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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.

HAPTOGLOBIN METABOLISM IN INJURY. K. Abdul-Karim*and R. A. Zeineh* (Spon: A.A. Hakim). Department of Microbiology, The Chicago Medical School, Chicago, Illinois 60612.

The serum level of haptoglobin (Hp) characteristically increases after injury. This study reports on the serum Hp-level, its rate of synthesis, turnover, and extra-vascular/intra-vascular ratio after aseptic injury. Native labeled ^{14}C-Hp (Sp. activity 39,000 cpm/mg) was administered by IV injections (0.25 mg/kg) to sixteen 10-20 kg normal dogs which were placed in metabolic cages. At time intervals serum and urine samples were collected and radioactivity was assessed. A month later, Hp-level was back to normal and no radioactivity in serum. Injury was produced with 0.1 ml/kg of sterile turpentine administered S.C. into the gluteal region followed by a second dose of ^{14}C-Hp and the study was repeated. The half-life of ^{14}C-Hp in serum was 3.3 and 1.7 days, the EV/IV ratio was 0.75 and 0.55 in normal and injury, respectively. In a second group of 8 dogs with a sustained injury ^{14}C-glucosamine (2×10^5 cpm/kg) was administered by IV injections and serum Hp was immunoprecipitated, counted and specific activity was calculated. Two hours after IV administration of ^{14}C -glucosamine, ^{14}C-amino acids or (35) S-methionine, the maximum uptake of the labels was increased three folds in injury over normal. Therefore, in injury, Hp-synthesis predominates catabolism. Immunocore electrophoresis against Hp sera revealed 8 precipitin bands in normal dog serum, and the pattern changed after injury.

HYDROCORTISONE AND LIPID METABOLISM IN THE RAT LUNG. M. Abe and D. Tierney, Department of Medicine, University of California at Los Angeles, Los Angeles, California 90024

Large doses of hydrocortisone are commonly used to treat a variety of conditions with acute lung injury. Prolonged hydrocortisone administration to adult rats increases the number of type II epithelial cells (J. Picken, et.al., Am. Rev. Resp. Dis. 110, 746-753, 1974). We have examined the effect of large doses of hydrocortisone upon lipid metabolism in the rat lung. Eight rats (270-340 g) were separated into two groups (experimental and control) and hydrocortisone sodium succinate or saline was injected intraperitoneally twice a day for seven days, with a dose of 4 mg/rat or 0.1 ml/rat, respectively. Lung slices (200 mg) were incubated at 37° for 30, 60, 90 min, in 4.5 ml of Krebs-Ringer Bicarbonate buffer with 5 grams of bovine serum albumin per 100 ml. After each incubation period, slices were washed twice with cold saline and the lipids were extracted. The lipids were separated using DEAE-Cellulose column chromatography and thin-layer chromatography and method of Shimojo, et.al., (J. Lipid Res., 15, 525-527, 1974) to separate phosphatidylcholine (PC). The experimental lung had a 22% increased content of saturated-PC, however, total PC showed no change. In experiments using radioactive glycerol and palmitate, the incorporation of both precursors into total-pc and saturated-pc increased significantly ($p. < .05$) compared with that of the control; however, incorporation into other lipid fractions was not significantly different at 90 min. The incorporation of lysolecithin into PC was 10 times that of glycerol and palmitate but did not vary between control and experimental animals. In summary, we conclude that hydrocortisone increased de novo synthesis of PC in the rat lung and may also have increased the synthesis of saturated-PC.

BEHAVIORAL REDUCTION OF PREOPTIC TEMPERATURE--A CLOSER LOOK. Eleanor R. Adair and Robert O. Rawson. John B. Pierce Fndn. Lab., New Haven, CT 06519.

Corbit has reported (Science, 166:256, 1969) that rats, previously trained to regulate skin temperature behaviorally, will rapidly learn to reduce the temperature of a water perfused thermode (.049" O.D.) implanted in the anterior hypothalamic preoptic area. Similar experiments on 4 squirrel monkeys (Saimiri sciureus) in our laboratory have featured highly localized preoptic temperature changes via a 1 x 2 mm microheater inserted into a .039" O.D. implanted thermode. In screening experiments, all monkeys responded to preoptic microheating by behaviorally selecting a cooler air (skin) temperature. Then, with ambient temperature held constant at 37°C, the monkeys were offered a rope to pull for 15-sec respites from preoptic microheating to 41.5°C. Learning was slow, requiring 5 or more 6-hour sessions, suggesting that the reinforcement for rope-pulling was not immediate but somehow delayed. Once learned, the response rate could be manipulated by altering either microheater or ambient temperature. Raising the microheater by 8-9 mm in the implanted thermode (to the level of fornix or corpus callosum) eliminated the response. These results suggest that localized preoptic temperature changes are not sensed per se but stimulate autonomic response changes that are sensed at other loci and can serve as delayed reinforcements to support learning. (Supported by USPHS Grant NS 11517.)

CARDIOVASCULAR EFFECTS OF INHALED METHYLENE CHLORIDE IN THE CONSCIOUS DOG. By J. D. Adams* and H. H. Erickson, Environmental Sciences Division, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.

Human inhalation exposure to detrimental levels of methylene chloride (CH_2Cl_2) is not uncommon, due to its widespread domestic and industrial use as a solvent, aerosol spray, etc. In this study, its effects on coronary hemodynamics, left ventricular function and cardiac rhythm were studied in 8 mongrel dogs. The heart was chronically instrumented with a flow transducer around the left circumflex coronary artery and a solid-state pressure transducer in the left ventricle to determine left ventricular pressure and dP/dt. A catheter was placed percutaneously in a carotid loop to measure arterial pressure. With each dog, 2-hour exposures to 500, 1,000, 2,000 and 5,000 ppm CH_2Cl_2 in air were conducted via an endotracheal tube inserted in a tracheostomy. Coronary blood flow increased 20-25% with 1,000, 2,000 and 5,000 ppm. Myocardial contractility (dP/dt) increased 10% and arterial pressure, 16%. Heart rate did not change significantly. Respiration and body temperature decreased and visual signs of CNS depression were observed. Methylene chloride was found to be arrhythmogenic in 4 of 8 dogs and predisposed the heart to epinephrine-induced arrhythmias. Atrioventricular blocks, paroxysmal ventricular tachycardia, and preventricular contractions were observed. Propranolol blocked the PVC's; atropine temporarily eliminated the A-V block; but arrhythmias returned after 24 hrs. These results suggest that methylene chloride may have direct effects on neural pathways or effector mechanisms.

ROLE OF THE CAROTID CHEMORECEPTORS IN THE HYPERPNEA OF EXERCISE. D. Aggarwal*, H.T. Milhorn and L.Y. Lee*, Dept. Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Ms. 39216

To determine whether the sensitivity of the peripheral chemoreceptors is increased during exercise, a set of experiments was performed as follows. Activity of the carotid body of the cat was monitored while the blood supply to the carotid body was controlled independently of the systemic circulation. By this technique, fluctuations in the arterial blood were unable to affect chemoreceptor activity. The left common carotid artery was cannulated at the proximal and the distal ends which were connected to each other by a 3-way stop-cock. The third end of the 3-way stop-cock was connected to a blood reservoir, the height of which could be changed to adjust the arterial pressure perfusing the carotid body. Under normal conditions, the 3-way stop-cock was connected so that the cat supplied blood to its own carotid body. For controlled conditions, the 3-way stop-cock was connected so that the reservoir supplied the carotid body with blood of controlled Po_2 and Pco_2. While the carotid body was being perfused by the controlled blood, the number of impulses per second in the sinus nerve was recorded. After a few minutes of steady state recording, the cat was suddenly made to exercise for 1 minute by electrical stimulation of the hind limb muscles. Chemoreceptor discharge was found to be unchanged in 12 experiments, 6 while perfusing with normoxic blood and 6 while perfusing with hypoxic blood. Thus, it must be concluded that alteration of carotid chemoreceptor sensitivity does not occur during electrically induced exercise in anesthetized cats.

CHOROID PLEXUS ACCUMULATION OF ^{3}H Δ^{9} TETRAHYDROCANNABINOL. W.F.Agnew, C.L.Rumbaugh,* J.T.Cheng,* and T.G.H.Yuen,* Cerebrovascular Laboratory, Huntington Institute of Applied Medical Research, Pasadena, CA.91105.

In vitro experiments. One-hour incubations of lateral ventricle choroid plexus and brain cortex slices of the rabbit with bovine serum albumin microsuspension of ^{3}H Δ^{9} Tetrahydrocannabinol (Δ^{9} THC) in artificial cerebrospinal fluid (CSF) gave tissue-media ratios of 52.9 and 6.8 respectively. This accumulation against a concentration gradient in these tissues had both active and passive transport components. The saturable component was inhibited by ouabain, potassium cyanide, p-chloromercuribenzoate, iodoacetate and low temperature (4°C). A Hofstee plot of the transport values for the saturable component in choroid plexus yielded a transport constant (K_t) of 21 μM. Thin layer chromatographs of incubated choroid plexus indicated that the radioactivity present was due entirely to unchanged Δ^{9} THC. Autoradiographs demonstrated that the Δ^{9} THC was preferentially localized in intracellular lipid bodies of incubated choroidal epithelium. In vivo experiments. One hour following intravenous injections of alcoholic solutions of Δ^{9} THC in rabbits, choroid plexus tissue : plasma ratio was 1.69, more than twice the uptake of parietal cortex, frontal cortex, midbrain, cerebellum or corpus callosum. Taken together, these results indicate that Δ^{9} THC is not only actively accumulated by the choroidal epithelium but may also be taken up from CSF and transported across the epithelial stroma into the capillary circulation. This suggests that the choroid plexus participates in the regulation of Δ^{9} THC concentrations in CSF and indirectly in brain by means of the "sink" function of the CSF.

(Supported by NIH Grant DA 00126 and The O'Neill Brothers Foundation.)

EFFECT OF ARGININE VASOPRESSIN (AVP) ON INTRARENAL BLOOD FLOW DISTRIBUTION AND ON ELECTROLYTE EXCRETION. Nobuharu Akatsuka*, Mary L. Morgan*, Michael F. Wilson, Walter H. Moran, Jr., and Ping Lee, West Virginia University Medical Center, Morgantown, WV 26506.

This study was designed to extend results of previous experiments which used Xe-133 washout method to measure intrarenal flow distribution during steady-state AVP infusions (Fed. Proc. 34: 364, 1975). Lightly anesthetized dogs were hydrated to suppress endogenous ADH. AVP was then infused for 45 min. to produce plasma AVP concentration of 16 μU/ml. Microspheres (15 μ) labeled with Sr-85 and Cr-51 were injected before and after AVP infusion. The renal cortex was sectioned into 4 shells of even thickness (I to IV from outer cortex). Pooled segments of each shell were weighed and counted in a gamma counter. The fraction (%) of total glomerular flow to each shell (f_{TGF}) was calculated assuming a renal ellipsoidal structure (McNay and Abe). Infusion of AVP induced a small decrease in heart rate without change in mean aortic pressure, a decrease in urine flow, and an increase in urine osmolality making free water clearance negative. Fractional unit flow decreased to outer cortex and increased to inner cortex [I .39 → .35; II .33 → .27 ($P < 0.02$); III .18 → .21; IV .10 → .18 ($P < 0.003$)]. The f_{TGF} also shifted from outer to inner cortex [I 46% → 43%; II 33 → 28 ($P < 0.03$); III 15 → 17; IV 7 → 12 ($P < 0.003$)]. Increased excretion of Na^{+} (> 4X) and K^{+} (> 1.5X) occurred with no change in filtered load (calculated from creatinine clearance). The blood flow shifts were anatomically well defined but their functional relationship to altered electrolyte excretion requires further investigation. (Supported in part by Am. Heart Assoc., WV Affiliate, Grant No. 74-AG-4N)

THE DIFFERENTIAL EFFECTS OF LENGTH AND TEMPERATURE ON O_2 CONSUMPTION OF RESTING AND CONTRACTING FROG SKELETAL MUSCLE IN VITRO. P.D.Allen* and M.J.Kushmerick, U.S. Army Research Institute of Environmental Medicine Natick, MA., 01760, and Harvard Medical School, Boston, MA. 02115

Although initial length is an important factor in governing the energy utilized by resting and contracting skeletal muscle, discordant results have been reported as to the direction and magnitude of the change. One important difference among the studies which may have affected the interpretation has been the muscle temperature.

Sartorii from both R.pipiens(RP) and R.Temporaria(RT) were studied in an in vitro polarographic muscle chamber at 0.8, 1.0 and 1.25 L_o at 5°, 15° and 26°C. A reversable increase in the oxygen consumption of unstimulated muscles (VO_2R) was found with increasing length above L_o. It was a graded function of the amount of stretch and was present at all temperatures. For example at 1.25L_o VO_2R increased by 50% in RP and 175% in RT while at 0.8L_o VO_2R was unchanged. Log VO_2R increased linearly as muscle temperature increased with a slope of 2.4 per 10°C. When the same muscles were tetanized isometrically for 2.5 seconds total suprabasal O_2 consumption during recovery (ΔO_2) had a different and relatively much smaller temperature dependence than did VO_2R. Log ΔO_2 was not a linear function of temperature, having a greater temperature dependence at lower temperatures. This relation was maintained when tetanic tension and ΔO_2 were decreased at 0.8L_o and 1.25L_o.

Thus: 1. Passive stretch increases VO_2R in sartorii of both RP and RT at all three temperatures studied; 2. The relative increase in ΔO_2 with temperature is less than that of VO_2R; and 3. At 0.8 and 1.25L_o ΔO_2 was less than at L_o in proportion to the lower isometric tension, but the form of the temperature dependence of ΔO_2 was similar at all three muscle temperatures.

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FUNCTIONAL DISTRIBUTION OF CARDIAC SYMPATHETIC NERVES IN THE CYNOMOLGUS MONKEY. William A. Alter III, Delbert E. Evans* and L. John Parkhurst*. Armed Forces Radiobiology Research Institute, Bethesda, Maryland.

This study was undertaken to define the functional anatomy of the cardiac sympathetic nerves in a primate species, cynomolgus, which might serve as an alternative to the rhesus. Ten cynomolgus monkeys (Macaca fasicularis) were anesthetized and prepared for recording arterial blood pressure, heart rate, right atrial force and right ventricular force. The stellate ganglia, middle cervical ganglia and thoracic vagi were exposed and all discernible branches stimulated. The largest cardiac sympathetic trunk on the right side was the middle cervical cardiac nerve, stimulation of which resulted in a significant increase in all recorded parameters. Right stellate nerves passing directly to the heart were not observed in cynomolgus, but small stellate branches coursing into the vagus were consistently found and stimulation of these branches usually resulted in a significant increase in all parameters. Sympathetic fibers also entered the vagus at the level of the right middle cervical ganglion and then emerged in the craniovagal and caudovagal cardiac nerves. After administration of atropine, stimulation of these cardiac vagal nerves resulted in significant positive chronotropic and inotropic responses without any significant changes in arterial blood pressure. The right phrenic nerve was also found to have significant effects on heart rate and right cardiac function. The major pathway on the left side affecting rate and force was the ventromedial cardiac nerve which originates in the middle cervical ganglion. These results indicate that the cynomolgus is a suitable alternative to the rhesus for studies of neural control of the heart.

EFFECTS OF TRANSIENT FLOW RESISTIVE LOADING AND UNLOADING ON INSPIRATORY MUSCLE FORCE. M.D. Altose*, S.G. Kelsen*, and N.S. Cherniack. University of Pennsylvania, Philadelphia, PA 19104.

Inspiratory muscle force, measured by the mouth pressure during airway occlusion, increases with hypercapnia. At any P_{CO_2}, occluded mouth pressure is greater during mechanical loading. In the present study, the dynamic changes in inspiratory muscle force during inspiratory flow resistive loading and unloading were examined in 10 normal subjects. The airway was occluded for the first 100 msec of every inspiration by an electrically activated shutter and the pressure at the end of the occlusion (P_{100}) was measured. During rebreathing 7% CO_2 in O_2, an inspiratory flow load of 10 cm H_2O/L/sec was introduced randomly for one to five consecutive breaths. At any given P_{CO_2}, P_{100} of the first loaded breath was the same as control determinations. However, P_{100} of the second loaded breath was greater (121 $\pm$ SE 5% control at P_{CO_2} 55 mm Hg). During subsequent loaded breaths there was little further increase in P_{100} so that P_{100} of the fifth loaded breath at P_{CO_2} 55 mm Hg was 124% of control. Upon removal of the inspiratory load, the P_{100} remained elevated during the first unloaded breath (124 $\pm$ SE 6% of control) but then returned to control values. When graded loads were applied in 5 subjects during rebreathing, the change in P_{100} increased with increasing loads. P_{100} at P_{CO_2} 55 mm Hg (% Control):

Load (cm H_2O/L/sec)	Second Loaded Breath	First Unloaded Breath
6	116 $\pm$ 5	113 $\pm$ 4
10	121 $\pm$ 7	123 $\pm$ 9
13	131 $\pm$ 4	130 $\pm$ 4

It is suggested that the responses to mechanical loading develop rapidly, increase with the magnitude of the load and are determined from information obtained from previous breaths.
(Supported by NIH Grant HL - 08805)

ADH ACTION IN ISOLATED CORTICAL COLLECTING TUBULES: EVIDENCE FOR INCREASES IN LUMINAL MEMBRANE FLUIDITY. G. Al-Zahid*, J. A. Schafer and T. E. Andreoli. Depts. of Medicine (Nephrology), and Physiology and Biophysics. Univ. of Alabama in Birmingham, Birmingham, Ala. 35294

We have recently proposed that the hydro-osmotic effect of ADH in isolated rabbit cortical collecting tubules depends on hormone-induced increases in the fluidity of luminal membranes which increase the partition of water into hydrophobic regions of these membranes, and that ADH-dependent osmosis through apical membranes is wholly diffusional in nature (J. Clin. Invest. 51:1264, 1972; J. Gen. Physiol. 64:201, 1974). To test this view, we evaluated the effects of ADH on the reflection coefficients (σ_f) and diffusional permeability coefficients (P_f) of lipophilic species. Three results obtained. First, highly lipophilic solutes such as butanol ($K_{oil} > 10^{-1}$) had zero reflection coefficients with or without ADH; and, P_f for such solutes was unaffected by ADH. Second, the ADH-dependent values of σ_f for moderately lipophilic ($K_{oil} = 10^{-3}$ to 10^{-2}) branched and straight chain homologues, such as isovaleramide and n-valeramide, were uniformly less than unity (range 0.3-0.6), but σ_f for the branched species was greater than for the straight chain homologue. Third, ADH produced nearly twofold increases in P_f for such species. For example, with isobutyramide, P_f was 0.16 $\pm$ 0.02 (SEM) without ADH and 0.27 $\pm$ 0.04 with ADH ($p < 0.05$). We conclude that ADH-dependent changes in fluidity of plasma membranes results in increased diffusion rates for both water and moderately lipophilic solutes, both branched and unbranched, but, that the membranes remain sufficiently "organized" to discriminate between branched and straight chain homologues. (Supported by: AHA Grant 72-899, NIH Grant 5-T01-AM14873, and NSF Grant BMS 74-13645.)

THE INTERRELATIONS OF SENSORIMOTOR CORTICAL AND SUBCORTICAL CIRCUITS SUBSERVING CONTACT PLACING IN THE KITTEN. Vahe E. Amassian and Richard Ross*, Dept. Physiology, SUNY, Downstate Medical Center, N.Y. 11203

A (precritical) period of development lasting for the first 3 weeks was previously distinguished in the kitten, during which, removal of sensorimotor cortex was followed by temporary recovery of contact placing (CP) of the contralateral forelimb within hours or even minutes (Amassian and Ross, 1973, J. Physiol., 230:55-56P). However, when cortical outflow was acutely removed during the last week of the precritical period by cooling the internal capsule, CP to contact of the ulnar aspect of the forepaw was reversibly lost (Amassian and Ross, 1975, J. Physiol., 246:101-105P). The onset of such short term cortical influence on CP has now been determined by aseptically implanting a cooling device epidurally over sensorimotor cortex. The earliest loss detected of contralateral ulnar CP occurred with cooling at 8-7 days. Cortical cooling behind the ansate sulcus was ineffective. These results imply that a subcortical circuit manages CP at least until the end of the first week. Subsequently, the sensorimotor cortex influences CP, but if removed before the start of the fourth week, the subcortical circuit can soon reacquire full control of CP, secondarily losing this 'stand alone' capacity when the operated kitten ages, e.g. by 2 months. The sensorimotor cortex might influence CP during the precritical period either through a steady state (precontact) output or as part of a dynamic (reflex) circuit. In preparations under gallamine-procaine, resting discharge by individual PT neurons was minimal up to 6 days, but prominent by 10 days, suggesting a possible role in CP of such steady state activity during the mid and late precritical period.
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EFFECT OF CHRONIC EXPOSURE TO SO_2 ON GAS EXCHANGE AND MECHANICAL PROPERTIES OF THE LUNG OF BEAGLE DOGS. R. Amyot*, J. Gauthier*, and R.R. Martin, Meakins Christie Labs., McGill University Clinic, Montreal, Quebec.

In an attempt to produce an animal model of chronic bronchitis we have exposed 6 beagle dogs to 350 PPM of SO_2 for 3 hours on alternate days for 4 months, plus 2 shams. Great care was taken to prevent infection. We measured gas exchange, lung volumes (V_L), elastic recoil (Pel), airway resistance (R_L), flow volume curve on air and on helium ($\Delta\dot{V}max$), the slope of the alveolar plateau ($\Delta N_2/l$) and closing volume (CV). Each dog was studied before and after 2 months, 3 months and 4 months of exposure. R_L was partitioned in all animals on the day of their last study.

No consistant changes were seen in the shams. The exposed dogs showed significant increase in the $(A-a)DO_2$, R_L, and CV at 3 months and 4 months and a very significant increase in $\Delta N_2/l$ but only after 3 months. No significant changes were seen in V_L nor in $\Delta\dot{V}max$ and there were no loss of Pel. When compared to the shams 4/6 exposed dogs had increased peripheral resistance expressed as % of the total. This correlated fairly well with CV but not with $\Delta\dot{V}max$. We have thus produced an animal model of airway disease with certain features similar and others dissimilar to human chronic bronchitis.
(Supported by the MRC of Canada).

HYPOPHOSPHATEMIA IN THE DOG: EFFECTS OF GLUCOSE, SALINE AND ACUTE THYROIDECTOMY. J.J.B. Anderson and Sam W. Boye*. Dept. of Nutrition, Sch. of Public Health, Univ. of North Carolina at Chapel Hill, 27514.

Investigations were designed to determine what short-term effect, if any, calemic and phosphatemic hormones of the thyroid-parathyroid complex have on the well established glucose-induced hypophosphatemia. Following an overnight fast, female mongrel dogs (10-18 Kg) were: anesthetized; surgically prepared for intravenous (right femoral) infusion (90 ml per hour for 3 hours) of either 0.9% sodium chloride or 10% glucose in water; thyroparathyroidectomized (TPTX), sham-operated (Sham TPTX) or left intact in the neck region; ventilated; and sampled via a right femoral arterial catheter at 15-30 minute intervals prior to, during, and 2 hours following the infusion. Extracellular volume expansion (ECVE) was only about 3%, but it did cause a net average decrease in plasma calcium (Ca) of 0.6 mg/100ml in the glucose-infused dogs versus 0.3 in the saline-infused animals during the 3-hour infusion. For 2 hours after the infusion was stopped plasma Ca remained constant or rose slightly. Plasma inorganic phosphate (Pi) fell in all animals, but maximal mean decreases of 1.5-1.7 mg/100ml occured in glucose-infused Sham TPTX and TPTX dogs versus 0.9 in saline-infused intact dogs. Following the cessation of infusion plasma Pi rose steadily. Plasma glucose was significantly elevated in all groups of infused animals, including those receiving a simple saline ECVE. The data suggest that, in addition to parathyroid hormone-mediated and renal mechanisms, a third hypophosphatemic mechanism exists when plasma glucose is elevated; namely, glucose transfer out of plasma into extrahepatic tissues, including the kidney, results in the obligatory co-transfer of phosphate and, hence, hypophosphatemia. (Supported in part by GRS Grant No. 1-0-107-4660-AF451.)

EFFECT OF DIETARY RESTRICTION AND OVARIAN STEROIDS ON FETAL SURVIVAL AND DEVELOPMENT IN THE PIG. L. L. Anderson and D. W. Dunseth*. Dept. Animal Science, Iowa State University, Ames, Iowa 50010

On Day 30 after mating 50 Yorkshire pigs were laparotomized to determine ovulation rate and confirm pregnancy; half the animals then were ovariectomized and given daily intramuscular injections of progesterone (80 mg/100 kg bodyweight) and estradiol benzoate (500 μg/100 kg bodyweight). Half the pigs continued receiving a control diet (1.82 kg/day; 5008 kcal) and the other half a restricted diet (0.80 kg/day; 2208 kcal) from Days 30 to 70 or 110. There were 8 experimental groups of 6 or 7 pigs per group. Ovulation rate (15.5 ± 1.26, mean and SE) was similar ($P > 0.05$) for all groups. Bodyweight declined from Days 30 to 70 or 110 in pigs given restricted diet, whereas those on control diet gained during these periods of the gestation. Mean number of living fetuses at Day 70 in laparotomized controls given control diet was 10.2 ± 1.07 vs. 9.6 ± 1.63 in those on restricted diet; ovariectomized pigs given progesterone and estradiol benzoate had 9.2 ± 1.45 living fetuses on control diet and 7.9 ± 1.42 on restricted diet. Number of living fetuses was similar ($P > 0.05$) regardless of level of dietary intake or exogenous steroid treatment. Mean number of living fetuses at Day 110 in laparotomized controls on full diet was 9.8 ± 1.14 vs. 8.0 ± 0.41 in those on restricted diet; number of living fetuses in ovariectomized pigs given progesterone and estradiol benzoate was 9.8 ± 0.86 on full diet and 8.0 ± 1.15 on restricted diet. Number of living fetuses at Day 110 was similar ($P > 0.05$) regardless of level of diet or exogenous hormone treatment. Number of degenerating fetuses (1.2 ± 0.59) was similar ($P > 0.05$) in all groups at Day 70 and Day 110. Fetal development at Day 70 was less ($P < 0.01$) in laparotomized controls given restricted diet, but similar ($P > 0.05$) in ovariectomized pigs on restricted and full diets.

ACTIVATION OF CONTRACTION IN FROG VENTRICLE. T.W. ANDERSON*, C. Hirsch* and F. Kavaler. Dept. of Physiology, Downstate Medical Center, SUNY, Brooklyn, N.Y. 11203.

The force of contraction and transmembrane potential were recorded from extremely short segments of frog ventricle strips. Thus, longitudinal voltage distribution, during clamp, was relatively uniform. Extracellular ionic composition could be changed rapidly. Large and abrupt increases in intracellular $[Ca^{++}]$ have no detectable effects on subsequent contractions. In contrast, an increase in extracellular $[Ca^{++}]$ is associated with a progressive increase in contraction extending over several beats. A slow inward current was observed, which was sensitive to changes in extracellular $[Na^{+}]$ but not to changes in extracellular $[Ca^{++}]$. Displacement of transmembrane potential during an action potential affected contraction in a manner opposite to that to be expected if a calcium current were to play a significant role in activation. The activation process could be saturated by sufficient displacement of transmembrane potential to high inside positive levels. The voltage displacement necessary for saturation was less the higher the extracellular calcium concentration. Force development occurring after displacement of transmembrane potential to levels beyond the equilibrium potential for calcium was rapidly sensitive to alterations in extracellular composition, including: addition of 10 mM Mn^{++}; increase in $[Ca^{++}]$; decrease in $[Na^{+}]$. It is concluded that activation of contraction in frog ventricular muscle is mediated exclusively, or almost exclusively, by an influx of calcium into the cell. This is true throughout the range of voltage dependence of activation: from threshold to saturation. The observations suggest that such transsarcolemmal calcium movement is brought about by driving forces which add to those of electrodiffusion. (Supported by grant HL-12774 from NHLI.)

