which gave it better capability for survival. 272 isolated hearts were serially placed in specially designed modules, which monitored the surface electrogram and contractility at a constant 5°C. Contrary to the usual procedure of perfusing the tissue with oxygenated Tyrodes at 30° to 37°C, our method was to seal off the bloodless heart alone without oxygen or nutrients. The denervated hibernating heart had everything endogenous to stay "alive" electrically for many hours. Summer active hearts and arousing hearts survived for only short periods under these restrictive conditions. Hearts from winter hibernating, or summer hibernating (induced by blood trigger) animals exhibited excitability as shown by rhythmic electrical activity for 8 to 48 hrs. Active summer hearts survived .5 hrs. fall and winter non-hibernating hearts survived 3.5 hrs. This suggested an endogenous change. Hearts of arousing animals (arousal completed in .5, 1, 1.5, or 2 hrs) showed an inverse relationship between survival and arousing time. The .5 hr. arousing heart survived for 3 hrs, whereas the 2 hr arousing heart survived only 1 hr. Long arousing meant short survival, perhaps due to depletion of vital materials, such as hibernation blood trigger, from active cardiac sites. *(Supported by NIH Grant HL 08682)*

ECG RESPONSE TO EXERCISE OF HEALTHY INDIVIDUALS VIA QUANTITATION OF THE ST-SEGMENT. Ramachandra Srinivasan*, and David Cardus. Dept. of Rehabilitation, Baylor College of Medicine, Houston, Texas.

The electrocardiographic response to exercise of healthy male subjects is assessed via quantitation of the ST-segment of the electrocardiogram. ECG data are collected during exercise on bicycle ergometer using bipolar electrodes in the V_5 position at various loads ranging from rest to approximately 85% of predicted maximum. A representative complex is obtained from 15 to 20 second recording of the ECG by averaging complexes selected on the basis of a histogram of RR-intervals. No other filtering is employed. If necessary, "linear" baseline correction is applied to the selected complexes in order to remove excessive baseline shifts. As a first attempt, the parameter measured is the so-called ST-integral; it is the area of the ECG signal from a fixed interval past the R-peak to the end of the T-wave minus the area under the T-wave, assuming it to be symmetric about its peak. The parameter measured is empirically related to the heart rate and work intensity. The variation in the above empirical relationship is used as a measure of the normal variability in the exercise response of healthy subjects.

POST-DENERVATION CHANGES IN SUBCELLULAR FRACTIONS FROM ALD AND PLD SKELETAL MUSCLES. William T. Stauber *+ and Byron A. Schottelius. Dept. of Physiology and Biophysics, University of Iowa, Iowa City, Iowa, 52242.

Seven day post-denervated anterior (ALD) and posterior (PLD) latissimus dorsi muscles of the chicken were separated into five subcellular fractions by differential centrifugation following homogenization. These fractions were tested for cytochrome oxidase, cathepsin D, catalase, 5'-nucleotidase, Ca-ATPase, and EGTA-ATPase enzyme activities. Calcium uptake abilities in the presence of oxalate was measured in all fractions. In the PLD, there was an increase in the specific activities of cytochrome oxidase, cathepsin D and catalase, but a decrease was observed in Ca-ATPase and 5'-nucleotidase activities. The total calcium uptake per mgm of muscle protein did not change with denervation, but the subcellular distributions and the specific activities of individual fractions were markedly altered. The enzyme activities of the ALD, however, were reduced, except for small increases in cathepsin D and catalase. The calcium uptake ability of the ALD resembled that of the normal muscles in specific activity and distribution in subcellular fractions.

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COMPARATIVE UPTAKE OF BROMSULPHTHALEIN BY ISOLATED KUPFFER AND PARENCHYMAL CELLS. T. Stege*, L. D. Loose* and N. R. Di Luzio. Dept. Physiology, Tulane University School of Medicine, New Orleans, La. 70112.

Recent techniques for the isolation of metabolically active and structurally intact hepatic cells has provided an opportunity for studying the comparative functional expression of the two major liver cell types, parenchymal and Kupffer. Although isolated hepatic cell preparations have revealed distinct biochemical and functional differences between Kupffer and parenchymal cells, the cellular basis of classical liver function tests, such as bromsulphthalein (BSP) removal has not been resolved. The relative role of specific liver cells in the uptake of BSP was ascertained by the utilization of enzymatically isolated rat hepatic Kupffer and parenchymal cells. Isolated cells were incubated with BSP (100 μg) for 60 minutes and BSP disappearance from the medium was measured spectrophotometrically. The formation of BSP-glutathione conjugates were determined utilizing cellulose acetate thin-layer chromatography. BSP uptake and the formation of a BSP-glutathione (BSP-GSH) conjugate were demonstrated to be an exclusive function of parenchymal cells. The rate of uptake of BSP by the parenchymal cells was inversely related to the concentration of serum or albumin in the incubation medium. In contrast to parenchymal cell uptake, Kupffer cells neither removed BSP from the incubation medium nor formed a BSP-GSH conjugate. Parenchymal cells incubated in solutions containing 100 to 400 mg% ethanol for 30 minutes prior to the addition of BSP were found to have unaltered BSP uptake. These data establish the uptake of BSP to be an exclusive expression of the hepatic parenchymal cell population.

VENTRICULAR PERFORMANCE MEASURED DURING EJECTION: STUDIES OF THE RATE OF CHANGE OF VENTRICULAR POWER. Paul D. Stein and H. N. Sabbah.* Univ. Oklahoma College of Medicine and VA Hospital, Oklahoma City, Oklahoma.

An attempt was made to develop an expression for the evaluation of ventricular performance that would satisfy the characteristics of an ideal index. An expression representative of the rate of change of ventricular power during ejection was derived. It is calculated as:

$$\text{Rate of change of power (dynes-cm sec}^{-2}) = \dot{Q}\,\frac{dp}{dt} + p\,\frac{d\dot{Q}}{dt}$$

where p is intraventricular pressure (dynes cm^{-2}), $\dot{Q}$ is aortic flow (cm sec^{-1}), dp/dt and $d\dot{Q}/dt$ are their respective rates of change. This expression has the particular attribute of being capable of measuring ventricular performance during ejection. It expresses a meaningful concept. It is derived on the basis of principles of fluid dynamics with no implied assumptions. It serves in an integrative fashion by combining terms previously shown to be of functional value. Studies in dogs show that it reflects alterations of the inotropic state, yet is relatively independent of alterations of preload or afterload. In 9 dogs isoproterenol caused the peak rate of change of power to increase from 10 ± 2 to $15 \pm 3 \times 10^8$ dynes-cm sec^{-2} (mean ± S.E.) ($P < .01$). Propranolol produced a reduction from 10 ± 2 to $6 \pm 1 \times 10^8$ dynes-cm sec^{-2} ($P < .001$). An increased afterload of 20%, induced by angiotensin, caused no change of the peak rate of change of power. Augmentation of the preload with dextran, which caused a 40% increase of the end-diastolic volume, produced a statistically insignificant increase of the peak rate of change of power from 12 ± 3 to $16 \pm 4 \times 10^8$ dynes-cm sec^{-2}. These results indicate that the rate of change of ventricular power, measured during ejection, is a useful and meaningful indicator of ventricular performance that has many of the attributes of an ideal index.

PASSIVE INTESTINAL TRANSPORT OF ASCORBIC ACID IN PASSERIFORMES BIRDS: CONTRAST WITH ACTIVE INTESTINAL TRANSPORT IN MAN AND GUINEA PIG. Nancy R. Stevenson. CMDNJ-Rutgers Medical School, Piscataway, N.J.

Intestinal transport studies done in man, guinea pigs, rats, and hamsters demonstrate that ascorbic acid is transported by a Na^+-dependent active transport system only in those species which have a nutritional requirement for the vitamin. Studies of the mechanism of intestinal transport of ascorbic acid in Passeriformes birds with and without a nutritional requirement for the vitamin were done in order to determine if a similar relationship existed among members of the Aves class. In vitro tissue uptake studies were done using part or all of the intestine of 5 synthesizing and 4 non-synthesizing species. In all species 1) the ascorbic acid initially present in the intestinal tissue was, at least in part, mobile and could be detected in the media after incubation in ascorbic acid-free media; 2) transport against a gradient was not observed; 3) saturation kinetics were not observed over the range of ascorbic acid concentrations tested (up to 10 mM or greater in all but one case); and 4) the presence of glucose (10 mM) or phlorizin (0.5 mM) did not alter the observed uptake. In contrast, ouabain (0.1 mM), 2,4-dinitrophenol (0.1 mM) and Na^+ ion partial replacement by K^+ ion (25 meq/l Na^+) caused a greater inhibition of transport in the non-synthesizing than in the synthesizing species. From this work it is concluded that active transport was not demonstrated in the synthesizing species and that the non-synthesizing species may have a rudimentary active transport system which is of little physiological importance in insuring an adequate vitamin intake. Thus, a nutritional requirement for ascorbic acid is not necessarily related to a functioning active transport system for its intestinal absorption. This work was supported by a NIH Post-doctoral Fellowship FO2 AM37687, NIH Grant AM10696, and Am. Phil. Soc. Travel Grant 893.

ROLE OF ATP IN CORONARY FLOW REGULATION IN THE ISOLATED PERFUSED GUINEA PIG HEART. D.F. Stowe*, T.E. Sullivan*, J.M. Dabney, J.B. Scott and F.J. Haddy. Dept. of Physiol., Michigan State Univ., E. Lansing, MI. 48824.

We previously reported dilatory levels of ATP in canine coronary sinus blood during stellate ganglion stimulation but not during reactive hyperemia (RH) (Physiologist 15:104, 1972). The source of ATP was uncertain. To test if ATP is released from myocardial cells, we perfused the coronaries of isolated guinea pig hearts prepared after the Langendorf method at constant pressure (65 cmH_2O) with a non-recirculating modified Krebs-Ringer's HCO_3^- solution fortified with glucose and pyruvate, and equilibrated with 5% CO_2, 95% O_2 (pH 7.4) at 38°C. After stabilization (30 min), effluent was collected during RH (30 sec occlusion), anoxia (3 min of 5% CO_2, 0% O_2) and addition of ATP (range:140 - 10,200 nmols/L) to the perfusate; coronary flow (CF) was measured and [ATP] analyzed by the firefly luminescence technique (detection limit $>$1.8 nmols/L). Results:

	CONTROL(N=16)	RH(N=16)	ANOXIA(N=10)	ATP in PERFUSATE(N=10)
CF(ml/min/g)	5.5±0.2	10.8±0.4	10.2±0.8	8.5±0.8 SEM
ATP(nmols/L)	undetec.	4.3±1.2	2.0±0.9	40 - 1200(range)

ATP was found in the effluent of 12/16 hearts during RH and 4/10 hearts during anoxia. During ATP addition, the [ATP] in the effluent averaged only 11.5±2.6% of the [ATP] in the inflow. ATP remaining in, or added to the effluent remained stable between 2 and 90 min after sampling. Clearly, ATP did not appear in vasodilator concentrations in the effluent during anoxia or RH. However the high disappearance rate of ATP and the apparent absence of ATPase in the effluent suggest marked rapid cardiac breakdown of ATP. Thus, this study does not rule out a role for ATP in the dilation produced by anoxia and occlusion, but suggests that the source of the increased ATP levels observed in the earlier study during stellate ganglion stimulation was from nerves and/or formed elements in the blood. (Supported by Grants from the National Heart and Lung Institute.)

CALCIUM DEPENDENCE OF INACTIVATION IN FROG DENERVATED SINGLE MUSCLE FIBERS. S. C. Stuesse* and B. D. Lindley, Dept. of Physiol., Case Western Reserve University Med. Sch., Cleveland, Ohio, 44106.

One to 8 weeks after section of the sciatic nerve in one leg of Rana pipiens, single muscle fibers were dissected from the semitendinosus muscle for acute experiments. Denervated or contralateral control fibers were depolarized by conditioning exposure to K^+ solutions (Na- and Cl-free, tris and methanesulfonate used as replacements) containing 5 to 60 mM K^+. The ability of the fiber to give maximal contracture in 100 mM K^+ was then tested, and the length of exposure for reduction to 50% of control 100 mM K^+ contracture height determined. At each level of membrane potential (-58 mv to -22 mv), denervated fibers inactivated more rapidly than controls. Rates of inactivation were sensitive to Ca^{++} in the external medium. For denervated fibers, mean times (sec) to reach 50% inactivation were:

	K^+ concentration					
	15 mM	20 mM	25 mM	30 mM	40 mM	60 mM
1.5 mM Ca^{++}	--	21.3	18.6	7.4	4.7	1.8
0.4 mM Ca^{++}	8.5	--	3.4	1.6	0.5	--

Steady state inactivation was complete even at depolarizations below mechanical threshold. Plots of the log of the time to reach 50% inactivation versus membrane potential gave straight lines with similar slopes for denervated and control fibers, at normal and low calcium, indicating that although the inactivation rate is shifted with denervation, the mechanism is not altered. Supported by grants from the N.E. Ohio Amer. Heart Association, and USPHS No. NS-10196.

INFLUENCE OF POSTURE ON FLOW-DEPENDENCE OF DISTRIBUTION OF INHALED ^{133}XE BOLI. G. Sybrecht*, L. Landau*, R.R. Martin* L. Engel*, J. Milic-Emili, and P.T. Macklem. Meakins-Christie Laboratories, Royal Victoria Hospital, Montreal.

We measured the flow-dependence of distribution of ^{133}Xe boli inhaled at constant inspiratory flow rates varying between 0.2 - 2.5 lps in 7 normal subjects both upright and supine. Boli were inhaled from a lung volume = upright FRC in both postures. We confirmed the results of Bake et al (Physiologist 15: 75, 1972) who found that upright, as inspiratory flow increased from 0.5 and 1.5 lps the apex received a progressively greater share of the bolus so that the ventilation of apical zones/ ventilation of basal zones ($\dot{V}a/\dot{V}b$) became asymptotic to ca. 0.9. This redistribution was attributed to a shorter time constant (T) of apical vs. basal zones. In the supine posture we found $\dot{V}a/\dot{V}b$ was ca. 0.7 when flow = 0.2 lps and that the redistribution to the apex was more flow-dependent than it was upright so that at 1.5 lps, $\dot{V}a/\dot{V}b$ was ca. 1.1. As T differences between apex and base should be minimal in the supine posture, the greater flow-dependence of bolus distribution suggests that the pressure swing (ΔP) was greater over apical zones than basal zones and that the differences in ΔP increased as flow increased. Supported by the MRC of Canada.

INTERACTION OF SEQUENTIAL STIMULI APPLIED DURING THE RELATIVE REFRACTORY PERIOD OF THE DOG VENTRICLES. J. Tamargo* and G.K. Moe. Masonic Med. Res. Lab., Utica, N.Y. 13501

An ineffective stimulus applied to cardiac tissue within the relatively refractory period may alter the response to an immediately subsequent stimulus, as first described about 50 years ago. In re-examinimg this interaction we have observed three response patterns, all of which may coexist at different sites of stimulation in the same heart. (1) A stimulus of 2 to 10 times diastolic threshold, applied too early to elicit a propagated response, becomes effective when a stimulus of equal strength is delivered 10 msec earlier. (2) A stimulus applied just late enough to evoke a response will fail to do so when a stimulus of equal strength precedes it by as much as 30 msec. (3) Two stimuli, separated by 10 msec, both of which are late enough to be effective when given alone, fail to yield a propagated response when applied together. These results have a bearing on the use of trains of stimuli, bracketing the vulnerable period, in the assessment of the ventricular fibrillation threshold. Possible interpretations are based on the temporal dispersion of recovery from the refractory state. (Supported by HL 15759, N.I.H.)

THE EFFECTS OF CHOLECYSTOKININ (CCK) ON THE CANINE GASTROINTESTINAL (GI) TRACT AT DIFFERENT PHASES OF THE INTERDIGESTIVE MYOELECTRIC COMPLEX (IDMEC). Luke Tan° and Charles F. Code. Mayo Foundation, Rochester, Minnesota 55901

This study was done to delineate the direct effects of CCK on the electric activities of canine GI tract at different phases of the IDMEC. Gastric and small gut electric activities of 4 conscious, healthy female mongrel dogs were detected using previously implanted silver-silver chloride electrodes. The dogs underwent numerous 8-12 hour recording sessions after fasting 24 hours. CCK-PZ (Jorpes) 1/8 u to 4 u/kg were injected intravenously over 30 seconds during either phase I or III of the IDMEC. During either phase this produced simultaneous bursts of action potentials over the entire small gut within 30 seconds. The bursts lasted 3 to 10 minutes, depending on the site of gut observed. The lower jejunum and upper ileum showed longest effects, upper jejunum and lower ileum intermediate and duodenum shortest. Increased doses of CCK caused longer responses in all sites. The stomach responded unpredictably with either bursts of action potentials, exaggerated slow waves or no reaction. In 1/3 of the experiments, 45 to 60 minutes after CCK injection, negative deflections propagated from the lower jejunum to the stomach. These were immediately followed by 1 to 2 minutes of gastric and duodenal action potential bursts. These bursts were associated with vomiting in 30% of cases.

The effect of CCK on the IDMEC itself was variable. It would delay, abolish or not change an active phase III in a given segment of small gut; accelerate, delay or not change the onset of the subsequent IDMEC cycle.

DEPENDENCE OF CANINE GALLBLADDER FILLING ON THE INTRINSIC COMPETENCE OF THE INTRAMURAL COMMON BILE DUCT. M.F. Tansy, D.L. Innes*, J.S. Martin* and F.M. Kendall*, Dept. of Physiol. & Biophys., Temple University School of Dentistry, Philadelphia, Pennsylvania.

The purpose of these studies was to determine if it could be inferred that filling of the canine gallbladder could be influenced by intrinsic properties of the intramural portion of the common bile duct. Acute experiments were carried out on 15 nightly fasted mongrel dogs of both sexes anesthetized with chloralose-urethan. After anesthesia all animals were bilaterally cervically vagectomized and a laparotomy was performed. In all cases hepatic secretion of bile was driven by an intravenous infusion of a 2% solution of sodium taurocholate which was administered at a rate of 1 ml/min. Constancy of biliary flow was monitored via hepatic duct cannulation. Gallbladder bile accumulations were measured by aspirating the contents at 30 minute intervals by means of a cannula inserted into the fundus of the viscus. The following briefly summarizes some of the findings. Enforced patency of the intramural portion of the common bile duct precludes gallbladder filling. The degree of filling of the gallbladder is dependent upon the fraction of the length of intramural common duct which is patent. Gallbladder filling is possible with the intramural common duct exteriorized from the duodenum. Gallbladder volume accumulations show abrupt reductions when more than 2 mm of the excised duct is removed. We interpret these observations to indicate that gallbladder filling is dependent upon the intrinsic competence of the intramural portion of the common bile duct and that the degree of competence is a function of the length of intact intramural duct.

Cells of Origin of the Cutaneous Subdivision of the Dorsal Spinocerebellar Tract. Daniel Tapper, Michael D. Mann, Paul B. Brown, and Barbara Cogdell* New York State Veterinary College and Section of Neurobiology and Behavior, Cornell University, Ithaca, New York 14850.

The dorsal spinal gray neurons of cat which are somatotopically connected to skin supplied by the sural and posterior femoral cutaneous nerves and which project to the cerebellum in the cutaneous subdivision of the dorsal spinocerebellar tract were found to be a separate cluster of cells located apart from both Clarke's Column neurons and those dorsal gray neurons in the primary segments of entry of the hindlimb skin nerves. Both projections were located in laminae IV and V of rostal lumbar 5 and lumbar 4. This result was determined in decerebrate, decerebrate-decerebellate and in cats anesthetized with pentobarbital sodium. The rostro-caudal extent of the neuron cluster was determined by recording the potential evoked by electrical stimulation of the sural and posterior femoral cutaneous nerves in the ipsilateral inferior cerebellar brachium and selective sectioning of the dorsal column and the dorsolateral funiculus at various levels of the spinal cord from the first sacral to first lumbar segment. The location of these neurons and their cutaneous connectivities was determined by single unit recording, antidromic stimulation from the inferior cerebellar brachium and selective stimulation of various skin mechanoreceptors. (Supported by USPH Grant NS07505).

EVALUATION OF THE "FILTRATION THEORY" RELATIVE TO THE INTESTINAL SECRETION ASSOCIATED WITH CHOLERA TOXIN. A. E. Taylor and N.A. Mortillaro. Dept. Physiol., Univ. Miss. Sch. Med., Jackson, MS

Net volume movement into the intestinal lumen can be caused by altering capillary forces(capillary pressure-colloid osmotic pressure) which ultimately alter intestinal tissue forces(tissue pressure, tissue colloid osmotic pressure and lymph flow). Several investigators have implicated changes in capillary forces as responsible for the intestinal fluid loss associated with cholera toxin. This paper will describe a series of experiments in which potential difference(PD) and secretion rates were measured in dog ileal loops that were forced to "secrete" by either decreasing plasma colloid osmotic pressure or by placing cholera endotoxin(Wyeth) into the loops. The PD(serosa relative to mucosa) decreased to an average of -11 mv at the end of 2 hrs and the secretory rate averaged .2 ml/min/100 gm in loops exposed to cholera toxin. The secretion caused by decreasing colloid osmotic pressure averaged 1.04 and PD did not change during the course of the secretion. The secreting loops were then exposed to cold(20°C) and compared to control absorbing loops. The control groups demonstrated an immediate decrease in PD and zero absorption at 15 min. For cholera toxin loops, the PD averaged -3 mv at 30-60 min and 5 of 7 loops reached zero secretion rates between 15 and 30 min. For the secretion caused by decreasing colloid osmotic pressure, the PD did not change when exposed to cold and the secretion rate increased to 1.95. These experiments demonstrate that the secretions resulting from altering capillary forces are passive in nature as far as their response to changing temperatures; in addition, it appears that the transport process associated with cholera toxin secretion is much less temperature sensitive than the normal transport systems. Supported by NIH grants HL 15680 and HL 11477.

TURNOVER OF CYTOCHROME C IN SKELETAL MUSCLE DURING STEADY-STATE EXERCISE TRAINING. Ronald L. Terjung. Univ. of Illinois, Urbana, 61801

Exercise training of the endurance type can increase the cytochrome c (cyto c) concentration of working muscles nearly twofold. We have recently shown that, although the synthesis of cyto c is increased, the primary factor responsible for the increased cyto c is a decrease in the degradation rate constant (J.B.C. 248:7404,1973). The present study was designed to evaluate whether this increase in cyto c concentration is maintained in fully trained rats by similar changes in degradation and synthesis as occurred during the transition period. Delta-aminolevulinic-^{14}C acid was used to label cyto c in rats after 12-wk of training. This training program produced an approximate 85% increase in the cyto c concentration of the gastrocnemius muscle. A steady state condition was verified by a constant cyto c concentration. The half-life of cyto c determined between 12 and 18 wk of training was 42 d as compared to 31 d for paired weight untrained rats. The synthesis rate for cyto c was approximately 35% greater than for the sedentary controls. These results indicate that the increased level of cyto c found in fully trained rats is maintained by a combination of increased synthesis and decreased degradation rates. Thus, factors affecting the degradation process seem to be important during the transition period when the onset of training brings about the increase in cyto c concentration and, as seen in this study, also during steady-state training.

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ACUTE CHANGES IN ADENINE NUCLEOTIDES AND CONTRACTILE FORCE IN ISCHEMIC AND NON-ISCHEMIC MYOCARDIUM FOLLOWING CORONARY OCCLUSION. J.X. Thomas*, C. E. Jones, and J. C. Parker*, Univ. Med. Center, Jackson, Miss. 39216.

Adenine nucleotide (ATP, ADP, AMP) and metabolites (IMP, inosine, hypoxanthine, adenosine)were determined in dog left ventricle at 10 min. intervals for 40 min. following occlusion of coronary arterial branches. After 30 min. a sample was also obtained from non-ischemic muscle. In ischemic muscle ATP decreased progressively to a 75% reduction after 40 min.; ADP and AMP increased transiently. All metabolites increased during ischemia. However, the increase in concentration of metabolites did not account for the decrease in concentrations of nucleotides and metabolites. In non-ischemic muscle 30 min. following occlusion, ATP was reduced 40%, but the levels of metabolites were not increased, probably due to washout. In a second group of animals contractile force was monitored continuously for 45 min. following occlusion. In ischemic myocardium, contractile force decreased within 1 min. to 45% of its initial value. It remained approximately at this level during the 45 min. of observation. The immediate response of contractile force in the non-ischemic muscle was variable. However, after 10-15 min. contractile force in the non-iscehmic muscle was always 10-20% greater than the preocclusion value. Mean arterial pressure was never changed following coronary occlusion. The reduction in nucleotide levels in the non-ischemic muscle is believed to result from the hyperfunction of this muscle. (Supported by NIH grant No. NHLI-72-2948.)

CHARACTERISTICS OF ATRIAL RECEPTORS WITH NON-MEDULLATED VAGAL AFFERENTS. Peter Thorén (intro. by John T. Shepherd). Mayo Clinic and Foundation, Rochester, Minnesota.

Activity from atrial receptors with non-medullated afferents were recorded in the right cervical vagus in anesthetized thoracotomized cats. The receptors were localized to the atria by occlusion of the ascending aorta, mitral and tricuspid orifices and the pulmonary artery, and also by probing of the opened heart. The receptors seem to be localized throughout the atria, the atrial appendices and the intra-atrial septum. The conduction velocity in the vagal nerve was (0.3-2.2 m/sec, mean 1.0 m/sec) and the total conduction time varied from 42-380 msec. The receptors are normally silent or have a low irregular or cardiac modulated rhythm, coinciding with the a or v-wave (mean 1.4 imp/sec). With an increase in right and left atrial mean pressures caused by occlusion of the pulmonary artery and aorta respectively the activity of the receptors increased; the increase was related mainly to the v-wave or became continuous. The threshold was 3 to 12 mm Hg; the maximal activity in right atrial receptors of 10 imp/sec occurred during pulmonary occlusion at a right atrial mean pressure of 15 mm Hg. The maximal activity in left atrial receptors of 12-25 imp/sec occurred during aortic occlusion at a left atrial mean pressure of 20-30 mm Hg. Thus there exists a population of atrial receptors signalling in vagal c-fibers, which respond to moderate changes in atrial volumes. (Supported by NIH Grant HL 5883).

INTERDIGESTIVE GASTRIC AND DUODENAL MYOELECTRIC ACTIVITY IN THE UNANESTHETIZED RHESUS MONKEY. A. Thouin*, R. E. Braitman*, T. E. Chaddock*, C. L. Hamilton and G. M. Carlson*. Dept. of Physiology, Univ. of Pennsylvania School of Medicine, Philadelphia, Pa. 19174

Cyclical myoelectric activity patterns have been reported in the gastrointestinal tract of the dog during the interdigestive state (Szurszewski, Am. J. Physiol., 217:1757, 1969) while only random contractile activity was observed in the rhesus monkey (Weisbrodt et al., J. Appl. Physiol., 30:276, 1971). We were interested in this discrepancy. Three rhesus monkeys were chronically implanted with monopolar Ag-AgCl electrodes located on the stomach and duodenum. The animals were preconditioned to restraint chairs at least 2 wk before surgery and recordings were started 2 wk following surgery. Definite cyclical activity patterns were observed in both the stomach and duodenum of all monkeys. The cycles consisted of a phase with only slow wave (SW) activity and no action potential (AP) activity, a phase where SW's were associated with random AP activity, and a phase where SW's were associated with intense AP activity. These phases occurred almost simultaneously in both the stomach and duodenum. Sometimes phase 3 was followed by a 4th phase which occurred in the duodenum only. This phase consisted of AP's which were fused over several SW's (duration 10 to 19 sec) and which were separated by intervals of 44 to 55 sec. The fused AP's were propagated retrograde at a velocity of ~4 mm/sec. Two to 5 fused AP's occurred during phase 4. The total time from the start of phase 1 to the start of a 2nd phase 1 was ~80 min. Frequency of the SW in the stomach was ~3.5/min and the velocity of SW propagation ranged from 2 to 3 mm/sec. Frequency of the SW in the duodenum was ~16/min. In summary, SW and AP activity can be recorded from the stomach and duodenum of the chair restrained monkey. The AP activity occurs in a cyclical fashion if the animal has been properly conditioned to the laboratory environment.

Mechanical dipole changes due to movement of the heart as reflected by the spatial vectorcardiogram.
Olav Thulesius[X], Clifford V. Nelson and Brian Hodgkin[X]
Departments of Research & Cardiology, Maine Medical Center, Portland, Me 04102

Certain periods of the ventricular cardiac action potential coincide with the mechanical activity of the heart and the cardiac dipole is moving in relation to fixed points of surface ECG leads. Theoretically, therefore, cardiac movement may affect surface ECG both normally and in heart disease with altered kinetics of myocardial contraction. - Experiments were performed in 8 baby pigs (6 - 8 weeks, weight 10 - 12 kg) anesthetized with sodium pentobarbital. Vectorcardiograms were recorded using a specially designed lead system (Nelson et al., 1971) after application of intracardiac and epicardial electrodes, 10 - 25 mm apart at various locations. Electrodes were stimulated by a battery operated General Radio Model 1307 A oscillator with intensities of 150 - 270 μA and 400 c/sec. In this way an AC signal was superimposed on the ordinary vectorcardiogram. Spatial magnitude M, and two angles, the vertical V_o and horizontal H_o were calculated from the X Y and Z voltages. Variations in the superimposed dipole magnitude and direction probably due to cardiac movement were observed mostly during the ST and T segments. Dipole variation was affected by Isoproterenol and Propranolol.

Nelson, C.V., Gastonguay, P.R., Wilkinson, A.F. and Voukydis P.C.: Lead system for direction and magnitude of the heart-vector. In Vectorcardiography 2, edited by I. Hoffman, R.I. Hamby, and E. Glassman. Amsterdam, North-Holland, 1971, pp 85 - 97.

THE POSSIBLE INVOLVEMENT OF THE PINEAL GLAND IN PREGNANCY. Peter V. Tigchelaar (intr. C.D. Barnes). Terre Haute Center for Medical Education, Indiana University School of Medicine, Terre Haute, Indiana 47809.

The possibility of the involvement of the pineal in ovulation and pregnancy was examined in the rat. Ovulation rates, ovarian and uterine weights, pituitary LH and FSH content, and serum LH concentration were compared among pinealectomized, sham-operated, melatonin-injected and saline injected rats killed on day 1, 8, 16, 22, or 23 (day of parturition) of pregnancy. No difference was noted either in the time of ovulation or in the number of ova released among the four treatment groups. Also, no difference was noted in the number of pups or fetuses, number of implantation sites, or number of reabsorbed fetuses. The ovarian weights of pinealectomized rats were higher and the ovarian weights of melantonin-injected rats were lower than their respective controls only on day 1 and the day of parturition, i.e., on the days when the animal is not, in fact, pregnant. A 5-10 fold rise in pituitary LH content in all four treatment groups during pregnancy with no concomitant change in serum LH indicates that the rise in pituitary LH during pregnancy may represent only an increased storage of LH by the pituitary with little LH release. The sharp decline in pituitary LH content between day 22 and day 23 corresponds with a rise in serum LH over the same time interval. A fourfold increase in pituitary FSH is noted by day 16 in all four groups. The pituitary content of FSH remained high until day 22 and fell by the day of parturition to a level equal to that on day 1. It appears, therefore, that under "normal" laboratory conditions the role that the pineal gland plays in ovulation and pregnancy is minimal at best. The greatest effect of the pineal on the parameters measured appears to occur on days 1 and 23, i.e., before fertilization and after parturition.

Influence of Aging on Ligament Weight and the Strength of Bone-ligament Junctions of Rats. Charles M. Tipton, Ronald D. Matthes*, and Robert K. Martin*, Exercise Physiology Laboratory, University of Iowa, Iowa City, Iowa 52242.

The effects of aging on selected properties of the knee ligaments were studied using 228 male (M) and female (F) rats from 28 litters that were assigned to 10 separate age groups for each sex. The initial group was sacrificed after 15 days while the final group was terminated after 735 days. At all ages the weight of the ligament (LW) and the strength of the medial collateral ligament-tibial junction (JS) were dependent upon the body weight (BW) of the animal; however, this relationship was more pronounced before the rats were 135 days old. For both M & F, the LW at 12 months had plateaued although the LW of the F was 60% of the value recorded for the M. On an absolute basis (Newtons) and after 90 days, M were significantly stronger than F, M=24±1.3, F=16.7±1.1. Strength was also evaluated on JS/BW basis. After 30 days and thereafter, the F always had higher values than M. At 45 days this ratio was 5.98±.25 for the M and 6.97±.25 for the F. When strength was interpreted on a LW basis (grams/mg) the highest values were at 15 days: M=583±52, F=761±78. These results at 735 days were 127±8 for the M and 123±7 for the F. As expected, elastic stiffness (kg/mm) progressively increased up to 135 days after which it plateaued. There were no significant differences in this measure between M and F rats at any time period. These results at 15 days and 735 days were: M=.13±.009 and 1.06±.088 and F=0.12±.002 and 1.15±.022 respectively. These composite findings indicate that there are sufficient differences between M and F rats at various ages to consider when planning and evaluating ligamentous research studies. Supported in part by NIH Grant AM-08893-9.

EFFECTS OF ANXIETY AND ANGER ON THE DREAM CONTENT. Clara Torda
Mt.Sinai Sch.Med.& Downstate Med.Center,N.Y.,N.Y.,10029

The effects of anxiety and anger of various intensities on the dream content have been studied. Dreams were defined as a mental product in which visual imagery has been used to describe everything. Dreams consist of a changing combination of last day's events and old memory traces. The content of dreams of 10 college students has been studied. Anxiety or anger have been induced by posthypnotic suggestion. The occurrence of anxiety or anger has been ascertained by the differences in the free fatty acid content of the blood plasma, and by changes of the galvanic skin resistance, blood pressure and heart rate. The effects of mild and moderate anxiety and anger have been compared with the effects of exposure to intensive anxiety or rage producing exogenous presleep experiences.The results suggest that endogenous affects modify the content of concurrently ongoing dreams.The anxiety or anger became incorporated into the dream content and became part of the engram of last day's residue.Therefore, future anxiety or anger acquired the ability to retrieve these dreams.The results also suggest that excessive sensory stimuli, if sufficiently threatening, may disrupt the process of engramming the past day's residue. Instead of promoting the engramming, these intensive emotions will promote the retrieval of past memory traces in an attempt to remove the intensive anxiety or anger.The results seem to clarify the probable role of dreams in formation of longterm memory.

REGIONAL MYOCARDIAL BLOOD FLOW (RMF) MEASUREMENT USING TRITIATED WATER (THO) AND TRACER MICROSPHERES (SPHERES). M.R. Tripp*, M. Meyer, S. Einzig*, C.R. Swayze*, H.B. Burchell and I.J. Fox. Dept. of Physiology, University of Minnesota, Minneapolis, Minnesota.

During the first 10 seconds of a 20-40 sec constant-rate injection of THO, 7-10 μ ^{141}Ce-labeled spheres were injected into the left atrium of 15 open-chested dogs under pentobarbital anesthesia. Simultaneously blood was sampled serially from the aortic arch (a) to define the arterial THO concentration-time curve and (b) for a reference sphere flow. At the end of the THO infusion the heart was rapidly excised, sliced and frozen. RMF was measured in 150-300 mg tissue samples from the inner, middle and outer thirds of the left ventricular (LV) wall. Flow was varied using nitroglycerin, dipyridamole or A-V shunts. In 7 dogs relative tissue THO and tissue sphere concentrations (Ci and Mi, respectively) were both determined by liquid scintillation spectrometry while sphere concentration of the remainder of the LV and in the reference flow were determined by γ-counter. In this series, comparison of $Ci/\overline{Ci}$ with $Mi/\overline{Mi}$ for the 24-27 samples from each heart resulted in a mean correlation coefficient (ρ) of 0.77 (range: 0.58 to 0.94). In the next 8 dogs in which Mi was determined with greater precision by γ-counter, comparison of $Ci/\overline{Ci}$ with $Mi/\overline{Mi}$ resulted in a mean ρ of 0.78 (range: 0.35 to 0.96). Mean number of spheres/sample for all experiments was 1030. In 11 of the 15 dogs acceptable reference flows permitted calculation of RMF which ranged from 0.3 to 2.3 ml/min/gm. $RMF_{THO}/RMF_{spheres}$ in the inner, middle and outer LV layers averaged 0.96 (sem 0.03), 1.00 (sem 0.04) and 1.02 (sem 0.05), respectively. It is concluded that THO and spheres give similar estimates of RMF under the conditions tested. Whether absolute RMF is determined by either technique as well as the comparability of the 2 techniques in ischemic myocardium or at high flows requires further study.

EFFECT OF MANGANESE CHLORIDE ON AUTOMATICITY OF DIGITALIZED PURKINJE FIBERS. Warren W. Tse* and Jaok Han. Dept. of Medicine, Albany Medical College, Albany, N.Y.

Digitalis enhances automaticity of Purkinje fibers by increasing the slope of phase-4 depolarization. The underlying ionic mechanisms responsible for this change are still unknown. It has been shown that manganese chloride ($MnCl_2$) prevents the development of transient depolarizations of Purkinje fibers induced by digitalis. This suggests that $MnCl_2$ may also inhibit the increase in phase-4 depolarization induced by digitalis. In the present study, the effects of $MnCl_2$ on phase-4 depolarization of digitalized Purkinje fibers were studied using conventional microelectrode techniques. The studies were made on isolated Purkinje preparations either beating spontaneously or driven by basic stimuli at a cycle length of 630 msec. In spontaneously beating preparations, ouabain alone consistently increased the automatic rate by increasing the slope of phase 4, while no such increase was observed when the preparations were superfused with a mixture of ouabain and $MnCl_2$. $MnCl_2$ was also shown to be effective in reversing the enhanced automaticity induced by ouabain. $MnCl_2$ alone did not have a significant effect on the automatic rate of Purkinje fibers. In the driven preparations, ouabain alone consistently enhanced phase-4 depolarization, but such a change was not observed in the preparations treated with a mixture of ouabain and $MnCl_2$. In short, $MnCl_2$ prevented the ouabain-induced increase in automaticity of Purkinje fibers. The results suggest that an inward Ca^{++} current may play a role in the development of digitalis-induced increase in the slope of phase-4 depolarization in Purkinje fibers.

PROXIMAL TUBULE VOLUME REABSORPTION IN ANTI-GBM NEPHRITIC RATS. J. B. Van Liew and H. R. Von Baeyer°. Departments of Medicine and Physiology, SUNY at Buffalo and VA Hospital, Buffalo, N.Y.

Progressive membranous nephritis was produced in rats by the injection of sheep anti-rat glomerular basement membrane serum. This lesion uniformly affects all glomeruli and results in a massive and sustained proteinuria (control - 5.7 $\pm$ 2.0, nephritic - 189 $\pm$ 89 mg/24 hr x 100g BW). There is a concomitant decrease in total serum protein and most noticeably in serum albumin (total protein g/100 ml: control = 6.43 $\pm$ 0.45, nephritic = 4.27 $\pm$ 1.15; Albumin: control = 3.60 $\pm$ 0.95, nephritic = 1.19 $\pm$ 0.66). GFR and SNGFR exhibit parallel reduction (GFR ml/min x g KW: control = 1.07 $\pm$ 0.31, nephritic = 0.61 $\pm$ 0.29; SNGFR nl/min x g KW: control = 27.6 $\pm$ 10.3, nephritic = 16.6 $\pm$ 9.6). Calculated plasma colloid osmotic pressure (COP) decreased in all animals (control: 18.6 $\pm$ 3.3, nephritic: 10.2 $\pm$ 3.1 mmHg). Proximal tubule fractional volume reabsorption [end proximal (TF/P)Inulin] is constant and at near normal levels over a wide range of SNGFR. The average (TF/P)Inulin exhibits a slight decrease from control values (control: 2.69, nephritic: 2.38) and represents a 5% decrease in proximal reabsorption. The (TF/P)Inulin is linearly correlated with COP. A 1 mmHg decrease in COP results in an approximately 1.2% depression in reabsorption. This relationship is similar to that found in peritubular perfusion or chronic volume expansion experiments. These findings indicate that glomerular-tubular balance is maintained overall in this experimental model with the restriction that peritubular oncotic forces exert a slight but significant influence on proximal reabsorption.

THERMOREGULATORY RESPONSE OF THE RAVEN (CORVUS CORAX) TO TEMPERATURE EXTREMES. James H. Veghte. Aerospace Medical Research Laboratory, Wright-Patterson AFB, Ohio 45433.

The problems addressed concerned the interaction of the thermoregulatory system with duration of exposure to various temperatures, redundant seasonal exposures, and hysteresis effects. Continuous $\dot{V}_{O_2}$ and T_B of five birds were measured for 13 hours in an open metabolic system as temperatures were varied every two hours (+15°C, 0°C, and +30°C) or four hours (-45°C). Significant seasonal differences in absolute $\dot{V}_{O_2}$ and T_B responses to these temperatures were observed, but no seasonal effects were seen if these data were normalized except for $\dot{V}_{O_2}$ values obtained at T_A + 30°C. No habituation effects occurred with repeated summer or winter exposures. Aschoff and Pohl's (1970) predictive model for passerine birds best describes the lowest resting $\dot{V}_{O_2}$ obtained during T_A + 30°C. RQ's varied from 0.70 to 0.77 with a slight seasonal difference. $\dot{V}_{O_2}$ and T_B were found to cycle independent of environmental temperature every 203 and 210 minutes respectively. The sequence and duration of temperature exposure proved important.

DISAPPEARANCE HALF-TIME OF AUTOGENOUS ANTRAL GASTRIN IN CIRCULATION. Hugo V. Villar*, David D. Reeder, Edward N. Brandt, Jr.*, Lavenia LaGrone* and James C. Thompson. Univ. Texas Med. Branch, Galveston, Texas.

The half-life ($T_{\frac{1}{2}}$) of exogenous 17-amino acid gastrin (G-17) is about 2 min. Exogenous 33-amino acid gastrin (G-33) has a half-life of about 15 min. We studied the half-life of endogenous gastrin released by acetylcholine (Ach) irrigation of the antrum in 5 awake mongrel dogs. The dogs had isolated antral pouches, gastric fistulas and chokers around the vascular pedicles of the antrum. Method: After baseline collections, the antral pouch was irrigated continuously with a 0.5% Ach for 60 min, after which the antral venous drainage was abruptly occluded by constricting the chokers. Serum gastrin was measured by radioimmunoassay at intervals throughout this study and gastric acid was collected every 15 min. The gastrin concentrations were analyzed by linear regression analysis to determine the disappearance half-time. Results: Basal serum gastrin was 100 pg/ml and rose following Ach irrigation of the antrum to 251, 299 and 301 pg/ml at 20, 40 and 60 min, respectively; 1 min after the chokers were constricted, gastrin levels fell to 220 pg/ml and continued to fall. After 1 hr of antral vascular occlusion, serum gastrin level was 113 pg/ml. Regression analysis indicated that the disappearance curve could best be fit by a single exponential. The average calculated disappearance half-time was 8.62 min. Basal acid secretion of 0.1 mEq/15 min rose to 1.8 mEq/15 min during Ach irrigation, and fell to 0.2 mEq/15 min after the chokers were constricted. Conclusions: $T_{\frac{1}{2}}$ of endogenous gastrin is longer than that of exogenous G-17 (2.07 min) and shorter than that of exogenous G-33 (15 min). Physiologically released gastrin is, in all probability, a mixture of the two molecular forms, and the $T_{\frac{1}{2}}$ of 8.62 min in this study is the disappearance half-time of that mixture.