CIRCULATORY RESPONSES OF RHESUS MONKEYS TO PROLONGED EXPOSURE TO MAINTAINED HYPERTHERMIA. E.T. Angelakos, A. Sternberg*, and R. West*. Dept. of Physiology & Biophysics, Hahnemann Medical College, Philadelphia, PA 19102

Previous work in this laboratory indicated that monkeys (M. Mulatta) exposed to progressive hyperthermia died in respiratory failure. To extend these findings seven anesthetized monkeys were heated and then maintained at 42.5° C. Systolic and diastolic arterial pressure (AP), left ventricular pressure (LVP), dP/dt, heart rate (HR), respiration rate (RR), arterial pO_2, pCO_2, pH and rectal temperature (TR) were measured continuously or every 15 min. Up to 41° C, cardiovascular parameters were within normal limits or increased as previously reported. Although the TR was maintained at 42.5° C, progressive cardiovascular deterioration developed over a period of 3 hours. The gradual hypotension which began at 41° C continued while at 42.5° C until respiratory failure and death supervened. Attempts to correct this trend by artificial respiration or infusions of saline did not prolong survival time appreciably. Seven additional experiments were performed using metaraminol bitartate as a vasopressor. This maintained blood pressure above 60 mmHg and increased survival time by 3-5 hours compared to untreated controls, artifically respired, or saline infused. Subsequently, there was a progressive decrease in the blood pressure response to the drug and the animals died in severe hypotension. Arterial pO_2 and pCO_2 were both reduced prior to terminus (from 99 to 83 and from 33 to 12) while pH first rose and then declined (7.41 to 7.49 to 7.42). It is concluded that peripheral circulatory factors and possibly lack of sympathico-medullary response (ultimately combined with decreased blood vessel responsiveness) are dominant factors in death at 42.5° C. (Supported by ONR contract N00014-72-A-0317-0002.)

PREJUNCTIONAL AND POSTJUNCTIONAL SUPERSENSITIVITY IN THE RAT PORTAL VEIN AFTER SYMPATHECTOMY BY 6-HYDROXYDOPAMINE. O. Aprigliano* and K. Hermsmeyer. Dept. Pharmacology and The Cardiovascular Center, University of Iowa, Iowa City, Iowa 52242 (Spon: M. J. Brody)

Sympathectomy of the rat portal vein was produced in vitro and in vivo by 6-hydroxydopamine (6-OHDA) to study denervation supersensitivity in vascular muscle. In vitro incubation of the isolated veins with 6-OHDA abolished the responses of the adrenergic nerves to transmural stimulation, eliminated ^{3}H-NE uptake, and produced depletion of catecholamines to levels indetectable by fluorescence histochemistry. Concentration-response curves showed a 1.5 fold increase in sensitivity of the vessel strips to l-NE (prejunctional supersensitivity due to elimination of neuronal uptake) but no change in resting membrane potential. In vivo treatment of rats with 6-OHDA decreased the responses to transmural stimulation, reduced ^{3}H-NE uptake, decreased catecholamine fluorescence, and produced a 3.5 fold increase in sensitivity to NE. In contrast to the acute denervation, the chronic (3 days) denervation produced a partial depolarization of the vascular muscle cells (40.7 ± 0.5 mV vs. 36.4 ± 0.6 mV, control and treated, respectively). The data suggest that the sympathetic denervation of the vascular muscle of the portal vein produces a postjunctional supersensitivity for which partial depolarization is a component of the mechanism.
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HYPOGLYCEMIA IN CONSCIOUS DOGS IN LIVE ESCHERICHIA COLI SEPTICEMIA: A CHRONIC STUDY. Linda T. Archer* and L. B. Hinshaw (SPON: A.K. Weiss) V.A. Hosp. and Dept. Physiol. and Biophys., U. Okla. Hlth. Sci. Ctr., Okla. City, Okla. 73190

Recent data from this laboratory in anesthetized dogs injected with E. coli endotoxin documented progressive hypoglycemia with a correlation between endogenous blood glucose levels and survival. The purpose of the present study was to determine if the hypoglycemic response to endotoxin could be elicited in awake animals administered live E. coli organisms alone. Experiments were conducted on unanesthetized dogs with previously implanted carotid artery and jugular vein cannulae. Paired animals were infused with 1-2 cc/kg viable E. coli (10^{9} organisms/cc). Thirteen animals were subjected to E. coli alone while 12 dogs were administered E. coli but were treated for 6 hours with 50% glucose. Data document that blood glucose levels continuously fall; insulin response is normal in conscious dogs in live bacteremic shock; there is a correlation between blood glucose concentration and survival in animals given E. coli alone; and the hypoglycemia is a progressive phenomenon, not merely a terminal event. Results indicate during hypertonic glucose infusion, arterial pO_2 in glucose-treated dogs was higher ($p<0.025$) and pCO_2 was lower ($p<0.05$) compared with the non-treated group, suggestive of improved hemodynamic status; however, the survival rate was not improved. Termination of glucose infusion caused these parameters to be indistinguishable from controls indicating the possible need for an extended infusion time of 50% glucose in order to decrease mortality. Factors other than blood glucose levels seemed operative in determining lethality. The present results emphasize the need for further research into the metabolism of shock. (Supported by V.A. Hosp. and U.S. Navy Contract N00014-68-A-0496).

COMPARATIVE STUDIES OF MITOCHONDRIA AND SARCOPLASMIC RETICULUM FROM EXERCISED-TRAINED AND STELLECTOMIZED DOG HEARTS. G. K. Asimakis*, H. L. Stone and L. A. Sordahl, Division of Biochemistry, University of Texas Medical Branch, Galveston, Texas 77550.

Studies have indicated that the sympathetic drive to the heart is markedly decreased in exercised-trained animals. Mitochondria (M) and sarcoplasmic reticulum (SR) were isolated from exercised-trained (E-T), stellectomized (S) and sedentary control (C) hearts. The mitochondrial respiratory activity was measured by polarographic techniques. Calcium binding and uptake by M and SR was determined by Ca^{45} rapid filtration and dual-beam spectroscopy. There were no significant differences in respiratory activity between mitochondrial preparations of E-T, S and C dog hearts. M calcium uptake of E-T preparations was slightly lower than C, while S preparations exhibited slightly higher rates than C. A rapid, spontaneous release of M calcium after uptake was seen in all E-T preparations but not in any C preparations. Some of the S preparations also showed early release of M calcium. SR studies indicated that initial binding rates and total uptake of calcium in both E-T and S preparations were less than C. It is suggested that alterations in sympathetic activity in the E-T heart may produce changes in myocardial cellular calcium metabolism which may be related to changes in cardiac function in exercised-trained animals.

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PARADOXICAL HYPERTENSION DURING SLEEP IN DOGS WITH BUFFER NERVE SECTION. D.B. Averill*, C.M. Ferrario, J.W. McCubbin and G. Nadzam*. Research Division, Cleveland Clinic Foundation, Cleveland, Ohio 44106 and Biology Department, Cleveland State University, Cleveland, Ohio 44115.

The unexpected rise in blood pressure of dogs with neurogenic hypertension has not been studied in detail (Ferrario et al., Circ. Res. 24:911, 1969). We have, therefore, investigated the effect of slow wave sleep (SWS) and desynchronized sleep (DS) on blood pressure of dogs before and 1 to 42 days after section of their carotid sinus and aortic depressor nerves. The electroencephalogram was recorded from supradural silver electrodes chronically implanted in the skull; blood pressure was measured from a catheter indwelled into an iliac artery. Before sinoaortic denervation blood pressure remained stable and unchanged during SWS. It fell slightly during episodes of DS. After sinoaortic denervation, SWS was accompanied by rises in pressure that ranged from 20 to 60 mm Hg above values measured prior to onset of SWS. Hypertension during SWS was not accompanied by changes in cardiac rate. On the other hand, marked fluctuations in mean arterial pressure occurred during DS episodes ranging from exceedingly low values (50 mm Hg) to frank hypertension (160 mm Hg) and, in these cases, were paralleled by similar changes in heart rate. After buffer nerve section rises in arterial pressure accompanying SWS suggest that in the dog baroreceptor afferents normally have a modulating influence on the activity of serotonergic pathways that have been implicated in cardiovascular control during sleep. (Supported in part by grant HL-6835 from NHLI.)

PROTECTION OF RATS AGAINST HEMOLYTIC HEMOGLOBINURIA FROM ORAL DISTILLED WATER BY HIGH INTAKE OF DIETARY NaCl. S. Ayachi,* C.E. Hall and O. Hall* (SPON: R.D. Baker). Dept. of Physiology & Biophysics, The Univ. of Texas Medical Branch, Galveston, Texas 77550

Previous studies have demonstrated the occurrence of hemolysis and hemoglobinuria in rats following the oral administration of distilled water. However rats that have been maintained for a prolonged period on a high NaCl intake are protected against that effect. Under conditions where all rats on a normal sodium chloride intake displayed postabsorptive hematuria, only half of those drinking a 1% NaCl solution and none of those drinking a 5% sucrose, 1% NaCl solution (which greatly augments NaCl consumption) so responded; this despite the fact that all drinking fluids were withheld for two hours prior to gavage with water. Rats on a high NaCl intake did not have higher than normal plasma osmolalities, nor did they display a slower rate of water resorption. Inspection of peripheral blood samples indicated that hematuria was preceded by a marked intravascular hemolysis. This was evident in all rats on a normal diet and in about half of those drinking 1% NaCl solution: very few animals drinking 5% sucrose and 1% NaCl showed any hemolysis, and none had detectable hematuria. The hemolysis leading to hemoglobinuria appears to be caused by hypoosmolality of blood plasma due to the rapid entry of water into the vascular bed, and possible factors which might account for the protective effect of dietary NaCl against this phenomenon will be discussed.

(Supported by grant HL-15319 from NHLI.)

LOSS OF VENTILATORY STIMULUS FOR ACUTE ACID-BASE INFUSIONS IN EXERCISING DOGS AFTER CAROTID BODY DENERVATION. Cedric R. Bainton, Depts. of Anesthesia and Physiology, U.C. Medical Center and V.A. Hospital, San Francisco, California, 94143.

Recent work in awake dogs (The Physiologist 15: 75, 1972) indicates that exercise amplifies the ventilatory stimulus of acute acid-base disturbance some 10 fold. The present study evaluates the effect of carotid body denervation (c.b.d.) on this response. Studies were done in three dogs prepared with chronic tracheostomies and carotid loops. Ventilation ($\dot{V}_E$) was measured during 3 mph exercise before and after infusions of 250cc normal saline alone or HCl (23 mEq.) or HCO_3^- (90 mEq) in 250cc saline. P_AO_2 was maintained at 100 mmHg. Arterial P_{CO_2} was held constant for each dog at the mean resting $PaCO_2$ for that dog plus 2 mmHg CO_2. Inhaled CO_2 was adjusted as necessary to maintain constant $PaCO_2$. Acid-base changed rapidly after infusions but was stable during the 20-30 minute period of exercise. At that time, the mean changes (n=18) in Base Excess (mEq HCO_3^-/L) were; saline - .6; HCl - 3.3, and HCO_3^- +5.5. The changes in ventilation (L/min/mEq HCO_3^-) associated with these acid-base changes were +1.1 $\pm$2, +1.7 $\pm$.2 and -.8 $\pm$ .1 before c.b.d. and 0.0, 0.0, and -.4 $\pm$ .1 respectively after c.b.d. We conclude that the carotid body is the exclusive sensor for acute H^+disturbance and partial sensor for HCO_3^- changes in these studies and that exercise then amplifies this input. (Supported in part by USPHS GM 15571, GM 00063, KO4-GM 42350)

THE ROLE OF VAGAL AFFERENTS AND SINO-AORTIC BARORECEPTORS ON RENAL HEMODYNAMICS DURING RAPID BLOOD VOLUME SHIFTS IN THE ANESTHETIZED RABBIT. D.G. Baker* and Y.C. Lin, Dept. of Physiol., Univ. of Hawaii Sch. of Med., Honolulu, Hawaii 96822.

Recent studies suggest that "low pressure" receptors play a role in the neurogenic control of renal blood flow. To determine in the rabbit if receptors subserved by vagal afferents influence renal blood flow we have monitored changes in renal blood flow and resistance as well as other cardiovascular variables during rapid shifts in blood volume (± 10% body weight). Measurements were made in the presence and absence of high and low pressure baroreceptors. Sino-aortic denervation (SAD) was accomplished by section of glossopharyngeal and aortic nerves respectively. Cardio-pulmonary receptors were removed by vagal section. Cardiac output (Q_t) and kidney blood flow (Q_r) were measured by thermodilution techniques. In sino-aortic intact rabbits vagotomy caused a significant elevation in blood pressure (BP, 9%), and total peripheral resistance (TPR, 11%), with no change in Q_r or kidney resistance (R_k). SAD resulted in a significant increase in BP (18%), TPR (29%), and R_k (34%). Vagotomy following SAD resulted in a further elevation in BP, TPR and R_k where Q_t fell and Q_r did not change. Blood volume shifts resulted in appropriate changes in heart rate and TPR with baroreceptors intact and no appropriate changes after SAD. Renal resistance did not change during increases or decreases in blood volume in the presence or absence of the cardiopulmonary or sino-aortic receptors. It is concluded that vagal afferents exert a profound tonic inhibitory input to the vasomotor center after SAD. No evidence was found to suggest kidney involvement in neurogenic compensatory mechanisms to blood volume shifts via high or low pressure baroreceptors. (Supported by NIH grant HL 16482.)

NEURONS IN THE CAT ABDUCENS NUCLEUS WHICH PROJECT TO THE OCULOMOTOR COMPLEX. R. Baker and S.M. Highstein, Div. of Neurobiol., Univ. of Iowa, Iowa City, Ia. 52242 and Dept. of Neuroscience, Kennedy Center for Research, Albert Einstein College of Medicine, Bronx, N.Y. 10461

In this study we have identified a class of neurons located in the cat abducens nucleus which can be antidromically activated by electrical stimulation of their axons in the oculomotor complex. These neurons appear to be distinct from abducens motoneurons as we did not find any electrophysiological evidence for axon-collaterals from identified abducens motoneurons directed towards the oculomotor complex nor was there any indication of motoneuron axon-collateral effects on these neurons. However, oculomotor stimulation produced short latency orthodromic EPSPs and occasionally IPSPs (ipsilateral) in these neurons as well as abducens motoneurons. Combinations of ipsi- and contralateral MLF lesions anterior to the abducens nucleus demonstrate that these cells have predominantly a contralateral axonal projection. Following contra- and ipsilateral vestibular nerve stimulation, disynaptic EPSPs and EPSP-IPSPs, respectively, are found in this population of cells. The latter observation suggests this new class of neurons should respond in a fashion similar to abducens motoneurons during eye movements. Based on this new and previous physiological evidence we now submit these neurons are excitatory, not inhibitory, on contralateral medial rectus motoneurons. Since lesions in the abducens nucleus produce a lateral gaze paralysis we conclude that these neurons are responsible for mediating conjugate third-sixth nucleus interactions. Finally, if these cells are essential for lateral gaze mechanisms then we propose that interference with their axons in the MLF (and not those of pontine reticular neurons) underlies the syndrome of anterior internuclear ophthalmoplegia. (Supported by PHS grants EY-01074 and NYC HRC I-781)

ENZYMATIC CHANGES IN FAST-TWITCH SKELETAL MUSCLE IN RESPONSE TO BILATERAL COMPENSATORY OVERLOAD. K.M. Baldwin*, W.G. Cheadle*, and O.M. Martinez*(Spon: P.F. Hall). Dept. of Physiol., Univ. of Calif., Irvine 92664

Little is known concerning the quantitative enzymatic adaptation to chronic compensatory overload of skeletal muscle. Female rats were assigned to the following groups: (1) normal-sedentary (NS); (2) normal-exercise (NE); (3) bilateral-plantaris-overload-sedentary (BS); and (4) bilateral-plantaris-overload-exercise (BE). Overload was accomplished by partial ablation of the gastroc-soleus muscles. Exercising rats walked up a 65% incline, 0.2 mph, 2 hrs/day, 5d/wk. Groups (N=6), equated for body wgt, were sacrificed after 1,3,5, and 8 wks, and the plantaris muscles were analyzed for the following: wet wgt, protein, citrate synthase (CS), phosphofructokinase (PFK), and myofibril ATPase (MATPase). After 5 wks, absolute wet muscle wgt was increased (peak) by 2%, 39%, and 38% in NE, BS, and BE respectively as compared to NS. Enzyme patterns (expressed per mg protein) were similar in NE as in NS except that CS was increased by 23% after 8 weeks of exercise. However, in both BS and BE, PFK and MATPase were decreased by 30% and 18% respectively throughout as compared to NS. CS was initially decreased by 20% in BS and BE and remained decreased in BS. However, in BE, it was increased by 33% above NS after 8 weeks of exercise. These results suggest that the enzyme pattern of differentiated skeletal muscle is modified both quantitatively and qualitatively in response to compensatory overload coupled with exercise. (Supported by American Heart & Orange Co. Heart Grants.)

RAT BRAIN OSMOLALITY DURING ISCHEMIC ANOXIA. N.M. Bandaranayake* and E.M. Nemoto. Dept. of Anesthesiology, University of Pittsburgh, Pittsburgh, PA 15261.

With complete cessation of brain circulation, rapid degradative metabolic changes occur in the order of seconds and minutes. We hypothesized that these degradative changes lead to an increase in brain solute concentration and osmolality, and, therefore, to postischemic water imbibition. Anesthetized rats were decapitated and heads maintained for 4, 8, 16, 20, 30, 60, 90, and 120 minutes at 37° C. At the exact times, the brains were frozen in liquid Nitrogen and brain osmolalities were measured. For control brain osmolality, a rapid brain sampling technique developed in our laboratory was used. Normal whole brain osmolality was about 320 mOsm. There was an almost linear rise in osmolality up to 30 min of ischemia which plateaued at 90 min. In the regional study, normal cerebellar, cerebral cortex and midbrain osmolalities were 335, 320, and 325 mOsm, respectively. There was a linear increase in cerebellar osmolality up to 60 min of ischemia. The cerebral cortex and midbrain osmolalities were relatively unchanged at 16 min. Midbrain osmolality rose rapidly to 350 mOsm at 30 min. Between 60 and 120 min, little change occurred in the three regions, but cerebellum and midbrain osmolalities plateaued at higher levels than for cerebral cortex. The ratio of experimental to control osmolality, which estimates the percentage increase in water volume showed a 7.7% rise, at 30 min of ischemia. We demonstrated that the greatest change in brain osmolality occurs between 16 and 30 min of ischemia which should result in severe brain edema.

CONTRACTILE RESPONSE OF RAT FEMORAL ARTERIES DURING THE ONSET OF RENAL HYPERTENSION. N.R. Bandick and P.R. Finn*. Natural Science Dept. Oregon College of Education, Monmouth, Oregon 97361

It has previously been reported (Am. J. Physiol. 219:348, 1970) that helically cut strips of femoral arteries from renal hypertensive rats exhibit an enhanced norepinephrine sensitivity, develop less maximum contractile tension, have decreased extensibility, and develop spontaneous contractions more frequently than equivalent strips from normotensive rats. This former study was conducted with rats that were sacrificed 21 days or more after unilateral nephrectomy and contralateral renal artery clamping. The present study was designed to determine the sequential appearance of these elastic and contractile changes as the rat converted from a normotensive to a hypertensive state following surgery. All strips taken from hypertensive rats had spontaneous contractions but equivalent contractions did not appear in the controls (n = 7). These autorhythmic contractions could be observed within 24 hours of renal artery clamping. Maximum active tension and norepinephrine sensitivity were the same in both types of strips for the first two weeks (n = 8). During this same early period both types of strips had equal stiffness. It appears that, with the exception of autorhythmicity, the transitional passive and active arterial wall changes must occur sometime during the third week of renal hypertension. (Supported by HL-14874 from NHLI and the H.R. Kaiser Foundation)

EARLY DETECTION OF UNEVEN VENTILATION BY WHOLE BODY PLETHYSMOGRAPHY. M.R. Banerjee, Dept. of Bio. Sci., Tenn. St. Univ., Nashville, Tenn., M.J. Jaeger, and J.N. Evans,* Dept. of Physiology, U. of Fla., Coll. of Med., Gainsville, Fla.

We have shown on theoretical grounds that if the time constants in parallel lung compartments are unequal and therefore dynamic compliance is frequency dependent, mean alveolar pressure (P_A) determined by body plethysmography is not in phase with flow rate at the mouth ($\dot{V}_m$). The phase lag was predicted to be largest at normal breathing rates (Fed. Proc. 33:324, 1974). In the study reported here a body plethysmograph in which the subject rebreathes gas at BTPS conditions was used to determine P_A. $\dot{V}_m$ was plotted against P_A on an oscilloscope to determine the phase lag. In addition, standard pulmonary function tests (PFT: VC, RV, FRC, FEV_1, and Raw) and three "sensitive" tests (Closing volume, MMFR, and slope of Phase III) were performed by standard techniques.

Three groups of subjects were studied: 1) in 12 non-smoking healthy subjects with normal PFT no detectable phase lags were found; 2) in 51 healthy college students with a smoking history of 1-5 pack years all PFT were normal, but phase lage were detectable in 6; 3) in 51 subjects ranging in age from 20 to 66 years (mean: 29 years) and a smoking history of at least 10 pack years 2 subjects were judged abnormal on the basis of PFT while 28 had a plethysmographic phase lag. This phase lag correlated well with the three other sensitive tests.

We conclude that this plethysmographic technique is a valuable tool for the detection of uneven ventilation in smokers. Presumably it provided the same information as the dynamic compliance.
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VAGALLY-MEDIATED INCREASE IN PHRENIC DISCHARGE EVOKED FROM THE DOG LUNG BY CO_2. R.B. Banzett*, H.M. Coleridge and J.C.G. Coleridge. Cardiovas. Res. Inst. UCSF, San Francisco, CA 94143

Adding 3-10% CO_2 to the inspired O_2 of spontaneously breathing dogs with cardiopulmonary bypass stimulates breathing by a vagal reflex (Bartoli et al. J. Physiol. 240, 91, 1974). We have used a simpler preparation in order to determine the range of CO_2 concentrations over which the reflex operates. In anesthetized dogs with open chest, the right and left lungs were ventilated separately at constant volume. The left pulmonary artery was occluded; the circulation to the right lung was intact. $FETCO_2$ from each lung was measured continuously. Efferent phrenic impulses were recorded in the neck. In the control period both lungs were ventilated with O_2. Addition of 5% CO_2 to the O_2 ventilating the test (left) lung caused an increase in phrenic firing, without change in $PaCO_2$ or in $FETCO_2$ of the right lung. Ventilation of the test lung with 8% CO_2 in O_2 caused a further increase in phrenic discharge in half the experiments. The increases in phrenic discharge were abolished by left vagal section. Occlusion of the left pulmonary artery and the washout of CO_2 from the left lung usually produced a unilateral increase in peak left airway pressure, which reverted to the previous level upon addition of 5% CO_2. There was no further alteration in left airway pressure when the ventilating gas was changed to 8% CO_2 in O_2. We do not think therefore that the reflex increase in phrenic discharge with increase in $FICO_2$ to the test lung can be fully explained by changes in vagal afferent activity secondary to changes in lung mechanics. We conclude that CO_2 can increase ventilatory drive by direct stimulation of vagal afferents in the lung. (Supported by NIH grants HL 3875 and HL 6285.)

GLUCOSE TRANSPORT BY ISOLATED PERFUSED SNAKE PROXIMAL RENAL TUBULES. Delon W. Barfuss and William H. Dantzler. Dept. of Physiology, College of Medicine, Univ. of Arizona, Tucson, Arizona 85724.

Glucose transport was studied in isolated perfused proximal portions of snake (Thamnophis spp.) proximal renal tubules. With equal concentrations of ^{14}C-labeled glucose and unlabeled glucose in bathing medium and perfusion fluid, net transepithelial glucose transport occurred from lumen to bath. An apparent maximum rate of transport of about 1.2×10^{-12} moles mm^{-1} min^{-1} was reached at a glucose delivery rate of about 4×10^{-12} moles min^{-1}. Transepithelial permeability to glucose determined from passive flux down a concentration gradient from bath to lumen was about 2.3×10^{-6} cm sec^{-1}. Removal of sodium from perfusion fluid reduced net glucose transport from lumen to bath by about 50%. Phlorizin (0.1 mM) in perfusion fluid reduced net glucose transport from lumen to bath by about 70% without affecting volume reabsorption. Cell-to-bath glucose concentration ratio (C/B ratio) for non-perfused tubules incubated in glucose was about 0.25. Cell-to-perfusion fluid glucose concentration ratio (C/PF ratio) for tubules perfused with equal concentrations of unlabeled glucose in bath and perfusion fluid but labeled glucose only in perfusion fluid was about 0.1. Preliminary data on tubules perfused with equal concentrations of labeled and unlabeled glucose in bath and perfusion fluid indicate that C/B and PF/B ratios are less than 1.0. These studies indicate apparent active transepithelial transport for glucose from lumen to bath in isolated perfused tubules but do not clearly support the concept of an active transport step on the luminal membrane. (Supported by research grants NSF GB 38033, NIH AM 16294; NIH training grant HL 05884).

ROLE OF CARDIOACCELERATION AND THE FRANK-STARLING MECHANISM DURING INTRAVENOUS VOLUME INFUSION. G.E. BARNES* B.C. CHEVIS* AND H. J. GRANGER (SPON: J.W. CROWELL). Dept. Physiology & Biophysics, University of Mississippi Med. Ctr. Jackson, MS 39216

To determine the contribution of cardioacceleration and the Frank-Starling mechanism to the augmentation of cardiac output during rapid volume infusion, dogs were instrumented for continuous monitoring of aortic flow, heart rate, stroke volume, transverse ventricular diameter, left atrial pressure and arterial pressure. In chronically-instrumented conscious dogs, cardioacceleration accounts for 75% of the increase in cardiac output during i.v. infusion. The small increase in stroke volume occurs in the face of an elevation in arterial pressure and is accompanied by a small increase in end-diastolic ventricular diameter. In open-chest, anesthetized dogs, resting heart rate was manipulated and the effect of initial heart rate on the contribution of cardioacceleration and the Frank-Starling mechanism was studied. At high initial heart rates, increase of cardiac output was accomplished through the large increment in stroke volume accompanying dramatic increases in end-diastolic ventricular diameter. Heart rate decreased or did not change. At lower initial heart rates(90 b/min), cardioacceleration and increased stroke volume contributed equally to the elevation of aortic flow. In conclusion, in normal conscious dogs, cardioacceleration is the major mechanism utilized by the cardiovascular system to augment cardiac output when venous return is increased by volume infusion. However, the relative contribution of cardioacceleration and changes in stroke volume are modulated by the initial heart rate, possibly through the influence of cardiac frequency on end-diastolic dimensions. Supported by Miss. Heart Assn. grant and NIH grant HL 11678.

MICROTUBULE ASSEMBLY IN RENAL MEDULLARY SLICES: EFFECT OF ADH AND VINBLASTINE Larry D. Barnes*, Y. S. F. Hui* and Thomas P. Dousa (SPON: C. G. Strong), Mayo Clinic and Foundation, Rochester, Minnesota 55901

To evaluate the effect of vasopressin and some vasopressin inhibitors on the polymerization of microtubules in unbroken cells, an assay was developed to assess microtubule polymerization in isolated renal rabbit medullary slices. Slices were first incubated for 90 min at 0° to depolymerize microtubules to free tubulin and then incubated at different temperatures to promote microtubular assembly. At the end of the second incubation, slices were homogenized in a microtubule-stabilizing medium (55% glycerol, 10% DMSO, 5 mM $MgCl_2$, 5 mM Na_2HPO_4 and 0.5 mM EGTA) and centrifuged at 10^5 x g for 60 min. The pellet was resuspended in GTP-phosphate buffer and incubated at 0° for 90 min to depolymerize formed microtubules into free tubulin. The depolymerized mixture was centrifuged for 60 min at 10^5 x g and the quantity of tubulin in the supernate was assessed by [^{3}H]-colchicine-binding assay. It was found that polymerization was proportional to the increase in temperature in the range of 25° to 37° and progressed in time up to 90 min. Polymerization was inhibited by 2.5 x 10^{-6}M vinblastine and at 0° no polymerization occurred. Addition of 2.5 x 10^{-7}M [8-Arginine]-vasopressin did not influence the extent of polymerization. These results indicate that polymerization of free tubulin into microtubules can be detected indirectly in the unbroken renal medullary cells in vitro and low temperature or vinblastine blocks or inhibits assembly of the tubulin into microtubules. Vasopressin does not have an apparent effect on the extent of microtubule polymerization under these conditions.
(Supported by NIH grant AM-16105, AHA #73689 and by Mayo Foundation)

DYSTROPHIC SARCOPLASMIC RETICULUM MEMBRANES. Ronald J. Baskin and Stephen D. Hanna*. Department of Zoology, University of California, Davis, California 95616.

Analysis of the ultrastructure and of the functional properties of fragmented sarcoplasmic reticulum isolated from dystrophic chicken muscle is complicated by the finding that chicken muscle microsomal membranes obtained following sucrose density centrifugation show a large non-calcium dependent ATPase activity. Present evidence indicates that a major portion of this ATPase activity is related to the sarcoplasmic reticulum fraction, however, contamination by mitochondrial membrane fragments as well as by other membrane fragments has not been ruled out. Poly-acrylamide gel electrophoresis of normal and dystrophic membrane preparations showed a strong band identified as the 106,000 dalton ATPase protein. Several faint, lighter bands were also seen in both preparations. Freeze-etch micrographs of dystrophic membrane preparations showed a characteristic difference from normal membrane preparations. Dystrophic membranes show a significantly lower density of 80 Å membrane particles (identified as the ATPase enzymes) than do normal membrane preparations. While a decreased particle density could be related to functional differences between normal and dystrophic muscles, such a conclusion requires more certain information on preparation homogeneity than is presently available.

(Supported by grant HL-12978 from NHLI.)

COLLATERAL VENTILATION-EFFECT OF POSITION ON RESPONSE TO HYPOXIA AND CO_2. G.K. Batra*, R.J. Traystman*, H. Rudnick* and H.A. Menkes. The Johns Hopkins Medical Institutions, Baltimore, MD. 21205.

The mechanics of collateral ventilation were studied in anesthetized paralyzed dogs. A double lumen catheter obstructed a peripheral bronchus. Through one lumen, compressed air or 5% oxygen (hypoxia) was administered locally at a constant flow ($\dot{V}$). Through the other lumen, pressure (Ps) was monitored. At functional residual capacity, resistance to collateral flow (R_{coll}) = $Ps/\dot{V}$. The time constant for collateral ventilation (T_{coll}) was the time for Ps to fall 63% when $\dot{V}$ was stopped. Both R_{coll} and T_{coll} increased with hypoxia ($p < 0.05$). When the studies were done in a dependent portion of lung, R_{coll} increased from 0.057 $\pm$ 0.033 cm H_2O/ml/min with compressed air to 0.078 $\pm$ 0.039 cm H_2O/ml/min ($p < 0.05$) with hypoxia. In nondependent portions of lung, R_{coll} increased from 0.023 $\pm$ 0.004 cm H_2O/ml/min to 0.027 $\pm$ 0.005 cm H_2O/ml/min (p = N.S.) with hypoxia. The percentage increase was greater in the dependent region ($p < 0.05$). The increase in R_{coll} and T_{coll} with hypoxia was not abolished with the administration of atropine. In previous experiments, we found that 5% CO_2 produced a decrease in R_{coll} and that the percentage decrease was greater in the nondependent portion of lung (Fed. Proc. 34(3), 1975). Thus, the response to hypoxia is greater in dependent portions of lung where perfusion is higher and the response to CO_2 is greater in nondependent portions of lung where the ratio of ventilation to perfusion is higher. It is possible that hypoxia acts by decreasing local perfusion especially in high perfusion areas, producing a fall in CO_2 tension. This would explain our previously reported finding that 5% CO_2 abolishes the increase in R_{coll} produced by hypoxia.

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EFFECTS OF WEAK LOW FREQUENCY ELECTRIC FIELDS ON CALCIUM EFFLUX FROM ISOLATED CHICK AND CAT BRAIN. S.M. Bawin* and W.R. Adey, Depts. Anatomy & Physiology and Brain Research Institute, University of California Los Angeles, 90024

Freshly isolated chick cerebral hemispheres were equilibrated with a calcium Ringer's solution containing $^{45}Ca^{2+}$ for 30 min. Washed tissue portions were then exposed to sinusoidal electric fields at either 1,6, 16 or 32 Hz, with electric gradients of 5,10, or 56 V/M in air for each frequency for 20 min. $^{45}Ca^{2+}$ efflux was then measured in 0.2 ml of supernatant, and compared with efflux from unexposed control samples. All tissues were maintained at 36C, and checked for specific activity after the experiments. A frequency sensitive "tuning curve" showed sharply reduced efflux of 15 to 20 per cent at 6 Hz ($p<0.05$) and 16 Hz ($p<0.01$) for 10 V/M fields. Similar but slightly smaller reductions ($p<0.05$) occurred at 56 V/M. Threshold was around 10 V/M, but non-significant trends occurred at 5 V/M. Cat visual, auditory, suprasylvian and sensorymotor cortex tested at 1,6,16,32 or 75 Hz, 56 V/M showed significantly decreased effluxes at 6 Hz ($p<0.05$) and 16 Hz ($p<0.01$), but with non-significant trends at all other frequencies tested. At 10 V/M, non-significant decreases occurred at 6 and 16 Hz. Oscillating ELF fields at 6 to 30 Hz thus reduce Ca efflux, whereas weak VHF fields amplitude modulated at the same frequencies increase efflux (Bawin, Kaczmarek and Adey, 1975). A model for both effects based on cooperative interactions of Ca with fixed charges on stranded biopolymers is proposed. Tissue components of these fields in a phantom monkey head averaged 0.1 μV/cm. We have reported interactions of Ca, glutamic acid, GABA and taurine in cerebral tissue (Kaczmarek and Adey, 1973, 1974, 1975). Supported by Contract N 00014-69-A-0200-4037 ONR, Contract USPHS 1 RO1 FD 678-01 with BRH and Contract AF F-44620-75-C-0030 with AFOSR.

GLUCOCORTICOID UPTAKE BY MYOCARDIAL SLICES. Anthony C. Beardsley,* Minoru Okuda* and Allan M. Lefer. Dept. of Physiology, Jefferson Med. College, Thomas Jefferson Univ., Philadelphia, PA 19107

Uptake of dexamethasone (DEXA) and methylprednisolone (MP) was studied in cat left ventricular slices. Glucocorticoid concentrations in the incubation medium were 0.171 mM DEXA and 0.805 mM MP, equivalent to those employed in myocardial infarction. Left ventricular tissue was washed and sliced (0.5 mm thickness), and incubated in Krebs-Henseleit solution with 10 mM glucose gased with 95% O_2 and 5% CO_2. Uptake of tritiated DEXA or MP was calculated by liquid scintillation counting techniques. At 37°C, both glucocorticoids showed a significant increase in uptake by cardiac tissue. After 60 minutes of incubation, steroid uptake (corrected for extracellular space by the use of ^{14}C-sorbitol) plateaued at 0.21 μ moles DEXA/g tissue and 0.95 μ moles MP/g tissue. Incubation at 0°C however, retarded steroid uptake, by about 50% (0.1 μ moles DEXA/g tissue, 0.5 μ moles MP/g tissue at 60 minutes). Increasing the concentration of either glucocorticoid resulted in a linear increase in the uptake of that steroid. The optimal pH range for uptake of glucocorticoids was 7.3-7.4. Incubation in the presence of metabolic inhibitors (i.e., 95% N_2 + 5% CO_2, 2,4-DNP 0.5×10^{-2}M) produced no significant changes in glucocorticoid uptake by the heart slices. Incubation in the presence of SH-inhibitors (i.e., PCMB, 1.2×10^{-2}M; KSCN, 0.1 M) slightly reduced steroid uptake. In conclusion, myocardial cells are capable of accumulating large quantities of glucocorticoids. Most of their uptake appears to be a non-specific binding to cellular components. The uptake process does not appear to be an energy dependent phenomenon. These data are consistent with the membrane stabilizing action of these glucocorticoids in acute myocardial infarction.

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MECHANISM OF "SYMPATHOLYSIS" IN EXERCISING SKELETAL MUSCLE. Orren Beaty III*, Gertrude M. Tyce* and David E. Donald. Mayo Clinic and Foundation, Rochester, Minnesota 55901.

The mechanism of the reduced vasoconstrictive responses to sympathetic stimulation (SS) or to intra-arterial norepinephrine (NE) observed during the early minutes of simulated exercise (22% and 36% of steady state values, respectively) were studied in the dog hindlimb, contracting rhythmically in response to electrical stimulation, and perfused at constant flow. The venous-arterial difference in plasma K^+ across the hindlimb muscle bed increased from 0.06 mEq/l at rest to 0.75 mEq/l at 2.5 minutes of exercise. Thereafter, it declined to a steady state value of 0.2 mEq/l by 27 minutes. The vascular response to SS or NE during this period of exercise was temporally and inversely related to the release of potassium from the exercising hindlimb. There was no significant difference in the amount of fluorometrically determined norepinephrine released by SS at 3 minutes (5.33 ± 1.58 ng/ml) and at 32 minutes (3.75 ± 0.85 ng/ml) of exercise. After 30 minutes of exercise when the vascular response to SS or NE had reached a steady state, venous plasma K^+ was increased by intra-arterial infusion of KCl, to levels similar to those observed in the first moments of exercise. This significantly reduced the vasoconstrictive response to SS by 22.3 ± 8.66% and to NE by 23.6 ± 4.5%. These data suggest that the reduced ability of alpha adrenergic stimulation to constrict muscle resistance vessels in the early stages of exercise is due to a direct effect on the alpha receptor of K^+ released from the contracting skeletal muscle cells, and not to a reduction in the amount of NE released by SS. (Supported in part by NIH grants HL 6143, HL 00168, and NS 9143.)

A CHRONIC PREPARATION FOR HIGH FIDELITY LEFT VENTRICULAR PRESSURE MEASUREMENT IN NON-THORACOTOMIZED DOGS. J.W. Beazell* and J.M. Criley* (SPON: J.M. Tormey) UCLA School of Medicine, Los Angeles, CA 90509

In the past we have chronically implanted fluid filled catheters in the left atrium (LA) and left ventricle (LV) of dogs via the intra-atrial septum. Modifying this technique to introduce a catheter-tip transducer (CTXD), we have implanted these devices to take high fidelity recordings of pressures in the LV of conscious, non-thoracotomized dogs. The technique uses a 7 Fr. bore polyethylene sheath sharpened at the distal end, which is advanced down the jugular vein to the right atrial septum at the fossa ovalis. A transseptal needle is advanced down the sheath to perforate the septum, the sheath passed over the needle into the LA and the needle withdrawn. A CTXD is inserted into the LV, and the sheath withdrawn. Fluid filled catheters can be placed in the LA and the aorta to confirm pressures from the CTXD. The catheters are tunneled under the skin to exit at the dogs side. After suturing the wounds and placing the catheters in a jacket, the dog is allowed to recover. Placement of the CTXD has been accomplished 6 times. Survival of the preparation has been up to two weeks. No mortality resulted from placement of the CTXD. Post mortum examination revealed no perceivable clot formation on the CTXD. The point of passage through the septum was sealed around the CTXD and little trauma could be detected. Commercially available CTXDs have top frequency responses of 1-25kHz, an acceptable response for measuring dp/dt. Preliminary studies, using the CTXD as described, have yielded an average dp/dt of 2902 mmHg/sec conscious and 2168 mmHg/sec anesthetized dogs. We conclude that this can be a useful chronic preparation for studying LV hemodynamics in the conscious, unthoracotomized dog.

ALVEOLAR SURFACTANT CHANGES IN CATS EXPOSED TO ACUTE STRESS. D.L. Beckman, D.R. Bergren* and J.D. Sexton*. Dept. Physiology, Univ. North Dakota, Grand Forks 58202.

Previous work has shown that sympathetic stimulation via the stellate ganglion in cats as well as sudden lethal head injury by captive bolt and also hyperbaric oxygen exposure (6 atm, 30 min) results in a high minimum surface tension (ST) in the absence of any change in lung water content as indicated by lung wet wt/dry wt and lung wt/body wt ratios. The results from the present experiments, carried out to determine a possible cause of these ST changes, showed a striking cholesterol increase in these acutely stressed cat lungs. Normal total cholesterol levels in 30 ml of lung wash from 14 cats was 1.3 ± 0.2 (SE) mg vs 7.0 ± 1.6 in 5 stellate stimulated cats ($P < 0.001$), 4.3 ± 0.6 in 6 cats exposed to mechanical head injury ($P < 0.001$), and 3.3 ± 0.3 in 8 cats exposed to hyperbaric oxygen ($P < 0.001$). Min ST values for the 14 controls averaged 4.4 ± 1.1 dynes/cm and for the 3 stressed groups 20.0 ± 1.3, 20.2 ± 2.5, and 20.0 ± 1.6, respectively ($P < 0.001$). Addition of as little as 0.04 micrograms cholesterol to control lung wash fluid raised the min ST to 18.5 dynes/cm. Most (85%) of the increase in wash fluid total lipid content in stellate stimulated cats was accounted for by cholesterol. Lung wet/dry and lung wt/body wt ratios showed a slight decrease in response to this stress tending to rule out edemagenic factors. The results from the present study suggest that high alveolar cholesterol levels may account in part for pulmonary changes following exposure to acute stress. [Supported by ONR Contract No. N00014-68-A-0499 (NR 101-753)]

FRUCTOSE DIPHOSPHATASE FROM KIDNEY AND LIVER OF A DIVING MAMMAL, THE HARBOR SEAL. H.W. Behrisch* and R. Elsner. Institutes of Arctic Biology and Marine Science, University of Alaska, Fairbanks, Alaska 99701.

Renal blood flow is drastically reduced in the diving harbor seal (*Phoca vitulina*). Isolated perfused kidneys of this species have been shown to tolerate prolonged warm ischemia much better than dog kidneys (Halasz, Elsner, Garvie and Grotke, Am. J. Physiol. 227, 1331-1335, 1974). This study was undertaken to look for cellular adaptations related to regional ischemic tolerance in the seal. The regulatory properties of fructose diphosphatase (FDPase) from liver and kidney were examined. In both tissues of the seal the enzyme occurs as one form with a pI of 5.85. Seal FDPase has a pH optimum near 7.0 and is relatively insensitive to pH in affinity for substrate; Km for FDP is 20 μM at pH 7.4 and 25 μM at pH 6.8, a pH value likely to occur at the end of a long dive. An activator of FDPase, phosphoenolpyruvate (PEP), reduces the apparent Km for FDP over a pH range from 6.5 to 7.5 and also enhances the degree of interaction between the substrate binding sites; nH values are around 2 in the absence of PEP and are between 3 and 4 in the presence of 100 μM PEP. Seal FDPase is inhibited by 5'AMP but appears to have a low affinity for the inhibitor over a wide pH range. PEP reduces FDPase-AMP affinity and also maintains Km for AMP independent of pH. These observations, particularly the marked insensitivity of the enzyme to large pH changes, which contrasts strongly with that of the non-diving mammal, suggest a mechanism for extended control by this key enzyme in the diver. (Supported by NSF grant GB 20476, NSF grants to Scripps Institution of Oceanography in support of the Alpha Helix Program, and by NIH Grant HL 16020)

EFFECTS OF RANDOM AND SELECTIVE REMOVAL TRAPPING ON ADRENAL AND REPRODUCTIVE RESPONSES OF WILD DEER MOUSE POPULATIONS. R.W. Belknap*, M. Ryan-Kline*, and R.V. Andrews. (SPON: H.J. Phillips) Creighton U., Omaha, NE 68178.

Cycles in breeding and endocrine function follow seasonal patterns in undisturbed, wild Peromyscus populations. Such populations maintain numbers at constant levels by precisely regulating breeding and recruitment. When mouse density is altered by removal trapping a higher fertility and fecundity rate is apparent among resident animals. When both density adjustment and juvenile removal are managed by removal trapping, the fertility and fecundity rates remain high well into the winter season. Although the onset of winter is ordinarily accompanied by a suppression of reproductive hormones and behavior, such suppression is not seen as early and in as many animals when population density was decreased. Moreover juvenile removal from the population modified the usual adrenal response to cold onset. Seasonal adrenal secretory responses appear to be affected by changes in both social and climatic factors, and appear to be more sensitive to juvenile emergence than to other density related or physical environmental challenges.

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FAILURE OF LIVER DENERVATION OR INTRAPORTAL GLUCOSE INFUSIONS TO EFFECT FOOD INTAKE IN DOGS. L.L. BELLINGER* and L.L. BERNARDIS* (SPON: J.M. Bode) Dept. of Surgery, SUNY at Buffalo, N.Y. 14215.

Hepatic glucoreceptors have been hypothesized to control food intake. In the 23 hr. fasted dog 3 gm. of intraportally infused glucose has been reported to produce anorexia for at least 40 min. (Russek, M. Physiol. Behav. 5:1207.1970). Increases in the level of hepatic glucose are theorized to decrease neural activity in the glucoreceptors and the lack of neural activity is thought to result in satiety. Transection of hepatic nerve fibers should result in either aphagia or hypophagia. Eleven mongrel dogs (16-22Kg) were conditioned for 6 wk. before the study began. These animals were then fed for one hour a day only ad libitum for 7-8 days and the time of their onset of eating and their hourly intakes were measured. At the end of this period a total denervation of only the liver was attempted on 6 of the dogs. At the same time, the portal vein was cannulated and the polyethylene cannula was exteriorized. Five dogs were sham-operated and also cannulated. All denervated and sham dogs returned to within one standard deviation of their pre-operative food intake levels by 8 days post-surgery. After a 23 hr. fast the denervated and sham dogs were infused with either 6,12, or 25 gms of glucose and the dogs were presented with food 3-10 min. later. Only one trial was run on each dog a day. In 20/20 trials the denervated dogs began eating within 30 sec. of food presentation, while this was observed in 22/22 trials on the sham dogs. In both groups once feeding began it lasted for at least 3 min. These results question the existence of hepatic glucoreceptors or cast doubt on their role as a major controller of food intake.

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NOREPINEPHRINE AND CORONARY VASCULAR DYNAMICS. F.L. Belloni, R.E. Smith*, and H.V. Sparks. Univ. of Michigan, Ann Arbor, Mich. 48104

Norepinephrine (NE) has several effects on the coronary circulation-direct vasoconstriction and vasodilation mediated via vascular alpha and beta adrenergic receptors and vasodilation due to increased metabolic activity mediated via myocardial beta receptors. In order to ascertain whether the alpha constrictor effect has a net slowing effect on the coronary vascular response to NE, we compared the time courses of myocardial oxygen consumption ($\dot{V}O_2$) and coronary vascular resistance following intracoronary infusions of NE (0.5-5 ug/min) and isoproterenol (ISO, 1-2 ug/min). We used an open-chest dog heart preparation in which the left main coronary artery was pump perfused with blood at constant flow. Coronary perfusion pressure (CPP) and coronary sinus O_2 content (cs_{O_2}) were continuously monitored. We viewed the time course of changes in $\dot{V}O_2$ as indicating the arrival of drug at the tissue. After corrections were made to account for the effects of vascular transit between tissue and sinus sampling site, we found that the vasodilation accompanying NE infusion lagged behind the change in metabolic activity ($t_{\frac{1}{2}}$ for cs_{O_2} = 42.1 ± 1.9 sec; $t_{\frac{1}{2}}$ for CPP corrected for vascular transit = 48.1 ± 2.5 sec; $p < .05$, n = 5 dogs). This supports the hypothesis that the vasodilation seen is metabolic in origin. In contrast, the vascular and metabolic time courses are not significantly different from one another with ISO infusion ($t_{\frac{1}{2}}$ for cs_{O_2} = 51.8 ± 4.5 sec; $t_{\frac{1}{2}}$ for corrected CPP = 47.0 ± 5.7 sec; $p > .2$, n = 5). We conclude that alpha vasoconstriction results in a net slowing of the coronary vascular response to NE. This may exaggerate the transient discrepancy between O_2 utilization and O_2 supply observed following step increases in heart rate (The Physiologist 17: 178, 1974). (Supported by USPHS grant HL 16760.)

PATHOPHYSIOLOGICAL RESPONSES OF THE RHESUS MONKEY TO LIVE ESCHERICHIA COLI. Bruce Benjamin*, Linda T. Archer*, Beverly Beller*, J. J. Coalson*, and L. B. Hinshaw. (SPON: G. A. Brecher). V.A. Hosp. and Dept. Physiol. and Biophys., U. Okla. Hlth. Sci. Ctr., Okla. City, Okla.73190

Progressive hypoglycemia has been documented in this laboratory in both canine and subhuman primate animal models. The purpose of the present study was to develop a model more applicable to the clinical patient. Eleven lightly anesthetized unrestrained rhesus monkeys were monitored for a twenty-four hour observation period. Doses of E. coli varying from 7.6×10^9 to 3.0×10^{11} organisms/kg were infused over a thirty minute period and hemodynamic, respiratory, and metabolic parameters were monitored. Controls administered saline survived the twenty-four hour period with minimal changes in measured parameters. Two of the nine experimentals survived the E. coli while remaining animals died between three and twenty-seven hours. Results revealed two patterns of response: acute death and prolonged life. The acute response was characterized by marked hypotension, hypoglycemia, hypoinsulinemia, decreased pH, increased lactate and respiratory depression. The other response revealed sustained hypotension, hypoglycemia and hypoinsulinemia in some but not all animals and elevations in lactate, BUN, potassium, creatinine, SGOT, LDH, and F-LDH. Renal fibrin thrombi, prominent in baboons administered E. coli were absent in the rhesus monkey regardless of dosage. This study suggests the operation of a multifactorial mechanism of septic shock with interactions between hemodynamic and metabolic factors varying within the primate species. (Supported by V.A. Hosp. and U.S. Navy Contract N00014-68-A-0496).

EFFECT OF CHRONIC CO EXPOSURE ON LEFT VENTRICULAR CONTRACTILITY IN THE RAT. M. L. Benjamin* and D. G. Penney. Univ. of Ill. at Chicago Circle, Chicago, Ill. 60680

Depressed contractile function is reported in myocardium hypertrophied from pressure-overload, whereas normal contractility is associated with volume-overload hypertrophy. The present study examined possible alterations in contractile function in CO enlarged left ventricles (LV). Compared to 12 controls, continuous exposure of 15 rats to 500 ppm CO (COHb = 37.8%) for 7 - 8 weeks produced 49.1% and 16.2% increases in Hb and wet weight of the LV + septum, respectively. Testing involved a modified Langendorff non-recirculating perfusion apparatus containing Krebs-Ringer bicarbonate solution plus 5 mM glucose (27 - 30°C). Hearts were paced at 240 beats/min. and pressure changes monitored via a latex balloon in the LV. After initial oxygenation for 30 min, hearts were made anoxic for 10 min, followed by 30 min. of oxygen recovery. CO-exposed LV showed significantly depressed max. dP/dt and max. systolic pressure (Pmax) values compared with controls during preanoxia and aerobic recovery, but not during anoxia. Mean preanoxic Pmax for CO-exposed LVs was 54.3 $\pm$ 2.6 mmHg, while control was 69.2 $\pm$ 3.2 mmHg. Percent of mean preanoxic Pmax was significantly higher for CO LVs compared with controls during min. 3 (69.0 $\pm$ 1.8 vs 52.3 $\pm$ 1.9) and 9 (50.9 $\pm$ 2.5 vs 43.6 $\pm$ 2.2) of anoxia. Also, time from onset of anoxia to 0.67 preanoxic Pmax was significantly prolonged in CO LVs (2.80 $\pm$ 0.37 min. vs 1.19 $\pm$ 0.21 min.). Since CO and control Pmax fall to similar values during anoxia, the maintenance of a higher proportion of preanoxic Pmax during anoxia in CO LVs is attributable only to their initially depressed values. Time from onset of stimulus to peak of contraction tended to be prolonged in CO LVs relative to control. Overall, LV contractility of the CO enlarged LV is diminished in oxygen, while similar to control during anoxia. (Funded by grant HL-16367, NHLI.)

THE PULMONARY INTERSTITIAL COMPARTMENT AND HYPOXIC PULMONARY VASOCONSTRICTION. J.L. Benumof*, J. Mathers*, and E.A. Wahrenbrock. Dept. Anesthesia, UCSD, La Jolla, CA 92037

We tested the hypothesis that the mediator of hypoxic pulmonary vasoconstriction (HPV) is released into the pulmonary interstitial compartment. In six mongrel dogs, the right main lymph duct was cannulated and pulmonary lymph collected during random periods of ventilation with F_IO_2= 1.0 and F_IO_2=0.08 (bilateral hypoxia). In 3 of these dogs lymph was also collected with one lung F_IO_2=1.0 but with the other lung F_IO_2=0.00-0.06 (unilateral hypoxia). The pulmonary lymph was tested on helically cut strips of pulmonary artery (prepared according to Gorsky, B.H. and T.C. Lloyd, J. Appl. Physiol. 23:683-686, 1967) which had been shown to react to serotonin. We found that 1 cc of the lymph collected during bilateral hypoxia and unilateral hypoxia caused a change in the resting tension of the vessel strip of 58±13 mg and 35±9 mg respectively, whereas 1 cc of lymph collected during hyperoxic conditions caused a tension change of -1±8 mg. We conclude that a vasoactive substance or substances is released into the pulmonary lymph during ventilation hypoxia and this may represent the mediator of HPV.

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VASCULAR REACTIVITY IN RENAL AND DOCA HYPERTENSIVE RATS. Kathleen H. Berecek* and David F. Bohr. Dept. Physiology, Univ. of Michigan, Ann Arbor, MI 48104. (Spon: R. L. Malvin)

Further studies were undertaken to determine if the changes in vascular smooth muscle sensitivity previously seen in renal hypertensive rats (RHR) (Fed. Proc. 34:920, 1975) could be demonstrated in another type of hypertension; and secondly, if changes in vascular reactivity seen in RHR to norepinephrine (NE) could be demonstrated for other vasoconstrictors. Constant flow perfusion with blood was carried out on single hindlimbs of RHR (n = 8), DOCA hypertensive rats (DHR, n = 6), and age, sex and weight matched normotensive (NR) controls (n = 8). Rats were studied 4-12 weeks after induction of hypertension. Vascular beds of both RHR and DHR demonstrated significantly ($p<.025$) greater resistances than NR both before (PRU_{100} = 29.4 ± 3.2, 29.6 ± 1.1, 19.5 ± 1.2, respectively) and after (PRU_{100} = 15.5 ± 2.1, 14.3 ± 6.6 and 9.3 ± 0.6) papaverine vasodilatation. In response to NE (.001 μg - 6.4 μg) DHR as well as RHR demonstrated significantly ($p<.0005$) greater maximum pressor responses than NR, a shift in the dose-response curves to the left and a lower threshold dose of NE for vasoconstriction. Threshold to maximum doses of serotonin (5-HT) (.00001 μg - 10 μg) were injected i.a. Although characteristics of the dose-response curves in RHR to 5-HT and NE were similar, the maximum response of RHR to NE was 1.6 times greater than NR, while to 5-HT it was 2.4 times greater. Haeusler, G. and Finch, L. (Arch. Pharm. 272:101, 1972) argue that structural change alone should potentiate the maximum responses to all agonists equally. A differential increase in responsiveness in RHR to two agonists adds further support to the hypothesis that distinct changes in vascular smooth muscle sensitivity as well as structural changes occur in hypertension. (Supported by NIH grant HL-03756 and PHS-4620.)