SYNTHETIC AMINO ACIDS AND THE BLOOD-BRAIN BARRIER TRANSPORT OF THE NEUTRAL AMINO ACID, L-DOPA. Lester A. Wade* and Robert Katzman. Albert Einstein Coll. Med., Bronx, N.Y.

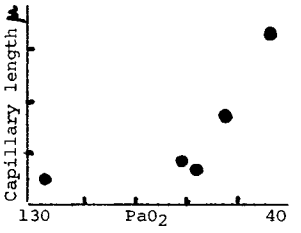
Measurements of amino acid transport at the rat blood-brain barrier have demonstrated significant variation in the rate of transport of neutral amino acids. These data suggest the possibility that the brain capillary endothelium might contain a transport system similar to the Ehrlich ascites cell "L" system (Christiansen, 1973), but lacks the "A" system for neutral amino acids. These systems can best be differentiated by the use of the non-metabolized synthetic amino acids, 2-amino-norbornyl-2-carboxylic acid (BCH), specifically transported by the "L" system, and α-(methylamino)-isobutyric acid (MeAIB), specifically transported by the "A" system. Using the carotid injection technique of Oldendorf, we measured the blood-brain barrier uptake of radioactive amino acids. We found that radioactive (±)-b-BCH-^{14}C was taken up by a saturable mechanism when tested over a concentration range of 0.1 to 4 mM. The amount of BCH-^{14}C transported was less than L-DOPA-^{14}C at a corresponding concentration. The regional rate of BCH-^{14}C uptake was similar for the cortex, striatum, hypothalamus, and midbrain. These results parallel our previous findings for L-DOPA-^{14}C and L-3-O-methyl-dopa-^{14}C of a saturable uptake mechanism and a similarity in the rate of uptake between the brain regions. The data suggest an uniformity among regional capillaries in their transport capacity for the amino acids tested. In another series of experiments, non-radioactive BCH or MeAIB was added to the injectant of L-DOPA-^{14}C. Total L-DOPA-^{14}C uptake over an injected concentration range of 0.1 mM to 1.0 mM was inhibited 50% to 35% by BCH (0.5 mM). When MeAIB (0.5 mM) was added to the injectant, a smaller and less defined inhibition of L-DOPA-^{14}C total uptake was produced than with BCH. (Supported by U.S.P.H.S. grants NS 09649 and MH 06418.)

COMPARISON OF INERT GAS AND O_2 TRANSFER IN ABNORMAL LUNGS. P.D.Wagner, J.W. Evans* and J.B. West. Univ. Calif. San Diego, La Jolla, CA.

Both in homogeneous lungs and lungs with ventilation-perfusion ($\dot{V}_A/\dot{Q}$) inequality theoretical studies show that arterial P_{O_2} (P_{aO_2}) can be accurately predicted from measurements of inert gas transfer provided that diffusion equilibration is complete for all gases in all units of gas exchange. However if diffusion across the blood-gas barrier is sufficiently impaired to produce hypoxemia, P_{aO_2} will be overestimated from measurements of inert gases because their rates of diffusion equilibration are an order greater than that of O_2. On the other hand, impaired gaseous diffusion in terminal airways will preferentially impair exchange of high molecular weight (MW) gases, so that if the poorly soluble gas used to identify low $\dot{V}_A/\dot{Q}$ regions is SF_6 (MW 146), there will be underestimation of P_{aO_2} since MW of O_2 is only 32. If diffusion equilibration is complete and all of the $\dot{V}_A/\dot{Q}$ inequality occurs between lung units in parallel, the distributions of blood flow measured from arterial inert gas levels and of ventilation measured independently from expired levels will be internally consistent in that at any point in the $\dot{V}_A/\dot{Q}$ domain, ventilation can be accurately calculated from the product of blood flow and $\dot{V}_A/\dot{Q}$ ratio. However, if there is series inequality of convective ventilation resulting in an alveolar-endcapillary difference within single lung units, this internal consistency will be lost, although P_{aO_2} will remain predictable. From these arguments, in 10 of 13 patients with chronic obstructive pulmonary disease, the results suggested presence of series inequality without evidence for diffusion impairment either within the terminal airways or across the blood-gas barrier. Three patients with interstitial lung disease had no evidence of impaired diffusion across the blood-gas barrier at rest, but did during exercise since P_{aO_2} was over-predicted by 14 mm Hg. (Supported by NIH Grants 13687-04, 14169-04, and 16698-01.)

PULMONARY CAPILLARY RECRUITMENT WITH HYPOXIA IN THE DOG. W. W. Wagner, Jr., and L. P. Latham,* Univ. of Colo. Med. Center, Denver, Colo.

Although airway hypoxia causes elevation of pulmonary artery pressure (P_{pa}), the effect of hypoxia on the pulmonary capillaries is not understood. To study this, windows were inserted in the chest wall of 9 pentobarbital anesthetised dogs. In each animal, an observer who had no knowledge of the dog's inspired oxygen tension used a microscope with an image superimposing device to make drawings of the perfused capillaries under the window. The total length of all perfused capillaries in the field was obtained by adding the lengths of each perfused segment. Total perfused capillary length was obtained at a number of arterial oxygen tensions (PaO_2). Recruitment of previously unperfused capillaries occurred in all cases; at a PaO_2 of 40 torr, the total length of perfused capillaries was about 2.5 times greater than during normoxia. There was no correlation between the recruited capillaries and alterations in left atrial pressure, only a weak correlation with cardiac output changes, but a very strong correlation with P_{pa}. This implies that recruitment was probably caused by vasomotion within the lung. This pulmonary microcirculatory response serves to increase the surface area for gas exchange and therefore could be advantageous to the animal during airway hypoxia.



InVitro EFFECTS OF HIGH PHOSPHORUS (P_1),LOW CALCIUM (Ca), AND LOW GLUCOSE (CHO) ON BONE MATRIX COLLAGEN, SOLUBILITY, SYNTHESIS, AND RESORPTION. Winona Wagner* and Dorothy H. Henneman, Univ. Del. & VA Hosp.,Wilmington, Del.

Studies in vivo (Am J Physiol 225: 269, 1973; J Clin Invest 52: 1052, 1973) demonstrate that levels of Ca and P_1 without endogenous parathyroid hormone profoundly affect bone formation, mineralization, and resorption. Studies were designed to determine whether high P_1 and low Ca in synthetic media of in vitro systems would also produce changes in bone collagen formation and resorption rates, solubility and content, and whether hyper- or hypo-CHO might modify these effects. Increased P_1 produced marked increases ($p < 0.001$) in collagen solubility accompanied by the reported decrease in resorption. Hypo-CHO under the same conditions significantly inhibited the high P_1 effect. Total bone collagen decreased markedly but collagen biosynthesis (^{14}C-proline incorporation) increased ($p < 0.001$). Low Ca decreased both solubility and resorption; hypo-CHO diminished these responses also. The data suggest that in vitro changes of cellular environmental levels of P_1, Ca, and CHO significantly affect bone collagen metabolism; that hypo-CHO protects bone from the increased solubility, loss of matrix, and decreased resorption (perhaps related to the observed fall in lactate production); and that the marked decrease in matrix collagen relate to changes in collagen solubility rather than to decreased osteoblastic synthetic activity.

Supported by Div.Health Sciences & UDRF grant.

EFFECTS OF INCREASED PULMONARY PRESSURE ON GLUCOSE METABOLISM IN THE PERFUSED RAT LUNG. S. A. Wali*, R. A. Rhoades (intr. by E. P. Hiatt) Pennsylvania State University, University Park, Pa. 16802

Rat lungs were perfused for 1 h (flow 15 ml/min), with a medium containing washed bovine RBC's resuspended to a 10% Hct with Krebs-Henseleit bicarbonate buffer - 5g% Pentex bovine serum albumin. Glucose and palmitate concentrations were 6mM and 1mM, respectively. 10 μCi of D-glucose-^{14}C(U) (specific activity 15 mCi/mMole) was added as a single pulse to the medium. Left atrial pressure was increased by 15 cm of H_2O in the experimental lungs. Post-perfused wet:dry ratios were not significantly different between controls and experimentals. Glucose uptake increased 26% in the experimental lungs, while circulating lactate and pyruvate levels were unaltered. Glucose utilization was significantly ($P>0.05$) accelerated in lungs with elevated pulmonary pressure as seen by a 36% increase in glucose incorporation into total lipids (T.L.) and phospholipids (P.L.). CO_2 production also increased by 46%. The addition of papaverine (8.6 mg%) to the perfusate resulted in a reduction in pulmonary arterial pressure and a significant increase in glucose uptake and lactate production compared to control lungs. Circulating pyruvate levels showed a significant 3-fold reduction. Glucose oxidation to CO_2 and glucose incorporation into T.L., P.L., and neutral lipids was significantly depressed. The data indicate that increased pulmonary pressure stimulates both glucose uptake and utilization while papaverine stimulates anaerobic glycolysis and depresses lipid synthesis. (Supported in part by N.I.H. grant H.L. 16247.)

PULMONARY VASCULAR IMPEDANCE AND HYDRAULIC POWER IN THE LAMB, IN UTERO AND NEW-BORN. William E. Walker*, Beat Kehrer*, J. Alex Haller*, and William R. Milnor. The Johns Hopkins School of Medicine, Baltimore, Md.

To determine whether changes in pulmonary arterial impedance parallel the known changes in pulmonary vascular resistance during ventilation in utero and after normal delivery, experiments were performed in fetal lambs at term, and in new-born lambs. Three were studied in utero at ∿145 days (term = 147 days), through a left thoracotomy. Pulsatile flow (Q) and pressure (P) were measured in the proximal pulmonary artery (PA): (1) lungs collapsed and ductus arteriosus (DA) open; (2) DA occluded; (3) DA open, lungs ventilated with air for 5 minutes; (4) DA occluded, lungs ventilated. Two lambs were studied in a similar way ½ and 2½ days after normal birth. Results were as follows (R_{PA} and Zo_{PA} = input resistance and characteristic impedance, respectively, of the PA, expressed in dyn sec cm^{-5} x 10^3. W = hydraulic power associated with PA flow, in milliwatts.):

Utero	Vent.	Ductus	P(mm Hg)	Q(ml/sec)	R_{PA}	Zo_{PA}	W
In	No	Open	51 ±1.5	6.2 ±0.1	10.8 ±.29	1.2 ±.08	53 ±3
In	No	Closed	74 ±1.2	2.6 ±0.3	32.7 ±.39	2.0 ±.18	34 ±3
In	Yes	Open	40 ±3.4	6.2 ±0.5	8.5 ±.21	1.0 ±.19	40 ±5
Ex	Yes	Closed	23 ±1.0	7.3 ±0.2	4.2 ±.20	1.2 ±.11	32 ±1

The effects of DA occlusion prior to, and during, ventilation were similar. Resistance and characteristic impedance of the pulmonary bed alone (R_{pulm} and Zo_{pulm}) were assumed to equal R_{PA} and Zo_{PA} with DA occlusion. R_{pulm} decreased by 64% during ventilation in utero, but Zo_{pulm} did not change significantly. R_{pulm} was 87% higher in utero with the lungs collapsed than after birth, but Zo_{pulm} was essentially the same in the two conditions. Closure of the DA also reduced the pulmonary arterial input impedance phase angle. As a result, W decreased by only 40% after birth, even though the mean P fell 55%.

EFFECT OF CARBACHOL ON LIPID LEVELS IN THE NON-WORKING CANINE MYOCARDIUM
D. Wallick*, C. Aravanis*, M. Pindok*, and V.V. Glaviano. The Chicago Medical School, Chicago, Illinois 60612

Previous work has showed that the intracoronary administration of the cholinergic agent, carbachol, (carbamylcholine chloride) in the paced hearts of dogs subjected to complete cardiopulmonary bypass caused an increase in the myocardial uptake of free fatty acids (FFA) and triglycerides (TGFA) as compared to control dogs. Continuous monitoring of arterial perfusion pressure and myocardial contractile force showed a 14 and 44% decrease respectively, while coronary flow was observed to increase by 45%. The action of carbachol on myocardial lipids was blocked with atropine, while reserpine did not alter the increased uptake of the two substrates. These data suggested that parasympathomimetic stimulation of the heart leads to an increase in intracellular levels of FFA and TGFA. Simultaneously infused tritiated FFA as palmitic acid (9,10-^{3}H) and TGFA as tripalmitin (^{14}C-FFA, carboxyl-^{14}C) were subsequently administered to dogs subjected to a 12 min intracoronary infusion of carbachol (1 μg/kg/min) on cardiopulmonary bypass. Left ventricular levels of FFA and TGFA were analyzed together with the isotope incorporation of the two lipid substrates in both control and carbachol-treated dogs. Both FFA and TGFA pools of the heart incorporated the labeled substrates by a 3 fold increase above that found in the non-treated hearts. Concentration studies of FFA agree with the increase in FFA incorporation since the concentration of FFA rose 69%. However, the TGFA concentration only increased 6%. The results indicate that the increases in myocardial uptake of FFA and TGFA in previous experiments with carbachol resulted in an increase in the intracellular concentration of these two substrates. (Supported by NIH grant HL 14673 and ONR N0014-67-0397-01).

REGIONAL PERMEABILITY OF THE AORTA OF NORMAL AND HYPOTHYROID NEONATE SWINE.[1]
J. L. Walter*, D. P. DeVore*, S. D. Carter*, and J. B. Boatman. Battelle's Columbus Laboratories, Columbus, Ohio.

A comparison was made of the regional permeability of the aortae of normal and hypothyroid neonate swine. Half of a litter of swine, weaned at 2 weeks was made hypothyroid by 0.5% propylthiouracil in hog chow supplemented with 18% protein and 2% cholesterol, the remaining half was maintained on normal diet with 18% protein. At 10 weeks of age, control animals had increased body weight by 15 kg, the hypothyroid group by 3.8 kg, from age of weaning. Evan's Blue and I^{131} albumin were given intravascularly and 4 hours later all animals were terminated, aortae removed, and punch biopsies taken of the arch, the thoracic and abdominal regions from both blue and white areas. Additional samples were taken for light and scanning electron microscopy. The distribution of dye on the normal arterial surface showed almost uniform and intense staining of the arch, with sharply defined streaking of the thoracic aorta and little or no involvement of the abdominal aorta. Labeled albumin distribution corresponded generally in concentration to the dye. The hypothyroid arteries did not dye as intensely or extensively, and labeled albumin levels were significantly lower in both the dyed and faintly dyed areas. Microscopically, the hypothyroid aorta showed fewer smooth muscle cells between elastic laminae which were thinned, and the subendothelial space was markedly narrowed, with endothelial nuclei darkly stained and rounded. Atypical surfaces were seen under scanning electron microscopy with broadened foldings of the intimal surface. Hypothyroidism during growth was considered to reduce active influx of plasma constituents by inhibition of growth-mediated remodelling of the arterial wall and/or depression of metabolic control of active transport.

[1] Supported in part by NIH Grant HE-14031 and by Battelle Memorial Inst.

PROLONGED HYPERPOLARIZING POTENTIALS IN THALAMIC NEURONS DURING CORTICAL EEG SPINDLES. M. Waszak (intr. by R. Bowman). VA-Hospital and Dept. Neurosurg., SUNY, Upstate Med. Center, Syracuse, N. Y. 13210.

Synchronization of the EEG in the form of spindles occurs periodically on the cortex of barbiturate-anesthetized as well as in immobilized encephale isole cats; however, the membrane potential changes in thalamic neurons accompanying spindles in these two preparations are unequivalent: In unanesthetized encephale isole cats neurons in n. ventralis lateralis (VL) and n. ventralis anterior (VA) have a stable membrane potential and fire at irregular intervals while the EEG on the anterior sigmoid gyrus is desynchronized. EEG spindles, occurring spontaneously or triggered by a single thalamic or caudate stimulus, are accompanied by a prolonged hyperpolarizing shift in membrane potential, often in excess of 10 mV in amplitude, which persists throughout the period of EEG synchronization (up to 1.5 sec). Depolarizing waves arising out of the sustained membrane hyperpolarization reach firing level very rarely and are reduced by the intracellular injection of hyperpolarizing currents (1.0-4.0 nA), suggesting that they are disinhibitory potentials. Stimulation in the brachium conjunctivum at intensities consistently evoking spikes in VL cells during EEG desynchronization fails to do so during the prolonged hyperpolarization. The i.v. administration of small amounts of the short-acting barbiturate Brevital is followed by an increase in membrane potential level, and a drastic reduction in firing during periods of EEG desynchronization. During barbiturate spindles the depolarizing waves become much more pronounced, often reaching firing level. Thus, in the absence of anesthesia spindles are accompanied by almost total inhibition of discharges, whereas during barbiturate narcosis firing is strongly increased during EEG synchronization.

SUPPRESSION OF GASTRIC SECRETION BY ANTIBODIES TO GASTRIN. Takaho Watayou*, Robert A.D. Booth*, Hugo V. Villar*, Phillip L. Rayford*, David D. Reeder and James C. Thompson. Univ. Texas Med. Branch, Galveston, Tex.

There is preliminary evidence that antibodies to gastrin (Ab_G) may inactivate circulating gastrin and might eventually be useful in treating patients with duodenal ulcer or, more especially, the Zollinger-Ellison syndrome. Methods: To test this hypothesis we administered, to 16 dogs, varying doses of either normal rabbit serum or Ab_G generated in rabbits. The Ab_G was capable of binding 2 μg of gastrin/ml; in the radioimmunoassay the Ab_G, at a final dilution of 1:100,000, binds 20 picograms (pg) of gastrin. Serum samples obtained from dogs injected with as little as 0.005 ml/kg of Ab_G bound greater than 20 pg gastrin; serum levels of gastrin could not be detected, therefore, in the radioimmunoassay. After a single dose of 0.07 ml/kg Ab_G, basal gastrin levels could not be detected for 47 days. Gastric secretion in response to food was not diminished by Ab_G doses as high as 0.07 ml/kg/day for 10 days. Gastrin-stimulated gastric secretion was not affected by injecting 0.03 ml/kg Ab_G; however, 0.1 ml/kg caused 60% suppression and 0.4 ml/kg abolished acid output. Gastric secretory response was normal the next day. Mucosal levels of gastrin in antrum, fundus and duodenum doubled after 10 days of Ab_G (0.07 ml/kg/day). Normal rabbit serum did not influence serum or mucosal gastrin or gastric secretion. Conclusions: Administration of small doses of antibodies to gastrin interferes with the measurement of circulating gastrin by radioimmunoassay for as long as 47 days. Ab_G caused an increase in mucosal levels of gastrin, presumably by interfering with hormone release or catabolism. Since relatively large doses of Ab_G are required to diminish acid output, therapeutic use will depend, inter alia, on availability of large amounts of Ab_G.

AN ELECTROPHYSIOLOGICAL INVESTIGATION OF NEURAL PATHWAYS IN THE INTERMESENTERIC NERVE. William A. Weems (intr. by J. H. Szurszewski). Mayo Foundation, Rochester, Minnesota.

The intermesenteric nerve (IMN) forms an anatomical connection between the solar plexus and the inferior mesenteric ganglion (IMG). Experiments were designed to determine (1) if mechano-sensory fibers from the distal colon make synaptic contact with neurons in the solar plexus via the IMN, and (2) if peripheral nerves of the solar plexus synapse with IMG neurons via the IMN. In vitro experiments were conducted on preparations consisting of the guinea pig solar plexus (which contains the superior mesenteric ganglion (SMG) and the right and left celiac ganglia) connected to the IMG by the IMN. Major nerve trunks associated with these ganglia were stimulated by external electrodes. In some preparations the distal colon remained attached to the IMG via the colonic nerves. Electrical activity of ganglion cells was recorded with intracellular electrodes. Neurons in the SMG and left celiac ganglia received excitatory synaptic input upon stimulation of the IMN. Most of these neurons also showed excitatory synaptic input following stimulation of the colonic nerves. When the distal colon remained attached to the IMG via the colonic nerves, spontaneous EPSPs were also observed.

Neurons in the IMG receive excitatory synaptic input from the IMN and mesenteric nerve trunks associated with the solar plexus. However, maximum stimulation of the IMN produced greater synaptic input than maximal stimulation of the mesenteric nerve. This suggests that not all the fibers in the IMN which synapse with neurons in the IMG are excited by stimulation of these peripheral trunks. We conclude that the IMN contains pathways which furnish neurons in the solar plexus with sensory information from the distal colon and neurons in the IMG with sensory information from proximal regions of the gastrointestinal system.

MECLOFENAMATE AND INDOMETHACIN AUGMENT THE PULMONARY PRESSOR RESPONSE TO HYPOXIA AND EXOGENOUS PROSTAGLANDIN $F_{2\alpha}$ ($PGF_{2\alpha}$). E. K. Weir*, J. T. Reeves and R. F. Grover. Univ. Colo. Med. Center, Denver, Colo.

Prostaglandins are naturally occurring substances with powerful vasoactive effects. The balance between constrictor ($PGF_{2\alpha}$) and dilator (PGE) prostaglandins may modulate vascular responses. We wished to see if inhibitors of prostaglandin synthetase (meclofenamate [M] and indomethacin [I]) would alter the pressor effect of hypoxia or exogenous $PGF_{2\alpha}$ on the pulmonary vasculature. In 17 anaesthetised mongrel dogs (mean weight 22 $\pm$ 1 kg.) the pulmonary arterial pressure, pulmonary arterial wedge pressure, systemic arterial pressure and cardiac output responses to twenty minutes of hypoxia (P_{IO_2} 9%), and $PGF_{2\alpha}$, 2 µg/kg I.V., were measured before and after the administration of M or I (2 µg/kg. I.V. followed by 2 µg/kg/hour I.V.). Following M or I the rise in pulmonary vascular resistance throughout hypoxia was increased by 10% ($p < .01$) and pulmonary arterial pressure was also elevated ($p < .05$). Pulmonary vascular resistance measured within a minute of the injection of $PGF_{2\alpha}$ increased from 4.0 $\pm$ .4 to 7.4 $\pm$ 2.0 mm Hg/L/min prior to M or I, and from 3.9 $\pm$ .4 to 9.2 $\pm$ 2.4 mm Hg/L/min after their administration ($p < .05$). We conclude that a dilator influence, possibly that of PGE, is removed by the use of M or I, thus enhancing the pressor response to hypoxia or exogenous $PGF_{2\alpha}$.