LATERALIZATION OF EVOKED PHRENIC ACTIVITY TO ELECTRICAL STIMULATION OF RESPIRATORY AFFERENTS

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We electrically stimulated right and left pharyngeal branch of the glossopharyngeal (PGLN), internal branch of the superior laryngeal (ISLN), and carotid sinus (CSN) nerves at various frequencies and intensities in anesthetized, paralyzed, artificially ventilated cats. We simultaneously recorded, averaged, and compared bilateral evoked phrenic nerve (PHR) activity. In paired comparisons low intensity stimulation of PGLN and ISLN during inspiration evoked a short latency excitation predominant in the contralateral PHR. This lateralized excitation had a latency of 5.2msec±0.2SE(16 cats) for PGLN, and 3.8msec±0.1 SE(13 cats) for ISLN. This excitation could be evoked at frequencies up to 100Hz. Stimulation during expiration, even at high intensities, did not result in a lateralized short latency excitation. The initial excitation is followed by bilateral inhibition of on going PHR activity. Both intravenous strychnine and picrotoxin did not prevent either the lateralized response or the inhibition, though a delayed bilateral excitation to high intensity PGLN stimulation was diminished after strychnine. This delayed (latency 18.7msec±0.7SE) bilateral excitation is what others have termed the sniff reflex. This excitation is also evoked during expiration. CSN stimulation did not result in lateralized excitation at conditions which produced marked increases in integrated PHR activity and changes in blood pressure. We suggest that the lateralized low threshold evoked response results from a gated paucisynaptic reflex pathway involving afferent fibers in the PGLN and ISLN, the respiratory neurons in the ipsilateral dorsal respiratory group, and contralateral PHR motorneurons. (Supported by USPHS Grants 5 F03 GM53152 and GM15571)

INFLUENCE OF CALCIUM CONCENTRATION ON THE MECHANICAL RESPONSE OF ISOLATED ATRIA TO TEMPERATURE VARIATION. S.R. Bergmann*, J.C. Torres, and E.T. Angelakos. Dept. of Physiology & Biophysics, Hahnemann Medical College, Philadelphia, PA 19102

Force-frequency and dF/dt-frequency determinations were performed on isometrically contracting rabbit left atria cooled from 30° to 21° C. With normal bath calcium (2.16 mM), peak developed force (F) increased progressively to a maximum at 21°. Peak rate of F development (dF/dt), electronically obtained, increased to a maximum at 25° and then declined. At 21°, the dF/dt of atrial preparations in 2.16 mM Ca was significantly lower than 30° values. Substituting 1.8 or 1.0 mM Ca for the normal concentration yielded qualitatively similar responses to cooling. At 30°, these low-Ca preparations exhibited lower values of F and dF/dt than normal-Ca preparations at all frequencies studied. However, with cooling, F and dF/dt in these low-Ca preparations showed proportionally greater increases than normal-Ca preparations, with maximal values still occurring at 21° and 25° respectively. Peak dF/dt values at 21° of the low-Ca preparations were greater than 30° levels, but not significantly so. Time to peak force development (TTP) was increased with cooling with no significant difference among the three concentrations of calcium used. Warming atria from 30° to 40° resulted in force-frequency and dF/dt-frequency curves that were progressively depressed at all Ca concentrations. The data substantiates that with moderate cooling, F, dF/dt, and TTP increase in the isolated rabbit atria, and suggest that these responses to cooling are not critically dependent on the Ca concentration.
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STUDIES OF FACTORS RESULTING IN AMMONIA ELEVATION IN HYPOXIA AND SUPERIMPOSED HYPERCAPNIA. R.A. Berkman*, and R.E. Dutton. Dept. Physiology, Albany Medical College, Albany, N.Y. 12208

Previously we reported that systemic hypercapnia resulted in an elevation of the systemic arterial NH_3 concentration via NH_3 release from the intestine (Fed. Proc. 34: 430,1975). The present study was designed to determine both the effect of hypoxia alone and with hypercapnia (HH) on systemic arterial NH_3 concentrations. Ten mongrel dogs (30-40 Kg.) were anesthetized, artificially ventilated, and electromagnetic flow probes were placed on the portal vein(PV) and hepatic artery(HA). At the end of 30 min. of 6% O_2 inhalation, arterial NH_3 rose from 167.7 µg % to 182.9 µg % ($P<.01$) while PaO_2 decreased from 88.2 mm Hg to 34.5 mm Hg ($P<.01$). The effect of 6% O_2 + 6% CO_2 inhalation was to raise the arterial NH_3 concentration from 170.7 µg % to 196.6 µg % ($P<.01$). $PaCO_2$ increased 30 mm Hg to 63.3 mm Hg ($P<.01$) and the PaO_2 decreased from 47 mm Hg to 41.6 mm Hg ($P<.01$). Hypoxia alone resulted in a 529.0 µg/min ($P<.05$) decrease in NH_3 uptake from the intestine and a 640.5 µg/min ($P<.01$) decrease in liver uptake of NH_3 below controls. In contrast, superimposition of hypercapnia resulted in a 476 µg/min ($P<.05$) increase in the mean NH_3 uptake from the intestine, and a 337.6 µg/min ($P<.05$) increase in the mean liver uptake of NH_3 above control. PV flow decreased from 527.0 ml/min to 381.2 ml/min ($P<.01$) in hypoxia and increased from 514.5 ml/min to 713.7 ml/min ($P<.01$) in HH. These results indicate that the rise in arterial NH_3 during hypoxia is at least in part a result of decreased liver uptake of NH_3. Superimposition of hypercapnia appears to increase NH_3 release from the intestine. Part of this NH_3 load is either shunted past parenchymal liver cells, or exceeds their ability to extract the NH_3. (Supported by USPHS Grant HL 12564.)

REPTILIAN FEBRILE RESPONSE. H.A.Bernheim* and M.J.Kluger. Dept. Physiology, Univ. of Michigan Medical School, Ann Arbor, Mi. 48104

We previously reported that the lizard Dipsosaurus dorsalis would develop a fever in response to an injection with dead Aeromonas hydrophila, by shuttling between a hot and cold side of a chamber. In order to determine if Dipsosaurus would develop a fever when placed in an environment more closely resembling the natural desert, a simulated desert was designed in which night (1800-0600 h) T_a= 12°C and day (0600-1800 h) T_a= between 30 and 55°C depending on the location within the chamber. Injection of 6 lizards with dead Aeromonas (0.2 ml of $2x10^{10}$ bacteria/ml) led to a body temperature averaging 40.3°C over a 9 hour period following the injection, some 3.6°C higher then the control lizards' body temperature. Further investigations on the response of Dipsosaurus to Aeromonas infection were conducted at the Univ. of Wisconsin's Biotron where there exists a simulated desert environment with the light intensity, temperature, and humidity closely paralleling a typical southwestern desert spring day (see Porter et al., Oecologia 13, 1-54, 1973). Injection of 7 lizards with the dead bacteria led to an average body temperature of similar magnitude (40.5°C) but with a longer latency then that found at the Univ. of Michigan. Injection of 5 lizards with live Aeromonas (0.5 ml of $1x10^{10}$ bacteria/ml, sub-cut.) in the simulated desert at Michigan, led to a daytime fever averaging 3.1°C (mean b.t.= 41.1°C) over a 5 day period. On the 6th-7th day, each lizard's body temperature returned to the normal or afebrile level. Injection of sodium salicylate (0.2 ml of 75 mg/ml) along with dead Aeromonas resulted in the attenuation of the normal febrile response. These results demonstrate a striking similarity among reptilian, avian and mammalian fever and suggests a common origin and perhaps function for the febrile mechanism. Supported by NSG GB 42749X.

VENTILATORY ACCLIMATIZATION OF NORMAL PONIES DURING FOUR DAYS OF EXPOSURE TO HYPOXIA. G.E. Bisgard, H.V. Forster, J.A. Orr*, D.D. Buss* and B. Rasmussen*. Dept. of Vet. Sci., Univ. of Wisconsin, Madison 53706 and Dept. of Env. Med., Medical Coll. of Wis., Milwaukee, 53226

In previous studies, we found $\dot{V}_E$ of normal awake ponies after 4 days of altitude sojourn (3400 and 4300 m) to be unchanged from sea level, but Pa_{CO_2} at altitude was 8-12 mmHg lower than at sea level. Accordingly, to determine whether ventilatory acclimatization to hypoxia (H) does indeed occur in ponies, 4 normal ponies were studied in a hypo/hyperbaric chamber after 2 days at 740 mmHg and then repeatedly during 4 days at 460 mmHg. The major reduction in Pa_{CO_2} during H occurred during the first hr (Δ-6.9 mmHg, $P<.05$), but there was a further 4-6 mmHg reduction ($P<.05$) evident by 21 hrs which was sustained for the duration of H. This pattern of change was consistent over all ponies. In contrast, changes in $\dot{V}_E$, $\dot{V}_A$, and $\dot{V}_{CO_2}$ were more variable (measured only after 5, 21, 44, 68, and 92 hrs). In 3 ponies $\dot{V}_E$ and $\dot{V}_A$ increased between control and 5 hours of H (44 and 35%), and between 5 and 21 hrs (35 and 17%), and $\dot{V}_{CO_2}$ remained unchanged over this time period. In the fourth pony $\dot{V}_E$ increased 115%, $\dot{V}_A$ remained unchanged, but $\dot{V}_{CO_2}$ decreased 25%. In all ponies, $\dot{V}_E$ was lower after 44 hrs than at 21 hrs and it continued to decrease progressively to near normal levels at 92 hrs. After 21 hrs of H, $\dot{V}_A$ and $\dot{V}_{CO_2}$ tended to decrease in parallel but the changes were not progressive nor consistent over all ponies. Calculated P_{ACO_2} (from $\dot{V}_{CO_2}/\dot{V}_A$) closely paralleled Pa_{CO_2} throughout the period of H in all ponies. We conclude that changes in $\dot{V}_{CO_2}$ during H can mask the ventilatory stimulus associated with altitude sojourn and that changes in Pa_{CO_2} provide a valid index of the hypoxic response and of ventilatory acclimatization to H. (Supported by PHS Grant HL15473)

THE ROLE OF NEURAL FACTORS IN THE CARDIOVASCULAR RESPONSE TO ACUTE VOLUME LOADING. Vernon S. Bishop and D. Fred Peterson, Dept. Pharmacology, University of Texas Hlth. Sci. Ctr., San Antonio, Texas 78284

The influence of the cardiac sympathetic nerves (CSN) and arterial baroreceptors on the cardiovascular responses to acute volume loading (AVL) was investigated in 20 conscious dogs. All animals were previously instrumented with electromagnetic flow probes for measurement of cardiac output (CO), catheters for measuring left atrial pressure (LAP) and arterial pressure (AP). AVL increased LAP (15 mmHg), CO (+1439 cc/min), HR (28 b/min) and AP (13 mmHg) while decreasing peripheral resistance (PR) (-0.87 PRU, 37%). In 5 animals, baroreceptor denervation did not alter the above responses to volume loading. Surgical section of the sympathetic innervation to the heart, in 6 animals significantly reduced the ΔHR to volume loading (35 to 21 b/min) and, consequently, the CO was less (1863 to 977 cc/min). Since the AP response was unaltered, the decline in PR to volume loading was significantly less -0.52 PRU as compared to -0.88 PRU. In 5 animals, selective removal of the left CSN had no effect on the responses to AVL while in other animals, initial removal of the right CSN significantly reduced ΔHR response from 35 to 17 b/min. Vagal blockade resulted in a fall or no change in HR during AVL. However, a small positive ΔHR response to AVL was observed after combined vagal blockade and bilateral cardiac sympathectomy. Epinephrine infusions augmented the ΔHR response to AVL with or without cardiac sympathetic innervation. These observations suggest the ΔHR is mediated via the vagus and the magnitude is modulated by the cardiac sympathetic nerves. (Supported by NIH grant #HL12415-07 and AFOSR 71-2075).

PLACENTAL DIFFUSING CAPACITIES AT VARIED CARBON MONOXIDE TENSIONS. J.M. Bissonnette, W.K. Wickham* and W.H. Drummond*, Dept. Obstetrics & Gynecology, University of Oregon Health Sciences Center, Portland, Oregon 97201

In nine near term ewes under spinal anesthesia the umbilical circulation was perfused with adult sheep blood at 50 ml min^{-1}. Various quantities of blood equilibrated with carbon monoxide (CO) were added to the oxygenator. Alternately oxygenator (fetal) CO tension could be lowered by diluting with blood. Samples were drawn simultaneously from the umbilical artery, umbilical vein and maternal uterine vein. Blood CO content was determined by the standard ferricyanide method (Coburn et al, J.Appl.Physiol. 19:510, 1964). Fetal to maternal CO transfer ($\dot{V}_{CO}$) was calculated by the Fick principal. Placental diffusing capacity ($D_{P_{CO}}$) was estimated from $\dot{V}_{CO}$ divided by the difference in CO partial pressure between the umbilical vein and maternal uterine vein. Twenty four measurements of $D_{P_{CO}}$ were made at carboxyhemoglobin concentrations (COHb) in the umbilical artery between 2.5 and 70 percent. $D_{P_{CO}}$ at 2.5 to 25% COHb was 0.71 ± 0.39 ml min^{-1}/mm Hg per 100 grams of placental tissue (mean ± S.D.; n = 14). In contrast at COHb levels between 25 and 70%, in the umbilical artery, $D_{P_{CO}}$ fell to 0.36 ± 0.17 ($n = 10$; $p < 0.02$). In five preparations (14 measurements) we simultaneously measured the placental permeability of urea ^{14}C which decreased 8.4 ± 9.3 percent. This decrease, however, was related to duration of the perfusion and not to carboxyhemoglobin levels. We conclude that placental permeability of CO is in part due to facilitated diffusion and that the carrier is saturated at the higher tensions of carbon monoxide.
(Supported by grant HL-17150 from USPHS.)

MODE OF STIMULATION BY cAMP OF THE SODIUM EFFLUX IN BARNACLE MUSCLE FIBERS. E. Edward Bittar, Geoffrey Chambers* & Ronald Schultz†, Department of Physiology, Univ. of Wisconsin, Madison, Wisconsin 53706.

The radiosodium efflux in muscle fibers from Balanus nubilus is stimulated by the microinjection of cAMP. This response to cAMP is enhanced by pretreatment with ouabain and is observed with a cAMP concentration as low as 10^{-6}M. Ouabain, however, when applied after the onset of stimulation is without effect. This substantiates the seesaw theory. To find out whether the response involves a change in the Ca^{2+} gradient, experiments were done with EGTA and a Ca^{2+} free medium. Fibers pre-injected with 100 & 500mM-EGTA before 3 x 10^{-2}M-cAMP show 118.1 ± 22.9% (n=11) and 105.0 ± 8.4% (n=6) stimulation of the efflux. (Controls: 302.4 ± 44.6, n=9, $P < 0.01$ and 212.6 ± 24.1%, n=6, $P < 0.05$, respectively). Fibers bathed in a Ca^{2+}-free medium respond to injected 3 x 10^{-2}M-cAMP by showing 128.4 ± 8.6% (n=15) stimulation. (Controls: 348.0 ± 62.3%, n=8, $P < 0.001$). Replacement of external Na^+ by Li^+ fails to alter the response to cAMP. To test the idea that membrane phosphorylation is an absolute requirement, fibers were preinjected with the protein inhibitor of Walsh. The results show 80.5 ± 13.4% (n=16) stimulation by injected 3 x 10^{-2}M-cAMP (Controls: 378.9 ± 40.6%, n = 13). Fibers bathed in a Ca^{2+}-free medium and injected with 500mM-EGTA and protein inhibitor before 3 x 10^{-2}M-cAMP show 57.7 ± 19.1% stimulation (n=8). That phosphorylation of the fiber membrane also leads to Na:H exchange is suggested by the observation that protonation of a HEPES-containing medium augments the magnitude of the response to cAMP. As for the role of the adenyl cyclase system (ACS) in the cascade mechanism, this was investigated by employing ethacrynic acid (EA). The results show that EA completely abolishes stimulation by a raised pCO_2 of the ouabain-insensitive Na efflux into a Ca^{2+}-free solution as well as reduces the response of these fibers to injected cAMP.

RENIN RELEASE AFTER PAPAVERINE AND FUROSEMIDE IN CONSCIOUS SHEEP E.H. Blaine, Dept. Physiol., Univ. Pittsburgh, Pittsburgh, Pa. 15261.

Under sterile conditions a right nephrectomy was performed in 6 sheep and indwelling catheters were placed in the left renal artery and vein and into the ureter. A flow probe was placed around the left renal artery. After recovery, experiments were performed on the conscious animals 3-5 days following surgery. Statistical analysis compared the difference between experimental and control values using Student's t test. Papaverine (7 mg/ml) into the renal artery for 20 min (n=12) produced statistically significant changes in BP (4% decrease; $p<0.01$), RPF (8% increase; $p<0.01$) and GFR (21% decrease; $p<0.01$). Renal Na excretion decreased by an average of about 50% but was not significantly altered because of high variability. Renal venous minus arterial plasma (V-A) renin activity was 0.97±0.44 (mean±S.E.) ng AI/ml/hr during saline infusion into the renal artery and 0.69±0.33 during the papaverine infusion (N.S.). Increasing the papaverine to 10 mg/min in 6 experiments did not alter the variables further. In 4 animals approximately 1 mg/kg furosemide was injected IV while continuing the papaverine infusion. Increases in urine flow above control were continuously replaced by IV saline. Maximum renal Na excretion occurred at 40 min post furosemide injection and was approximately 4.6X greater than during the papaverine only infusion ($p<0.05$). V-A plasma renin activity difference also reached maximum at 40 min being approximately 3X greater than during the papaverine only infusion (4.46±1.46 vs 1.45±0.49; p 0.05). At this time there were no significant changes in BP, RPF or GFR. The data indicate that papaverine at levels which reduce GFR and increase RPF significantly, do not alter renin secretion. Further, furosemide stimulated renin release is not blocked by papaverine and this finding supports the concept of an intrarenal receptor sensitive to alterations in ion transport by the renal tubules. (Supported by HL-16483).

EFFECT OF L-DOPA ON PLASMA RENIN ACTIVITY AND BLOOD PRESSURE FOLLOWING PERIPHERAL DOPA-DECARBOXYLASE INHIBITION IN DOGS. M.L. Blair*, I.A. Reid and W.F. Ganong (SPON: R.H. Steinberg), Dept. Physiology, University of California, San Francisco, California 94143

Previous work from this laboratory has shown that clonidine acts within the central nervous system to lower plasma renin activity (PRA) and blood pressure (BP), possibly by stimulating alpha-adrenergic receptors. This study was undertaken to determine if catecholamines also act centrally to decrease PRA. L-DOPA (10-20 mg/kg) was administered I.V. to pentobarbital-anesthetized dogs 35 min after treatment with carbidopa (MK486), 20 mg/kg I.V. This DOPA-decarboxylase inhibitor does not cross the blood-brain barrier. Falls in renal perfusion pressure (RPP) were minimized by adjusting a supra-renal clamp. Carbidopa alone caused no change in PRA or BP, while the combination of L-DOPA (20 mg/kg) and carbidopa produced statistically significant decreases in PRA and BP as shown below:

time (min)	Control	+15	+30	+60	+90	+120
PRA (+)	19.3±2.8	13.1±2.0*	12.5±2.1*	11.3±2.5*	17.6±4.9	21.1±5.0
Syst BP	164 ±7	124 ±6*	125 ±7*	134 ±9*	144 ±10*	159 ±9
Dias BP	125 ±4	89 ±6*	91 ±7*	99 ±7*	109 ± 8*	124 ±6
RPP (mm Hg)	92 ±1	90 ±2	87 ±3	89 ±3	91 ± 2	92 ±1

*p<.02, Student's t-test, n=7. +ng angiotensin I/ml/3 hr. BP in mm Hg. A lower dose of L-DOPA (10 mg/kg) caused a smaller fall in BP which was not accompanied by a statistically significant change in PRA (n=8). L-DOPA without carbidopa increased renin secretion. These data support the hypothesis that stimulation of central adrenergic receptors decreases renin secretion. (Supported by USPHS grants NS00045 and AM06704 and the Skaggs Foundation).

EFFECTS OF INTRAVENOUS INFUSION OF CATECHOLAMINES ON PLASMA LH AND PROLACTIN. Charles A. Blake. Department of Anatomy, Duke University Medical Center, Durham, N.C. 27710

Dopamine (D), l-norepinephrine (N), l-epinephrine (E), or l-isoproterenol (I) was infused at a constant rate through an atrial cannula from 1345-1730 hr in unanesthetized proestrous rats and blood was withdrawn through a second cannula for radioimmunoassay of LH and prolactin (P). Infusion of D at .8, 8, 80, or 800 µg/hr did not interfere with the spontaneous LH surge or ovulation but the two highest doses blocked the spontaneous P surge and depressed basal P levels. After the end of infusion, plasma P rose rapidly. Infusion of N at .4, .8 or 8 µg/hr had no effect on the rises in plasma LH and P. Infusion of N at 80 µg/hr caused death in some of the rats. In those that survived, N partially suppressed the LH surge, did not block ovulation and suppressed the P surge but only after approximately 2 hr of infusion. Infusion of E at .0007 µg/hr had no effect on the two surges. However, in some rats given .007 or .07 and in all rats given .7, 7 or 70 µg/hr the LH surge and ovulation were blocked. The highest dosage did not alter pituitary LH release in response to administration of exogenous LRF but it did affect plasma P in a manner similar to that of N at the 80 µg/hr rate. Infusion of I at .2 µg/hr did not block ovulation or interfere with P release but it did suppress the LH surge. Raising the dosage of I to 0.7 µg/hr blocked LH release and ovulation without altering the rise in P. However, I infused at 20 or 80 µg/hr blocked both the LH and P surges. The results are consistent with the view that D may be PIF and indicate that E but not N is highly effective in inhibiting LH release by an action exerted either directly or indirectly on the brain. D and E may exert these effects by stimulating β receptors. (Supported by the Duke University Research Council and personal funds of the author.)

AMELIORATION OF POSTISCHEMIC ENCEPHALOPATHY BY SODIUM THIOPENTAL AFTER 16 MINUTES OF GLOBAL BRAIN ISCHEMIA IN MONKEYS. A.L. Bleyaert,* E.M. Nemoto, S.W. Stezoski,* H. Alexander,* and P. Safar. Dept. of Anesthesiology, University of Pittsburgh, Pittsburgh, PA 15261.

Recent studies suggest that barbiturates protect the brain from focal infarction, but has not been demonstrated after global ischemia in primates. We evaluated the effect of IV sodium thiopental (90 mg/kg) administered 5 min postischemia (PI) in our recently developed monkey model of 16 min global cerebral ischemia, with 7 days postischemic life support and monitoring. At five minutes PI, the sodium thiopental was infused over one hour with Levophed used to maintain normal arterial pressure. Neurologic deficit score, EEG, and intracranial pressure (ICP) were monitored and neuropathologic changes examined at sacrifice. Compared to our previously reported (Nemoto et al, Fed. Proc. 34:384, 1975) control (no therapy) studies, recovery in the pentothal treated group was remarkable. Neurologic deficit score in the nontreated monkeys ranged from 70% to 40% (maximum deficit 100%) for up to 7 days PI, whereas, in three of four pentothal treated animals, neurologic deficit score was less than 10% within 72 hrs and was essentially normal at 4 to 5 days PI. The other monkey received 70 mg/kg of pentothal and had a neurologic deficit score of 35% at seven days. While the control monkeys were unable to walk, sit, stand, or feed themselves at 7 days PI, the treated monkeys were normal. Brain histology and EEG changes were quantitated. In conclusion, sodium pentothal treatment after global cerebral ischemia ameliorates PI encephalopathy. Although the mechanism of pentothal protection is unkown, reduction of ICP and metabolic rate PI have been proposed. However, in the nontreated control studies significant elevation of ICP was not observed which suggests that its efficacy is not related to a reduction of ICP.

Ca^{++} FLUX IN BEATING HYPERPERMEABLE HEART MUSCLE CELLS. S. Bloom* (SPON. C. Baker). Dept. of Pathology, Univ. of South Florida College of Medicine, Tampa, Fla. 33620.

Beating myocardial fragments were prepared as previously described. Ca^{45} uptake and release were measured under conditions favorable for spontaneous beating. In phosphate-buffered medium containing 10 μM total calcium, uptake was ATP dependent and proportional to time, temperature and protein concentration. Concentration gradients of $[Ca^{++}]_i/[Ca^{++}]_o$ = 8,000 were generated, using a calculation based on cell calcium distribution in an estimated 4.7 ml total cell water/gm protein. This gives a gross underestimate of the gradient. At 25°C, the initial uptake rate was 5.4 nmoles/min/mg protein, corresponding to an influx of 50 μmoles of calcium/kg myocardium/beat at the observed contraction frequency of approximately 18/minute. The washout medium used for these experiments was similar to the uptake medium except that Tris buffer was substituted for phosphate so that re-uptake did not interfere with washout, and EGTA and calcium were sometimes added. By contrast to uptake, the initial Ca^{45} efflux rate, measured in prelabelled cells suspended in a large volume of unlabelled medium, was less than 0.2 nmoles/min/mg protein at 25°. This is less than 2 μmoles/kg myocardium/beat. The Ca^{45} washout rate increased with temperature between 0 and 35° and also increased if ATP was omitted from the medium. It is unlikely that the Ca^{45} influx measurements exclusively reflect "contractile calcium". However, the results are compatible with $[Ca^{++}]_o$ as the source of contractile calcium. Since the sarcolemmae of this preparation are permeable to calcium, the slow efflux either argues against a regenerative release mechanism or indicated that contractile calcium does not have full access to the sarcolemma. (Supported by Grant 74-867 from AHA, and HL-16956 from NHLI).

ACTION OF HUMAN GASTRIN I AND II (HGI, HGII), CHOLECYSTOKININ (CCK) AND VASOACTIVE INTESTINAL POLYPEPTIDE (VIP) ON THE PYLORO-DUODENAL JUNCTION (PDJ) OF DOGS. W. E. Bloomquist* and T-M Lin (SPON: P. Stark) Lilly Research Laboratories, Indianapolis, Indiana 46202.

Intralumenal pressure in the PDJ of the anesthetized and conscious dog was recorded with 3 open tip catheters. The catheter in the middle was located in the high pressure zone (HPZ) and the others were 1-cm on each side of the HPZ. In anesthetized dogs, infusion of synthetic 15-leu HGI at 0.25-2 μg/kg and pure natural HGI at 0.05-1.0 μg/kg over a 10-min period increased the amplitude of intralumenal pressure in all 3 catheters; baseline pressure on the antral side of PDJ was increased while that on the duodenal side was decreased by HGI at the high dose range. CCK infused at a dose of 0.25-4.0 units/kg over a 10-min period also increased the pressure-amplitude in all 3 catheters. In the conscious dog, natural HGI and II at 1-100 ng/kg both increased the pressure-amplitude in all 3 catheters. VIP reduced the intralumenal pressure in PDJ at 1-8 μg/kg when infused in a 10-min period. PDJ pressure recorded during continuous infusion of HGII 5-6 ng/kg-hr was inhibited by 4 and 8 μg/kg of VIP. Conclusion: HGI and II and CCK augmented intralumenal pressure in the PDJ of the dog. VIP decreased and counteracted the action of HGII.

Note: Pure natural Gastrin I and II prepared by Drs. R. A. Gregory and H. Tracy were distributed by Dr. M. I. Grossman of CURE, Los Angeles, California. CCK (20% pure) was obtained from Dr. V. Mutt of GIH, Karolinska Institute, Stockholm. VIP samples were the kind gifts of Drs. S. Said, U. of Texas Medical School, Dallas, Texas and Dr. V. Mutt of Karolinska Institute, Sweden.

RECIPROCAL CHANGES IN DUCK ERYTHROCYTE 2,3 DIPHOSPHOGLYCERATE (2,3-DPG) AND INOSITOL HEXAPHOSPHATE (IHP). T.A. Borgese and L.M. Lampert*, Dept. of Biological Sciences, Lehman College-CUNY, Bronx, N.Y. 10468.

Adult duck (Anas domesticus) and duckling red cells are unique in that they contain appreciable amounts of IHP and no measurable 2,3-DPG. We are now able to report that ion-exchange chromatography of neutralized trichloracetic acid (TCA) extracts of 22 day old duck embryo red cells reveals a considerable concentration of 2,3-DPG. The identification of this intermediate is based on (1) its elution position on the chromatogram and (2) the chromotropic acid test for 2,3-DPG as described by Bartlett. Also present, at this time, as the major phosphorylated intermediates are inorganic phosphate (P_i), ATP and IHP. Their respective concentrations are 2.25, 2.00 and 0.30 umoles/ml cells. The concentration of 2,3-DPG was 4.82. ADP was present in extracts from all age groups studied but represented a relatively minor component. The one day old duckling has no measurable 2,3-DPG and approximately 5.45 umoles of ATP and 1.74 umoles of IHP per ml of cells. Replicate experiments with adult duck red cell extracts indicate that ATP decreases somewhat to 3.15 umoles while IHP increases and reaches a stable value of about 4.54 umoles/ml cells. The reciprocal changes in 2,3-DPG and IHP during development in the duck may have some bearing on the mechanism of oxygen unloading from duck hemoglobins. It appears that these reciprocal changes in 2,3-DPG and IHP parallel the switch from embryonic to adult type hemoglobins.

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A QUANTITATIVE ANALYSIS OF GLYCOLYSIS AND THE PENTOSE PHOSPHATE PATHWAY IN TETRAHYMENA PYRIFORMIS STRAIN HSM. M.J. Borowitz*, R.B. Stein* and J.J. Blum, Dept. Physiology & Pharmacology, Duke University Medical Center, Durham, N.C. 27710

A detailed model of glycolysis and the pentose-phosphate pathway (PPP) has been developed. The equations allow computation of the flux of labeled and unlabeled carbon through these pathways under steady-state conditions and thus of the specific activity of each carbon of every intermediate. The model, which contains 18 independent flux parameters, was tested using T. pyriformis, which has transaldolase and transketolase but lacks the oxidative enzymes of the PPP. Cells in proteose-peptone medium were incubated for up to 80 min in a mixture of glucose (6 mM), fructose (6 mM), ribose (3 mM), and glycerol (3 mM). Each flask also contained one of 10 ^{14}C-labeled forms of these substrates. Twenty-seven measurements of label incorporation into CO_2, lipid, and glycogen were made. The $^{14}CO_2$ production from labeled glucoses, fructoses, and [1-^{14}C]ribose increased parabolically with time, in contrast to the linear time dependence of the other measurements made. The data were treated as if the system were in the steady state for short intervals during the incubation. The equations were programmed on a digital computer and sets of fluxes were found which gave good fits to the data for each interval. The analysis indicates that addition of sugars to these cells causes an approximately linear increase with time of the flux through phosphofructokinase. In addition, flux through the non-oxidative portion of the PPP is quantitatively significant and also increases with time.
(Supported by grant 5 RO1 HD01269 from NIH.)

THE EFFECT OF ELECTRICAL STIMULATION ON THERMOSENSITIVE PREOPTIC AND SEPTAL NEURONS. J. A. Boulant and H. N. Demieville.* Dept. of Physiol., Univ. of So. Fla. College of Med., Tampa, Fla. 33620, CIBA-GEIGY, Basel Switzerland and Pierce Fndn, New Haven, Ct. 06519.

In urethan-anesthetized rabbits, the responses of preoptic and septal single units were observed during changes in local, preoptic temperature, controlled by implanted thermodes. Each rabbit was also implanted with stimulating electrodes in three different locations; i.e., hippocampus, reticular formation, and either the lateral lemniscus or the lateral spinothalamic tract. Therefore, in addition to local thermosensitivity, each unit was tested separately for its response to electrical stimulation (0.3 - 1.0 Hz for 60-90 sec.) in each of the three locations. Approximately 30% of all units tested showed increases or decreases in their level of firing rate during electrical stimulation. Of these responsive units, most were affected by only one of the three stimulation sites, and the most predominant response was an initial excitation. Stimulation of the reticular formation elicited slightly more unit responses than did stimulation of the other sites. A relatively low proportion of the temperature-insensitive units was affected by electrical stimulation. This is in contrast to the warm-sensitive and cold-sensitive units, which showed a high incidence of response to electrical stimulation at the three sites. In some of these units, the response to preoptic temperature was determined before, during, and after extended electrical stimulation. Such determinations indicate that the electrical stimulation can alter the local thermosensitivity in some of the temperature-sensitive neurons. (Supported in part by NIH 5501 RR0574902 and ES00123.)

MEAT WRAPPER'S ASTHMA: EFFECTS OF FUMES OF POLYVINYL CHLORIDE ON AIRWAYS FUNCTION. H.A. Boushey*, Empey, D.W.*, and Laitinen, L.A.* (SPON. A.M. Rudolph). Univ. of California, Cardiovascular Research Institute and Department of Medicine, San Francisco, California 94143.

In 1973, Sokol et al suggested that workers employed as meat wrappers develop respiratory symptoms when exposed to the fumes of polyvinyl chloride (PVC) film cut with a hot wire (J.A.M.A. 226:639-641, 1973). Others have since reported that PVC fumes have little effect on pulmonary function. We studied the effects of PVC fumes on pulmonary function in ten meat wrappers who had respiratory symptoms attributed to their work. Each was exposed under simulated working conditions for 1 1/2 to 3 h. There was no significant change in total lung capacity or its subdivisions, in expiratory flow rates, in diffusing capacity, or in airway resistance (R_A). We tested airway reactivity to ten breaths of 0.2-1.6% histamine aerosol in each subject. Increased bronchial reactivity (a rise in R_A of more than 100% above control) characterized a subgroup which had more severe symptoms at work and a greater change in pulmonary function after exposure to PVC fumes. We then tested in all 10 subjects the effects of 1 1/2 to 3 hrs exposure to PVC fumes on bronchial reactivity to histamine. After such exposure the rise in R_A provoked by histamine increased from a mean of 32% to 125% ($p=0.01$) even though mean baseline R_A was not changed by exposure to the fumes (1.66 vs 1.73 cm H_2O/LPS; $p=0.49$). Our conclusions are: that increased bronchial reactivity to histamine characterizes patients who develop severe respiratory symptoms on exposure to PVC fumes; that inhalation of PVC fumes for periods up to 3 h does not alter pulmonary function in subjects with normal bronchial reactivity; and that such inhalation may itself induce a state of bronchial hyperreactivity. (Supported in part by HL-06285, HL-14201, and USPHS Fellowship F05 TW 2129).

EFFECT OF HINDLIMB ISOLATION PROCEDURE ON ISOGRAVIMETRIC CAPILLARY PRESSURE. R.A. Brace and A.C. Guyton. Dept. Physiol. & Biophys., Univ. Miss. Med. Ctr., Jackson, MS 39216.

Previously measured isogravimetric capillary pressures (Pci) in the dog hindlimb have averaged 15-16 mm Hg. However, past isolation procedures have involved 1-2 hrs of surgery, during part of which the hindlimb was denervated and autoperfused. After isolation the leg usually has been perfused at normal arterial (Pa) and venous (Pv) pressures for 1/2-1 hr before Pci was determined. The above may cause fluid to filter into the interstitial spaces, leading to an increase in interstitial fluid pressure and thus an increase in capillary pressure. We have examined the effects of the above procedures on Pci by very rapidly isolating the hindlimb with a clamp distal to the hip joint and by perfusing at reduced pressures during the stabilization period so that no weight changes occurred. Using these procedures Pci and plasma colloid osmotic pressure (πp) were measured in 4 groups of dogs. The average results ($\pm$ SE) are

	n	Pci	πP	πP - Pci
Limbs isolated immediately after anesthetization	11	8.8 $\pm$ .6	17.0 $\pm$ 1.0	8.2 $\pm$ .6
Isolated 1 to 2 hrs after anesthetization	6	13.5 $\pm$ .4	18.0 $\pm$ .5	4.6 $\pm$ .7
Anesthetized 1/2 hr, denervated 1/2 hr, then isolated	5	16.3 $\pm$ .7	17.5 $\pm$ .6	1.3 $\pm$ .9
Above plus perfused at normal Pa and Pv for 1/2 hr.	5	16.6 $\pm$ .8	18.0 $\pm$ 1.0	1.4 $\pm$ 1.1

These data suggest that previously measured isogravimetric capillary pressures may have been heavily influenced by the method of isolation.

EFFECTS OF RADIOPAQUE CONTRAST MEDIA ON THE BLOOD-BRAIN BARRIER: PHYSIOLOGICAL AND MORPHOLOGICAL CORRELATION. I.M. Bradley, G.T. Kitten, L.S. Holloway, P.R. Sterrett. Department of Physiology and Anatomy, Texas Tech University School of Medicine, Lubbock, Texas 79409.

Anesthetized rabbits were infused with a single bolus (0.25 cc) of Na diatrizoate (Hypaque 50) via the left internal carotid artery. A flow rate of .05 ml/sec. was used that would rinse the pial blood vessels of blood as confirmed by a burr hole in the left parietal region. The osmolality of the above contrast medium was 1.27 mOsm/ml. H^3 Inulin or horseradish peroxidase (HRP) was administered via the femoral vein prior to the bolus. Rabbits were sacrificed 5, 30 and 60 minutes after the contrast media infusion for physiological and morphological analysis of blood-brain barrier permeability and structural alteration. Uptake of H^3 Inulin in the brain parenchyma (esp. cerebral cortex and midbrain) and cerebrospinal fluid (CSF) was significant within 5 min. after the bolus infusion. Electron micrographs showed a shrinkage of adjacent endothelial cells of capillaries, arterioles and venules with a resultant opening of the tight junctions. Leakage of HRP through the opened junctions into brain extracellular space was observed. Increased pinocytosis was evident primarily in the arterioles. Brain edema, especially of the perivascular glial cells, became more apparent with time. The choroid plexus also showed shrinkage with a resultant increase of extracellular space between two adjacent choroidal cells. However, the apical tight junctions remained closed. Pinocytosis was increased significantly as shown with HRP. This increase is one possible explanation of the significant uptake of H^3 -Inulin in 5 minutes. The osmolality of the contrast medium appears to be a major cause of the above changes. Volume fractions are now being done to determine the osmolality threshold of Na diatrizoate using the above methods.
(Supported by NIH Grant #NS11883-02).

THE OXYGEN COST OF BREATHING DURING MAXIMUM SUSTAINED VOLUNTARY VENTILATION. M.E. Bradley and D.E. Leith. Harvard School of Public Health, Boston, MA 02115.

As part of a study of the effects of ventilatory muscle training, we measured the oxygen cost of breathing during maximum sustained voluntary ventilation. In all, twelve subjects (four endurance trainers, four strength trainers, and four controls) were studied before and after completing a five week training program limited to the ventilatory muscles. Pulmonary ventilation was maintained at a constant level for at least five minutes and oxygen consumption was continually monitored. Thus "steady-state" conditions of work were obtained. A total of 103 determinations of "steady-state" oxygen consumption were made under these conditions at pulmonary ventilations ranging from 103 to 250 liters/min. Over this range of ventilations for these twelve subjects, the oxygen cost of breathing was best expressed by a linear regression (R-.81) with A = minus 647 and B = 8.126. The subject group who undertook endurance training increased by 15% the level of hyperpnea that they could sustain for 15 min and increased their oxygen consumptions during this hyperpnea by as much as 75%. These changes were not seen in the strength training group or controls. We conclude that ventilatory muscle endurance training can appreciably increase the aerobic work capacity of the respiratory muscles.
(Supported by USPHS NIH Grant HL14580 and BUMED 4306.01.8011)

EFFECTS OF NEUROHYPOPHYSECTOMY ON SINGLE NEPHRON GLOMERULAR FILTRATION RATES (SNGFR) IN THE DESERT QUAIL. Eldon J. Braun. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724.

The nephron population within avian kidneys consists of a large number of reptilian-type (RT) and smaller numbers of mammalian-type (MT) nephrons. SNGFRs of both types of nephrons have been estimated in desert quail (Lophortyx gambelii), using the sodium ferrocyanide infusion technique. Previous studies have shown that physiological doses of arginine vasotocin (AVT) cause a reduction in the number of filtering RT nephrons. To further assess the role of AVT in regulating SNGFRs within the avian kidney, the endogenous source of AVT was removed from desert quail by neurohypophysectomy. Following neurohypophysectomy, all RT and MT nephrons were filtering (4.6 and 11.3 nl/min respectively) but at significantly ($P < 0.01$ for both) lower rates than during control conditions (controls 6.4 and 14.6 nl/min respectively). Following neurohypophysectomy the systemic blood pressure decreased (101.3 to 92.5 mmHg). The decrease in systemic blood pressure coupled with a possible decrease in resistance at the level of the afferent arterioles allowed all the nephrons within the quail kidney to filter following neurohypophysectomy but at a lower rate. These data can be taken as further evidence that AVT functions to regulate SNGFRs within avian kidneys in addition to regulating tubular functions. (Supported by NIH AM 16294).

RENIN SECRETION AND SODIUM EXCRETION DURING INCREASED NEGATIVE INTRAPULMONIC PRESSURE. Berton Braverman. Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Dogs were anesthetized with chloralose and then either hemorrhaged (group A; 5 dogs) by 1% body wt or infused (group B; 5 dogs) with .45 NaCl plus 2.5% dextrose by 2% body wt. Clearance periods were 15 min with blood samples taken at the beginning and end of each period. After two control periods, the trachea was attached to a resistance so that inspiration required an intrapulmonic pressure of -5 to -10 mmHg; four clearance periods were done, followed by a 30 min recovery and two more clearance periods. Group A; renin secretion (arteriovenous difference X RPF; RIA) decreased transiently after 30 min of increased intrapulmonic pressure and returned to control levels before the inspiratory resistance was removed. Sodium excretion increased two-fold and remained elevated throughout the four periods, while right atrial pressure decreased from a control of 1.8 mmHg to -1.9 mmHg. No change was observed in renal blood flow (flowmeter), heart rate, mean blood pressure, urine flow, glomerular filtration rate, or potassium excretion. Group B dogs did not respond to increased negative intrapulmonic pressure with respect to renin secretion, Na excretion or any other renal or cardiovascular measurement. These results suggest that renal responses to increased intrapulmonic pressure are a) influenced by the state of hydration, and b), except for Na excretion, rapid or transient in nature.

(Supported by NIH HL 08682.)

FUROSEMIDE INHIBITION OF CHLORIDE TRANSPORT IN HUMAN RED BLOOD CELLS. P.C. Brazy* and R.B. Gunn. Dept. Physiology & Pharmacology, Duke Univ., Durham, N. C. 27710.

Furosemide, a potent chloruretic, inhibited the chloride self-exchange flux across human red blood cell membranes at 0°C in vitro. The inhibition was half-maximal in $2x10^{-4}$M furosemide, was fully effective within 3s, and was easily and completely removed by washing the cells in drug-free saline before the flux measurement. The maximum chloride self-exchange flux (Vm) and chloride concentration for half-maximum flux ($K_{\frac{1}{2}}$) were determined from a Lineweaver-Burk graph of data obtained using NH_4Cl additions to isotonic Na-acetate to vary internal and external chloride concentrations and using either $0,10^{-4}$M or $5x10^{-4}$M furosemide. Vm decreased from 478 mM/(kg cell solids·min) to 435 and 210, while $K_{\frac{1}{2}}$ increased from 31mM to 77 and 128 in the presence of furosemide. These data suggest that furosemide is a non-competitive inhibitor which reacted with a site distinct from the chloride binding site on the RBC Cl-carrier mechanism and decreased its transport capacity up to 98%. The pH dependence and apparent activation energy of the Cl flux were unchanged by the drug. Furosemide inhibited the equilibration of chloride containing cells placed in an acetate medium (bubbled with N_2) and dissociated the equality of the internal hydrogen ion x chloride ion product from that on the outside for up to 3 hrs. at 0°C, pH 7 to 8. C^{14}-acetate self-exchange and net flux were not inhibited by furosemide and were proportional to H^+ activity. This suggests that acetic acid was the major acetate transport species. We propose that HCl transport on the titratable chloride-carrier is the primary pathway for Cl efflux into acetate solutions and furosemide inhibits the carrier both in the self-exchange mode and the HCl transport mode.
(Supported by grant HL-12157 and the National Kidney Foundation)

THE USE OF METAL BINDING PROFILES TO MEASURE CHANGES IN TROPONIN CONFORMATION. Norman Briggs, Edward Gleason* and R. John Solaro*. Department of Physiology, Medical College of Virginia, Richmond, Virginia 23298, USA.

It has been suggested that tropomyosin, actin and myosin all influence Tn-C conformation and thus its affinity for calcium. The effect of myosin (crossbridge attachment) is of particular importance because of its proposed role in calcium activation of myofilament activity. In the studies to be presented changes in Tn-C conformation have been deduced from divalent metal binding profiles (Fuchs, B.B.A. 245, 221, 1971). By comparing the relative metal binding activities (binding profiles) of IZI filaments with Fuch's troponin data we conclude that tropomyosin and actin have little effect on Tn-C conformation. Comparison of our myofilament binding data with our IZI data indicates that crossbridge attachment alters not only affinities but profiles. Attachment increased affinities for Mn, Cd, Ca, Sr and Ba. The increase in affinity was, however, 2 times greater for Cd than for Ca and 4 times greater for Ba than for Ca. These results suggest that crossbridge attachment produces a conformational change in Tn-C which can be analyzed by studying a broad spectrum of divalent metals.
(Supported by AHA Grant #74865 to Dr. R. John Solaro.)

EFFECT OF LACTATE AND ORNITHINE ON UREA SYNTHESIS IN ISOLATED RAT LIVER CELLS. Stephanie Briggs* and R. A. Freedland, Dept. Physiological Sciences, University of California, Davis, CA 95616

In the perfused rat liver, ornithine (orn) has been shown to stimulate urea production from ammonia. Optimal orn concentration was reported by Hems et al. to be 2.7 mM. In isolated rat hepatocytes we have found that as orn concentration is increased from 0 to 10mM, urea production from ammonia continues to increase. Furthermore, addition of 10mM lactate results in a 2- to 4-fold increase in urea production at all levels of orn studied. This is in contrast to the findings of Hems et al. in perfused liver which showed no effect of lactate on urea production. The level of added lactate at which urea production is half maximum appears to be about 1.5mM, although there is considerable variability between rats. The lactate effect seems not to be through provision of energy. 2mM oleate and butyrate inhibit urea production. Likewise, lactate's effect appears not to be a result of altering oxidation-reduction state, as pyruvate also has a stimulatory effect, although not so great as that of lactate. Alanine, glutamine, and asparagine stimulate urea production from ammonia to varying degrees, but to a lesser extent than lactate. Citrulline accumulation appears to be primarily a function of orn concentration and is independent of lactate when lactate is 5mM or less. At 10mM lactate there may be some inhibition of citrulline accumulation. The level of orn for which citrulline accumulation is half maximum is about 8mM.

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CHANGES IN AUTONOMIC CONTROL OF CARDIOVASCULAR FUNCTIONS AFTER BIRTH. C. R. Brinkman, III, J. R. Woods, Jr.*and N. S. Assali, Dept. Obstet. and Gynecol., UCLA School of Medicine, Los Angeles, Calif. 90024

Previous studies in fetal lambs between 60 days and term gestation showed that: a) parasympathetic and sympathetic control of cardiovascular functions takes place at different periods of development, and b) systemic and pulmonary vascular responses to cholinergic and adrenergic agonists increases with fetal age, due to progressive maturation of effector system. Present report deals with data obtained in neonatal period. Newborn lambs 3-4 days old were chronically-instrumented for measurements of arterial and pulmonary artery pressures, and pulmonary and ascending aortic flows. Same lamb was tested at regular intervals until 60-70 days of age. Dose-response data to acetylcholine, norepinephrine and isoproterenol were obtained and blocking effects of dibenzyline, trimethaphan, propranolol and atropine were tested. Results show: 1) acetylcholine which produced profound pulmonary vasodilatation in the fetus had insignificant effects in the neonate. When neonatal pulmonary vascular resistance was raised with hypoxia (6-10% O_2), acetylcholine exerted vasodilating action similar to that in fetus; 2) neonatal cardiovascular system is considerably more sensitive to adrenergic agonists than fetal and sensitivity increases during neonatal development until it becomes similar to that of adult; 3) neonatal cardiovascular responses to autonomic blocker approaches adult nonpregnant pattern during neonatal development. Conclusion: a) autonomic control of cardiovascular functions changes significantly after birth; b) response of pulmonary vascular bed to vasoactive agents such as acetylcholine depends on initial status of its resistance in the resting state.

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CORONARY HEMODYNAMICS DURING HYPOXIC AND CARBON MONOXIDE HYPOXIA. B. Bromberger-Barnea, D. Peters*, and F. Khalafbeigui*, Johns Hopkins University, School of Hygiene and Public Health, Department of Environmental Medicine, Baltimore, Maryland 21205

We have previously reported coronary hemodynamic changes in isolated hearts perfused by a donor animal resulting from carbon monoxide and hypoxic hypoxia (Physiologist, 15:257, 1972). In order to eliminate humoral effects from the donor animal, the present study involved perfusion of isolated hearts with a pump oxygenator system during exposure of the heart to hypoxic hypoxia (decreasing PaO_2) and carbon monoxide hypoxia at normal PaO_2. When arterial O_2 content (CaO_2) was lowered from 20 vol % to 5 vol %, coronary bloodflow (Q_{CBF}) more than doubled, while the dP_{LV}/dt of the ventricular pressure pulse fell 30%. Heart rates remained relatively constant throughout the hypoxic exposures. There was no significant difference between hypoxic and CO hypoxia in Q_{CBF}, heartrate, dP_{LV}/dt, and rate of ventricular relaxation. However, oxygen consumption (VO_2/beat) decreased more and vascular volume (VV) increased more with CO hypoxia than with hypoxic hypoxia, especially at the severest level of hypoxia reached. The equal increases in Q_{CBF} during CO and hypoxic hypoxia were proportional to arterial oxygen content (CaO_2) rather than arterial oxygen tension (PaO_2). The larger decrease in VO_2/beat with CO hypoxia is consistant with some metabolic inhibition by CO. Finally, the larger increase in vascular volume (VV) with CO hypoxia are probably due to increases in venous compliance. The changes in vascular volume were independent of total vascular resistance which decreased equally in CO and hypoxic hypoxia causing total coronary bloodflow to increase to the same extent under both conditions.

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PROGESTERONE SECRETION FROM THE ADRENAL GLANDS OF RATS AND HAMSTERS DURING THE ESTROUS CYCLE. G.P. Brown*, G.A. Courtney and S.F. Marotta, Departments of Physiology and General Nursing, University of Illinois at the Medical Center, Chicago, IL. 60612

Adrenal venous progesterone secretory rates were determined every 12 hr. throughout the estrous cycles of four-day cyclic rats and hamsters. Progesterone was quantitated by the competitive protein binding method after extraction, and separation on sephadex LH-20 columns. In four-day cyclic rats, adrenal progesterone secretory rates varied from 57±9 to 130±18 ng/min., with the highest rates noted on proestrus. A significant decline in rates occurred between 2000 hr. on proestrus and 0800 hr. the following morning. These results indicate that adrenal progesterone secretion is associated with the events leading to ovulation in rats. The data also suggest that cyclic variations in peripheral levels of reproductive hormones during the estrous cycle of rats influence adrenal progesterone secretion. In hamsters, adrenal progesterone secretory rates varied from 3.8±0.8 to 8.5±1.4 ng/min. during the estrous cycle. The rates noted on proestrus were among the lowest observed and did not differ from those noted on the following morning. These data indicate that adrenal progesterone secretion may not be associated with events leading to ovulation in hamsters, and suggest a relative lack of influence of female reproductive hormones on adrenocortical function in hamsters.

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OBSERVATIONS OF THE EFFECTS OF INTRAVENOUS HISTAMINE ON PULMONARY MECHANICS IN NORMAL MAN. R. Brown,* R.H. Ingram, Jr.* and E.R. McFadden, Jr. Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass. 02115

We studied 6 normal volunteers on 25 occasions before and during the intravenous infusion of 0.1 and 0.2 μgm/kg/min of histamine base as part of the assessment of the role that this humoral mediator of the type I allergic reaction plays in the production of clinical asthma. In a pressure compensated variable volume plethysmograph, we measured total lung capacity and its subdivisions, static and dynamic compliance (Cdyn), lung resistance (R_L), partial expiratory flow volume curves and density dependence of maximal expiratory flow. Factorial analysis of the pooled data showed a statistically significant effect of histamine on only Cdyn ($p<.001$). No significant effects were found on any of the other parameters measured. Our results suggest peripheral airway obstruction and with respect to lung volumes and R_L differ from those previously reported in the literature. We do not believe this to be due to the administration of insufficient quantities of histamine, for the doses used produced marked systemic effects that caused considerable subject discomfort. We conclude that, when administered by infusion, the effects of histamine on normal lungs are minimal. (Supported by an MRC(C) Fellowship and grants HL 00013 and HL 17382 from NHLI.)

ADRENERGIC INHIBITION OF PARASYMPATHOMIMETICALLY-CHALLENGED GASTRO-DUODENAL JUNCTIONAL TISSUE FROM THE RAT IN VITRO. L.A. BRUCE* and I.E. DANHOF, Dept. Physiology, U. of Texas Health Science Center at Dallas, Dallas, Tx. 75235

This investigation is addressed to the question of whether gastroduodenal junctional tissue (GJT) has unique properties which functionally separate it from adjacent tissues in influencing gastric emptying and/or preventing reflux of duodenal contents. GJT from rats may be identified from either histological studies or functionally from its unique contractile wave forms in vitro. Adjacent duodenal or antral tissues display different types of contractile waves in vitro and histologically can be distinguished from GJT. Data presented in this report suggest that the GJT also has unique pharmacological properties when compared to adjacent tissues. Norepinephrine (N) and epinephrine (E) inhibit parasympathomimetically-challenged GJT; whereas, isoproterenol, a beta adrenoreceptor stimulant, shows no observable effect. An alpha blocker, phentolamine, blocks the inhibition from both N and E. These data suggest that the inhibition seen with N and E is mediated through alpha adrenoreceptors, whereas, beta adrenoreceptors appear to be functionally absent from rat GJT with chemical stimulation. Adjacent areas of the tract have two target sites for inhibition (alpha and beta adrenoreceptors), whereas, the GJT apparently has only one avenue for inhibition. Theoretically, the GJT, in vivo may be more excitable to physiological levels of acetylcholine and/or vagal stimulation because of fewer inhibitory adrenoreceptors available to physiological levels of N and E than adjacent tissues. However, an increased sensitivity of alpha adrenoreceptors to adrenergic drug inhibition cannot be ruled out from this study.

REDISTRIBUTION OF BLOOD FLOW IN THE NEWBORN DURING ACIDOSIS. Richard L. Bucciarelli* and Donald V. Eitzman, University of Florida, Coll. of Med., Dept. of Ped., Div. of Neonatology, Gainesville, FL.

Distribution of blood flow was studied using radioactive spheres in 21 newborn goats (post C-Section) ranging from 128-148 days gestation, and in 18 goats aged 1-37 days. Injections were made 10 minutes after production of the experimental condition. Acidosis was produced with decreased ventilation, lactic acid infusion, post hypoxia or stress. Pressure was measured directly in left atrium, pulmonary artery, and femoral artery. Oxygen consumption was measured with a closed system and oxygen content calculated from the pulmonary artery and left atrial samples. At the end of the experiment, individual organs and the entire carcass were ashed and counted. Resistance was calculated and total flow was checked by the Fick Principle. In general, there was an increase in flow to the brain with all types of acidosis. This increase was most marked with respiratory acidosis and was most consistent with infusion of lactic acid. There was a smaller and less consistent increase in coronary flow with all types of acidosis. Flow to kidney, gut, and carcass was variable with mean change in flow being a small decrease.

Summary of change in flow during acidosis in all age groups

	Brain	Body	Heart	Kidney	Gut
No. Increasing Flow	35	15	23	8	14
No. Decreasing Flow	4	24	18	33	26
Mean % Change	+83.2	-5.3	+34	-20.5	-12.4

(Supported by NIH Training Grant HD00054 and Research Grant HL14829.)