INSTANTANEOUS INSPIRATORY FLOW AT 100 MILLISECONDS: A NEW METHOD FOR EVALUATING VENTILATORY RESPONSE IN MAN. Richard B. Weiskopf and Ronald A. Gabel*. U.S. Army Research Institute of Environmental Medicine, Natick, MA and Department of Anesthesia, Peter Bent Brigham Hospital, Boston, MA.

Recently, attention has been drawn to the measurement of the pressure generated against an occluded airway, at 100 milliseconds of inspiration ($P_{0.1}$), as a method of assessing respiratory center output. We reasoned that with constant external resistance to ventilation, the measurement of inspiratory flow at 100 milliseconds of inspiration ($\dot{V}_{0.1}$), except for the effects of the small changes in lung volume (5-150 ml) during this time, should be as valid a measure of ventilatory activity. In several subjects, we measured $\dot{V}_{0.1}$ during repeated isocapnic progressive hypoxia and CO_2 rebreathing tests. In these experiments each breath produces a data point, thus yielding 120-200 or more points per test for comparison of $\dot{V}_{0.1}$, $\dot{V}_E$ and P_{O_2} or P_{CO_2}. Both $\dot{V}_{0.1}$ and $\dot{V}_E$ demonstrated linear relationships to P_{CO_2}, and similar curvilinear relationships to P_{O_2}. $\dot{V}_{0.1}$ maintained a relatively constant linear relationship to $\dot{V}_E$ during all experiments (range of r=0.93-0.99). In separate similar experiments, $\dot{V}_{0.1}$ also showed a linear relationship to $P_{0.1}$ (range of r=0.95-0.99). We conclude that $\dot{V}_{0.1}$ is a valid reproducible measure of human ventilatory activity, with the advantages of: (1) convenience and ease of measurement; (2) non-interference with ventilation, thus obviating resultant compensatory events; (3) availability of a large volume of data in each experiment, a point per breath. Perhaps the most interesting implication of these findings is that by as early as 100 milliseconds of inspiration, the final outcome of the breath has already been determined by the respiratory system.

INCREASED PERMEABILITY TO GLUTAMINE (gln) IN MITOCHONDRIA FROM ACIDOTIC RAT KIDNEYS. Tomas C. Welbourne. Dept of Medicine, Montreal University, Montreal, P.Q. Canada.

In acidosis (A) renal NH_3 production increases as the result of mitochondrial glutaminase I (glu'ase I) activation. The activity of this enzyme may be controlled by the permeability of the mitochondrial membrane. To determine this, gln permeability was evaluated by two independent methods. In the first, the D-isomer of gln was employed to exclude metabolic effects, and the volume of distribution measured. In nonacidotic (NA) mitochondria this volume represented 69 $\pm$ 4 per cent of the total mitochondrial H_2O which was not significantly different from the sucrose volume (63 $\pm$ 6 per cent) suggesting gln enters the outer, but not the inner, glu'ase I containing, compartment. In A mitochondria gln was distributed in 103 $\pm$ 9 per cent suggesting the inner mitochondrial membrane had become permeable. In the second, gln's reflection coefficient (σ), was determined. In NA mitochondria, σ= 1.05 $\pm$ 0.08 for D-gln and this fell in A to σ = 0.50 $\pm$ 0.06. These results are consistent with the hypothesis that glu'ase I activity is regulated by mitochondrial membrane permeability.

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DISTANT CHEMORECEPTION IN APLYSIA. L. J. Wells*, B. Jahan-Parwar, S. M. Fredman*. Worcester Fndn. Exptl. Biol., Shrewsbury, MA 01545.

In a progressive series of y-maze experiments, the ability of Aplysia to find food by distance chemoreception was tested, and partial characterization of the nature of food attractants was accomplished. Subjects (Ss), 5 Aplysia californica, were kept in individual y-mazes (60 cm long, 3.5 liter capacity) through which seawater was continuously flowing at the rate of 200 ml/min in each arm and out the foot. In the first series of 15 daily experiments, Ss were placed at the foot end of the maze, one gram dried seaweed (Rhodymenia palmata) was placed in one randomly selected arm, and responses were recorded for 30 minutes with a time-lapse movie camera. Mean responses were: 77% correct (food choice); 11% incorrect; 5% undecided at the choice point; 7% no movement. In 10 subsequent similar experiments, 1 drop/sec. of a standard seaweed extract, SSWE (5 gm dried seaweed standing in 1 liter seawater for 30 min., then filtered) served as the test substance. Responses were: 94% correct; 6% incorrect. Six experiments with 100 X diluted SSWE produced: 63.3% correct; 33.3% incorrect; 3.3% no movement. To characterize the nature of food attractants, SSWE was further filtered through an Amicon UM05 ultrafilter (cut off point approximately 500 MW), and 10 X diluted ultrafiltrate was tested in 9 experiments. Responses were: 82% correct; 18% incorrect. In 40 control runs (30 min long, one preceeding each experiment) with plain seawater, Ss chose 44% the left arm, 40.8% the right arm, 3.2% undecided, and 12% no movement, suggesting no significant side preference. These results indicate that Aplysia are capable of distant food chemoreception and that some seaweed constituents with MW < 500 can serve as food attractants.

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IN VIVO AND *IN VITRO* UPTAKE OF β-PHENYLETHYLAMINE-1-C^{14} (PEA) BY RAT BRAIN SYNAPTOSOMES. C.E. Whalley* and R. Greenberg. University of Illinois, College of Medicine, Chicago, Illinois, 60680.

PEA has been characterized as a neuromodulator by Giardina *et al.* (Life Sci. 12:153, 1973). Previously Nakajima *et al.* (JPET 143:319, 1964) and Oldendorf (Am.J.Physiol. 221:1629, 1971) reported that PEA is concentrated in brain subsequent to i.v. injection. Conflicting reports have been published as to whether or not PEA is present in synaptosomes; however, there are no previous studies to demonstrate whether an active synaptosomal uptake exists for PEA. We examined rat brain synaptosomes subsequent to *in vivo* i.v. injection of PEA-C^{14} by the Oldendorf technique (Brain Res. 24:372, 1970). PEA-C^{14} was regularly found in the synaptosomal fraction; however, most of the label was in the soluble fraction. Also, we have investigated the *in vitro* uptake of PEA-C^{14} by synaptosomes incubated at 37°C and 0°C in the presence of 154 mM Na^+ or 0 mM Na^+. No significant differences in PEA-C^{14} uptake were demonstrated. Therefore, it is most likely that a Na^+ dependent, active transport system for PEA does not occur.

FREQUENCY RESPONSE PROPERTIES OF THE DORSAL COLUMN NUCLEI. D. Whitehorn, J.P. Walsh*, O. Limcaco,* and M.C. Mackey*. Dept. of Physiol., Univ. Vermont, Burlington, Vt. 05401

Prior studies (Bromberg and Whitehorn; Physiologist, 15,72; Blum and Whitehorn; Fed. Proc., 32,73) suggest the presence of two major cell types in the dorsal column nuclei (DCN), separable by their ability to reproduce inputs of varying steady state frequency (SSF). Here we report freq. resp. measurements for DCN output and for inhibition. Output was calculated as the area (determined by automated digital integration) under the evoked response (latency:2-3 msec.,duration: 8-14 msec.) recorded from the contralateral medial lemniscus (ML) upon stimulation of the dorsal columns at C_2. Inhibition was quantified as the ratio of test to conditioned test areas. Total ML resp. was reduced as input freq. was raised from 1 to 100 Hz. However, the earliest portion of the resp. (ML1; duration: 2 msec.) was unaltered to 100 Hz., while the remainder (ML2) was markedly reduced, particularly between 1 and 10 Hz. Inhibition evoked from the ipsilateral (ISR) or contralateral (CSR) superficial radial nerves influenced ML1 and 2. When the SSF of the inhibitory input was varied, inhibition from ISR was reduced to 50% of max. at 100 Hz., while that from CSR was absent above 10 Hz. Inhibition upon ML1 or ML2 gave similar results. These findings further document the heterogenity of the ML and are consistent with the concept of two inhibitory system in the DCN, differing in freq. resp. character. The data indicate that ML cells, regardless of SSF properties, are influenced by both inhibitory systems. (Supported by NINDS, NS 09472).

MITOCHONDRIAL RESPIRATION AND SUBSTRATE UTILIZATION FOLLOWING EXPERIMENTAL MYOCARDIAL INFARCTION IN DOGS. Albert J. Whitty, Michael J. Dimino and Charles G. Todoroff (intr. by J. A. Rillema). Sinai Hospital of Detroit, Detroit, Michigan, 48235

Infarction was induced in dogs by ligating the left anterior descending coronary artery and regions of normal, ischemic, injured, and infarcted tissue of the heart were delineated by measurements of intramyocardial oxygen tension using coaxial pO_2 electrodes. Mitochondria were isolated from samples of myocardium removed from each region and their oxidative phosphorylation was measured with various substrates. Progressing from normal to infarcted cardiac tissue, there was a pari passu decrease in respiratory control and ADP:O ratios when the substrates were succinate and palmitoyl-carnitine, but not when glutamate or pyruvate-malate were used; however, oxygen uptake decreased with all four substrates as the injury became more severe. These results suggest that mitochondria from periischemic tissue may still be able to utilize glutamate and pyruvate-malate efficiently for oxidative phosphorylation. Mitochondrial protein per g of infarcted tissue was about 20% less than that found in normal myocardium. To study this apparent loss of mitochondria, preparations from normal and infarcted areas were fractionated by rate zonal centrifugation using an iso-osmotic Ficoll gradient. Both normal and infarcted areas yielded two peaks of functional mitochondria, with the heavy mitochondria generally having higher ADP:O ratios than the light ones. However, one hour after infarction, there was a 50% loss of heavy mitochondria, suggesting that the decrease in respiratory activity observed in the infarcted tissue may have been due to the loss of a specific mitochondrial population. (Supported by USPHS Grant 637362 and by a grant from the Michigan Heart Association)

Serum Gastrin Levels in Fed and Fasted Rats after Vagotomy or Atropine Treatment. Donald E. Wilder and Lyle A. Hohnke (intr. by Jay W. Constantine). Pfizer Central Research, Groton, Connecticut 06340.

Relatively few reports have considered factors important in the control of circulating gastrin levels in rats. Using radioimmunoassay techniques, serum gastrin levels were determined in rats of differing nutritional states both before and after bilateral truncal vagotomy (BTV) or atropine administration. Serum gastrin levels after 24 hours of fast were 39 $\pm$ 30 pg/ml (N=24). Similar determinations in animals allowed free access to food were 137 $\pm$ 47 pg/ml (N=12). In controlled food intake studies fasted rats receiving 4 ml of a standard carbohydrate, fat or protein meal by gastric intubation showed peak gastrin levels in the serum 30-50 minutes after feeding; the greatest increases were observed with protein containing meals. Serum gastrin levels in fasted rats were not changed significantly by reductions (pH 1) or increases (pH 9) in intragastric pH using 0.15 M HCl or 0.15 M $NaHCO_3$, respectively. Following atropine treatment (100 mg/kg - i.p.) or BTV significant increases in serum gastrin levels occurred that were proportional to intragastric pH. The highest levels were observed in rats with BTV and an intragastric pH of 9 (700 $\pm$ 300 pg/ml). Parallel studies in fed rats showed a similar pattern of serum gastrin levels although values were uniformly higher than comparably treated fasted animals. The studies suggest that in rats circulating levels of immunochemically reactive gastrin are controlled in part by the vagus and that the amount of vagal control is proportional to intragastric pH.

ROLE OF Na^+ IN PANCREATIC AMYLASE SECRETION

J.A. Williams. Department of Physiology, University of California, San Francisco, California.

Amylase release from mouse pancreatic fragments incubated in vitro was found to be influenced by the concentration of Na^+ in the medium. Replacement of Na^+ by choline, Tris, sucrose or Li^+ increased basal amylase release while inhibiting the increased release induced by bethanechol or caerulein. Both effects were also seen in tissue incubated in Ca^{++} free medium. The effects of removing Na^+ from the medium were reversible and concentration dependent. Pancreatic amylase release can also be stimulated directly by Ca^{++} by use of the Ca^{++} ionophore A23187 which allows cellular entry of Ca^{++} from the medium. A23187 in the absence of Ca^{++} has no effect. In contrast to amylase release induced by normal stimulators, amylase release induced by A23187 plus Ca^{++} is not inhibited by removal of Na^+ from the medium. Electrophysiological data has shown that pancreatic stimulators increase the acinar cell permeability to Na^+. It is suggested that Na^+ entry is the coupling mechanism between the stimulator-receptor interaction at the cell membrane and release of intracellular Ca^{++} which then promotes pancreatic enzyme release by exocytosis or other means. (Supported by NIH grant GM 19998 and a grant from the National Cystic Fibrosis Research Foundation).

THE INFLUENCE OF RESPIRATORY LIKE ACTIVITY (RLA) ON THE BAROREFLEX IN THE FETAL LAMB. R.L.Williams, M.A.Day, I.Edwards & A.Bator (intr. by P. Sekelj). Dept. of Physiology & McGill University-Montreal Children's Hospital Research Institute, Montreal, Canada.

Spontaneous respiratory like activity (RLA) in the chronic fetal lamb preparation is known to be accompanied by alterations in the electrocorticogram and electrooculogram. Experiments were performed on the fetuses of 7 mixed breed ewes ranging in gestational age from 116 to 130 days to test whether this central nervous activity influences a cardiovascular reflex known to have synaptic connections in the lower brainstem. Vinyl catheters were inserted into the amniotic cavity, the fetal trachea, carotid artery and jugular vein. Electrocardiographic leads were sewn to the chest wall and a balloon catheter advanced from the femoral artery into the descending thoracic aorta. Studies were performed at least 5 days after operation on healthy fetuses with normal arterial blood gases ($pO_2 > 20$ mmHg and $pCO_2 < 45$ mmHg) and pH (>7.32) and resting heart rate of < 195 beats/minute. Fetal baroreflex sensitivity was quantitated by transiently elevating proximal aortic blood pressure by balloon inflation and plotting successive R-R intervals as a function of pulse pressure (Circ Res 31: 710, 1972). The slowing of heart rate per unit rise in pulse pressure averaged 1.25 ± 0.22 (S.E.) msec. per mmHg during spontaneous RLA and 2.96 ± 0.49 (S.E.) msec. per mmHg in fetuses with no RLA (P less than 0.01). There was no difference in resting heart rate between the 2 groups. These data suggest that there is an interaction between spontaneous RLA and the fetal baroreflex which may involve the brainstem.

EFFECT OF CHRONIC CONSTRICTION OF THE ASCENDING AORTA ON RENAL SODIUM EXCRETION IN RATS. J. H. Wong* and A. D. Baines Dept. of Clin. Biochem., Univ. of Toronto, Toronto, Canada.

In congestive heart failure, according to Guyton, decreased GFR is a factor responsible for the renal retention of sodium. Using chronic aortic-constricted (AC) rats as a model of low-output cardiac failure, we studied the cardiovascular changes and renal sodium excretion before, during, and after acute blood volume expansion (BVE). All animals received ADH and aldosterone during the experiment. With an average 40% reduction (P<.001) in cardiac output (CO), AC rats had mean arterial pressures (MAP) similar to sham-operated (C) controls. GFR, Na excretion and urine flow were lower. During BVE, CO, MAP, GFR, Na excretion and urine flow rose in both groups. CO was 30 percent lower in AC rats (P<.05). Although MAP and GFR were similar, Na excretion in AC rats was 30% less. After BVE, GFR in AC rats was elevated above the original level (P<.025) while that of C rats returned to control level. AC rats continued to excrete less sodium and the cumulative excretion 100 min after BVE was 25% less than C rats (P<.025). Thus following BVE, renal retention of sodium in a low cardiac output state relates to CO but is independent of MAP, ADH, aldosterone, and large changes in GFR.

	GFR, ml/min/100gBW		$U_{Na}V$, μEq/min/100g		MAP, mm Hg	
	C	AC	C	AC	C	AC
Before	0.94	0.72^a	2.48	1.26^a	121	121^c
During	1.18	1.13^c	15.70	11.20^a	141	136^c
After	0.91	0.84^c	4.32	3.28^b	121	122^c

(a=P<.001, b=P<.01, c=not significant)

SOURCE OF PURINES IN NUCLEATED VERTEBRATE RED CELLS. Lyle Wong*, Jean E. Vorhaben* and James W. Campbell. Rice University, Houston, Texas

The capacity for purine synthesis de novo is lost during differentiation of mammalian reticulocytes. Mature red cells must therefore rely upon an external source--mainly the liver--for preformed purines. Whether or not nucleated vertebrate red cells are also incapable of purine synthesis de novo was not known. The latter cells do retain some biosynthetic capabilities, e. g., for heme. We found mature amphibian, reptilian and avian red cells to have little or no capacity to incorporate [U-^{14}C]glycine into either adenine or guanine. These cells, with the exception of Necturus, were, however, capable of incorporating [2-^{14}C]4-amino-5-imidazole carboxamide (AIC) into the two purines indicating that they, like mammalian cells, have a dysfunction in the pathway prior to the formation of AIC ribotide. Cells lacking the ability to synthesize purines de novo utilize preformed purines via the purine phosphoribosyltransferases, enzymes converting the free bases to the nucleotide monophosphates. Since the main purines supplied by the liver may be the oxypurines, hypoxanthine-guanine phosphoribosyltransferase (HGPRT) may be especially involved. We found HGPRT activity in all vertebrate red cells examined: fish, amphibians, reptiles, birds as well as mammals. The highest activities were in chelonid reptiles and the lowest, in dogs. Indirect evidence was also obtained for high levels of 5'-nucleotidase in reptilian cells. We therefore conclude that the loss of ability to synthesize purines may occur universally during reticulocyte differentiation in vertebrates and is not necessarily associated with the physical loss of chromatin in mammalian cells and also that all vertebrate red cells may utilize preformed purines via the purine phosphoribosyltransferases.

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THE EFFECTS OF Mg AND PROCAINE ON Ca REDISTRIBUTION WITHIN CHEMICALLY SKINNED HUMAN MUSCLE FIBERS. D. S. Wood*, J. P. Reuben and P. W. Brandt. Depts. Neurology and Anatomy, College of Physicians & Surgeons, Columbia U., New York 10032.

Ca within the matrix of skinned muscle fibers is distributed among 3 major compartments: sarcoplasmic reticulum (SR), troponin binding sites (Tc), and matrix sites (Mc). The redistribution of Ca among these compartments can be analyzed by observing the amplitude, duration, and development of isometric tensions following Mg (1-10 mM) or procaine (5-10 mM) treatment. Fibers exposed to subthreshold Ca levels in the presence of either agent develop large transient tensions upon the removal of Mg or procaine from the bathing solution. These large transient tensions are abolished and instead a small step decrease in tension occurs after destroying the SR's Ca accumulating ability with Brij-58. Following Brij treatment the addition of Mg or procaine causes a small (5-10% P_o) step increase in tension. Brij, by destroying the Ca accumulating ability of the SR, reduces to 2 the number of major Ca compartments within the matrix. The Mg and procaine effects following Brij treatment are interpreted as a shift of Ca from Mc to Tc. Prior to Brij treatment, however, the SR dominates Ca distribution within the matrix, and the magnitude of the effects of Mg and procaine on Mc may be obscured by their effects on the SR. That they do affect the SR is evidenced by their ability to attenuate or block CI and caffeine tensions. The demonstrated affects of Mg and procaine on both the SR and Mc must be considered when analyzing any modification of Ca induced tensions by either agent. (Supported by MDAA, NIH and NSF).

EFFECTS OF NICOTINIC AGENTS ON REBOUND EXCITATION OF GUINEA-PIG SMALL INTESTINE. J. D. Wood and B. A. Rose*. Dept. of Physiology, Univ. of Kan. Med. Ctr., Kansas City, Kan. 66103.

Poststimulus rebound contractions and associated action potentials of the circular muscle layer occurred following termination of transmural electrical stimulation. Low concentrations of nicotine (1×10^{-6} g/ml to 5×10^{-6} g/ml) either abolished or greatly reduced the poststimulus rebound response. The contractile force and time duration of the response were reduced, and the latency between termination of stimulation and onset of the response was increased by low concentrations of nicotine. The inhibitory action of low concentrations of nicotine was reversed by a one-step increase in concentration from 5×10^{-6} g/ml to 1×10^{-4} g/ml. The effects of low concentrations of nicotine were mimicked by DMPP, and they were antagonized by hexamethonium and pentolinium. Pretreatment with guanethidine produced a small reduction in the inhibitory action of nicotine. Propranolol and phentolamine reduced the amplitude of the poststimulus contractile response, but the specificity of the action was questionable. The effects of nicotine appeared to be mediated by an excitatory action on intrinsic inhibitory neurons. (Supported by NSF GB-31292)

Oxygen uptake and cardiac output in eels adapted to hypoxia. Stephen C. Wood and Kjell Johansen, Department of Zoophysiology, Aarhus University, DK-8000 Aarhus C., Denmark.