HYPERINSULINEMIA AND THE PATHOGENESIS OF THE HYPOGLYCEMIA OF ENDOTOXIN SHOCK. Bernard J. Buchanan and James P. Filkins. Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Endotoxin shock elicits a progressive and profound hypoglycemia in a wide variety of species. Since a significant relationship exists between the insulinemic state and the susceptibility to lethal endotoxin shock, the role of insulin in the genesis of the hypoglycemia of endotoxemia in the rat was investigated. Endotoxin (1 mg/300 gm rat) produced an early hyperglycemia which reached a zenith of 157 mg/dl at 90 min post endotoxin (saline control value 87 mg/dl), accompanied by an increase in serum insulin to 130 μU/ml (saline control, 17.6 μU/ml). The rats remained significantly hyperinsulinemic throughout the 12 hr observation period although the hyperglycemia rapidly subsided. Total body glucose oxidation, as evaluated by the recovery of $^{14}CO_2$ from [^{14}C-U]-D-glucose, reflected significant enhancement of glucose utilization in endotoxemic rats which was completely abolished in rats rendered acutely insulinopenic by mannoheptulose or streptozotocin. Rat hemidiaphragms demonstrated elevated glucose utilization, with utilization of glucose increased from 39.3 ± 0.9 μgm/mg dry wt/3 hr in the saline controls (N=25) to values at 1, 2, and 3 hrs post endotoxin of 46.7 ± 1.3(N=21), 46.7 ± 0.9(N=21), and 52.9 ± 2.5(N=21), respectively. Endotoxin in vitro had no influence on hemidiaphragm glucose utilization. These data indicate that enhanced glucose utilization plays a prominent role in the pathogenesis of the hypoglycemia and carbohydrate depletion of endotoxemia and that insulin is a key mediator of this potentially lethal action of endotoxin. (Supported by NIH HL 14540 and HL 08682.)

OSMOSENSITIVITY OF RAT THIRD VENTRICLE FOR THIRST AND INTERACTIONS WITH ANGIOTENSIN-INDUCED THIRST. J. Buggy(SPON: C. J. Imig). Dept. Physiology & Biophysics, University of Iowa, Iowa City, Iowa 52242

Adult male rats were prepared with intracranial cannula for injection into the anterior-ventral third ventricle. Following recovery from surgery, animals were tested for drinking responses to microinjection of hypertonic NaCl or sucrose, and angiotensin(AII). Short latency water ingestion was reliably elicited by 1-4ul injection of NaCl(1.3-2.5%). Thirst was also elicited by sucrose(4ul of 0.9M) but less consistently. Thirst elicited by hypertonic stimulation was water specific; feeding or drinking of 1.8% saline was not observed. In contrast, AII injection(0.1-200ng/1ul) through the same cannula resulted in short latency drinking of 1.8% saline as well as water. These behavioral differences between thirst elicited by AII or hypertonic solutions suggest that the neural substrates involved are not identical. It has been suggested that angiotensin induces thirst by facilitating entry of sodium into neurons subserving thirst since combined injections of AII and hypertonic saline in the goat have been reported to elicit drinking in excess of the additive sum drunk to each solution alone. Combined injections and infusions of AII and hypertonic NaCl were made into rat third ventricle to determine if drinking to the combined solutions would be greater than the sum drunk to each solution alone. In this study, artificial cerebrospinal fluid(CSF) served as a control injection and as vehicle. NaCl was added to the CSF for hypertonic NaCl. AII was prepared in a dose of 5ng/ul in the CSF vehicle and in the hypertonic NaCl. For single 2ul pulsed injections or for 30 minute infusions(1ul/minute), AII in hypertonic NaCl did not produce greater drinking than the sum of drinking to AII and hypertonic NaCl alone.

CARDIOVASCULAR AFTEREFFECTS OF HYPOTHALAMIC LESIONS IN AWAKE NORMOTENSIVE AND HYPERTENSIVE RATS. Ruben D. Buñag* and Adego Eferakeya* (SPON: G. N. Loofbourrow). University of Kansas Medical Center, Kansas City, Kansas 66103

If the hypothalamus causes hypertension by increasing sympathetic vasomotor activity, then the abolition of such activity should lower blood pressure more in hypertensive than in normotensive rats. To test this hypothesis, aortic pressures were recorded from indwelling catheters in awake rats before and 1 to 2 days after bilateral hypothalamic lesions were made. In normotensive rats posterior hypothalamic lesions reduced blood pressure and heart rate consistently while anterior hypothalamic lesions produced the opposite effects. Posterior hypothalamic lesions of approximately the same size and location elicited greater hypotensive aftereffects in renal and spontaneously hypertensive rats than in normotensive or Doca hypertensive ones. These findings indicate that the blood pressure elevation in spontaneous or chronic renal hypertension results mainly from sympathetic overactivity caused by posterior hypothalamic mechanisms. (Supported by grant HL-14560 from the National Heart and Lung Institute).

INCREASED APPETITE AND UNCHANGED METABOLISM UPON CESSATION OF SMOKING WITH DIET HELD CONSTANT. R.L. Burse*, G.D. Bynum*, K.B. Pandolf*, R.F. Goldman, E.A.H. Sims* and E.R. Danforth* (SPON: J.T. Maher). US Army Research Institute of Environmental Medicine, Natick, MA 01760 and University of Vermont Medical School, Burlington, VT 05401

Significantly decreased resting oxygen consumption ($\dot{V}O_2$), heart rate (HR) and protein-bound iodine level concomitant with increased body weight have been reported subsequent to cessation of smoking (S.C. Glauser, et al., Arch. Environ. Health 20:377-381, 1970). Since dietary composition influences calorigenesis, the metabolic and cardiorespiratory responses of 4 habitual 1 pack/day smokers, ages 23-27, were evaluated at rest and during exercise, while diet was held constant in both calories and composition: (a) while smoking, (b) after 3 weeks without smoking and (c) 3 weeks after resumption. Analysis of variance showed no significant differences ($P>.10$) between the smoking and non-smoking states for the following variables: weight; basal, resting or walking metabolic rate (Weir conversion); resting or exercise $\dot{V}O_2$, CO_2 production, respiratory quotient, minute volume, respiration rate, tidal volume and ventilatory equivalent ($\dot{V}O_2/\dot{V}_E$); resting HR; and resting body core and mean skin temperatures after both supper and breakfast. HR when walking at 5.6 km/hr was less after cessation of smoking ($P<.01$) and remained so after resumption ($P<.05$), suggesting a practice effect. Desire for food was increased after smoking stopped ($P<.05$), but decreased upon resumption. Statistical re-analysis of the metabolic, serological, cardiorespiratory and body weight data reported by Glauser, et al., also failed to yield significance for the differences between the smoking and non-smoking states. The weight gains reported after cessation of smoking are thus more likely due to increased caloric intake rather than to decreased basal or resting metabolic rate.

AN ANESTHETIZED DOG HEATSTROKE MODEL. G. Bynum* and J. Patton (SPON: LeeRoy G. Jones). US Army Research Institute of Environmental Medicine, Natick, MA 01760.

Twenty mongrel dogs anesthetized with Nembutal were heated with a water blanket over a 1-1/2 hr period to the rectal temperature range of 43.0 - 43.4°C established by Shapiro as the minimum rectal temperature for heatstroke in unanesthetized dogs. Anesthesia was maintained during the subsequent passive cooling in 27°C air and was terminated at death or 18 hours, when survivors were sacrificed. Twelve were monitored with only a rectal probe; the other eight with a rectal probe plus surgically implanted needle thermocouples (brain, liver and kidney), 5 skin thermocouples for MWST and 5 heat flow discs for mean weighted surface heat loss (MWSHL) and, via a tracheostomy, expired air samples were obtained for calculation of metabolic rate (MR). There was no significant difference in survival rates as a result of the surgical procedures. Mean values for all animals were:

	Rectal °C	Liver °C	Kidney °C	Brain °C	MWST °C	MWSHL W/m^2	MR W/m^2
Initial	37.3	38.0	38.0	37.5	33.7	64.2	36.3
At Tre Max	43.1	43.5	43.5	42.7	41.1	115.5	78.6
Death	40.8	40.8	40.3	38.0	33.7	77.7	34.4

However, differences can be distinguished between severely heat traumatized dogs (i.e., survival times ($\leq$ 2 hrs) and those which could conceivably have responded to therapy. The 66% survival rate for Shapiro's unanesthetized dog model, across the rectal temperature range 43.0 - 43.4°C, is greater than the 25% for this anesthetized dog model suggesting that the stress (or disruption of thermoregulation) from Nembutal anesthesia may lower the threshold for heatstroke.

RAPIDITY OF ARTERIAL LACTATE APPEARANCE IN DOGS BREATHING N_2 OR MADE APNEIC. S. M. Cain. U. of Ala. Med. Ctr., Birmingham, AL 35294

To see whether lactate appeared in arterial blood promptly in response to tissue O_2 depletion, the $P\bar{v}o_2$ at which lactate appeared was compared between two types of fulminating anoxia and to a previous study in which hypoxia was more prolonged (Am. J. Physiol. 209:604, 1965). Ten dogs were anesthetized, paralyzed, and V_T adjusted at f=10 on a respirator so that $Pa_{CO2} \sim 40$ mmHg. After control data collections, either N_2 was breathed at the same $\dot{V}_E$ or the respirator was turned off at end-expiration. Arterial and mixed venous blood gases were measured every minute as well as arterial lactate and pyruvate. A final set of samples was taken as mean arterial pressure fell rapidly below 70 mmHg in a typical circulatory failure and recovery on room air was followed for 1 hr post-anoxia. The alternate procedure was then performed and recovery from the second anoxia was again followed for 1 hr. N_2 breathing was first in half the experiments, and apnea was first in the other half so that each animal experienced the 2 types of anoxia and any effect of order was minimized. With washout of O_2 stores by N_2 breathing, the O_2 stores estimated to have been used would have supported control $\dot{V}o_2$ only 1.3 min in N_2 but 2.7 min in apnea for which all O_2 stores were available. These times corresponded to a $P\bar{v}o_2$ of 23.1 and 20.1 mmHg respectively. Arterial lactate increased at corresponding $P\bar{v}o_2$ of 20.5 and 23.0 mmHg. In other words, lactate rise exactly corresponded to full development of tissue O_2 depletion. Further, $P\bar{v}o_2$ at which excess lactate appeared in previous "steady state" experiments was nearly the same, 22 mmHg. The identification of tissue O_2 lack by appearance of lactate in arterial blood had little error attributable to a lactate delay time.

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ROLE OF BRANCHIAL ION EXCHANGE IN ACID-BASE BALANCE OF TELEOST FISH. James N. Cameron, Institute of Arctic Biology, University of Alaska, Fairbanks, Alaska 99701.

In resting, unanesthetized Arctic grayling acclimated to 10C, branchial uptake of Cl^- was 8.03 ueq·hr^{-1}·$200g^{-1}$, and the uptake of Na^+ was 15.49 ueq·hr^{-1}·$200g^{-1}$. Acute temperature increase from 10 to 17C was followed by an alkalosis, which was compensated gradually over the next 24 hours. Corresponding to this alkalosis, there was an increase in Cl^- uptake (presumably in exchange for HCO_3^-), and an increase in the ratio of Cl^- to Na^+ uptake from 0.33 to 0.50. Uptake rates following temperature increase were significantly greater than both the 10C control rates, and rates for a control group acclimated to 17C. Similarly, respiratory acidosis induced by 1% CO_2 was compensated over a 24-hour period. This compensation was found to be accompanied by an increase in Na^+ uptake, and an increase in the ratio of Na^+ to Cl^- uptake from 1.75 to 4.09. Since ventilation has been shown not to be involved in acid-base regulation in teleosts, it appears that these branchial ion uptake mechanisms, viz. Cl^--for-HCO_3^- and Na^+-for-H^+, can be the mechanisms by which blood pH is regulated. Changes in the relative activity of the two exchange pathways lead to either increase or decrease in the total buffering and pH of body fluids.

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A POLYGRAPHIC SURVEY OF THE HUMAN SEXUAL RESPONSE. Berry Campbell, William E. Hartman*, Marilyn Fithian*, and Irene Campbell*. University of California at Irvine and Center for Marital and Sexual Studies, 5199 E. Pacific Coast Highway, Long Beach, CA 90804

Information to establish a baseline of human sexual response to serve as a foundation for experimental work was gathered on 23 men and 57 women in 310 polygraphic recordings of 617 orgasms during masturbation or coitus. No critical information of this kind has been amassed before. The events during sexual response have been well described by Masters and Johnson but verbal material does not lend itself to the purposes at hand. We have studied especially vaginal pressure in the different segments of the vagina, rectal pressure, respiratory pattern, ECG, heart rate, and capillary pulse volume. We found that orgasm resulted in simultaneous contraction of all the muscles of the pelvic outlet; thus comparable records could be made from the rectum and vagina, allowing equivalent studies on both men and women and of couples in coitus. Consistency of pattern within the individual and the widest variation between individuals was found. Of the systemic parameters, heart rate only was found to be a reliable indicator of orgasm. What we have called the cardiac crisis is a constant feature of the sexual response. The widespread prevalence of premature ventricular contractions is shown. The study suggests that valid experimental series can be set up with a judicious matching of the response patterns.

INCREASED RESPONSIVENESS OF PITUITARY (AP) FROM STARVED RATS TO LRH-TRH TREATMENT. G.A. Campbell*, M. Kurcz*, S. Marshall*, and J. Meites, Dept. of Physiology, Michigan State University, East Lansing, Michigan 48824.

It long has been recognized that dietary deficiencies interfere with AP function, and can lead to reproductive failure. However, stimuli that elevate gonadotropin secretion have been shown to be effective during starvation. Questions therefore arise about the status of hypothalamic function and responsiveness of the AP to releasing hormones during inanition. Adult male rats were acutely starved for 7 days and maintained thereafter on 25% of ad libitum intake for up to 4 weeks. Serum hormone levels were determined by RIA in acutely and chronically starved rats before and after LRH and TRH administration. Basal levels of LH, TSH and prolactin were depressed by inanition while FSH was not. LRH-TRH treatment elevated serum LH, FSH and TSH to a greater extent in starved rats than in full-fed controls. The in vitro release of LH and TSH from AP of starved rats in response to LRH-TRH was greater than from AP of control rats, but prolactin release was not augmented. It can be concluded from these results that underfeeding does not impair and even increases AP response to LRH-TRH, and that diminished AP function in starved rats is brought about by reduced hypothalamic activity. (Supported in part by NIH grants AM 04784 and CA 10771).

EFFECT OF HEMATOCRIT ON CORONARY BLOOD FLOW MEASUREMENTS BY INDICATOR WASHOUT TECHNIQUE. Ronald D. Carlin* and Shu Chien. Dept. Physiology, College of Physicians and Surgeons, Columbia Univ. New York, N. Y. 10032

In the indicator washout method, the rate of blood flow per unit tissue weight is calculated as $k/\lambda bt$, where k (sec^{-1}) is the rate constant of the washout and λbt (gm/ml) is the partition coefficient between blood and tissue. λbt, in turn, depends on the relative partitioning of the indicator among erythrocytes, plasma, and tissue: $\lambda bt = \lambda pt[1+(\lambda cp-1)H]$. λpt (gm/ml) is the partition coefficient between plasma and tissue, after correction for trapped blood, λcp (ml/ml) is the partition coefficient between cells and plasma, and H is hematocrit/100. In the left ventricle of the dog, determinations under steady states showed $\lambda ptX = 1.09\pm0.20$ (S.D.) and $\lambda cpX = 3.31\pm0.06$ for ^{133}Xe; $\lambda ptI = 1.53\pm0.27$ and $\lambda cpI = 0.97\pm0.03$ for ^{131}I-iodoantipyrine. Therefore, for ^{133}Xe, $\lambda btX = 1.09(1+2.21H)$, and for ^{131}I-iodoantipyrine, $\lambda btI = 1.53(1-0.03H)$. After simultaneous injections of ^{133}Xe and ^{131}I-iodoantipyrine into left anterior descending coronary artery of dogs in which hematocrit was varied from 10 to 70%, the rates of washout of ^{133}Xe (k_X) and ^{131}I-iodoantipyrine (k_I) into the coronary sinus were determined. The ratio k_X/k_I, which is a measure of the ratio of the λbt for the isotopes under dynamic condition, varies linearly with H and agrees with the $\lambda btX/\lambda btI$ ratio obtained under steady state conditions (Supported by U.S.P.H.S. Grants HL 06139, HL 12738, and U.S. Army Contract DADA-17-72-C-2115).

A COMPARISON OF CORTICOSTEROID AND FLUID TREATMENT AFTER RATTLESNAKE VENOM SHOCK IN RATS. R. W. Carlson*, R. C. Schaeffer, Jr.*, F. E. Russell*, and M. H. Weil, USC School of Medicine, Los Angeles, California 90027.

Male Wistar rats (25 animals, 256-435 g) were studied in groups of 5 animals each. Rattlesnake (Crotalus viridis helleri) venom 2.0 mg/kg was infused intravenously over an interval of 30 min. At the end of venom infusion, five regimens of experimental treatment were instituted by bolus intravenous injection of corticosteroid analogs or infusion of fluids over an interval of 30 minutes. Experimental groups included: Control, 0.5 ml saline; methylprednisolone, 30 mg/kg in 0.5 ml saline; dexamethasone, 6 mg/kg in 0.5 ml saline; infusion of 20 ml/kg of Ringer's lactate; or infusion of 20 ml/kg of 5% human serum albumin. Arterial pressure decreased from 127 to 65 torr following venom. The arterial pH declined from 7.37 to 7.20 units, PCO_2 from 32 to 20 torr, and colloid osmotic pressure (COP) from 19.0 to 14.1 torr. Arterial blood lactate increased from 1.1 to 3.5 mM/L and hematocrit from 48.5 to 57.7%. Arterial pressure was restored and lactacidemia reversed 60 min. after treatment with albumin and Ringer's lactate. Hematocrit and COP were also returned to near normal values after infusion of the albumin solution. However, hematocrit and COP were not reversed by Ringer's lactate. All of the animals which were treated with albumin survived; 3/5 of animals treated with Ringer's lactate survived; and all other animals died within 60 min. These data confirm that volume and colloid deficits constitute the life-threatening disturbance that follows envenomation and that volume repletion, and especially colloid solution, is an effective method of experimental treatment for rattlesnake venom shock.

INTERACTIONS BETWEEN ANTICHOLINESTERASES AND αBUNGAROTOXIN (αBT) AT THE ACETYLCHOLINE RECEPTOR OF APLYSIA. D. O. Carpenter, W. Shain* and L. A. Greene*, Armed Forces Radiobiology Research Institute, Bethesda, Md. 20014 and Harvard Medical School, Boston, Mass. 02115.

Anticholinesterase agents such as eserine (ESER) and neostigmine (NEO) potentiate and prolong responses to acetylcholine (ACh) applied iontophoretically to Aplysia neurons, as expected by their inhibition of the esterase. However, both of these drugs also inhibit binding of ^{125}I-labelled αBT to homogenates of Aplysia ganglia, ESER being much more effective ($I_{50} = 4x10^{-6}$ M) than NEO ($I_{50} = 2x10^{-4}$). Kinetic analysis of the interactions between αBT and ESER using the methods of Cleland demonstrate that this inhibition is hyperbolic competitive, suggesting that αBT binds to a different site than does ESER. This contrasts with the linear competitive inhibition observed between αBT and carbamylcholine, which suggests that αBT binds to the ACh receptor. When compared for ability to block the esterase, NEO was found to be much more effective ($I_{50} = 1.4x10^{-8}$ M) than ESER ($I_{50} = 2.5x10^{-7}$ M). In electrophysiologic experiments we have demonstrated that 10^{-4} M ESER will both prolong the response to ACh and protect against the blockade of the response by αBT. In contrast, 10^{-4} M NEO prolongs the response but does not protect against the αBT blockade. These results suggest that some anticholinesterase agents block αBT binding to the ACh receptor by binding to a site near to but distinct from the ACh receptor, in addition to their ability to bind to and block the acetylcholinesterase. The relative affinities of different anticholinesterase drugs for these two sites are not identical.

URINARY KALLIKREIN AND PLASMA RENIN IN NEW ZEALAND RATS WITH GENETIC HYPERTENSION. O.A. Carretero, C. Polomski*, N.B. Oza and A.G. Scicli*. Department of Medicine, Henry Ford Hospital, Detroit, Michigan 48202.

Urinary kallikrein is an enzyme produced by the kidney which acts upon substrate (kininogens) to produce kallidin (lysyl-bradykinin), a potent vasodilator peptide. Kallikrein excretion is decreased in patients with essential hypertension and in animals with renal hypertension. We have studied urinary kallikrein excretion (UKE) in New Zealand genetically hypertensive rats (GHR) and in normotensive Wistar-Otago rats (WOR) between 8 and 25 weeks of age. In addition, plasma renin activity (PRA) was measured in GHR and WOR at 10 and 27 weeks. Blood pressure was similar in GHR and WOR at 8 weeks of age, but UKE was 27.34 ± 2.1 (± = SEM) in GHR and 40.05 ± 6.4 in WOR. This difference was statistically significant ($p < 0.05$). Blood pressure was significantly higher, and UKE lower in GHR at 9 weeks. UKE increased gradually to 69.51 ± 5.91 in GHR and 103.73 ± 4.88 in WOR at 25 weeks of age. These differences are highly significant ($p < 0.001$). PRA at 10 weeks was 3.33 ± 0.48 in GHR and 3.00 ± 0.73 in WOR, and 5.27 ± 0.43 and 2.00 ± 0.34 at 27 weeks ($p < 0.01$). Body weight in GHR was less than in WOR at all ages (195 g and 279 g at 25 weeks respectively). When UKE was expressed per 100 g of body weight, the differences were not significant. In conclusion, in GHR of any age, UKE is lower. However, it is not clear if these differences are a consequence of the lower body weight, of the higher blood pressure, or of a genetic defect that may play a role in the development of hypertension. (Supported in part by NIH grant HL 15839-03, and the Michigan Heart Association.

COUPLING OF VENTILATION TO CO_2 PRODUCTION DURING CONSTANT LOAD ERGOMETRY WITH SINUSOIDALLY VARYING PEDAL RATE. R. Casaburi, B.J. Whipp, S.N. Koyal* and K. Wasserman. Div. of Resp. Physiol. & Med., Harbor General Hospital-UCLA School of Medicine, Torrance, CA 90509.

We previously demonstrated that, in response to sinusoidal variations of work load, ventilation (V_E) was closely coupled to CO_2 production (V_{CO_2}) with no evidence of neurogenic response components (Fed. Proc. 34:431, 1975). We wished to investigate factors controlling ventilation under conditions where work load remained constant, but where hypothesized proprioceptive influences from the exercising limbs would be expected to vary. To accomplish this, 5 subjects exercised at a constant 50 watts work rate on a cycle ergometer at pedalling rates which varied sinusoidally between 40 and 80 rpm. Each subject exercised continuously for 30 mins at sinusoidal periods of 1,2,4,6 and 10 mins. $\dot{V}_E$, $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ were computed and displayed breath-by-breath. From these and steady state response data, digital computer routines extracted amplitude and phase relations between each variable and pedal rate fluctuation. The responses demonstrate that, although the work done on the flywheel was constant, sinusoidal perturbations in metabolic rate were engendered by the work required to move the legs at varying rates. $\dot{V}_E$ fluctuations were closely in phase with $\dot{V}_{CO_2}$ and the amplitudes of the fluctuations were highly significantly correlated ($r=0.83$, $p<0.001$); consequently, P_ACO_2 oscillated negligibly. Pedalling frequency, therefore, did not provide a ventilatory response independent of the effect of $\dot{V}_{CO_2}$. These results are inconsistent with a significant role for proprioceptive afferents from the exercising limbs and provide further evidence for coupling between $\dot{V}_E$ and $\dot{V}_{CO_2}$ in the hyperpnea of exercise. (Supported by NIH Grants HL-17107, HL-14967 and HL-11907).

FACTORS AFFECTING PROLACTIN RELEASE AFTER CERVICOVAGINAL STIMULATION. A. Castro-Vazquez* and S.M. McCann. Dept. of Physiology, University of Texas Health Science Center, Southwestern Med. Sch., Dallas, Tx. 75235.

The effect of handling (H) and of mechanical cervicovaginal stimulation (CS) on prolactin release was tested in several experimental conditions. H and CS were applied during 40 sec at 10 AM. Blood was collected by decapitation and prolactin determined in serum by radioimmunoassay. Intact animals were decapitated at 10 AM and used as controls. Experimental groups were sacrificed at 1 PM and 4 PM. In estrous rats, both H and CS induced a remarkable increase in serum prolactin (H: 162± 43 ng/ml; CS: 272±53 ng/ml) at 1 PM, as compared to 10 AM values (23±7 ng/ml). Prolactin remained elevated at 4 PM in both groups, but was higher in the CS rats (H: 82±15 ng/ml; CS: 216±32 ng/ml; $P<0.001$). No response either to H or CS was observed on diestrus II, after chronic ovariectomy (OVX) or near the end of lactation. Four days after a single estradiol benzoate (E) injection (5 µg) in the OVX rats, a prolactin surge was observed in both H and CS groups, reaching maximum values at 4 PM. However, no significant differences were observed between the H and CS groups at any time. Since Caligaris et al reported (J Endocr 60:205, 1974) that a single injection of E elicits a similar surge in the OVX rat, it is possible that neither H nor CS had any effect in the OVX, E-treated rat. However, when E was followed by progesterone (P, 2 mg) 3 days later, prolactin at 1 PM was much higher in the CS group (H: 42±15 ng/ml; CS: 470±114 ng/ml; $P<0.01$). Rats treated with P alone showed low prolactin values throughout the afternoon. It is concluded that the ability of CS to increase serum prolactin is remarkably modified by the endocrine status of the animal; apparently, both E and P priming are needed to permit the response to CS. (Supported by grants from NIH, the Ford Foundation and the World Health Organization.)

SENSITIVITY OF PURIFIED SARCOPLASMIC RETICULUM (Ca^{++} + Mg^{++})-ATPase TO PHOSPHOLIPID CONTENT. M.D. Cellucci*, E.J. Masoro and B.P. Yu, Dept. Physiology, Univ. of Texas Health Science Center, San Antonio, Texas, 78284.

Purification of the (Ca^{++} + Mg^{++})-ATPase from rat skeletal muscle sarcoplasmic reticulum (SR) by the cholate method of Meissner et al [Biochim. Biophys. Acta 298, 246 (1973)] yielded a preparation with an increase in specific activity commensurate with the extent of purification, i.e., approximately a 1.5-fold increase above that of the native membrane ATPase. This purified ATPase has a phospholipid:protein ratio about 0.5 that of native membranes. When this cholate method was carried out in the presence of dioleoyl lecithin or egg phospholipid or phospholipid isolated from SR, the specific activity of the purified ATPase is as much as 3 times that of the native SR membrane ATPase and its phospholipid:protein ratio is similar to or greater than that of the membranes. The partially delipidated purified ATPase preparation can be further delipidated by treatment with cholate and these preparations can be relipidated by the addition of phospholipid to yield increased ATPase specific activity as the phospholipid:protein ratio increases; e.g., at phospholipid:protein ratios (μg lipid-P/mg protein) of 8.7, 14.2 and 22 the μmoles of ATP hydrolyzed per mg protein per minute at 34°C were 1.6, 5.3 and 6.5 respectively. Although the increase in specific activity which occurs during the purification of the SR ATPase by the cholate method of Meissner et al indicates the procedure causes no loss of enzymatic activity, it is evident that the activity of this preparation can be markedly influenced by small changes in its phospholipid content.
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STUDIES ON SARCOPLASMIC RETICULAR CALCIUM PUMPS, AND ON MICROSOMAL REDUCTASES IN SKELETAL MUSCLE OF COLD ACCLIMATED HAMSTERS. R.R.J. Chaffee and J.P. Balcer* Departments of Ergonomics and Bio. Sci. University of California at Santa Barbara 93106.

In cold acclimated hamsters non-shivering thermogenesis develops and is the basis for the elevation in the resting metabolic rate (RMR). This is believed to involve elevated activity in a number of tissues including skeletal muscle (SM). But there is very little evidence for changes in SM metabolic potential i.e., there are few changes in oxidative enzymes. This suggests that any SM metabolic activity increase contributing to the RMR would depend on an elevated rate of intercellular ADP production. Recent work by others indicates that increased activity of Na^+/K^+ ATPase pumps in the plasma membrane may be an important ADP replenishing system. On the other hand, we have begun a series of studies to see if the sarcoplasmic reticulum Ca^{++} pumps may show altered activity in cold acclimation since the resorption of sarcomeric Ca^{++} is an ADP replenishing system and Ca^{++} itself dictates the extent of activation of the myosin-actin ATPase. Our preliminary studies seem to indicate a possible change in SR particulate Ca^{++} uptake in cold acclimation, but due to high variability in the method, proof awaits the results of further investigation now in progress. In other studies on the SR we assayed NADPH- and NADH-cytochrome c reductase, since liver microsomes are known to show striking changes in these reductases in cold acclimation. But in the SR there are no NADPH-cytochrome c reductase changes and possibly a decline in NADH cytochrome c reductases.
Supported by U.S. Navy Grant N0014-75-C-0506 and NIH Grant AM18895-01.