Oxygen uptake ($\dot{V}_{O_2}$) was measured at 20 °C in control eels (kept in aerated water) and hypoxia adapted eels (kept for 2 weeks at water P_{O_2} of 20-40 mm Hg). These data, with our previous measurements of blood gases (Am. J. Physiol. 225: 849, 1973) were used to calculate cardiac output ($\dot{Q}$) and thereby more fully allow evaluation of the physiological significance of the earlier finding of increased oxygen affinity of blood in hypoxia-adapted eels (Nature New Biol. 237: 278, 1972. We found that adaptation to hypoxia includes a reduction in $\dot{V}_{O_2}$ (from 0.63 to 0.46 mlO_2 $\times$ min^{-1} $\times$ kg^{-1}) in addition to the previously reported three-fold increase in arteriovenous O_2 content difference (from 1 to 3 vol %). These factors of the Fick equation reveal a 76 % decrease in $\dot{Q}$ (from 63 to 15.3 ml $\times$ min^{-1} $\times$ kg^{-1}) in hypoxia adapted eels which is explained mainly by the increased O_2 affinity and capacity of the blood. If the hypoxia adapted eels are returned quickly to aerated water the higher O_2 affinity becomes detrimental and the arteriovenous O_2 content difference is reduced from 3 to 1 vol % (compared with 2 vol % for control eels). Adapted eels must then compensate with a correspondingly higher cardiac output ($\dot{Q}$ = 46.0 compared with 31.5 ml $\times$ min^{-1} $\times$ kg^{-1} for controls) until the increased O_2 available to the red cells induces replenishment of ATP stores and thus lowers oxygen affinity once again.

Supported by a grant from the Danish Natural Science Research Council. Present address of SCW: Department of Biology, Southern Illinois University, Edwardsville, Illinois 62025.

REGIONAL MYOCARDIAL INOTROPIC RESPONSES TO BILATERAL CAROTID OCCLUSION, NOREPINEPHRINE AND THORACIC VENTRAL ROOT STIMULATION. R. D. Wurster and J. E. Norris*. Loyola University, Stritch School of Medicine, Dept. of Physiology, 2160 South First Avenue, Maywood, Illinois 60153.

On 10 vagotomized dogs strain gauges were placed on 6 areas of the anterior and posterior surfaces of both ventricles. Bilateral carotid occlusion increased systolic and diastolic blood pressure an average of 71 and 55 mm Hg, respectively. Heart rate increased 26 beats/min. Contractile force increased from 3 to 24% being highest on the posterior surface of the right ventricle and least on the left apex. Norepinephrine (0.4 μg/Kg,i.v.) increased contractile force from 90 to 183% being highest on the apex of the left ventricle and minimal on the posterior basal regions. Systolic and diastolic blood pressure increased 38 and 28 mm Hg, respectively. Heart rate increased 28 beats/min. Left ventral root stimulation increased force of contraction up to 114% being greatest on the left posterior surface. Systolic and diastolic blood pressure increased 32 and 18 mm Hg, respectively. Heart rate increased 14 beats/min. Right ventral root stimulation increased force of contraction up to 116% being maximal on the anterior basal regions of both ventricles. Systolic and diastolic blood pressure increased by 18 and 13 mm Hg, respectively. Maximal heart rate increased an average of 50 beats/min. Thus, bilateral carotid occlusion, norepinephrine and ventral root stimulation resulted in different patterns of inotropic responses which are not solely explained by different heart rate and blood pressure responses. These results support the concept of differential control of regional myocardial inotropic responses. *(Supported by NIH Grant HL 08682)*

ELECTROGENIC SODIUM PUMPING IN MYTILUS SMOOTH MUSCLE. H. Yamaguchi* and B. M. Twarog, Department of Biology, Medford, Massachusetts 02155.

The possible contribution of an electrogenic sodium pump to the resting membrane potential of smooth muscle cells of Mytilus ABRM has been investigated using microelectrode and double sucrose gap methods. In artificial sea water (ASW) containing 10^{-4}M ouabain or in potassium-free ASW no depolarization of the membrane was observed during the first hour. After several hours of soaking in potassium-free or ouabain-containing ASW, depolarization of 4-5 mV occurred. After restoration to control ASW, the membrane transiently hyperpolarized (10-12 mV). The hyperpolarization increased with the duration of the soaking. In addition, when the internal sodium ion content was augmented by brief exposure to isotonic NaCl - EGTA solution during soaking in potassium-free ASW the transient hyperpolarization was enhanced. This hyperpolarization was blocked by 10^{-4}M ouabain. The evidence suggested the existence of an electrogenic sodium extrusion mechanism; however, its contribution to the normal resting membrane potential seemed negligible. (Supported by USPHS Grant NS 10554-07).

LUNG CAPILLARY PERMEABILITY TO SODIUM WITH THE INSTANTANEOUS EXTRACTION METHOD. T. Yipintsoi*, T. Nivatpumin*, P. Chandler* and F. Veith. Montefiore Hospital and Medical Center, Bronx, N.Y.

^{24}Na and ^{131}I-albumin was injected as a bolus into the right atrium of six anesthetized and ventilated dogs. Sequential blood samples were collected from the femoral artery. The peak extraction, E, for sodium and the permeability surface area of the lung capillaries (PS = - F $\log_e$ (1-E)) were calculated. Total plasma flow, F, was varied by transient occlusion of the venae cavae. E was 5-10% when total flow was 0.2 to 1.0 L/min. The extravascular sodium volume, v_E, ranged from 0.2 to 0.3 g/g lung tissue and appeared constant from 2 to 60 minutes after the bolus injection. Blood volume, v_b, was 0.1 to 0.2 g/g. Comparable myocardial values for v_E and v_b were 0.05-0.10 and 0.13-0.17. Because of the low PS with low F, the distribution of 9u diameter microspheres in 1-2 lung pieces was compared at both high and low F. Regional flow as a function of total F per unit lung weight varied from 0.3 to 3.0. When total F was reduced those regions which initially had higher than average flows showed greater relative amount of microsphere while those regions which initially had lower than average flows showed disproportionately much less. This suggests that with decrement in total F, some areas of the lung may not be perfused. In normal lung, the low E for Na, the large v_E and the very high lung flow per unit weight imply that the instantaneous extraction technique may not measure true PS for sodium, but may qualitatively denote conditions where there are increases of PS.

CONTROL OF PLASMA SODIUM CONCENTRATION(PNa) BY THE ADH-THIRST MECHANISM. D. B. Young*, and A. C. Guyton. Univ. Miss. Sch. Med., Jackson, MS

The ability to control PNa and fluid volume during changes in Na intake was studied in intact dogs, in dogs lacking responsive aldosterone mechanisms and in dogs without responsive ADH-thirst mechanisms. In intact animals an increase in Na intake from 10 to 200 mEq/day resulted in a 1% increase in PNa from 142.1 $\pm$ .5 to 143.8 $\pm$ 1.8 mEq/L. Extracellular fluid volume estimated by ^{22}Na space increased from 30.8 $\pm$ .8 to 33.1 $\pm$ 2.3% body weight(B.W.), an 8% increase. In animals adrenalectomized and maintained on a constant replacement of aldosterone(130 ug/day) a similar increase in Na intake resulted in a 2% increase in PNa, from 141.4 $\pm$ .5 to 144.4 $\pm$ .9 mEq/L while ^{22}Na space increased 13%, from 33.4 $\pm$ .9 to 37.8 $\pm$ 2.1% B.W. after 3 days high Na intake. A third group of animals was maintained on constant infusion of ADH(Pitressin, Parke-Davis), 18U/day, and a controlled water intake(700 ml/day) during the low and high Na intake periods. Throughout the experiment urinary osmolarity remained maximally concentrated. In these dogs the increase in Na intake produced a 12% increase in PNa, from 131.5 $\pm$ 4.2 to 147.1 $\pm$ 3.1 mEq/L, and a 6% increase in ^{22}Na space, from 28.2 $\pm$ .9 to 29.8 $\pm$ .6% B.W., after 4 days high Na intake. By the end of the high intake period the animals were in daily Na balance. The results suggest that PNa is regulated to a large extent by the ADH-thirst mechanism and is not significantly influenced by the aldosterone system. Supported by NIH grants No. HL 11678 and HT-5184.

EFFECT OF LUNG INFLATION ON PULMONARY ARTERIAL BLOOD VOLUME IN INTACT DOGS. S. Zarzecki*, A. Wanner*, and M.A. Sackner. Mount Sinai Medical Center, Miami Beach, Florida.

The isolated effects of lung inflation and transmural pulmonary arterial pressure (P_{TM}) on pulmonary arterial blood volume (V_{PA}) were investigated in 10 anesthetized intact mongrel dogs. Using transvenous phrenic nerve stimulation (Wanner, Sackner, J.Appl.Physiol. 34:489-494, 1973), changes in P_{TM} at a fixed transpulmonary pressure (P_{TP}) were produced by the Mueller maneuver and increases in P_{TP} at relatively constant P_{TM} by relaxation of the diaphragm against the closed airway following lung inflation which resulted in a Quasi-Valsalva maneuver. Also, both P_{TP} and P_{TM} were allowed to change during open airway lung inflation. V_{PA} was determined during these three maneuvers by multiplying pulmonary blood flow by mean pulmonary arterial transit time obtained by an ether injection method (Feisal, Soni, DuBois, J. Clin. Invest. 41: 390-400, 1962), and mean pulmonary arterial, intrapleural and mouth pressures were simultaneously recorded. It was found that during open airway lung inflation, mean (±SD) P_{TP} increased by 7.2 (±3.6) cmH_2O and P_{TM} by 4.3 (±3.4) cmH_2O for a mean increase in V_{PA} of 26.5 (±10.7) ml. A pulmonary arterial compliance term ($\Delta V_{PA}/\Delta P_{TM}$) calculated from the Mueller maneuver was 3.9 ml/cmH_2O, and an interdependence term ($\Delta V_{PA}/\Delta P_{TP}$) calculated from the Quasi-Valsalva maneuver was 2.5 ml/cmH_2O for a 19% increase in lung volume, and 1.3 ml/cmH_2O for an increase in lung volume between 19% and 35%. These results indicate that in the intact dog at lung volumes near functional residual capacity, the elastic recoil of the pulmonary artery has a greater effect on V_{PA} than the elastic recoil of the lung. It should be of interest to evaluate these relationships in disease states such as pulmonary arterial hypertension, pulmonary edema or emphysema.

COLD RESISTANCE OF THE OUABAIN SENSITIVE ^{42}K INFLUX IN PRIMARY CELL CULTURES OF GUINEA-PIG, HAMSTER AND GROUND SQUIRREL KIDNEY CORTEX. R.B. Zeidler* and J.S. Willis. Dept. of Physiology, Univ. of Illinois, Urbana, Illinois 61801.

Cell K regulation offers a sensitively graded criterion for testing whether the unusual cold resistance of cell function of hibernating mammals persists in cells grown in culture. Primary cell cultures of kidney cortex were grown for three days as a monolayer on plastic culture dishes at 37°C in a 5.0% CO_2 incubator. The uptake of 5.0 mM radioactive potassium was measured in the presence and absence of ouabain in cells at 37°C and at 5.0°C in cells pre-incubated for two hours at 5.0°C. The ratios of ouabain sensitive ^{42}K influx measured at 5.0°C over ouabain sensitive ^{42}K influx measured at 37°C for cell cultures from one day old hamsters and from one day old guinea-pigs are 0.17 and 0.06 respectively. The ratio for cells from adult guinea-pigs is 0.07, while cells from awake ground squirrels and hibernating ground squirrels have ratios of 0.09 and 0.13 respectively. Cell cultures from awake adult hamsters and from hibernating adult hamsters have ratios of 0.09 and 0.07. After two hours incubation at 5.0°C, monolayers from one day old guinea-pig, adult guinea-pig and awake adult hamster retain respectively 62%, 74%, and 86% of their initial intracellular K, while monolayers from hibernating hamster, and hibernating and awake ground squirrel retain 100% of their initial intracellular K. Thus while K influx in all of the primary cultures of kidney cortex was relatively cold resistant, cultures from hibernating ground squirrel were still more cold resistant than those from guinea pig. The pump-leak system of cultured cells of ground squirrels and of hibernating hamsters permits unaltered retention of K at 5°C. Supported by N.I.H. Grant, GM 11494.

ACTION OF Mn ON CONTRACTION, Ca UPTAKE AND CATION CONTENT OF FROG VENTRICLE. Gerald W. Zimmerman and Jean F. Delahayes (intr. by Emil Bozler) Dept. Physiol. Ohio State Univ., Columbus, Ohio.

The effect of Mn^{2+} on the contraction and cation exchange of frog ventricle was investigated. The mechanical responses of ventricular strips equilibrated either in 1.0 mM or 1.8 mM Ca-Ringer solution decreased with increasing $[Mn^{2+}]$ (0.1 mM to 5.0 mM), by 63.1% ($\pm$ 4.0 S.E.) and 42.0% ($\pm$ 2.2 S.E.) respectively in 1.0 mM Mn^{2+}. Responses depressed by Mn^{2+} were increased above control levels when 10^{-6} M epinephrine was added to the solution. Cation content was studied in whole ventricles perfused for 60 min with ^{45}Ca labeled, 1.0 mM Ca-Ringer solution, either in the presence or absence of 1.0 mM Mn^{2+}. Quiescent ventricles were pulsed by applying outside negative and positive pressure rhythmically to facilitate mixing of the extracellular space. One group was stimulated (12 beats/min) for the final 10 minutes. With and without stimulation, Mn^{2+} decreased the ^{45}Ca uptake, while the total Ca was diminished, but only in stimulated muscle. Mn^{2+} significantly depressed the Na^+ content of resting ventricles, but did not alter the K^+ content. It is concluded that the negative inotropism of Mn^{2+} is due to decreased uptake and total cellular content of Ca and possibly Na^+.

ADRENERGIC MECHANISMS IN THE CANINE GASTRIC CIRCULATION. Michael J. Zinner*, John C. Kerr*, and David G. Reynolds. Division of Surgery, Walter Reed Army Institute of Research, Washington, D. C. 20012

The effects of adrenergic stimulation and blockade on the gastric circulation were studied in anesthetized dogs. Right gastric (RGBF)and left gastric (LGBF) arterial blood flows were measured electromagnetically. Epinephrine (E), norepinephrine (N), and isoproterenol (I) were injected intraarterially over a range of 10^{-3} to 10^{0} μg (base) kg^{-1} before and after differential adrenergic blockade (phenoxybenzamine 1.5 mg kg^{-1} iv, n=5; propranolol 0.5 mg kg^{-1} iv n=5). E and N caused biphasic responses, constriction followed by dilation, at all doses, while I was a pure vasodilator. The left gastric artery (control flow 51 $\pm$ 9 ml min^{-1}) exhibited greater vasodilator responses to all three adrenergic amines ($p < .05$) than did the right gastric artery (control flow 72 $\pm$ 5 ml min^{-1}). At a dose of 10^{-1} μg kg^{-1}, E caused a decrease in LGBF of 36 $\pm$ 4 ml min^{-1} which was rapidly followed by an increase of 65 $\pm$ 7 ml min^{-1} above control. At the same dose E caused a fall of 54 $\pm$ 4 ml min^{-1} in RGBF followed by a rise of only 32 $\pm$ 7 ml min^{-1} above control. Alpha adrenergic blockade abolished or attenuated the constrictor responses while beta adrenergic blockade attenuated the dilator responses. At the highest dose of all three amines, there was a significant ($p < .01$) change in RGBF when the drugs were injected into the LG artery. N caused a decrease of 37 $\pm$ 8 ml min^{-1} in RGBF when injected into the LG. There ware minimal changes in LGBF when the drugs were injected into the RG artery. These data suggest that the subregional area served by the LG artery, the fundus and body of the stomach, exhibits different responses to adrenergic stimulation than does the subregion served by the RG artery, the antrum and duodenum.

Discharge Characteristics of Viseral Afferents in the Monkey. E.J. Zuperku, D.R. Kostreva, G.L. Hess, J. Neumark, R.L. Coon and J.P. Kampine, (Intr. by W.J. Stekiel) Med. Col. of Wisc., Milwaukee, Wisc.

Neural receptors in the walls of the heart and major vessels provide the feedback elements for the beat to beat regulation in the cardiovascular system. The discharge patterns of these receptors have been mainly studied in the dog and cat. This investigation was conducted to study the discharge characteristics of cardiac receptors in a non-human primate. Pigtail Macaque monkeys 10-15 Kg were anesthetized with phencyclidine (1-2 mg/Kg) and anesthesia was maintained with 40% N_2O in oxygen and halothane (0.5 to 1.0% inspired). The animals were ventilated with a Bird Mark VII respirator and anesthesia controller. The EKG, ventricular, atrial, and systemic arterial pressures were recorded on a polygraph and magnetic tape system. Nerve activity was recorded from the anterior ansa subclavia and stellate cardiac nerves with bipolar hook electrodes. Receptors were located by probing the walls of the left atrium and ventricle and aortic arch. Interventions such as increases in afterload (snare on descending aorta), preload (infusion of saline in large vein), and positive inotropic agents (Epinephrine) produced altered mechanical events and increased subsequent afferent neural activity. Frequency histograms of multiple fiber activity reveal that several types of cardiac receptors exist. Activity was grouped with respect to atrial contraction, ventricular contraction, near the peak of the atrial v-wave, and during the rapid filling phase of the ventricle. These discharge patterns are similar to those found in the dog and indicate that receptors located within the walls of the left atrium, ventricle, and ascending aorta may give rise to afferent nerve activity in the nerves studied.

Muscle Tissue Ionic Balance in Cancer magister Exposed to Different Salinities. G. Samuel Alspach, Jr. and Austin W. Pritchard. Western Maryland College, Westminster, Md. and Oregon State University, Corvallis, Ore.

Ion regulation was studied in the Dungeness crab, Cancer magister, after acute exposure for 24 and 48 hours to a range of five salinities from 25% to 125% sea water (100%=32°/oo). Measurements were made of sodium, potassium, chloride and calcium ion concentrations. Data were obtained also for total amino nitrogen. The muscle extracellular space (interfiber water) was determined with inulin-C^{14}. Muscle tissue of crabs in dilute sea water (blood hyperionic to the medium) shows reduction in muscle ion concentrations and free amino nitrogen compounds, while increases occur in tissue water content and muscle extracellular space. The blood:tissue gradient for potassium indicates intracellular regulation of this ion; no regulation of sodium and chloride is found. Decreases in free amino nitrogen compounds do not contribute significantly to decreases in cell volume through loss of osmotically active non-electrolytes in muscle. Muscle tissue of crabs in 125% sea water (blood isoionic to the medium) shows a decrease in tissue water content, muscle sodium and muscle chloride. Muscle potassium is regulated. Large increases in free amino nitrogen compounds are noted and appear to indicate intracellular adjustments by cells to the increased osmotic concentrations.

ELECTROPHYSIOLOGICAL STUDIES ON AN UNUSUAL MUSCLE. M. Anderson. Smith College, Northampton, Mass.

The proventriculus of the marine polychaete worm Syllis spongiphila is made of a single layer of myoepithelial cells oriented radially around the lumen. These cells consist of only one or two sarcomeres, and sarcomere length reaches 40 μ. The proventriculus is the section of the alimentary tract between the proboscis and the intestine. Its function is to expand its lumen to draw in sea water and particulate matter and then to close it to push material into the intestine. Microelectrodes were used to record electrical activity from the muscle cells. Spontaneous activity associated with swallowing behavior is characterized by a series of junction potentials (jp's) of one polarity, which sum, followed by a series of jp's of the opposite polarity. Changes in membrane potential were correlated with mechanical activity by photographing the proventriculus through the microscope during junctional activity evoked by indirect stimulation (constant intensity, 0.5 msec duration pulses applied to the head end of the animal at a frequency of 20 Hz). Results showed that at rest the lumen is slightly open, at depolarized membrane potentials it is opened wider, and at hyperpolarized potentials it is closed. Measurements of the lengths of the cells in the region of the microelectrode showed that the muscle cells shorten from rest length with depolarization and lengthen with hyperpolarization. The frequency of the applied stimuli, and not the intensity, determine the nature of the postsynaptic response. Low frequencies (< 4 Hz) elicit only hyperpolarizations; higher frequencies elicit hyperpolarizations and depolarizations.

"Decompression of Salmonids: Comparison with Mortality Due to Supersaturation at One Atmosphere"

D. Byer,* B. G. D'Aoust, and L. Smith,* University of Washington and Virginia Mason Research Center, Seattle, Washing.

The use of salmonids for evaluating critical conditions of gas separation in tissues (D'Aoust and Smith, Comparative Biochem. and Physiology, vol. 48A, 1974) requires definition of maximum saturation times and capacities for inert gas of the specimens used. Initial studies of fingerling (6 cm) steelhead (Salmo gairdnerii) using a two compartment chamber suggest either a large slow component in the saturation curve (consistent with a large diffusion limited tissue volume) or alternatively a considerably lower capacity for inert gas in the fishes' tissues than would be expected on the basis of water solubility. Using a weighted dose response bioassay and a 50% of maximum effect for an end point preliminary decompression experiments confirm previous work that in this size of fish at 11°C maximum scores are obtained in a minimum of one hour. Assuming maximum lethality is associated with maximum gas absorbed for any one decompression, it is concluded that for any given gradient, saturation is complete within one hour. Thus the well-documented lethal times of 18 hours for an over-saturation of 15% of one atmosphere (Rucker, 1972) indicates a time lag in achieving maximum effect which cannot be related to gas saturation or desaturation rates.

THE EFFECT OF CHRONIC HEAT STRESS ON INTESTINAL FUNCTION IN THE RAT. Mecca Carpenter* and X. J. Musacchia, Dept. of Physiol., and Dalton Research Center, University of Missouri, Columbia, Mo. 65201.

Male rats exposed to T_a 34°C for two weeks show alteration in intestinal function compared to pair fed controls at T_a 22°C. Active transport was measured by an everted gut sac method using three jejunal locations. The initial concentration of glucose was 18 mM in a Krebs-Ringer Bicarbonate buffer at both the mucosal and serosal surfaces. Incubation time was 30 minutes. The total amount of glucose transported per sac was significantly less in heat stressed animals for each jejunal location. Proximal to distal values for glucose uptake following heat exposure were 49.8 ± 2.2, 38.0 ± 3.4, and 36.7 ± 2.6 μM. Control values were 57.1 ± 2.0, 53.7 ± 4.3, and 47.4 ± 4.0 μM. However, when transport of glucose is expressed as μmoles/gm wet wt., there was no significant difference between sacs from the same location in the two groups of animals. Intestinal mass per gram body weight was reduced in heat stressed rats. The total dry gut weight to body weight ratio after heat exposure was .0033 ± .0002 compared to a control value of .0043 ± .0001 ($p < .005$). With heat exposure, gut tissue water was also significantly reduced from control values. Reduction in total absorptive capacity while maintaining a stable active transport system may be one adaptation to reduced metabolic demands with an increased heat load in the rat. (Supported by NASA NGL 26-004-021-S10).