EFFECTIVE MIXING COEFFICIENT AND SINGLE-BREATH N_2 WASHOUT CURVE. H.K. Chang, D.B. Taulbee* and C.P. Yu*, Faculty of Engineering and Applied Sciences, State University of New York at Buffalo, Buffalo,N.Y. 14214

Mechanisms which have been proposed as responsible for the mixing between inspired gas and lung gases include molecular diffusion, longitudinal velocity dispersion due to non-uniform mechanical properties and irregular geometry of the lung, Taylor dispersion, and cardiogenic oscillations. To elucidate the effect of these mechanisms on overall intrapulmonary mixing, experimental single breath N_2 washout curves were compared with computed curves based on the solution of a one-dimensional convective-diffusive equation for a trumpet-shaped lung model. When binary diffusivity between oxygen and nitrogen was used as the mixing coefficient in the transport equation, the computed curve showed a steeper and narrower frontal phase than the experimental curve. When an expression for longitudinal velocity dispersion was superimposed on the molecular diffusivity, agreement between theoretical and experimental curves improved, with the former still indicating a larger dead space. Consideration of Taylor dispersion did not yield significantly different results. No separate expression for the effects of cardiogenic oscillations was derived in this study; however, more accentuated logitudinal velocity dispersion terms were used to simulate such effects. These parametric studies provide a vehicle for assessing the relative influence of each mechanism on the three phases of a single breath N_2 washout curve.

A REFINED METHOD FOR MEASURING INTESTINAL ABSORPTION IN VIVO. Tapan K. Chaudhuri, Eastern Virginia Medical School & Veterans Administration Center, Hampton, Virginia 23667

Various in vivo methods have so far been employed in the study of intestinal absorption in animals and man. In the former, the methods include acute experiment (tied loop experiment), chronic experiment (intestinal fistula method) and the experiment involving circulation of fluid through a cannulated loop of intestine with intact blood supply. In the latter, the technique of intestinal intubation have been used, but the quantitative estimation of the intestinal absorption involved timed sampling of the test solution. More recently, recirculating perfusion systems with continuous monitoring of radioactivity have been developed. We have succeeded in developing a technique by means of which not only all the advantages of the above-mentioned techniques are achieved simultaneously, but also it presents certain additional important feature. An intubation system with a loop recirculation has been developed in which the absorption of water and nutrient (or an electrolyte) from the intestine can be simultaneously and continuously monitored. This technique offers a simple means of correction for fluid absorption or secretion in the quantitative estimation of the net absorption of a nutrient.

RELATIONSHIP BETWEEN NICOTINAMIDE ADENINE DINUCLEOTIDE AND SURVIVAL IN HEMORRHAGIC SHOCK. I.H. Chaudry, S. Zweig,* G.J. Planer,* M.M. Sayeed, and A.E. Baue, Dept. of Surgery, Washington University School of Medicine and The Jewish Hospital of St. Louis, St. Louis, Mo. 63110.

It has been shown that administration of nicotinamide following severe sepsis favorably affects the survival rate in rats. The object of this investigation was to determine if nicotinamide would also have a salutary effect in hemorrhagic shock. In the first group of rats, nicotinamide adenine dinucleotide (NAD), 25-100 μmoles, nicotinamide, 100 μmoles, or nicotinic acid, 100 μmoles, was infused intravenously following which the animals were bled to a mean arterial pressure of 40 mm Hg for 1½ hrs. The remaining shed blood was then returned slowly, the vessels ligated and the animals returned to cages. In the second group of rats, animals were bled to 40 mm Hg for 1½ hrs. NAD, nicotinamide or nicotinic acid was then given intravenously followed by return of the shed blood. Control animals were bled for the same period and given the shed blood and an equal volume of saline. Survival was measured over a period of 12 hrs. Mortality was 100% in control rats and also in the 24 rats receiving NAD, nicotinamide or nicotinic acid prior to shock. In the 50 rats who received NAD, nicotinamide or nicotinic acid following shock, no beneficial effect was observed. Experiments from our laboratory have also shown that during shock tissue NAD levels decrease significantly. Infusion of nicotinamide following shock resulted in restoring NAD levels in liver and kidney, but despite this, the animals failed to survive. These results indicate that infusion of nicotinamide, NAD or nicotinic acid failed to have any salutary effect on the survival of rats in hemorrhagic shock, whereas previous work from our laboratory has clearly shown a beneficial effect of ATP-$MgCl_2$ for animals in shock.

DYNAMICS OF CAPILLARY FILTRATION IN THE DOG'S HIND PAW. H.I. Chen,* H.J. Granger, and A.E. Taylor. (SPON: W.L. Williams) Dept. Physiology & Biophysics, Univ. Mississippi Medical Center, Jackson, MS 39216

The dynamics of capillary filtration and interactions of Starling forces were studied in the isolated dog's hind paw. Average capillary filtration coefficient of the soft tissue (total wt. - bone wt.) was 0.028 ml/min/mm Hg/100 gm. Interstitial compliance was 2% or 0.3 ml/mm Hg/100 gm in the negative range of interstitial fluid pressure (P_T), 10% or 1.5 ml/mm Hg/100 gm in the positive range of P_T. At an initial isogravimetric state, when the arterial pressure was set at 100 ± 3 mm Hg (mean ± S.E.M.) and venous pressure (P_V) at 5 ± 1 mm Hg, the average isogravimetric capillary pressure (P_C), capsule pressure (P_T), plasma oncotic pressure (π_P) and interstitial (lymph) oncotic pressure (π_T) were 12.5, -5.1, 20.7 and 3.6 mm Hg respectively. Calculated pressure gradient for capillary filtration (imbalance in Starling forces) was approximately 0.5 mm Hg. At another isogravimetric state, following elevation of P_V to 20 mm Hg, P_C, P_T, π_P and π_T averaged 24.8, -0.2,20.9 and 1.2 respectively. Lymph flow increased 5 to 12 times control values to maintain the tissue in an isogravimetric state. P_C was related to P_V (assuming a linear relationship) by: $P_{Ci} = 12/15\ P_{Vi} + 8.5$. Further elevation of P_V to 35 mm Hg resulted in an insignificant increase in lymph flow, a slight decrease in lymph protein concentration, a large increase in tissue volume (observable edema) and P_T increased to values ≈+9 mm Hg. Thus, when filtration forces are increased (<15 mm Hg) increased P_T, decreased π_T and the increase in imbalance of Starling forces(lymph flow factor) provides 40, 20, and 40 per cent respectively of the counterbalancing forces. At high elevations of filtration pressures (>15 mm Hg) the only tissue force that changes significantly to oppose filtration is P_T. (Supported by grants HL 11477 and HL 15680)

QUANTITATIVE EFFECTS OF ELEVATED GAS DENSITY (ρ), AMBIENT PARTIAL PRESSURE OF OXYGEN (P_{O_2}), AND AMBIENT PRESSURE (P) ON OXYGEN UPTAKE ($\dot{V}O_2$, ml/min/Kg) OF RATS AT REST AND DURING EXERCISE. L.H. Chen*, D.G. Baker*, and Y.C. Lin, Dept. of Physiol., Univ. of Hawaii Sch. of Med., Honolulu, Hawaii 96822.

Experiments were designed to partition the effects of P_{O_2}, ρ, and P at rest and during exercise in 1, 3, and 10 ATA normoxic and hyperoxic He or N_2 environments consisting of mixtures of varying ρ from 0.36 to 10.33, P_{O_2} from 142 - 1586 mmHg, and P_{N_2} and P_{He} from 0 - 7402 mmHg. P_{O_2} effect was deduced by comparing the $\dot{V}O_2$ in normoxic and hyperoxic mixtures at a given P, ρ, and P_{He} or P_{N_2}. The ρ effect was obtained by comparing the $\dot{V}O_2$ in various ρ at a given P and P_{O_2}. The P effect was obtained by comparing the $\dot{V}O_2$ at a given ρ and P_{O_2}. Hyperoxia produced insignificant effects on $\dot{V}O_2$ at rest and depressed $\dot{V}O_2$ 4.1, 8.4, and 6.7 units during exercise in 3 and 10 ATA N_2, and 10 ATA He, respectively. ρ produced negligible effects at rest, but affected $\dot{V}O_2$ by +2.8, -1.61, and -1.16 $\dot{V}O_2$ units per unit increment in ρ in the ranges of 0.36 - 1.0, 0.64 - 1.72, and 1.72 - 10.33. P depressed $\dot{V}O_2$ by 6.8 at rest and 6.7 units during exercise in P ranging from 3 - 10 ATA. At rest, $\dot{V}O_2$ was depressed by 7.6, 5.5, 1.4, and 5.3 units in 3 and 10 ATA normoxic N_2 and 3 and 10 ATA normoxic He, and was depressed by 5.7, 9.4, 1.8, and 1.1 $\dot{V}O_2$ units in 3 and 10 ATA hyperoxic N_2 and 3 and 10 ATA hyperoxic He. During exercise, $\dot{V}O_2$ was depressed by 8.1, 20.3, 2.5, and 8.8 units in 3 and 10 ATA normoxic N_2 and 3 and 10 ATA normoxic He, and was affected by -13.9, -25.5, +1.6, and -19.7 units in 3 and 10 ATA hyperoxic N_2, and in 3 and 10 ATA hyperoxic He, respectively. These effects can be explained by summing the individual effects of ρ, P_{O_2}, and P. The calculated effect matches the actually measured effect within the resolution of $\dot{V}O_2$ determinations.
(Supported by ONR contract N00014-67-A-0387-0014)

IN VITRO SYNTHESIS OF PROGESTERONE RECEPTOR BY HAMSTER UTERINE TISSUE. Tong J. Chen* and W.W. Leavitt. Dept. of Physiology, Col. of Med., Univ. of Cincinnati, Cincinnati, OHIO 45267.

Our objective was to determine the mechanism of uterine progesterone receptor (PR) formation. An in vitro incubation system was developed using uterine strips derived from ovariectomized hamsters. Each uterine horn was slit and the resulting strips were placed in 25-ml flasks. Flask pairs contained an equivalent amount of tissue from each donor animal. Strips were exposed to estradiol (E_2) ($3x10^{-12}$ to $3x10^{-6}$M) or ethanol vehicle (control) in 4 ml of sterile medium 199 at 25°C for 1 hr. Then the tissue was rinsed and incubated in fresh medium for 0.5, 6, 12 or 24 hr at 37°C under an atmosphere of 95% O_2 - 5% CO_2. The concentration of PR (p mole/gm tissue) was measured in the cytosol fraction by Scatchard plot analysis of specific ^{3}H-progesterone binding data. In control strips, the PR concentration increased progressively during 24 hr of incubation. PR formation increased significantly after strips were exposed to E_2 for 1 hr. The PR response to E_2 was dose dependent, and a maximal response was achieved using $3x10^{-8}$M E_2. The PR response was specific for E_2 in that testosterone, dihydrotestosterone and cortisol ($3x10^{-8}$M) did not increase the PR titer above the control level. Cycloheximide or Actinomycin D (10 μg/ml) blocked PR synthesis in both control and E_2-treated strips when added at zero time. When the inhibitors were added 6 hr after E_2 treatment, cycloheximide blocked PR synthesis but Actinomycin D was no longer effective. Sucrose-glycerol gradient centrifugation of ^{3}H-progesterone labeled cytosol revealed a single 6-7S receptor in all cases. The results demonstrate that PR formation in uterine tissue is mediated by RNA and protein synthesis and that PR synthesis is stimulated by estrogen action in vitro.
(Supported by Population Council Grant M74.113.)

THE SIGNIFICANCE OF ISOVOLUME MMEF IN THE EVALUATION OF AIRWAY OBSTRUCTION. W. Y. Chen* and J. F. Souhrada, National Jewish Hospital and Research Center, Denver, CO 80206

Some patients with obstructive airway disease (OAD) demonstrate no change or decrease in MMEF (maximal-midexpiratory flow rate) after the administration of the bronchodilative drug (BD) in spite of an increase in FVC and FEV_1. Olsen and Hale (Am. Rev. Resp. Dis. 98: 301, 1968) suggested that in those cases the isovolume MMEF should be used rather than the conventional MMEF. To clarify this issue, 343 patients with OAD (asthma, chronic bronchitis) have been studied with batteries of pulmonary function tests pre and post BD (Bronkosol or Isoproterenol). Spirometry (FVC, FEV_1, MMEF) multiple-breath helium washout (TLC, RV) and body plethysmography (Raw, TGV) were performed pre and post BD. It was found that in 26 of the 343 patients, the conventional measurement of MMEF failed to increase after BD administration. Spirograms of these 26 patients were analyzed and the isovolume MMEF was determined. In addition, the other pulmonary function parameters were analyzed and compared with the rest of the patient population. It was concluded that: 1) the incidence of decrease or no change in MMEF post BD is limited to adult population; 2) isovolume MMEF demonstrates a more sensitive measure of airway response to BD; 3) the above characteristics are not, however, related to the severity of airway obstruction nor to the lung hyperinflation.

EFFECT OF HYPOTHALAMIC LESIONS ON PLASMA LH AND PITUITARY RESPONSE TO LRF IN THE RAT. C. Cheung*, D. Tallentire*, R. Grant and J.M. Davidson. Dept. Physiology, Stanford University, Stanford, Cal. 94305

We have proposed (Adv. Biosci. 10:63, 1973) that deprivation of endogenous LRF (e.g. caused by steroids) reduces pituitary responsiveness on subsequent LRF exposure. To test this hypothesis sham or median eminence arcuate lesions were placed in adult Long Evans male rats 6 weeks after castration. Plasma LH and 10 min. responses to a submaximal dose of 10ng synthetic LRF were subsequently studied. After a transient increase 1 hr after lesioning, a progressive decline in plasma LH was found beginning on day 1 through 2 weeks postoperatively. A reduction in pituitary LH content associated with a decrease in pituitary weight was seen in the lesion group. LRF response was unaffected through day 7, but later dropped below control levels. All the lesions included in the study involved destruction of 95% or more of the area and animals with marked pituitary atrophy were excluded. Similar results were found in spayed females. Complete bilateral suprachiasmatic lesions in males did not affect basal LH and LRF response was unchanged until 4 weeks after the lesion, when it showed a slight decline. Thus it can be concluded that 1) the decline in pituitary sensitivity resulting from removal of endogenous LRF is a slowly developing process, requiring more than 1 week, despite a severe decrease in LH secretion already present at that time. 2) Although others have implicated the suprachiasmatic nucleus in LH regulation in males, its removal has little if any effect on LH release or pituitary LRF responsiveness in the castrated male rat. (Support by NIH grant HD-00778)

DYNAMIC REGIONAL LUNG STRAINS IN AWAKE DOGS. P.A. Chevalier, L. D. Harris*, J. F. Greenleaf, and R. A. Robb. Mayo Foundation, Rochester, Minnesota 55901.

Spatial distribution of pulmonary parenchymal strains in the intact thorax of awake standing dogs is determined from measurements of displacements of metallic (1-mm diameter) markers implanted percutaneously throughout the parenchyma of the right lung 3-4 weeks prior to the experiments. Tracking of these markers is accomplished by means of biplane orthogonal videoroentgenographic recordings which allow high temporal (60/sec) and spatial (± 1.5 mm) resolution measurements of the "tagged" lungs. Four dogs were trained to stand in a Pavlovian-type sling positioned on the fluoroscopic table while biplane recordings were made of the displacements of the parenchymal markers during spontaneous respiration. Analysis of regional parenchymal strains indicates considerable variability in the breathing pattern in an awake, non-medicated dog. With the dog in the standing position (Z-axis of lung horizontal), dynamic regional strains between markers lying along the horizontal Z-axis (i.e., no hydrostatic pressure gradient) were equal from apex-to-base indicating that the lung parenchyma behaves like a linear spring in the isohydrostatic pressure plane of the lung. In this case, since at least one of the "marker pairs" must lie across a lung fissure, similarity of regional strains suggests that "slippage" of lung lobes past one another during respiration contributes little to regional lung mechanics. (Supported in part by NIH grants HL-3532, HL-4664 and RR-0007; AF-44620; NASA-NGR-24003-001, and AHA CI-10.)

AUTOREGULATION OF HUMAN SKIN BLOOD FLOW DEMONSTRATED BY ^{133}XENON DISAPPEARANCE. J.E. Chimoskey, Depts. of Physiology and Surgery, Baylor College of Medicine, Houston, Tx. 77025 and G.A. Holloway,Jr.*,C.Daly*, and D. Kennedy*, Center for Bioengineering, Seattle, Wash. 98195

Blood flow was determined 209 times in the skin of the volar aspect of the forearm of 23 normal human subjects of both sexes aged 20-37 years. ^{133}Xe was injected intracutaneously in 0.02-0.03 ml sterile pyrogen-free physiological saline solution with a 30 gauge needle and Hamilton microsyringe. The first component of the disappearance curve was used to compute flow rate. The subjects were supine. They spent 20 minutes in the 21.0±0.5°C room to stabilize skin blood flow prior to the studies. The average of six blood pressures per subject ranged from 102/56 to 146/84. External pressure was applied to the skin through a 3 cm diameter plastic disc centered over the injection site. A servo controlled motor maintained constant average pressures of 0,5, 10,15,20,30,60,90,120 and 150 mmHg to the 7.07 cm^2 area with less than 1 mmHg tracking error and a system frequency response of 0.5 H_z. Pressures were applied in random order; pressure distribution was not determined. Flow rate decreased linearly for pressures from 0 to 10 mmHg (14.6 to 5.1 ml/min/100 gm), was constant at 10,15,20 and 30 mmHg (5.1, 4.8,4.5 and 4.9 ml/min/100 gm) and decreased from 30 to 150 mmHg (4.9 to 0.3 ml/min/100 gm). Reactive hyperemia was detected only following release of loads ≥90 mmHg. Denervated parasacral skin of 6 paraplegic subjects and parasacral skin of 6 normal subjects were studied at pressures of 0,5 and 15 mmHg. Flow decreased at pressures from 0 to 5 mmHg and was constant from 5 to 15 mmHg in both groups. Autoregulation of skin blood flow occurs by a nonneurogenic mechanism. Reactive hyperemia occurs following release of pressures which exceed the ability of skin to autoregulate. Supported by HL 15768-02 and HL 13330-05.

RESISTANCE OF THE RBC MEMBRANE TO OXYGEN UPTAKE. C.S. Chiu*, T. Robinson, and H. Rotman* (SPON: P.H. Abbrecht). University of Michigan Medical School, Ann Arbor, Michigan 48104

If the RBC membrane could be altered in such a way as to increase the apparent association velocity constant for O_2 and hemoglobin (k'c), then it would be justified to assume that in the intact state, the membrane offers finite resistance to O_2 uptake. A Hartridge-Roughton continuous flow rapid-reaction apparatus, modified so that changes in extracellular PO_2 were followed rather than actual oxyhemoglobin concentration, was employed to measure k'c in RBC before and after they were exposed to enzymes known to affect the membrane constituents or charge. Phospholipase C (3 experiments), Neuraminidase (3 experiments), pepsin (3 experiments) and papain (2 experiments) were incubated with RBC at 37° for 2 hours, k'c was measured and compared by paired Student t-test with untreated blood. Values for k'c in the treated and control bloods were: 122 mM^{-1} sec^{-1} and 131 mM^{-1} sec^{-1} for phospholipase C, 59 mM^{-1} sec^{-1} and 58 mM^{-1} sec^{-1} for neuraminidase, 94 mM^{-1} sec^{-1} and 101 mM^{-1} sec^{-1} for pepsin and 104 mM^{-1} sec^{-1} and 110 mM^{-1} sec^{-1} for papain. The hematocrit did not change, and the % hemolysis was in all cases less than 2% during the period of incubation.

It is concluded that either the RBC membrane in the intact state does not offer any significant resistant to O_2 uptake, and/or that O_2 traverses the membrane in a manner uninfluenced by the enzymes we employed.

EFFECTS OF ACUTE CHANGES IN PLASMA CALCIUM ON RENAL HEMODYNAMICS. B. Chomdej*, L. G. Navar and D. B. Young (SPON: W. A. Neely), Dept. Physiology & Biophysics, Univ. of Miss. Medical Center, Jackson, MS. 39216

This study was conducted to evaluate the effects of acute changes in plasma calcium on renal hemodynamics. Experiments were performed on mongrel dogs (14-20 kg) anesthetized with sodium pentobarbital. Hypercalcemia was induced by intravenous infusion of isotonic calcium chloride (100mM) at between 0.5 and 1.5 ml/min. To reduce plasma calcium 2% ethylenediamine tetraacetic acid (EDTA) was administered into the renal artery at rates of 0.5 to 0.8 ml/min. Renal arterial pressure (RAP) and renal blood flow (RBF) were monitored continuously; glomerular filtration rate (GFR) was determined from inulin clearance. To determine the renal autoregulatory capability, RAP was first raised by bilateral occlusion of the common carotid arteries, and then lowered by gradated aortic constriction while RBF and GFR were measured. Plasma and urinary calcium concentrations were determined by atomic absorption spectroscopy. During calcium chloride infusion, plasma calcium concentration was increased from 4.56 $\pm$ 0.1 to 8.75 $\pm$ 0.1 mEq/L (S.E.), leading to a decrease in fraction of ultrafiltrable calcium from 54 $\pm$ 5 to 40 $\pm$ 2 %. RBF and GFR were proportionally decreased from 4.49 $\pm$ 0.2 to 3.28 $\pm$ 0.3 and from .78 $\pm$ 0.1 to .60 $\pm$ 0.1 ml/min/g. However, the ability of the vasculature to autoregulate in response to changes in RAP remained. Following EDTA infusion, RBF and GFR were increased from 3.56 $\pm$ 0.3 to 4.05 $\pm$ 0.4 and from .66 $\pm$ 0.1 to .76 $\pm$ 0.2 ml/min/g. The ability of the kidney to autoregulate RBF in response to different levels of RAP was lost. The results of this study indicate that decreases in plasma calcium concentration can have an effect on renal autoregulatory capability.

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SOLUBILITY OF O_2 IN BLOOD AT LOW TEMPERATURES. C. Christoforides*, L.H. Laasberg* and J. Hedley-Whyte. Dept. Anaesthesia, Harvard Medical School, Boston, MA 02215

Roughton and Severinghaus recently (J. Appl. Physiol. 35:861-869, 1973) gave an indirectly computed value for the Bunsen solubility of O_2 in blood at 22 C of 0.0291 (Hb 15.5 g). We had provided for the FASEB Handbook "Respiration and Circulation" 1971, a value of 0.0277. At temperatures below 22 C there were also discrepancies. Consequently we determined Bunsen solubility coefficients for O_2 in blood at 12, 6 and 0 C. 20,000 units (1 ml) of heparin were added to 250 ml of blood. The blood with Hb 10.2 was obtained by substracting red cells after sedimentation. The other sample with Hb 15.7 was left unchanged. Both samples were treated with 500 mg $NaNO_2$/100 ml blood. 5 ml aliquots of blood were equilibrated with fully humidified argon free gas (99.5% O_2, 0.49 CO_2) in 125 ml capacity water jacketed tonometer flasks maintained at 12, 6, 0 C ± 0.1. The tonometer flasks were rotated at 190 rpm and were maintained at atmospheric pressure. After at least 30 min equilibration, 2 ml aliquots were withdrawn with a specially calibrated syringe which could deliver a sample to within 0.5% by weight. Other methods are in J. Appl. Physiol. 27, p 592, para. 7, line 12 onwards.

Results

Temp	N	α_B ± SE		α_B/α_{H_2O}*	
		Hb 15.7	10.2	15.7	10.2
12 C	14	0.0334 ± .0001	0.0328 ± .0001	0.93	0.91
6 C	14	0.0386 ± .0001	0.0378 ± .0002	0.93	0.91
0 C	14	0.0452 ± .0001	0.0443 ± .0001	0.93	0.91

*α_{H_2O} from J. Appl. Physiol. 26:56-60, 1969, NAPS Doc 00152.

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INCREASE IN ACTION POTENTIAL DURATION AND FORCE FOLLOWING THE REST STATE IN FROG VENTRICLE. L.H.S. Chuck* and W. W. Parmley, Cardiovascular Research Institute, University of California, San Francisco, Ca., 94143

A recent report on cat papillary muscle (Allen, D.G., B.R. Jewell, and E.H. Wood, J. Physiol. 238:29-30, 1974) indicated that the positive staircase following a rest state was associated with a decrease in the action potential duration. The present study was designed to investigate this phenomenon in frog ventricle. Simultaneous recordings of force and action potentials, using floating electrodes, were made from 5 frog (Rana pipiens) ventricular tips. Stimulation at 12 beats/min. following a 5 minute rest period produced a progressive increase of both the action potential duration and developed force.

The first and tenth contractions after rest from muscles in 1 mM calcium at 28°C. showed a prolongation of the action potential (measured at 90% repolarization) from 622 ± 39 (SEM) msec. to 652 ± 42 msec. (p less than .05 by paired t test). This was associated with an increase in force from 0.12 ± .02 to 0.35 ± .05 gms. (p less than .01). Measurements made at 23°C. showed an average increase in force of 0.2 to 0.45 gms. concurrent with an average increase in action potential duration at this lower temperature of 750 to 790 msec. A very slight fall in the resting potential and overshoot accompanied this prolongation of the action potential duration. In summary, in frog ventricle, the increase in action potential duration following a rest state was directionally opposite to that reported for cat papillary muscle, although the force increased in both instances. This may relate to the greater dependence of frog ventricle on extracellular calcium.

'AUTOMATIC' CARDIAC VENTRICLES. V. L'ACTIVITÉ EN PASSANT. Leon Churney. Department of Physiology, Louisiana State University Medical Center, New Orleans, Louisiana 70112.

En passant activity in frog or turtle ventr. strips may reflect the actions of multiple pacemakers. So, 2 independent rhythms may coexist, as in a dog heart where an S-A nodal rhythm is aperiodically interrupted by an ideoventricular pacemaker. Also, a regular run of single beats may be periodically interpolated with a regular run of burst activity. Actually, every part of a strip has pacemaker potential, as cutting experiments prove. Simultaneous recordings of mechanical (MG) and electrical (EG) activities reveal: 1. MGs may be everywhere alike, as are the EGs, 2. varying MGs may be associated with unvarying EGs, 3. unvarying MGs may be associated with varying EGs, 4. MGs and EGs vary uncoordinately. Where burst activity may safely be ascribed to a single pacemaker, the ratio (R) of the # of beats in a burst/burst duration is constant. Ex., a run of 23 bursts, each of 5 beats, and lasting 5 min gave an R of 0.46 s^{-1}. One and 3/4 hr later the strip with ever-failing energy reserves and active deterioration fired a run of 9 bursts lasting 25 min. The serial count/burst was 21, 21, 23, 23, 24, 24, 24, 25, 26. R was unchanged. Termination of a burst cannot be due to fatigue, since the last beats may be the largest. This also rules out inhibition developing with activity. Refractoriness is not involved, because the strip responds to a stimulus applied after the terminal beat. Not only does the heart "remember" to count and for how long, but it can at times follow instructions and "communicate" with the experimenter. So, a quiescent strip responded time and time again to a single stimulus with burst activity. A subthreshold pulse was ignored. More striking, a strip having fired a run of 10 bursts, each with a count of 3, changed the count from 3 to 4, then 4 to 5, then 5 to 6, following appropriate stimulations.

THE EFFECTS OF ACUTE HYPOXIA ON PLASMA ADH CONCENTRATION AND RENIN ACTIVITY. J.R. Claybaugh and J.E. Hansen. Tripler Army Medical Center, Honolulu, Hawaii 96819.