"Effects of Stress on Salmonid Blood Clotting Mechanisms"

E. Casellas,* L. Smith,* and B. G. D'Aoust, University of Washington and Virginia Mason Research Center, Seattle, Wa.

The effects of exercise stress on various hematological parameters in rainbow trout were examined in recent investigations. Blood coagulation times were found to decrease 55% of the original pre-stress values within a half hour after the termination of the stress period. Thrombocyte counts were found to increase three to four fold in the same period. Hematocrits and blood plasma glucose also rose significantly with respect to the stress applied. Red blood cell and white blood cell counts, however, did not increase in response to the stressor. The degree of the responses observed were compared between members of a wild trout population from Chester Morse Lake, Washington, and hatchery-reared Donaldson-strain rainbow trout. The wild strain showed a more rapid return to pre-stress conditions than the hatchery-reared population. This controlled variability in the blood coagulation rate is proposed as a mechanism to avoid disseminated intervascular coagulation [D.I.C.] in the poorly perfused muscles of fish.

Ganglionic Mediation Mechanisms of Lateral Cilia in Mytilus edulis Gill. Edward Catapane* and Edward Aiello, Fordham University: and George Stefano, New York City Community College.

Previous studies performed in this laboratory have demonstrated the localization of cholinesterase, serotonin (HT) and dopamine (DA) in the cerebral ganglia (CG), visceral ganglia (VG) and gill of the bivalve mollusc, Mytilus edulis. Acetylcholine, HT and DA have been postulated as being peripheral neurotransmitters of the branchial nerve. Present studies using the fluorescence techniques of Falck and Hillarp in conjunction with stroboscopic microscopy of gill lateral cilia are concerned with the intraganglionic role of these substances. Cilio-excitation was obtained with HT and cilio-inhibition with DA when applied topically to the VG. Electrical stimulation of the cerebro-visceral connective (CVC) resulted in cilio-excitation. Application of nicotine to the VG blocked the cilio-excitatory effects of electrical stimulation of the CVC. We are tentatively suggesting that 1) cilio-excitation is mediated by a serotonergic mechanism, possibly arising in the CG but regulated by the VG, 2) cilio-inhibition is mediated by a dopaminergic mechanism originating in the VG, and 3) intraganglionic mechanisms are mediated by a cholinergic system which is blocked by nicotine.

CENTRAL INTEGRATION OF HEART AND VENTILATORY ACTIVITY IN CANCER BOREALIS AND C. IRRORATUS. Philip E. Coyer (intr. by G. A. Wyse). University of Massachusetts, Amherst.

Crustaceans have intrinsic rhythmic motor outputs governing scaphognathite and heart activity. The heart is controlled by the cardiac ganglion and the scaphognathite by elements in the subesophageal ganglion. Since these two behavioral rhythms are both involved in gas transport, their control may be coordinated. This study provides evidence for coupling of the two respiratory activities in Cancer borealis and C. irroratus. In intact animals, heart rate and ventilation frequency were monitored simultaneously using an impedance pneumograph and a pressure transducer under normoxic and hypoxic conditions. The relationship between these rates and oxygen partial pressures was best expressed by a second-order polynomial equation. In addition, periods of simultaneous heart block and increased ventilatory rate lasting between 5-12 seconds were recorded. Histogram analysis has shown that there can be phase coupling between the cardiac ganglion burst and the scaphognathite movement, and that the degree of coupling may depend on oxygen conditions. In one animal at values between 80 and 90% air saturation, there was 91% coupling of the rhythms. With nitrogen bubbling and reduction in oxygen saturation values to between 50 and 60%. the coupling percentage dropped to 68%. When nitrogen bubbling was ceased, coupling returned to a value of 95% at 40% air saturation. The neuronal circuitry and possible role of command fibers in modulating these coupled behaviors is being considered.

Calcium Compartments in Turtle Heart, Thomas F. DeCaro, Widener College, Chester, Pa.

An attempt was made to elucidate calcium compartments in turtle heart, an organ lacking a well defined sarcoplasmic reticulum. In the past, this author demonstrated by twitch-tension and Ca^{45} washout studies that a loosely bound calcium moiety supports the contractile response in turtle atrium; i.e. calcium depleted atria subsequently loaded with calcium during either short or long soak periods in both cases showed a rapid decline in tension ($t_{\frac{1}{2}}$=3-9 min) when stimulated electrically. When calcium depleted atria were loaded with Ca^{45} in Ringer's Sol. for short and long periods and then washed out in cold Ringer's sol. a rapid efflux ($t_{\frac{1}{2}}$=8-10 min) occurred in both cases. In a recent study in comparison to controls, both atria and ventricles showed a + inotropic response when perfused with a Ringer's sol. containing 5 or 10 mM caffeine. Atria showed a +37-83% change in amplitude and ventricles a +20-50% change. Since caffeine is known to release calcium from its bound state these results may indicate the presence of a compartment that tightly binds calcium. Finally after washing calcium from atria and ventricles with a Ca free Ringer's sol. containing 1 mM EGTA, and then perfusing with an identical solution but containing 10 mM caffeine a + inotropic effect was noted, being more pronounced in the ventricle. These results seem to indicate the presence of three calcium compartments in turtle heart and that the previous results cannot be explained totally by an enhancement of calcium influx from the external solution by caffeine.

GLYCOSAMINOGLYCANS, COLLAGEN, AND ELASTIN OF THE AORTA OF NORMAL AND HYPOTHYROID SWINE NEONATE. D. P. DeVore*, J. L. Walter*, S. D. Carter*, and J. B. Boatman, Battelle, Columbus Laboratories, Columbus, Ohio

Aortae from normal and propylthiouracil-fed (hypothyroid) swine weaned at 2 weeks were removed at 10 weeks of age and separated into regions corresponding to the arch and the thoracic and abdominal areas. Procedures and results of studies of the regional permeability of the same swine aortae to Evans blue dye and I^{131}-albumin are reported elsewhere. Sections from abdominal and thoracic aorta were cleaned and minced, ground after lyophilization, and processed for total mucopolysaccharides, collagen, elastin, and total lipids. Plasma mucopolysaccharides were analyzed by methods modified from the tissue procedures. Protocols of analytical procedures will be reviewed. Hypothyroid animals exhibited significantly higher levels of total glycosaminoglycans (GAG) in plasma and in abdominal aorta sections. Electrophoretic analysis of abdominal aorta extracts indicated distinct qualitative differences between GAG's of control and treated animals. Collagen levels were depressed in hypothyroid animals and collagen:elastin ratios were subsequently affected. Total lipid levels were also significantly lower in abdominal aorta sections of treated animals although lipid levels in thoracic aorta sections were not so affected. Formation of structural moieties of specific tissues appeared to be dramatically affected by hypothyroid conditions during the growth period examined.

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MAST CELLS IN THE DEVELOPING RAT BRAIN. J. Dropp. Wilson College, Chambersburg, Pa.

Mast cells (MC's) were studied in the developing brains of 21 rats (Rattus norvegicus - Wistar strain), including time of appearance, distribution, and quantitative changes, beginning at one hour after birth and extending to two years of age. At birth MC's were present only in the stroma of some of the choroid plexuses (diencephalic and myelencephalic) and in the leptomeninges over the olfactory bulbs and the anterior-most portions of the cerebrum and dorsal thalamus. Thereafter, MC's appeared within other portions of the brain (some laminae of the olfactory bulbs - e.g., L. fibrosa, L. granulosa, L. granularis interna; some nuclei (e.g., N. olfactorius anterior) and tracts (e.g., T. olfactorius lateralis) of the olfactory peduncles, some laminae of the cerebral cortex, and some nuclei (e.g., N. lateralis, N. habenulae medialis) and tracts (e.g., Stria terminalis) of the dorsal thalamus). The total number of MC's in the brain increased dramatically at one and two weeks postpartum; thereafter, they progressively decreased with age. Age-related increases in MC number occurred only in the olfactory peduncles and in some nuclei of the dorsal thalamus. Elsewhere, dramatic decreases occurred with age. These changes in MC number correspond very closely to age-related changes in biochemically determined amounts of histamine in the brain.

ELECTRICAL ACTIVITY OF THE MAUTHNER NEURONS IN EMBRYOS AND LARVAE OF ZEBRAFISH, Brachydanio rerio. Robert C. Eaton* and Roger D. Farley. University of California, Riverside, California.

Histological and behavioral observations suggest that in newly hatched zebrafish, the tail-flip reflex is mediated by the giant Mauthner neurons (M-neurons) of the hindbrain. The objective of this research was to provide physiological evidence for this hypothesis. All experiments were performed on unanesthesized animals, 2 to 7 days of age. They were embedded in gelatin and mounted on a glass slide. Microelectrodes were positioned near the M-neurons under direct visual observation with the compound microscope. Tail-flip responses were elicited by vibrating a stylus against the ear vesicle. At the start of the response, the M-neurons produced a prominent negative potential like that previously noted in extracellular recordings in adult fish. The spike could be evoked by electrical stimulation of the spinal cord. In experiments on embryos, the M-spike was elicited as early as 48 hr after fertilization. By the time of hatching (4 days), the minimum spike latency was 7.5 msec. The first muscle contractions occurred 2.5 msec after the spike, thus giving a behavioral latency of 10 msec., a response comparable to that of the adult zebrafish. The presence of the tail-flip response during embryonic development may be to aid the animal's escape from the egg during attack by a predator. Because of the rapid and precise differentiation of this system, we suggest that it would make a useful preparation for studying the physiology and ultrastructure of synaptogenesis.

ENZYMATIC N-ACETYLATION OF BIOGENIC AMINES BY HONEYBEE BRAIN HONOGENATES. Philip H. Evans* and P. Michael Fox. State University of New York, College at Brockport, Brockport, N. Y.

Although the putative neurotransmitters serotonin, dopamine and norepinephrine are known to be present and to have pharmacological activity on the insect CNS no catabolic enzymes for these amines have been found in the insect CNS. Using radiochemical and spectrophotometric methods we found that tryptamine, serotonin, and dopamine were N-acetylated by enzymes from honeybee brain homogenates using acetyl Co-A as the acetyl donor. Norepinephrine was not acetylated, neither did it affect serotonin acetylation. Monoamine oxidase with tryptamine or serotonin as substrate was not found. We suggest that N-acetylation may be a major step for the inactivation of biogenic amine neurotransmitters or modulators in insects.

SEASONAL CHANGES IN METABOLISM AND CALORIGENIC RESPONSE TO NOREPINEPHRINE IN THE ALASKAN RED BACKED VOLE. Dale D. Feist and Mario Rosenmann.* Institute of Arctic Biology, Univ. of Alaska, Fairbanks, Alaska 99701.

In order to help define seasonal acclimatization in the northern red backed vole (Clethrionomys rutulis dawsoni), the metabolic responses to cold and to norepinephrine (NE) were determined in winter, summer, and fall groups of voles. At ambient temperatures tested between +30°C and -10°C the smaller winter voles (15g body wt.) showed a higher metabolic rate ($cc \cdot g^{-1} \cdot hr^{-1}$) but a 30% lower energy expenditure (cal/hr) per individual than did the larger summer voles (28g). Maximum metabolic rates (M_{max}) elicited with cold and helium (80%): oxygen (20%) were 1.7 times higher in winter than in summer voles and would be predicted to occur at an air temperature of -75°C in winter voles and -40°C in summer voles. In response to injection of NE (3mg/kg body wt.) at ambient temperature of +5°C, winter voles increased oxygen consumption by 130%, fall voles increased by 43%, and summer voles increased by only 11%. Red backed voles acclimated to +5°C in the laboratory exhibited lower M_{max} and lower response to NE than did winter acclimatized voles. The results suggest that seasonal acclimatization for winter conditions in the red backed vole involves an energetically economical weight depression, an enhanced maximum metabolic capacity, and increased sensitivity of thermogenic tissues to NE.

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CHANGES IN DENDRITIC STRUCTURE DURING DEVELOPMENT AND REGENERATION IN IDENTIFIED NEURONS OF THE LAMPREY BRAIN. Paul S. Fishman* and Melvin J. Cohen. Dept. of Biol. Yale Univ. New Haven, Connecticut.

The brain of the lamprey Petromyzon marinus contains the cell bodies of several giant reticulo-spinal neurons (Müller cells). We examined these cells with intracellular cobalt injection and electrophysiologically to observe changes in dendritic form and physiology during metamorphosis and also following injury and subsequent regeneration. Several bilateral pairs of giant neurons can be identified in the living brain of the larva and adult. The dendritic tree of each identified cell pair is divided into distinctive medial and lateral compartments which allows the identification of specific cells from animal to animal. However the fine details of branching pattern within a particular dendritic compartment show variation between animals. During metamorphosis the cell bodies may double in diameter and some of the dendrites lengthen. However there is no major change in the form of the dendritic compartments. Certain adult cells show a ventro-medial increase in dendritic branching. The eyes are non functional in the larva and the Müller cells are unresponsive to electrical stimulation of the optic nerve. In the adult, the eyes are well developed and all Müller cells respond to visual stimuli. The visual information in the adult appears to be conveyed through ventro-medial regions of the brain and this input may be responsible for the increased dendritic branching in the ventro-medial region of the adult cells. Chromatolysis in the giant nerve cell bodies does not occur until 2-3 weeks after axotomy. There is no significant change in the dendritic tree before the onset of chromatolysis. Preliminary results indicate that following chromatolysis and during subsequent regeneration there appears to be a decrease in the number of the fine terminal dendritic branches. Supported by PHS Grant NS08996-05.

STRUCTURE OF THE CUTICLE OF THE WAX-PRODUCING GLANDS OF THE WOOLY APHID. Helen Ghiradella, Department of Biological Sciences, State University of New York at Albany.

The wooly aphid produces long streamers of wax from specialized patches on the dorsum. The wax is produced by columnar epithelium cells which are vacuolated in their centers, i.e., tall goblet cells whose openings are contiguous with the overlying cuticle. The cuticle surface does not show any obvious pores or channels through which the wax may pass; however, the associated endocuticle has great gaps in it, giving it a spongy appearance. These gaps contain many tubules similar to those usually found in the pore canals of more typical insect cuticle and bearing a marked resemblance to the "pore tubules" described by other workers in insect olfactory sensilla. It is possible that all these tubule types are variations of a single basic structure which has been modified to suit the specializations of the different types of cuticles and which is generally important in cuticular development. (Supported by SUNY Research Foundation grant 020-7230A and NIH grant 2510A.)

IN VIVO BIOSYNTHESIS OF AN ISOPRENOIC ACID FROM MEVALONIC ACID IN THE FLY, SARCOPHAGA BULLATA. Robert D. Goodfellow and Yung-Sheng Huang. Fordham University, Bronx, New York.

The participation of mevalonic acid (MVA) in the biosynthesis of isoprenoids of many animals, plants and microbial organisms is well known. We report here the biosynthesis of an isoprenoic acid from MVA in this insect. Triglycerides (TG) are the dominant products of ^{14}C-MVA in the 7 day Sarcophaga larva, which radioactivities reached 35.7% of the labeled neutral lipids 48 hours after injection of labeled MVA. This labeled-TG fraction was purified by two successive thin-layer chromatography procedures and then saponified with alkaline methanol solution. The major radioactivities of these labeled TG was recovered in the acid fraction (94%). Results of extensive gas-liquid chromatography analyses of these acids, after methylation with diazomethane, indicated that most of the activity was found in a single peak (86.5%). The relative retention time of this peak was between that of myristate and palmitate methyl esters, and corresponded to that of the methyl ester of the isoprenoic acid, farnesenic acid. Further purification of this acid is under investigation. Furthermore, the presence of an isoprenol dehydrogenase is also reported here and suggests that a key reaction for the formation of isoprenoic acids is present in this organism. This work is part of our continuing investigation of the role of isoprenoids in the biosynthesis of the juvenile hormones of insects. (Supported by a Faculty Research Grant from Fordham University and in part by Grant AI 09626 from the USPHS).

REGULATION OF BODY TEMPERATURE. Robert E. Henshaw. NYS Dept. of Environ. Conservation, Albany, NY.

16 mm color film with sound, depicting mechanisms of thermoregulation in vertebrates from fish to man. Heat exchange by convection, conduction, radiation, and evaporation demonstrated using heat flux transducer. Behavioral thermoregulation in fish and hypothalamic mechanisms in the dog filmed in H.T. Hammel's laboratory. Human metabolic responses to heat and cold filmed in S.M. Horvath's laboratory. Vascular thermoregulation of appendages in the arctic wolf filmed in R.E. Henshaw's laboratory. Written and produced by Charles Finance. Released by Encyclopaedia Britannica Films; 22 minutes.

A NASAL SALT GLAND IN A TEIID LIZARD. Peter E. Hillman, F. Harvey Pough, Margaret B. Pough*, and Linda L. Hillman*. Section of Ecology and Systematics, Langmuir Laboratory, Cornell University, Ithaca, New York 14850.

Ameiva quadrilineata has a functional nasal salt gland and represents the fifth family of lizards known to possess such a gland. The table compares ion excretion of control lizards eating *Tenebrio* larvae with lizards 13-49 hours after salt loading with 1.0 mM NaCl/100 g.

Condition	N	Nasal Excretion (μEq/100 g hr, $\bar{x}$ ± SE)		
		Na^+	K^+	Cl^-
Control	18	1.12±0.16	0.14±0.02	1.10±0.17
Salt-loaded	7	2.63±0.24	2.50±0.30	5.52±0.37

Control lizards had a low K/Na ratio (0.13) in their nasal excretions despite a high ratio (4.9) in *Tenebrio* larvae. Seventy-two percent of the K^+ was discharged via urates. The response of the salt gland in the first 24 hours following NaCl administration was an increase in K^+ excretion to an average of 2.6 μEq/100 g hr. The K/Na ratio rose to 1.15. Excretion of Na^+ increased for the next 24 hours while K^+ showed little change and the K/Na ratio fell to 0.75. Intertidal amphipods are a major part of the lizards' natural diet. The amphipods have about 3 times the salt concentration of the lizards, and have a K/Na ratio of 0.67. Extra-renal salt excretion may be essential if the lizards are to exploit this food source during the dry season. (Supported in part by a Grant-in-Aid from the Cornell Chapter of Sigma Xi.)

TURNOVER RATES OF NOREPINEPHRINE IN HEART SPLEEN, AND BRAIN TISSUES OF THE GOLDEN HAMSTER IN TEMPERATURE ACCLIMATION. S. B. Jones* and X. J. Musacchia, Dept. of Physiol., and Dalton Research Center, University of Missouri, Columbia, Mo. 65201.

Tissue norepinephrine (NE) turnover rates were investigated in hamsters (Mesocricetus auratus) after 5-7 wk exposure to 7, 22 and 34°C. The drug α-methyl-p-tyrosine methyl ester, which competitively inhibits rate-limiting biosynthetic enzyme of NE, was injected (ip 200 mg/kg). At sequential periods after administration animals were sacrificed by cervical dislocation, tissues removed and frozen. Decay constants, half-life and turnover rates were determined. Heart NE turnover was highest in cold acclimated and lowest in heat exposed animals (.110 and .045 μg/g/hr, respectively); control values being intermediate (.081 μg/g/hr). Turnover is inversely related to tissue levels in these acclimated states. Spleen NE turnover was not different from that of heart, being lowest with heat and highest with cold exposure (34°C = .042 μg/g/hr, 22°C = .096 μg/g/hr, 7°C = .139 μg/g/hr). Brain NE turnover was not different with either 22 or 7°C acclimation, but was elevated with 34°C acclimation. Changes in peripheral organ turnover of NE are considered to be related to transynaptic induction of biosynthetic enzymes. Such transynaptic activity is reportedly mediated by peripheral sympathetic tone. Therefore, evidence reported herein suggests increased peripheral sympathetic tone with cold exposure and depressed peripheral tone with heat acclimation. (Supported in part: NASA NGL 26-004-021 S8-9.)

α-GLYCEROL PHOSPHATASE AND GLYCEROL KINASE ACTIVITY IN FAT BODY AND MIDGUT OF DEVELOPING SILKMOTHS *Hyalophora cecropia*. Arthur M. Jungreis, Ohio University, Athens Ohio

Magnesium metabolism has been studied in Cecropia silkmoths during the larval-pupal transformation (LPT) [Jungreis A.M., Am. J. Physiol. 224, 27-30 (1973)]. Throughout this period, magnesium accumulates in midgut, reaching a concentration of 0.5 Molar at ecdysis. This Mg^{++} is present as osmotically inactive $Mg_3(PO_4)_2$. Glycerol accumulation is also first noted during this period. I had proposed that the source of both glycerol appearing in hemolymph and magnesium in midgut was derived from hemolymph α-glycerol phosphate. To determine why net hydrolysis of α-glycerol phosphate occurred at this time, the levels of α-glycerol phosphatase (GP) and glycerol kinase (GK), respectively, were studied in midgut and fat body tissues during the LPT.

Total GP activity was lower in feeding larval and newly ecdysed pupal fat body and midgut than that of GK. Moreover, larval midgut possesses upto 3X the total and 10X the relative activities of GP measured in fat body, whereas pupal midgut retains only 5% of the total present in feeding larvae. Total GP activity doubles in fat body during the LPT.

Relative and total activities of GK in fat body and midgut tissues were comparable in feeding larvae, and both declined by some 70% by the fourth day after apolysis. However, following the pupal ecdysis, GK activity in midgut remained depressed, while that in fat body was not only restored to the larval level but continued to increase until levels 10X those in larval fat body were reached during diapause.

When total GP/GK activity ratios were determined in fat body, values were less than 0.5 and were frequently under 0.2 throughout the LPT. While ratios of 0.5 were also observed in both feeding larval and midgut tissues, ratios of 4.5 - 6.0 were encountered between 0-4 days after apolysis. The relative excess of GP versus GK in midgut immediately after apolysis results in the liberation of inorganic phosphate—derived from hemolymph α-glycerol phosphate—which then accumulates in midgut, and liberation of glycerol. Magnesium, present in excess in hemolymph, enters the midgut epithelial cells and complexes with inorganic phosphate to form insoluble magnesium phosphate.

Regulation of midgut GP activity has also been studied. GP has a K_m for α-glycerol phosphate of 52 μM, and is stimulated by Ca^{++}, Mg^{++}, glycerol, and UDP-glucose. It is non-competitively inhibited by GIP, G6P, ATP, ADP, AMP and 3-phospho-glycerate. Without effect were FI6P, T6P,T and phosphate.

THE POSSIBLE ROLE OF CARBAMINO-GABA IN HYPERBARIC OXYGEN-INDUCED CONVULSIONS. Philip Kashin, Dep't. of Biology, Queens College (C. U. N. Y.), Flushing, N. Y. 11367.

Oxygen at high pressure (OHP) induces generalized convulsions in animals, which in man resembles grand mal epilepsy. Although earlier studies attributed the onset of OHP-induced convulsions to reductions in brain γ - aminobutyric acid (GABA) levels during OHP exposure, more recent investigations show that treatment with drugs that increase brain GABA not only do not protect against OHP-induced convulsions, but actually potentiate them (Alderman, et al., in press). This apparently paradoxical finding may be explained as follows. OHP saturates erythrocytes and plasma with oxygen. At above 3 atm pure O_2, tissue requirements can be met entirely by the O_2 carried physically dissolved in plasma, and oxyhemoglobin (HbO_2) passes unchanged through capillaries. Since HbO_2 is a less effective buffer for H^+ from carbonic acid than deoxygenated hemoglobin, bicarbonate transport of CO_2 is reduced, and tissue P_{CO_2} rises by about 5 mm Hg. Increased tissue CO_2 concentration may react with endogenous brain GABA and cause a rise in the concentration of brain carbamino-GABA. Carbamino formation occurs rapidly, spontaneously, and reversibly between molecular CO_2 and amines. Evidence was already presented that GABA potentiates the stimulatory action of CO_2 in the insect CNS, and that carbamino-GABA may be the physiologically active species in the stimulation of specialized nervous tissue by CO_2 (Kashin, Comp. Biochem. Physiol. 44A, 829, 1973). The potentiation of OHP-induced convulsions with a rise in brain GABA may therefore be understood in terms of increased levels of both GABA and CO_2, leading to heightened formation of what may be an excitatory substance in the CNS, carbamino-GABA.

SODIUM DEPENDENT BIPHASIC POTASSIUM CONTRACTURES IN CRAYFISH ABDOMINAL EXTENSOR MUSCLE FIBERS. M. L. Koser (intr. by C. Edwards). S.U.N.Y. at Albany, New York and Brooklyn College, New York.

Contracture solutions containing 40-160 mM potassium elicit twitching responses in bundles of muscle fibers dissected from the deep extensor abdominal lateralis (DEAL) muscle of the crayfish. In single fibers, potassium-induced contractures were biphasic consisting of a rapid initial contraction with a duration of one second followed by a slower, more prolonged response. Lowering the concentration of sodium ions in solution by substituting Tris chloride for NaCl decreased and often abolished the initial contraction. Restoration of normal $[Na]_o$ levels restored the rapid twitch response. Tetrodotoxin (5×10^{-9}M) had no effect on the rapid phase. In the presence of a low (75 mM) level of sodium the K-contracture dose response curve was sigmoidal. The contracture response of muscle bundles dissected from adjacent deep extensor medialis (DEAM) and superficial groups did not exhibit the initial rapid response, nor did that of DEAL bundles prepared from lobster. Presentation of 10^{-3}M L-glutamate caused a rapid twitch response. It is postulated that potassium evoked depolarization causes the release of the neurotransmitter substance which exerts its effect only in the presence of sodium as demonstrated by Ozeki and Grundfest (Sci. 155: 478, 1967).

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SUPRAMEDULLARY INVOLVEMENT IN THE VAGOSYMPATHETIC ARTERIAL PRESSOR RESPONSE OF THE RAT. I.M. Lang,* D.L. Innes and M.F. Tansy.* Dept. of Physiol. & Biophys., Temple Univ. School of Dent., Phila., Pa. 19140.

The association of central vagus stimulation (CVS) with reflex alterations in the arterial blood pressures in dogs, cats, and rodents has been demonstrated over a considerable period of time. Our group has established the fact that in the dog the arterial pressor response to CVS is mediated via vagal afferent and splanchnic efferent nerve fibers. The pressor response to CVS is invariably accompanied by an apneic response in both the dog and the rat. Mogenson and Calaresu (Exp. Neurol. 39:166, 1973) demonstrated that electrical stimulation of the medial amygdala was associated with an arterial pressor response. The purpose of these experiments was to determine if it could be inferred that the pressor and apneic responses to CVS were mediated by a supramedullary neural pathway. In this study 54 adult male rats under urethan anesthesia were used. The head of each rat was stereotaxically positioned and electrolytic lesions were placed at various locations throughout the limbic system. At the end of each experiment the brain was removed, frozen, and sectioned to permit determination of the site of lesion by means of the Prussian blue reaction. We observed that ablation of the medial amygdaloid nucleus was associated with the abolition of the pressor response to ipsilateral CVS. The pressor response to contralateral CVS persisted. Ablation of the medial amygdaloid nucleii did not affect the apneic response to CVS in any case. The pressor response to CVS could also be completely abolished by the destruction of the post-commisural component of the stria terminales. Again the apneic response persisted. These results suggest the hitherto unexpected possibility that certain regions of the limbic system may be involved in the vagosympathetic pathway.

EYE AND OPTIC NERVE OF APLYSIA:CATECHOLAMINES AND NERVE TERMINATION. Judith L. Luborsky and Jon W. Jacklet. Dept. Biol. Sci., S.U.N.Y., Albany, N.Y.

The large synchronized compound action potentials recorded from the optic nerve and the numerous dense core vesicles (1000A) in the neuropile at the base of the eye suggested a neurosecretory function for the Aplysia eye. Using the fluorescence histochemical technique of Falck and Owman (1965) for the demonstration of biogenic amines, we found the secondary cells and optic nerve exhibit a green fluorescence (emission max. 470nm.) that is decreased by alpha-methyl-paratyrosine. Ligature of the optic nerve resulted in an accumulation of fluorescence at the constriction indicating the fluorescent material is transported to the cerebral ganglion. India ink injection of the aorta shows the eye and cerebral ganglion are extensively vascularized. Two large blood vessels intersect along the dorsal surface of the cerebral ganglion. Filling the optic nerve with cobalt chloride shows the majority of the optic nerve fibers end at the intersection of the two large blood vessels. Additional fibers originate from cells in the rhinophore nerve and elsewhere in the ganglion. It is concluded the secondary cells, previously shown to produce the compound action potentials (Jacklet, 1969) and a circadian rhythm of compound action potential frequency (Jacklet and Geronimo, 1971) also contain a catecholamine that is transported to endings in the cerebral ganglion. Supported by NIH predoctoral traineeship GM 02014 and NIH grant NS 08443.

Lustick, Sheldon, "The Effects of Wetting on Redwing Blackbird Energetics and Survival." Zoology Department, The Ohio State University. The energetics of both wet and dry redwing blackbirds were determined over an ambient temperature range of from 5 to 40° C. The lower critical temperature for a dry bird was 20° C and increased to 40° C for a wet bird. The maximum metabolic rate attainable for a wet bird was approximately 10 $cc O_2/g/hr$ and amounted to a fivefold increase over the standard metabolic rate in thermal neutrality (1.9 $cc O_2/g/hr$). Below an ambient temperature of approximately 15° C the wet birds could no longer maintain their high metabolic rate and thus the body temperature dropped. If the body temperature dropped below 31° C the bird could no longer rewarm itself by internal heat production (metabolism) when returned to an ambient temperature of 20 to 25° C. Since birds with a body temperature above 31° could increase their metabolism and rewarm themselves we also measured the effect of body temperature on nerve conduction and heart rate. Both nerve conduction and heart rate decreased linearly with a decrease to body temperature. The study points out the importance of the uropygial gland oil and preening (prevent wetting of feathers) to the overall energy budget and survival of the redwing blackbird.

A COMPARISON OF AEROBIC SUBSTRATE OXIDATION BY MODIOLUS DEMISSUS AND MYTILUS EDULIS GILL HOMOGENATES. Carl J. Malanga. School of Pharmacy, West Virginia University Medical Center, Morgantown, WV 26506.

The metabolic source of ATP required to maintain ciliary activity in the bivalve gill is not clearly understood. A study has been made to compare rates of O_2 uptake by 800xg supernatant fractions of Mytilus & Modiolus gill homogenates containing $2x10^{-4}M$ cytochrome c plus potential substrates & coenzymes. O_2 uptake was measured with an O_2 electrode. A previous report(Malanga & Aiello, 1972, Comp. Biochem. Physiol. 43: 795) showed that succinate stimulated O_2 uptake in Modiolus & Mytilus gill homogenates and accumulated as a major end-product of anaerobic glycolysis. In the present study, of the substrates & coenzymes tested only NADH stimulated O_2 uptake in Mytilus. In Modiolus, exogenous NAD or NADP($3x10^{-4}M$) stimulated O_2 uptake 154 & 80% respectively, presumably through oxidation of endogenous substrates. In order of effectiveness O_2 uptake was also stimulated by 0.3 to 6 mM NADH(127 to 290%) & by the following substrates at 15 mM in the presence of $3x10^{-4}M$ NAD or NADP as indicated: Malate-NAD(142%), Malate-NADP(100%), Isocitrate-NADP (85%), Isocitrate-NAD(33%) & Glutamate-NAD(16%). Lactate up to 50 mM produced a slight 10% increase. The results suggest that biochemical adaptations toward the more efficient utilization of a wider variety of aerobic substrates may have evolved to permit the survival of Modiolus in its high intertidal niche where it air-gapes apparently to survive long periods out of its aquatic environment. With the exception of succinate oxidation, O_2 utilization in Mytilus appears primarily directed toward the reoxidation of NADH$\longrightarrow$NAD probably to permit glycolysis to proceed optimally. Using the luciferase assay of Stanley & Williams (1969), in fact, Modiolus gills were found to contain higher endogenous levels of ATP than Mytilus gills.

COMPENSATORY RESPONSES TO HYPOXIC EXPOSURE IN THE LOBSTER *HOMARUS AMERICANUS*. B.R. McMahon. Department of Biology, University of Calgary, Calgary, Alberta, Canada.

Lobsters acclimated to well aerated water maintained high levels of blood oxygen saturation and tension at low levels of branchial pumping. Under these conditions hemocyanin apparently plays a minor role in oxygen transport. Oxygen consumption was maintained on exposure to ambient oxygen tensions down to 30-40 mm Hg. This can be attributed to a marked increase in branchial water flow together with increased participation of hemocyanin in oxygen transport.

INTERACTIONS OF URATE AND CATIONS IN LIQUID AND PRECIPITATED FRACTIONS OF AVIAN URINE. Roger A. McNabb and F. M. Anne McNabb*, Biology Dept., Va. Polytechnic Institute and State University, Blacksburg, Va. 24061.

Renal excretion of urate, H^+, Na^+, K^+, and NH_4^+ was examined in male domestic fowl (G. domesticus) given low or high protein feed and tapwater or 1% NaCl (LP, HP and TW, SW respectively). These components were determined in liquid and precipitated (except H^+) fractions of the urine. Ureteral urine was collected from glass, cloacal cannulae to prohibit cloacal modification of urine. All liquid fractions contained urates in excess of solubility limits; most contained colloidal urate in excess of colloidal limits set by H^+, NH_4^+ and/or Na^+ concentrations. These colloids must, therefore, be stablized by urinary mucoids. As total urinary urate increased, precipitated urate asymmptotically approached 98% of the total urate. In urine samples rich in precipitated urate (>80% precipitated), Na^+ and K^+ incorporation into the precipitate increased sharply, until about 70% of urine K^+ (especially in HPSW) and 80-90% or urine Na^+ (especially in LPTW and HPTW) was present in the precipitated fraction. Precipitation of NH_4^+ in the urine was lower, and never exceeded about 40%. Thus, conventional U/P ratios, based upon liquid bird urine, drastically underestimate the excretory abilities of the avian kidney, since the abundant, precipitated components do not contribute to the osmotic pressure of the urine. (Supported by NIH grant AM 14991.)

BODY TEMPERATURE CHANGES DURING DEVELOPING COLD ACCLIMATION OF THE HAMSTER. J. G. Minor and G. E. Folk, Jr. University of Missouri-Kansas City and University of Iowa, Iowa City, Iowa.

On exposure to cold hamsters have been shown to develop the initial physiological changes of acclimation within 8-10 days. The question of whether body temperatures from four areas (liver, rectal, inquinal, and subscapular) are effected by the cold environment was posed. The results indicate the temperatures of all four sites of the cold exposed animals were lower than those of control animals. On day 6 of cold exposure the temperature of all cold tissues increased towards the level of the control. Inquinal temperatures in cold hamsters exceeded control values on day 6 (34.3°C cold verses 34.1°C warm). The results thus indicate an unexpected "warming" trend during cold acclimation development. (Sponsored by AINA with support of ONR.)

HISTOCHEMICAL ANALYSES OF TISSUE CHANGES IN BROOK TROUT TO ACIDIFIED WATER. William H. Neff* (intr. by A. Anthony). Department of Biology, The Pennsylvania State University, University Park, Pennsylvania 16802.

The feasibility of using histopathological changes in brook trout as indicators of mine acid pollution of streams was investigated using both continuous gravity flow diluter and static aquaria systems. Exposure durations to low pH (ca. pH 4.0) were 4-5 and 28-30 days. Histochemical and cytophotometric analyses of respiratory, digestive and excretory organs included tests for nucleic acids, polysaccharides, lipids and proteins. Alterations in mucopolysaccharides and nucleic acids of the gill epithelium and renal Stannius corpuscle proved to be among the most reliable histopathological indices of short term exposure to sublethal levels of water acidity but were absent or less pronounced after four weeks of exposure. Use of a battery of histochemical tests is preferable to any single test since this often enables one to differentiate between acclimative and debilitative responses to water toxicants.

BEHAVIORAL AND ULTRASTRUCTURAL STUDIES OF COLOR VISION IN CRAYFISH. Richard Olivo and Douglas Miller*, Smith College, Northampton, Mass., and Williams College, Williamstown, Mass.

Crayfish are known to have violet- and yellow-sensitive receptors, and thus it has been assumed that they must have color vision. We tested for color vision behaviorally, using the animals' optomotor response. Crayfish were placed at the center of a rotating cylinder made of red (665 nm) and blue (440 nm) translucent stripes. Illumination by separate red and blue sources was adjusted with neutral density filters. Repeated tests were run in which a constant blue-stripe brightness was paired with various brightnesses of red stripes. If crayfish do use color vision, the response (walking in the direction of cylinder rotation) should be elicited by all red-blue brightness pairs. If they do not use color vision, the response should not occur for that brightness of red stripes that matches the brightness of the blue stripes. (A control experiment, using a cylinder made entirely of red stripes, was run to detect any rotational cues that might remain in the absence of both color and brightness contrast; it gives the baseline level of responses that would be expected for a perfect red-blue brightness match if the animals do not have color vision.) Our preliminary results suggest that crayfish do have color vision.

In a related experiment, crayfish were kept in either total darkness, white light, or dim red light ($\lambda > 600$ nm). After 3 months, the eyes were removed and prepared for electron microscopy. Severe degeneration had occurred throughout the rhabdoms of eyes kept in total darkness, while white-light eyes were normal. In dim red light, some rhabdomeres were normal while others in the same rhabdom had degenerated; the degenerated rhabdomeres presumably belong to the violet receptors, which can thereby be identified in the sections.

CHANGES IN HEMOLYMPH pH, BICARBONATE AND P_{CO_2} OF CRABS EXPOSED TO WATER AND AIR. Patricia M. O'Mahoney, C.F. Herreid II* and B.J. Howell*. (intr. by C.A. Privitera). Dept. of Biology and Dept. of Physiology, State Univ. New York, Buffalo, 14214.

Four species of crabs from different environments were exposed to water and air as respiratory media. Hemolymph was sampled in both conditions from the infrabranchial sinus at the base of the major cheliped. Aquatic species (Callinectes sapidus, Carcinus maenas) had lower normal hemolymph P_{CO2} then terrestrial species (Cardisoma guanhumi, Gecarcinus lateralis). When aquatic species were placed into humid air for 48 hrs., P_{CO2} levels rose dramatically. In Callinectes pH dropped from 7.87 to 7.71 while HCO_3^- rose from 9.38 to 19.12 mM/l. In Carcinus pH remained constant near 7.65 while HCO_3^- rose from 7.86 to 12.46 mM/l. Hemolymph values returned to normal within 48 hr. after the crabs were returned to water. When terrestrial crabs were placed into sea water P_{CO2} dropped. In Cardisoma pH raised from 7.59 to 7.65 while HCO_3^- dropped from 24.06 to 15.77 mM/l. After 48 hr. recovery in air, pH and P_{CO2} was near normal but HCO_3^- recovery was not complete (17.22 mM/l). Most Gecarcinus died during or shortly after they were exposed to water. pH remained constant in those crabs that survived, but it dropped precipitously in crabs that died (P_{CO2} rose dramatically). These results for crabs exposed to water and air are similar to data assembled for vertebrates. When aquatic animals are exposed to air, blood (hemolymph) P_{CO2} rises, pH drops and HCO_3^- rises. When air-breathing animals ventilate water, P_{CO_2} drops, pH rises and HCO_3^- drops. These results can be generally explained on basis of the differences in solubility of CO_2 in water and air.

HYPOTHALAMIC CIRCADIAN RHYTHMS IN HISTAMINE AND EVIDENCE FOR A PERI-PUBERTAL PHASE SHIFT. Edward L. Orr* and W. B. Quay. Department of Zoology, University of California, Berkeley, California; Waisman Center on Mental Retardation and Human Development, and Endocrinology-Reproductive Physiology Program, University of Wisconsin, Madison, Wisconsin 53706.

Probable contributions of hypothalamic amine rhythms to control of hypothalamo-hypophyseal gonadotropic mechanisms prompted this research on hypothalamic histamine (H) contents, histidine decarboxylase (HD) and histamine-*N*-methyltransferase (HMT) in male Holtzman rats maintained in a fixed 12-hour daily photoperiod (LD 12:12). Animals were sampled at six times per day (5-6 animals / time point) in replicate series and studies. H, HD and HMT were measured by means of a single isotope enzyme assay modified from Taylor and Snyder (1972). Peak hypothalamic H concentrations occurred in prepubertal rats during the light phase, with minima in the dark phase ($P<0.05$). While the reverse relationship was suggested in postpubertal hypothalamic H. At an intermediate (peripubertal) age, hypothalamic H levels were similar at all times. Transient loss in circadian H rhythmicity was correlated with a loss in HD circadian changes, while the prepubertal HMT rhythm continued. This appears to be the first demonstrated instance of a phasic change in a neurochemical circadian rhythm after its postnatal establishment. Possible relations of this phase shift to gonadal and gonadotropic hormones are to be investigated. (Supported in part by NIMH grant 1-F01-MH 54768 and Ford Foundation grant 630-0505A.)

FACTORS AFFECTING THE APPARENT OSMOTIC PERMEABILITY OF FROG SKIN. R.H. PARSONS, T. MAHONY* and D. KAUFMAN*, Department of Biology, Rensselaer Polytechnic Institute, Troy, New York, 12181.

The osmotic permeability of frog epithelia was measured by tying the cloaca and weighing the frogs at 1 hr intervals. The bathing solution was buffered 40mM sucrose (5mM Tris $SO_4^=$, pH 7.60). Aggitation (Shaking 120 cycles/min) was found to significantly increase ($P < .05$) the osmotic permeability, 0.53 to 1.28 $\mu l \cdot cm^{-2} \cdot hr^{-1} \cdot Atm^{-1}$. This does not appear to be the result of increased levels of antiduiretic hormone (ADH) since the same increase due to aggitation is observed after an injection of 10IU/gr arginine vasopressin. Changes in circulatory patterns were examined as a possible cause of the permeability changes due to aggitation. THO diffusion was shown to measure changes in circulation. Cutting the sciatic in one leg caused observable vasodialation and showed an increased THO permeability; tying the femoral artery caused a decreased THO permeability. Cutting the spinal cord on whole frogs increased the THO permeability as well as the osmotic permeability. The data appears to be consistant with the idea that circulation can affect the apparent osmotic permeability of frog skin. Supported by grant GB-40816 from National Science Foundation.

INTERACTING EFFECTS OF AGE AND CHRONIC CARBON MONOXIDE EXPOSURE ON POLYCYTHEMIA, CARDIAC HYPERTROPHY AND RIGHT-LEFT HEART SIZE RELATIONSHIP. David Penney, Karen Cook*, and Janet Sakai*. University of Illinois at Chicago Circle.

Groups of male rats of 1, 21, 70, 130 and 265 days of age were exposed to 500 p.p.m. carbon monoxide (COHb = 35 - 42%) for 35 days. Hemoglobin concentration increased 49 - 51% above same aged controls for the three intermediate-aged groups, while hemoglobin increased 39% in the oldest animals and 31% in the youngest group. Marked cardiac enlargement was observed in all groups relative to controls. Cardiac enlargement was greatest in the first group at 36 days of age (69%), intermediate in the second and third groups at 56 and 105 days of age (36 & 40%, respectively) and least in the two oldest groups (ca. 25%). Separated right ventricle (RV) and left ventricle + interventricular septum (LV + S) showed similar weight increases during CO-induced cardiac hypertrophy in all age groups but the youngest. There the RV showed a significantly larger weight increase relative to the LV + S. Atria in all age groups exposed to CO showed large gains in wet weight. These results suggest that the capacity of the heart to enlarge is greatest in animals shortly after birth and that this capacity declines with increasing age. It also suggests that the capacity of the right heart to enlarge relative to the left is greater in young rats, but that this difference in capacity is lost beyond several weeks of age. Both of these phenomena may be related to observations of other investigators that the ability of heart muscle cells to mitotically divide is lost around 21 days of age and that subsequent heart enlargement occurs only by volume increase of pre-existing cells.

Development of CNS suppression of the habituating gill withdrawal reflex in Aplysia. B. Peretz and K. Lukowiak*. U. Kentucky Med. Ctr., Lexington, Ky. 40506.

Habituation of the gill withdrawal reflex to locally applied tactile stimuli, 0.15g , is mediated by the neural plexus in the gill. With the innervation between the parieto-visceral ganglion (PVG) and the gill intact, the reflex is suppressed. Suppression is measured as a reduced reflex amplitude and a faster rate of habituation when compared before and after removal of the PVG (Peretz and Howieson, 1973). We report here that suppression of the reflex seen in mature Aplysia weighing 239 ± 7g (n=10) was not seen in immature Aplysia weighing 16 ± 7g (n=10), using 0.15g applied at a rate of 1/30 sec. Reflex amplitude and rate of habituation were not significantly different before and after PVG removal in immature Aplysia, but in mature Aplysia the differences were significant ($p<.01$). Comparisons between the two groups show that the reflex amplitude is greater and the habituation rate is slower in immature animals. Similar results were obtained using stronger stimulus intensities. The behavioral differences are attributed to a less developed PVG in immature Aplysia. Stimuli of 0.15, 0.3, and 2.0g evoked activity in PVG neurons in immature Aplysia. Thus, the pathways from the gill to the PVG are functional. A stimulus of 0.15g evoked activity in R2 in immature animals, yet activity in R2 in mature Aplysia was evoked only by stimuli of 2.0g and of greater intensity. We consider the greater responsiveness in R2 of immature Aplysia to be an expression of the absence of PVG activity responsible for suppression of the reflex. These results show that in Aplysia as in vertebrates behavioral inhibition is less in younger animals. (MH 18611; Found. Fund Psychiat. T64-205).

AMEBOID LOCOMOTION DUE TO PUSH-PULL GEL-TO-SOL AND SOL-TO-GEL CONVERSION. Donald L. Perkins and Stanley E. Babb*. Univ. of Oklahoma, Norman, Oklahoma.

Ameboid locomotion is usually considered to be a relatively primative form of movement, but how this movement is achieved is currently in dispute. This is particularly true for organisms represented by Amoeba and Chaos for which two theories of ameboid locomotion have been proposed. The more classical contraction-hydraulic theory is based on the posterior gel-to-sol conversion producing the motive force and the "fountain zone" frontal-eversion theory proposes that the anterior sol-to-gel conversion provides the motive force. Until now these theories have been considered as mutually exclusive. A consideration of published pressure, volume, and temperature changes associated with gel-to-sol/sol-to-gel conversions leads to the conclusion that the two theories are not mutually exclusive. Based on the above, ameboid locomotion, as found in Amoeba and Chaos, is due to a posterior-to-anterior pressure gradient. At the posterior end, the gel-to-sol conversion creates a positive pressure, the "push", which is additive to the reduced pressure, the "pull", established at the anterior end by the reverse process. In addition, it is proposed that the energy requiring component of the gradient is the sol-to-gel conversion at the anterior end.

THE EFFECT OF TEMPERATURE AND pH COMBINATIONS ON AMPHIBIAN EMBRYONIC DEVELOPMENT. F. Harvey Pough and Richard E. Wilson. Section of Ecology & Systematics, Cornell University, Ithaca, New York 14850.

We studied the effects of combinations of temperature and pH on embryonic development of the salamanders Ambystoma maculatum and A. jeffersonianum using dilute solutions of sulfuric acid or sodium hydroxide. Results are indicated in the table. Both temperature and pH optima were lower for A. jeffersonianum than for A. maculatum.

Temperature-pH Combinations Producing Hatching Success ≥ 90%

Temperature °C	A. jeffersonianum	A. maculatum
5	pH 5,6	none
10	pH 6	pH 7,8,9
15	none	pH 8
20	none	none

Temperature and pH extremes produced death before gastrulation. Yolk plug retraction, gill formation, and hatching were other stages at which high mortality occurred. There was no apparent effect of pH on rate of development. The pH tolerance of these salamanders may influence their survival in the immediate future. Rain in northeastern North America is a dilute mixture of sulfuric and nitric acids with an average pH near 4. The vernal ponds in which Ambystoma breed are formed by rainwater and melted snow and should reflect this acidity. In view of the cumulative effect of removal of buffering compounds from the soil, pH values in breeding ponds can be expected to drop below current levels which are near pH 6. (Supported in part from Federal Hatch Funds.)

THE PERMEABILITY OF THE "SYNAPTIC COMPLEX" OF MOTH NEUROMUSCULAR JUNCTIONS. Mary B. Rheuben. U.C.L.A., Los Angeles, Calif.

It has been suggested (Osborne, 1967; Belton, 1968) that the synaptic complex, which is formed by processes of the muscle cell interdigitating with glial cells around fine axon branches (Rakowski, 1972), protects the synapse from the ionic environment of the haemolymph. 3 possibilities were considered: a) the complex forms a structural barrier to the free passage of ions as does the nerve sheath; b) there is some flow of haemolymph but specific ion concentrations are regulated; c) there is free passage and no regulation of ions. To distinguish these, the following observations were made. Horseradish peroxidase and ferritin, used as extracellular markers, penetrated the layers of the complex and were found in the synaptic cleft. Of possible transmitters and blockers, glutamate and methysergide (10^{-3} to 10^{-2} M in the ringer) reversibly reduced the epp to 0 and caused disappearance of the mepps. Reduced Ca and increased Mg ion concentrations decreased the amplitude of the epp, presumably by interfering with transmitter release. 10mM Co blocked the epp and caused the disappearance of mepps, and may have prevented Ca influx through both pre and post-synaptic membranes. 1/10 normal K reduced the epp by up to 50%. High Na, high Ca ringer increased epp amplitude and average mepp amplitude. K, Na, and Ca appear to carry current post-synaptically. The above ions did not appreciably change muscle membrane potential or resistance at the concentrations used. The effects all occurred in less than 3 minutes on changing solutions. It can be concluded that the glial sheathes allow the passage of ions and transmitter-like molecules from the haemolymph to the axon terminal. No evidence was found that the concentration of a particular ion was being regulated, but the possibility was not excluded. Supported by NINDS special fellowship SFIO NS02558 & grants NS06232 & NS05670

ORGANIZATION OF A SKELETAL MUSCLE INSERTION IN THE CRAB CARCINUS MAENAS. K. L. Rossner and R. G. Sherman, Clark University, Worcester, Mass.

The insertion end of stretcher muscle fibers in the walking leg of Carcinus maenas (L.) was examined with a transmission electron microscope. Muscle fibers were found to attach to the exoskeleton through specialized epidermal cells, the tendinal cells, which contain a tremendous number of oriented microtubules that extend the entire length of the cell. The tendinal cells are attached to the ends of the muscle fibers by desmosomal junctions. Thin myofilaments anchor to one side of the desmosome and tendinal cell microtubules to the other side. The myo-tendinal cell attachment area is also heavily invested with collagen fibrils which may aid the desmosomes in securing these cells together. The apical end of the tendinal cell is secured to numerous dense cuticular rods called tonofibrillae which extend from within the cuticle into conical invaginations of the tendinal cell. The tonofibrillae and the tendinal cell form hemidesmosomes to which attach the tendinal cell microtubules. The microtubules presumably serve to transfer the tension developed by the muscle fibers to the exoskeleton. Adjacent tendinal cells are anchored together by desmosomal, septate and gap junctions.

TEMPERATURE-INDUCED ALTERATION OF HEPATIC ULTRASTRUCTURE AND FUNCTION WITHIN THE GOLDFISH, CARASSIUS AURATUS. A. J. Rotermund, Jr. and H. A. Johnson*. Loyola University, Chicago, Ill. and Brookhaven National Laboratory, Upton, N. Y.

Groups of goldfish were acclimated and then maintained for four weeks at temperatures of 10, 20, 30 and 37°C. Food intake was proportional to activity, and aqueous oxygen content ranged from 3.5 to 6.0 ppm. At the appropriate times, livers of acclimated fish were either fixed in buffered OsO_4-sucrose for electron microscopy, or homogenized for 5 min. in boiling 0.05 M tris-borate buffer, pH 9.2, for fluorometric estimation of Adenosine 5'-Triphosphate, or homogenized in iced, 0.25 M sucrose-EDTA, pH 7.4, for Disodium Phenyl-Phosphatase assay. Hepatocytic ultrastructure underwent dramatic modification over the 10-37°C spectrum of temperatures. At 10°C, miotchondrial cristae were well-defined, glycogen rosettes were abundant, and an extensive rough endoplasmic reticulum was evident. At 37°C, mitochondrial fine structure had degenerated, glycogen reserves were depleted, the R.E.R. had been replaced by a smooth endoplasmic reticulum, lipid droplets were present, and numerous vacuoles had appeared. Associated with these ultrastructural changes, hepatic ATP content was reduced fourfold at the highest temperature, from 0.4 µg ATP/µg protein (10°C) to 0.11 (37°C). DPPase activity had also been lowered, from 2.6×10^{-4} µg phenol/µg protein/min. (10°C) to 1.1×10^{-4} (37°C). These results indicate that prolonged exposure to high temperatures severely challenges the ability of goldfish' hepatocytes to generate sufficient ATP's to maintain the degree of biosynthetic activity which is characteristic of hepatocytes of cold-acclimated fish.
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AN IMPROVED BILE DUCT T-CANNULA FOR STUDIES ON FASCIOLA HEPATICA. **Pamela Sartori* and Hadar Isseroff. SUNY College at Buffalo, Buffalo, N.Y.**

Assembly of a short-armed T-cannula and its surgical implantation into the bile duct are described. The method has a number of advantages including: (1) Facilitation of external sampling without impeding normal bile secretion into the duodenum. (2) Long term studies are possible since the life span of the T-cannulated rats is several months. (3) Reduced allergic reactions because a medical grade adhesive is used. (4) Obstruction of the sampling tube is made less likely by the shortened arms of the 'T'. (5) The cannula is inexpensive to construct. (6) The procedure also permits infusion of materials into the biliary tract.

Experiments with T-cannulated rats indicate that infection with the bile duct fluke, Fasciola hepatica, does not significantly alter the rate of bile flow, and rates of flow with the T-cannula are within the range reported for other techniques.

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NEUROMUSCULAR BLOCKING ACTION OF NEREISTOXIN. Robert T. Schopp. Dept. Physiology, Southern Illinois University, Edwardsville, Illinois.

Nereistoxin (4-N,N-dimethylamino-1,2-dithiolane) is a neurotoxic substance which has been isolated from the marine annelid Lumbriconereis hetropoda MARENZ. These marine worms are used as bait by fishermen and many injuries have occurred through handling by a stinging mechanism associated with their bristles or by a bite of their jaws. The observation that some insects die following contact with the dead bodies of these marine worms has lead to experimentation with nereistoxin and related substances in regard to insecticidal activity. Reports of a paralytic action of nereistoxin (NT) provide a basis for further work on the influence of this toxin on junctional transmission. NT was administered intravenously into dog peroneal-tibialis anterior nerve-muscle preparations at a dose level of about 1 mg/Kg. Within 2 to 5 minutes the magnitude of indirectly induced muscle contractions was reduced by 50%. In the absence of corrective intervention, the paralysis was then complete within a few more minutes. An immediate, prominent and often long lasting antidote to the neuromuscular block of NT can be induced by close intra-arterial injection of 1 mg of Prostigmin. Close intra-arterial injection of acetylcholine (0.5 mg), 5-hydroxytryptamine (10 µg/Kg) or KCl (1 ml isotonic) partially oppose the NT block but in a more transitory manner than Prostigmin. During a partiial NT block tetanic contraction may be maintained for a short period but at a reduced magnitude. Post-tetanic potentiation may be evident. Intravenous administration of NT at the dose level employed will cause complete paralysis within a few minutes and, unless an antidotal agent or prophylactic procedure is employed, death will ensue apparently due to respiratory paralysis.

ACQUIRED THERMOTOLERANT EFFECTS ON PROTEIN, DNA, AND ATP SYNTHESIS IN SUSPENSION CULTURES OF L-929 MOUSE FIBROBLASTS. Robert D. Simpkin* and J. R. C. Brown, Department of Zoology, University of Maryland, College Park, Maryland

L cells (normally maintained at 35°C) surviving a 12 hour 40.5°C heat treatment were subjected to a second, similar heat treatment after a 36 hour recovery period along with previously unheated cells. Pulse labeling of aliquots at selected time intervals throughout the heat treatment was used to monitor metabolic activity. Cell number, ^{3}H-leucine incorporation into protein, and ^{32}P incorporation into ATP are reduced only 25% in reheated cells as compared to a reduction of > 50% in cells heated for the first time. Incorporation of ^{3}H-thymidine is reduced 80% in reheated cells and 98% in previously unheated cells. The mitotic index of the reheated cells undergoes a sharp reduction with a subsequent increase to control values during the last half of the heat treatment concomitant with a rise in protein synthesis. The mitotic index of the previously unheated cells remains approximately zero until 12 hours after the end of heat treatment. When grown at normal temperature (35°C) only minor differences are observed between previously heated and control cells; DNA and protein synthesis are slightly lower in previously heated cells and the number of multinucleated cells is higher. The results indicate a partial selection for cells exhibiting thermotolerance which is apparently short lived. This experiment was supported in part by Grant No. DA-ARO-D-31-124-73-G196, from the Army Research Office, Durham.

George B. Stefano and James E. White*
New York Community College of the City
University of New York

Serotonergic Neurons Compared By Histofluorescence and Electron Microscopy.

Previous studies have implicated serotonin as a possible neurotransmitter in cerebral ganglia of Mytilus edulis. Numerous nerve cell bodies in these ganglia histochemically exhibit specific yellow fluorescence attributable to serotonin. Cerebral ganglia were additionally prepared for fine structure studies by first orienting thick sections of tissue under the light microscope, followed by thin sectioning for electron microscopy. The unipolar nerve cell bodies were 15 μm in long dimension, radially oriented, and juxtaposed to the connective tissue sheath, which was devoid of cells. Multilobed nuclei were 6 μm in width. The cytoplasm contains numerous vesicle-like structures, approximately 0.25-0.50 μm in diameter, which upon higher magnification were found to contain spherical membrane-bound inclusions. We believe these vesicle-like structures contain serotonin since they appear identical in size and location to those found histochemically. These vesicle-like structures and numerous cytosomes (1 μm) were most numerous in the axon hillock region. Furthermore, vesicle-containing structures were not observed in non-fluorescent nerve cell bodies. Synaptic contacts were not apparent on the nerve cell bodies examined. In conclusion, we are tentatively suggesting the cells examined by both methods are the same.

RBC 2,3-DIPHOSPHOGLYCERATE IN HIBERNATING, HYPOTHERMIC, AND REWARMING HAMSTERS. George E. Tempel* and X. J. Musacchia, Dept. of Physiol., and Dalton Research Center, University of Missouri, Columbia, Mo. 65201.

Red cell 2,3-diphosphoglycerate (DPG) was investigated to provide information on the time course of recovery of DPG upon rewarming, and on mechanisms of DPG depression. Blood samples (cardiac puncture) were analyzed for hemoglobin (Hgb) and DPG in: control hamster (C), T_{re} 37°C at T_a 22 ± 2°C; hibernators (H 48), T_{re} 7°C for 48 hr; rewarming hibernators (RH 48) bled after reaching stable T_{re} 36 ± 2°C; hypothermic 12 hrs (Hy 12) induced with 80:20 cold He:O_2 and T_{re} 7°C; hypothermic 24 hrs (Hy 24) induced with 90:10 cold He:O_2 and T_{re} 7°C; recovered hypothermic (R_1Hy 24) bled after reaching stable T_{re} 36 ± 2°C; recovered hypothermic (R_2Hy 24) bled 2 hrs after reaching stable T_{re} 36 ± 2°C. Values for C were 16.9 ± 1.2 g% and 19.2 ± 1.1 µmoles/g Hgb for Hgb and 2,3-DPG respectively. Group H 48 showed a 22.5% increase in Hgb and decrease in DPG of 39.1%. By contrast the Hy 12 group did not differ from group C ($p>0.05$). However, in group Hy 24 a 19.5% decrease in Hgb concentration to 16.9 ± 1.2 g% and a 33.9% decrease in DPG concentration to 12.7 ± 0.7 µmoles/g Hgb resulted. DPG concentration, although decreased in the hypothermic animal, is 15% greater than the concentration in the hibernator. RH 48 and R_1Hy 24 did not differ from each other ($p>0.05$). Hgb returned to C values in both; however, DPG levels were approximately 10% less than C. R_2Hy 24 values for DPG were 17.5 ± 1.3 µmoles/g Hgb, 8.7% less than C values. DPG concentration decreases in both the hibernating and long term hypothermic hamsters. Differences between the two are slight and may be attributed to the long term cold exposure of the latter. (Supported by NASA NGL 26-004-021 S9 and 10, and Dalton Res. Center.)

THE ROLE OF THE THYROID GLAND IN THE DEVELOPMENT OF THERMOREGULATION OF JAPANESE QUAIL CHICKS. J. M. Ward, Jr., R. A. McNabb and F. M. A. McNabb*. Va. Polytechnic Inst. and State Univ., Blacksburg, Va. 24061.

Precocial birds that have been studied to date display some endothermy immediately after hatching, however complete thermoregulatory control is not achieved until 2-4 weeks later. Several factors which are necessary for the development of homeothermy in birds appear to be associated with, or perhaps controlled by, the thyroid gland. Short term (at 4, 8 and 16 days of age) and long term (4-10 days of age) studies were made of the effects of thyroxine (T_4) and thiouracil on body temperatures (T_B) of quail chicks. At 39C, T_4-injected chicks and thiouracil-fed chicks had significantly higher T_B's than controls, while at 35C or in a thermal gradient, only a few differences between the experimental and control chicks are significant and these show no consistent pattern. The lack of consistent differences between experimental and control groups maintained in a thermal gradient may be due to behavioral compensation. This possibility is being investigated now. The development of skin-plumage insulation with increasing age was studied and an inverse relationship was found between skin thickness and the quantity of heat required to maintain a constant temperature gradient across pectoral skin-plumage specimens. The time course of changes in skin thickness was inversely correlated with the time course of thyroidal iodine fluctuations, indicating that the thyroid gland may play an indirect, rather minor role in the development of homeothermy by affecting the insulative properties of the skin. In conclusion, thyroid hormones appear to influence the development of thermoregulation in birds through both direct and indirect actions. (NSF grant GB37966.)

ALTERATION OF SODIUM PERMEABILITY BY SEA NETTLE TOXIN. James Watrous, George Dubyak*, and Boris Sawula*, Saint Joseph's College, Philadelphia, Pa.

Experiments were conducted to study the effects of nematocyst toxin from Chrysaora quinquecirrha on sciatic nerve and gastrocmenius muscle of Rana pipiens, and on hamster small intestine. Whole toxin (WT), purified on Sephadex G-200 Superfine was resolved into 2 major protein peaks (P_1 & P_2). Only P_1(600 ug) significantly reduced action potential amplitude within 2 min. WT(240ug) or a combination of P_1 and P_2 also caused this effect. Partial blockage of the nerve was accompanied by a reduction in conduction velocity resulting from exposure to WT(240 ug) and P_1 (600 ug). Nerves bathed in choline chloride for 30 min to abolish action potential activity, then allowed to recover in a toxin-Ringers solution were significantly different in their recovery compared with control nerves. Conduction velocity during recovery increased in nerves exposed to WT(480 ug) for 5 min. WT caused an increased contracture in muscles. P_2 was especially effective in this respect. Preparations of everted hamster small intestine were exposed to buffer solutions containing glucose (100 mg%) and WT(1.34mg/ml). Tissues were incubated for 15 min at 37°C. Glucose concentration of intestinal tissue was then assayed. WT produced a significant depression in glucose uptake. Glucose transport results are explained in light of the Crane and the Fordtran model. Chrysaora toxin is thought to increase Na+ permeability in these membranes.

GLYCOLYTIC ENZYMES IN EXERCISED RAT HEART. J. W. YORK, D. G. PENNEY, and L. B. OSCAI*. Univ. of Illinois at Chicago Circle, Chicago, Ill.

Profound changes in the circulatory systems of both men and animals have been described in the course of physical training. One of the most striking changes is cardiac hypertrophy. Conflicting reports have appeared regarding changes in lactate dehydrogenase (LDH) isozyme pattern and activity and pyruvate kinase (PK) activity in hearts hypertrophied as a result of altitude and carbon monoxide exposure, anemia, and surgical induction of A-V fistulas and aortic constriction. The present study was undertaken to determine whether these glycolytic enzymes, as well as phosphofructokinase (PFK) and glycogen change in animals provided with a regime of strenuous physical training for several months following birth.

5 day old male Wistar rats were subjected to a program of swimming over a period of 16 weeks, 6 days a week. They swam in groups of 4-6 in plastic barrels filled with 35°C water. The duration of the exercise sessions was increased from 15 to 360 minutes per day over a period of 4 weeks. The animals were then maintained at this level until the time of sacrifice.

In the exercised group, heart weight was 25% greater than in paired weight controls. Heart PK activity increased 20% ($p<0.01$), while LDH activity increased by 32% ($p<0.001$). LDH composition in M subunits increased from 28.5% to 32.7% ($p<0.001$). PFK activity and glycogen content were unchanged.

These results suggest that changes in heart LDH isozyme pattern and activity and PK activity in response to physical training are similar to those which occur as a result of certain other cardiac hypertrophic stresses.