Eight male volunteers, 19-35 years of age, arrived at the laboratory after an overnight fast. After cannulation of the brachial artery, the subject was seated through 6 consecutive periods. Periods 1, 3, and 5 were 58 minutes long, during which the subjects breathed room air normally, and 2, 4, and 6 were 22-minute periods when 11.1, 13.9, or 20.9% oxygen in nitrogen gas mixtures were breathed through a mouthpiece. This resulted in corresponding mean Pa_{O_2} values of 36.7, 53.9, and 93.5 torr. The sequence of exposures to the various mixtures was randomized to eliminate a possible effect of order. The subjects voided urine before and 10 minutes after periods 2, 4 and 6, and during the last 2 minutes of these periods 72 ml of arterial blood were drawn. The volumes of blood withdrawn and the water lost through urine, and an estimated 40 ml of water for insensible water loss were replaced by oral administration of an equal volume of water 45 minutes prior to periods 2, 4 and 6. The hypoxia produced no detectable effects on mean arterial blood pressure, plasma concentrations of Na+ and K+, or osmolality, nor in urinary excretion rate or urinary ADH excretion. Mean values of plasma renin activity dropped from 0.95 to 0.78 to 0.61 ng Angio I/ml/hr at oxygen percentages of 20.9, 13.9, and 11.1, respectively, but this was also not significant. In all 8 subjects, the plasma ADH concentration was lower ($p<.01$) at 13.9% O_2 (mean=0.52 uU/ml) than at 20.9% (1.26 uU/ml), but at 11.1% (0.85 uU/ml) 6 of the 8 subjects had higher ADH levels than at 13.9%, and the mean was not significantly different from the other means. A possible biphasic action of hypoxia on ADH release is suggested by these data.

ELECTRO-MECHANICAL COUPLING IN THE CANINE TRACHEALIS MUSCLE (CTM). R.F. Coburn and T. Yamaguchi*, Dept. of Physiology, School of Medicine University of Pennsylvania, Philadelphia, Pennsylvania 19174.

Electro-mechanical (E-M) coupling in the CTM was studied in the double sucrose-gap apparatus. There usually was no spontaneous electrical or mechanical activity. Current pulses, either cathodal or anodal, resulted in electrotonic potentials and usually did not evoke action potentials. But occasional action potentials were evoked by cathodal current or anodal break, following depolarization of the membrane potential by 10 to 20 mV with elevated K^+. E-M coupling was studied during 59 mM K^+ and 1 x 10^{-7} to 1 x 10^{-6} g/ml 5-hydroxytryptamine (5-HT) contractions. Under these conditions, graded evoked changes in membrane potential with cathodal or anodal current caused graded changes in tension. Current-clamp reversal of the depolarization caused by 59 mM K^+ resulted in complete reversal of tension, but with 5-HT contractions, current-clamp reversal never completely reversed tension. The percentage of 5-HT tension that is membrane potential-dependent (voltage-dependent) was calculated from results of current-clamp reversal, or from comparison of isotension measurements of membrane potential depolarization with 5-HT and with 59 mM K^+. Voltage-dependent tension, at 5-HT tensions of 30 to 50% of maximal K^+ tension, was computed to account for 25 to 30% of total tension. Voltage-dependent 5-HT tension increased with increases in 5-HT concentration, giving tensions of 5 to 60% of maximal K^+ tension. The threshold 5-HT concentration for voltage-dependent and for voltage-independent tension was identical or similar. Voltage-independent tension was not due to amplification of effects of changes in membrane potential. The methods developed here should allow further study of voltage-dependent and voltage-independent tension in smooth muscle.
Supported by Grant 15061 (SCOR) from the NHLI.

EVALUATION OF THE RELATIVE DENSITY OF SYMPATHETIC NERVE TERMINALS IN THE CANINE RIGHT ATRIUM. C. J. Coglianese, W. C. Randall and J. P. FILKINS. (SPON: C. N. Peiss) Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois.

Uptake of ^{3}H-norepinephrine was used to map the relative densities of sympathetic nerve terminals in the complete right atria of intact and cardiac denervated dogs. Discrete localization was obtained via dividing each atrium into twenty sections using anatomical landmarks to achieve matched samples. ^{3}H-norepinephrine (5μCi/Kg) was infused into the superior vena cava of chloralose anesthetized dogs twenty minutes prior to extirpation of the heart and dissection of the right atrium. Each coded section was dispersed into perchloric acid using a Waring microblendor, centrifuged, and the supernatant assessed for tritium via liquid scintillation counting. Neurally intact right atria (N=10) displayed a gradient of ^{3}H-norepinephrine uptake, i.e., sympathetic terminals, with the highest concentration (DPM/gm) in the tip of the appendage and the lowest in the interatrial septum. The SA nodal region was not distinguished by enhanced uptake. The atria of chronically denervated hearts (N=8) had both markedly diminished ^{3}H-norepinephrine uptake and no gradient of uptake throughout the atrium. The data indicate: (i) the technique of evaluating ^{3}H-norepinephrine uptake in multiple contiguous sections of cardiac tissue provides a quantitative estimate of sympathetic nerve terminal density, (ii) the canine right atrium has marked concentrations of sympathetic terminals in the appendage and sparse content in the SA nodal region, and (iii) the technique of ^{3}H-norepinephrine uptake allows for evaluation of the status of cardiac denervation.
(Supported by NIH HL 08682.)

MULTI-TERMINAL SYMPATHETIC AFFERENT FIBERS SUPPLYING THE THORACIC ORGANS OF CATS AND DOGS. H.M. Coleridge, C. Kidd*, J.C.G. Coleridge and R.B. Banzett*. Cardiovas. Res. Inst. UCSF, San Francisco, CA 94143

Impulses were recorded from 85 single afferent fibers dissected from the 2nd, 3rd and 4th left thoracic sympathetic rami communicantes of anesthetized cats and dogs. Endings were located by probing the thoracic organs: 48 fibers had a single ending apiece; 37 had 2-9 endings each (average 4). Of the fibers with multiple endings, 26 innervated single organs (left ventricle, left atrium, pericardium, aorta, pulmonary artery, lung, trachea, esophagus and pleura), the receptive fields varying in size from one with a diameter of 8 mm to one that extended down the aorta from the left subclavian artery almost to the diaphragm. Eleven fibers innervated two or more structures: e.g., one fiber supplied endings in aorta, pleura, bronchus and esophagus. We measured conduction velocities of 29 fibers: 22 were myelinated A fibers (3.4-29.0 m/sec) and 7 were unmyelinated C fibers (0.9-2.1 m/sec). Conduction in peripheral branches was often slower than in the parent fiber. Some fibers had a spontaneous discharge related to events in a particular organ, but the effects upon impulse frequency and pattern of discharge of procedures such as cardiac distension or lung inflation were often unpredictable and evanescent. The innervation of several organs of widely different function by a single multi-terminal fiber suggests that these sympathetic afferents are unlikely to provide the CNS with specific information on events in a particular organ, and that they have a role very different from that of the vagal mechanoreceptors. (Supported by NIH grants HL 3875 and HL 6285 and by grants from the Royal Society and Wellcome Trust.)

REFLECTION MICROSPECTROPHOTOMETRIC EVIDENCE FOR PRECAPILLARY OXYGENATION IN PULMONARY ARTERIES OF QUICK-FROZEN CAT LUNGS. R.L. Conhaim* and N.C. Staub, Cardiovascular Research Institute and Dept. Physiology, University of California, San Francisco, CA 94143

Quickly frozen lungs of cats breathing 100% oxygen have been noted by us to have rims of red, oxygenated blood in their pulmonary arteries (pa) (Fed.Proc. 20:107abs, 1961). We are developing a microspectrophotometer to quantify the oxygen saturation (SO_2) in cross-sections of frozen blood vessels such as pulmonary arteries. The instrument measures intensities of reflected light at 660 and 800 nm (isosbestic point) from a 100 μm diameter field. In tonometered, frozen blood we found the average SO_2 based on 5 reflection readings to be within ±5% of the measured SO_2 over the entire saturation range. In 3 anesthetized, open thorax cats, we ventilated one lobe with 100% O_2 and the remaining lung with low O_2 gas to obtain $SpaO_2 < 35\%$. We froze the lungs quickly with liquid propane (-170°C) and cut cross-sections of frozen lung tissue in a cryostat (-25°C). We identified, photographed, and measured SO_2 of pulmonary arteries (diam. 475-2200 μm) on the cold stage (-25°C) of the microspectrophotometer. Of 31 frozen arteries from the 100% O_2 lobes, we found 18 with rims of SO_2 that averaged 30% higher than the core of the same vessel ($p<.05$). The remaining 13 arteries and those in the contralateral lower lobes had equal core and rim SO_2.
(Supported by HL6285 and Earl C. Anthony Trust.)

LEAD AND CADMIUM BLOCK ADRENERGIC SYNAPTIC TRANSMISSION AT THE RABBIT SYMPATHETIC NERVE-ARTERIAL MUSCLE JUNCTION. G.P. Cooper, D. Fretthold*, S. Shahbabian*, L.J. Galea*, and D. Steinberg*, Dept. Environmental Health, Univ. of Cincinnati College of Medicine, Cincinnati, Oh 45267.

Heavy metals, including lead (Pb^{++}) and cadmium (Cd^{++}) have been shown to interfere with cholinergic synaptic transmission in sympathetic ganglia and skeletal neuromuscular junctions. Their effects on adrenergic synapses have not been studied. In these experiments we examined the effects of inorganic Pb^{++} ($PbCl_2$) and Cd^{++} ($CdCl_2$) on the constrictor response of rabbit saphenous arteries produced by sympathetic nerve stimulation. The technique was adapted from that of Gillespie and Rae (J. Physiol. 223:109, 1972). A 1-3 cm length of artery was removed from 2-4 kg New Zealand rabbits, placed in a bath containing Locke's solution, and perfused with the same solution at a constant rate sufficient to maintain a 40-60 mm Hg perfusion pressure. Bath and perfusion solutions were oxygenated and kept at 35°C and pH 7.4. Periarterial nerve endings were stimulated with square pulses for a period of 30 seconds (2-10 volts; 1 msec duration; 30/sec). The resultant increase in perfusion pressure was reduced or completely blocked by the addition of 10-50 micromolar Pb^{++} or Cd^{++} to the bath solution for a period of 30 minutes. After complete block of the constrictor response to nerve stimulation, the response to norepinephrine (1-4 micrograms/ml) or to direct electrical stimulation of the muscle remained unaffected. During Pb^{++} or Cd^{++} blockade the constrictor response to nerve stimulation could be restored by a 2-5 fold increase in calcium concentration. It is concluded that Pb^{++} and Cd^{++} block the calcium-mediated release of transmitter agent at these junctions. (Supported by EPA contract #68-03-0429 and NIEHS grant #ES-00159).

AN ESTROGEN-INDUCED CHANGE IN PITUITARY LRH RESPONSIVENESS DURING THE DEVELOPMENT OF A DIURNAL GONADOTROPIN SURGE IN THE OVARIECTOMIZED RAT. K.J. Cooper* and J.M. Martinovic* (SPON: L. Krulich). Dept. Physiology, Univ. of Texas Health Sci. Ctr., Southwestern Med. Sch., Dallas, Texas.

The development of a daily signal for gonadotropin release following ovariectomy has been studied. Administration of a single sc injection of estradiol benzoate (20 µg) elicited a small surge of both LH and FSH on the afternoon of the 2nd day after ovariectomy. The same hormone regimen at 4,7,14 and 21 days after gonadectomy elicited a greater hormone output during the diurnal gonadotropin discharge, maximum hormone release being found in animals ovariectomized 14-21 days previously. The temporal character of this estrogen-induced LH surge was found to be similar to that observed in cycling animals ovariectomized at 10 AM on proestrus. Elevated plasma LH levels were first detected at 1 PM, reached a maximum value by 5 PM and declined to basal values by midnight. Irrespective of the interval between ovariectomy and estrogen treatment, the increase in LH output from 9 AM to 5 PM approximated 3-5 times the 9 AM value (from 1-4 ng at 2 days; 2-7 ng at 7 days; 7-30 ng at 21 days). These data indicate that the quantity of hormone released is related to pituitary LH stores which increase 5-7 fold by 21 days after ovariectomy. The contribution of an estrogen-dependent increase in pituitary LRH responsiveness in achieving the daily gonadotropin surge was also examined. A single iv injection of 100 ng LRH evoked a 3-5 fold greater LH release within 15 min in estrogen-treated rats than in non-estrogen treated controls. These data suggest that the estrogen may simply augment pituitary responsiveness to an endogenous discharge of LRH. The possibility that a diurnal surge of LRH may occur in non-estrogen treated, ovariectomized rats is being examined. (Supported by grants from NIH, the Ford Foundation and the Population Council.)

COUPLING BETWEEN ROD PHOTORECEPTORS IN SNAPPING TURTLE RETINA, D. R. Copenhagen* and W. G. Owen*. (SPON: K. T. Brown). Dept. Physiology, University of California, San Francisco, CA 94143.

Intracellular recording from rod photoreceptors in snapping turtle has revealed that the hyperpolarizing light response of an impaled rod is increased by the light-induced activity of neighboring rods. Each rod behaves as if it is functionally connected to as many as 200 nearby rods. We now show by simultaneous penetrations of two closely adjacent rods that extrinsic current passed into one of the rods can alter the membrane potential of the other rod. The coupled potential was always the same polarity as the potential induced by extrinsic current in the initial rod, and it added algebraically to the light response. This coupled potential disappeared when either of the electrodes was withdrawn from its rod. The magnitude of the coupled potential varied asymmetrically with the polarity of the extrinsic current. Hyperpolarizing currents produced larger potential changes than did depolarizing currents. The current-voltage relationship of the plasma membrane of individual rods proved to be rectifying in the depolarizing direction, which accounts for most of the polarity-dependent asymmetry in the coupling between rods. When a horizontal cell and rod were simultaneously penetrated, and currents were passed into the horizontal cell, no changes were observed in the rod potential. These results provide strong evidence for direct and specific intercellular pathways between rods. (Supported by U.S.P.H.S. postdoctoral fellowship EY 52502 (D.R.C.) and U.S.P.H.S. research grant EY 00468 to Dr. K.T. Brown).

METABOLIC AND MORPHOLOGIC DERANGEMENTS IN MYOCARDIAL REGIONS REMOTE FROM AN ACUTE CORONARY OCCLUSION. E. Corday*, L. Kaplan*, S. Meerbaum, J. Brash*, T.W. Lang*, C. Constantini*, J. Osher* (SPON: J. Katz) Cedars-Sinai Medical Center, Los Angeles, California 90029

Following an acute coronary occlusion, derangements in myocardial lactate extraction and potassium balance have often been observed in the nonoccluded (remote) segments of the heart. Such observations have previously been reported in both coronary occlusion and reperfusion studies. In this study, detailed histopathologic evaluations revealed frequent microinfarctions in the remote zone, and these correlated with measured metabolic derangements in the corresponding segment. Two series of closed chest dogs were subjected to intracoronary balloon occlusion of the proximal LAD. Series A (6 dogs) had 7 days of coronary occlusion, series B (7 dogs) had 3 hours occlusion followed by 7 days reperfusion. Mean remote infarct size (in cm^3 cardiac wall volume) was 2.8 cm^3 for series A and 1.3 cm^3 for series B. Corresponding mean primary infarct sizes were 46.4 cm^3 and 17.1 cm^3 respectively. In occlusion series A, 5 of the 6 animals exhibited remote region infarction, and there was correlation between metabolism and infarct finding in 5 cases. Six of the 7 dogs of series B had remote infarcts, and correlation was found in 5 instances. Of the possible mechanisms implicated, a correlation was noted with elevated postocclusion systemic vascular resistance which is associated with increased myocardial oxygen demands. Other factors may be catecholamine release, coronary angiospasms and myocardial edema. The data suggest that the remote lesions occurred during the first 3 hours of occlusion and could not be reversed by subsequent reperfusion. Results of this study indicate that the previously presumed uninvolved zones of the heart may become ischemic as a result of a remotely located acute coronary occlusion.

GLUCONEOGENESIS FOLLOWING PARTIAL HEPATECTOMY IN FASTING RATS. Robert P. Cornell, Division of Science, Northeast Missouri State University, Kirksville, Missouri, 63501.

The liver is unique among the organs of the body with respect to its ability for regeneration. Hepatic regeneration after partial surgical removal of the liver occurs in humans but is more rapid in lower mammals such as rats. Since the liver has a vital physiological role in regulating blood glucose levels, the present study investigated gluconeogenesis following partial hepatectomy in fasting rats. Male rats of the Holtzman strain (275 ± 10g) were fasted overnight and then subjected to partial (70%) hepatectomy under light ether anesthesia according to Higgins and Anderson at 8-10AM the next morning. Sham control rats underwent midline laporotomy and both groups continued to fast with tap water ad libitum. Hepatic gluconeogenesis was evaluated in vivo by radiotracer conversion of ^{14}C-alanine (4μCi in 1.0 mmole iv) into blood glucose just following (0 hr) and at 6, 12, 24, and 48 hr post-surgery. The remaining liver lobes (right and caudate) after hepatectomy , which were 30.7% of the total liver, increased in weight by 36.6% at 24 hr and 77.0% at 48 hr. Conversely, body weight decreased by 6.0% at 24 hr and 11.6% at 48 hr. Blood glucose levels measured at 30 min after alanine injection remained relatively constant (76 to 92 mg%) for all groups both experimental and control. Sham control rats had blood ^{14}C-glucose levels at 30 min post-injection that were almost identical to that in untreated controls ($1.41 \pm 0.04 \times 10^4$ dpm/ml) except at 48 hr ($1.29 \pm 0.04 \times 10^4$ dpm/ml). Gluconeogenesis in hepatectomized rats was significantly depressed as compared to sham control rats by 26.5% at 0 hr, 13.9% at 6 hr, 15.5% at 12 hr, and 22.1% at 24 hr. At 48 hr gluconeogenesis in hepatectomized rats($1.28 \pm 0.04 \times 10^4$ dpm/ml) was not significantly different from sham or untreated control rats. The results of these data suggest that structural and functional regeneration of the liver are time related.

EMBRYONIC CHICK INTESTINE IN ORGAN CULTURE: EFFECTS OF HYDROCORTISONE ON VITAMIN D_3-MEDIATED CALCIUM ABSORPTIVE MECHANISM. R. A. Corradino, Dept. Physical Biology, Cornell Univ., Ithaca, N. Y. 14853.

The apparent antagonism between glucocorticoids and vitamin D-mediated intestinal calcium transport remains incompletely understood. Previous studies used animals pretreated with glucocorticoids followed by measurement of calcium transport: therefore, direct vs indirect actions of the steroid on the intestine could not be distinguished. I have examined the effects of hydrocortisone (HC) in the organ-cultured embryonic chick duodenum, a system which responds to vitamin D_3 by increased cAMP production followed by de novo synthesis of an intestinal calcium transport protein (ICTP), and, consequently, enhanced uptake and transmucosal transport of calcium (Corradino, Endocrinology 94: 1607, 1974). Inclusion of 27.5 μM HC in the culture medium reduced calcium uptake and transport by the tissue after 12-24 hr. culture, regardless of the presence of D_3 in the medium. However, at ≤ 2.75 μM HC calcium uptake was reduced only in intestine cultured in the absence of vitamin D_3. At all HC levels tested, vitamin D_3 induction of ICTP was increased. In other experiments, HC (27.5 μM) was shown to stimulate phosphate, glucose and alanine uptake and, except for alanine, vitamin D_3 potentiated this action. As shown by others, HC stimulates alkaline phosphatase activity: this was also found here. HC also increased cAMP production. The data accumulated thus far indicate that HC acts on the intestine by a mechanism which, while reducing calcium transport, potentiates vitamin D induction of ICTP. Further, HC affects phosphate, glucose and alanine accumulation by the intestine. It seems clear that more study is necessary to determine the clinical importance of glucocorticoid therapy on nutrient absorption.
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HEPATIC VEIN CITRATE CHANGES IN SURGICAL STRESS. L. C. COSTELLO, R. STACEY*, AND R. FRANKLIN. Department Physiology and Biophysics, Howard University, College of Medicine, Washington, D. C. 20059.

That hypocitricemia results from surgical stress in humans and animal models has been conclusively established. The mechanism and mediation of the hypocitricemic effect remains to be elucidated. Recent studies demonstrated that renal handling of citrate (excretion and utilization) was not involved in this effect. Consequently we investigated possible alterations in citrate handling by liver. Rats were exposed to surgical stress by laparotomy under ether anesthesia. Control animals were anesthetized only. After a definitive post-op period (generally 10-20 hours) the animals were sacrificed and appropriate blood samples obtained for citrate assay. Typical results are presented below:

	Art. Cit.	Hepatic V. Cit.	Vena Cava Cit.
Surgery (12)	38 ± 5	21 ± 7	51 ± 5
Control (12)	124 ± 6.0	141 ± 6.3	109 ± 4

The vena cava sample was obtained above the renal vein and below the hepatic vein junctions. The results clearly (and repeatedly) estab- that the liver normally adds citrate to circulation. However in surgical stress the net production of citrate by the liver to circulation becomes less than zero. These results indicate that the liver might be directly involved in the hypocitricemic effect of surgical stress. (Supported by grant GM-17960 from NIGMS).

MUSCLE WATER AND ELECTROLYTES FOLLOWING VARIED LEVELS OF DEHYDRATION IN MAN. D. L. Costill, R. Coté* and W. Fink*, Human Performance Laboratory, Ball State University, Muncie, Indiana 47306

In an effort to assess the effects of dehydration on the content of water and electrolytes (Na^+, K^+, Cl^-, and Mg^{++}) in plasma and muscle tissue, eight men exercised in the heat (39.5° C, 25% relative humidity). Blood and urine samples were obtained before exercise and after the subjects had reduced their body weight by 2.2, 4.1, and 5.8%. At similar intervals tissue samples were obtained from the vastus lateralis muscle by needle biopsy. On the average, plasma and muscle water contents were found to decrease 2.4 and 1.2%, respectively, for each percent decrease in body weight. Muscle sodium and chloride remained unchanged with dehydration, while muscle magnesium declined 12% as a result of the 5.8% dehydration. In terms of intramuscular concentrations, potassium increased 7.2 and 10.6% at the 2.2 and 4.1% dehydration levels, respectively. Calculations of the resting membrane potential suggest that the water and electrolyte losses observed in these studies do not significantly alter the excitability of the muscle cell membrane. (Supported by grant AM 17083-02 from N.I.H.).

CALORIFIC EQUIVALENT OF OXYGEN AND CARDIAC ENERGETICS OF PRESSURE MAINTENANCE R. L. Coulson* (Spon: J. F. Spann)
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Isolated hearts [left ventricular (LV) wt 3.63±.07g±SEM] from 11 rabbits were paced and retrogradely flow-perfused at 25° C (modified Krebs solution with 10mM pyruvate) in a Dewar flask calorimeter. LV's contracted isovolumically against a volume-controlled balloon. Heat production [H, (mW)], oxygen consumption [$\dot{V}$, (μl/s)], and developed pressure index ($s^{-1}\int P.dt$) [P, (mmHg)] were measured at points on the Starling curve (ascending limb) including the apex. Linear regression of H upon $\dot{V}$ for all measurements yielded:
H=(.69±.41mW± SE)+(20.4±.27mJ/μl) x $\dot{V}$; n=81; r=.98. The intercept is anerobic metabolism. The slope is the calorific equivalent of oxygen and is in close agreement with the value (20.9mJ/μl) expected from summary pyruvate oxidation:
Pyruvate+2.5 O_2→3 CO_2+2H_2O+1280 KJ. Parameters were altered by volume decrementation from the apex of the Starling curve where H was maximal (Ho) and P, optimal (Pot). The change from Ho (H-Ho) was regressed upon the resultant ratio of P/Pot according to the equation H-Ho=-M+MxP/Pot: where Ho-M represents the sum of P- independent reactions including resting and calcium activation metabolism; M is the co-efficient of P-dependent or contractile actin-myosin reactions. Ho, M, and Pot were 46.63±0.55mW, 17.24±1.29mW, and 36.19±1.60mmHg respectively; n=81, r= 0.83. For the actin myosin reaction M corresponds with 4.75mW/g: LV or in steady state pyruvate metabolism 3.34μM: ATP/g: LV at 75 beats/min.

DISTRIBUTION OF γ-AMINOBUTYRIC ACID (GABA) SENSITIVITY ON THE CRAYFISH STRETCH RECEPTOR. W. Craelius* and R.W. Berry* (SPON: F. Gonzales).
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The distribution of GABA sensitivity was mapped on the crayfish tonic stretch receptor neuron by iontophoretic application of the compound. Small outward currents (0-10 nanoamps) from micropipets filled with 0.25-4.0 M GABA solutions at pH 4.5 were sufficient to completely abolish stretch-induced impulses when the pipet was positioned on the dendrites. Higher currents were required to stop impulse generation when the pipet was positioned at points on the soma, and increasingly larger currents were required to abolish impulse production at points at increasing distances from the cell body along the axon. Axonal points were often more than an order of magnitude less sensitive than were points on the dendrites. In each of the 20 cells tested, GABA sensitivity was shown to be a decreasing function of distance from the dendrites over an area extending from the receptor muscle to a point on the axon 200 μ from the cell body. Spatial resolution was approximately 8 μ since displacement of the micropipet by that distance off the neuronal surface, onto adjacent tissue, resulted in a sharply lowered sensitivity measurement. GABA effects on both dendrites and axon were reversibly antagonized by 1 mg/ml Picrotoxin and could not be reproduced by outward current from NaCl or KCl filled (pH 4.5) micropipets. These data indicate that a high degree of sensitivity to GABA is localized on the dendrites, near inhibitory synapses, but that some specialized sensitivity may exist in extrasynaptic areas on the axon.
(Supported in part by PHS Grant NS 11519 to R.W.B.)

MAGNESIUM AND CALCIUM TRANSPORT ACROSS HEALED JEJUNAL LOOPS OF RABBITS. C. F. Cramer and R. M. Couch*. Department of Physiology, University of British Columbia, Vancouver, B. C. V6T 1W5

The purpose of the study was to compare the characteristics of intestinal magnesium and calcium transport in vivo. Solutions of various concentrations of either magnesium or calcium made isotonic with NaCl, were perfused through jejunal loops 30 cm long for 30 minute periods in five unanesthetized rabbits. Ten experiments involved perfusion of only magnesium and 14 experiments involved perfusion of only calcium in the same rabbits. Net secretion of magnesium or calcium into the lumen was found at very low perfusate concentrations of these ions. Net magnesium and calcium absorption each followed Michaelis-Menten kinetics. Magnesium V_{max} (0.135 mM/h) was attained at about 24 mM magnesium concentration, while calcium V_{max} (0.09 mM/h) was attained at about 14 mM. The results imply that both magnesium and calcium transport in rabbit jejunum involve a carrier system. Magnesium transport seemed relatively simple, while calcium transport was characterized by wide variance in absorption rates, especially at higher perfusate calcium concentrations. Perfusion of solutions containing high calcium concentration reduced calcium transport rate in most experiments implying the existence of a negative feedback control.
(Supported by MRC MA-774.)

HYDROLASE-RELATED GLUCOSE TRANSPORT ACROSS THE INTESTINAL BRUSH BORDER MEMBRANE: SIGNIFICANCE IN VARIOUS ANIMAL SPECIES. R. K. Crane, K. Ramaswamy* and P. Malathi* Dept. Physiology, Coll. Med. Dent. New Jersey, Rutgers Medical School, Piscataway, N. J. 08854.

Hydrolase-related membrane transport (HRT) has been identified as a new way for simple sugars to get across a cell membrane and to be accumulated to high intracellular concentrations. HRT was first identified in hamster intestine in vitro (Malathi, et al., Biochim. Biophys. Acta.307(1973)613-626) and shown to differ from Na^+-dependent free glucose transport in two principle ways; namely, 1, HRT does not require Na^+ and, 2, the sugar to be transported must be presented as a glycoside susceptible of cleavage by a brush border membrane hydrolase rather than as a free monosaccharide (Ramaswamy, et al., Biochim. Biophys. Acta. 345(1974)39-48). Subsequent results to be reported show the presence of HRT in animals other than the hamster; namely, rat, mouse, rabbit and guinea pig and suggest that in rabbit and guinea pig, at least, HRT is of greater functional significance than Na^+-dependent free glucose transport. In each species, transport of free glucose and glucose derived from sucrose and trehalose was studied both in the presence and absence of Na^+. In all species tested, HRT of glucose was substantially greater than Na^+-dependent glucose transport, both measured in the presence of Na^+. In the rat, omission of Na^+ reduced HRT from sucrose or trehalose to levels comparable to Na^+-dependent glucose transport in Na^+ medium. In the mouse, omission of Na^+ reduced HRT from sucrose but not trehalose. In the rabbit, omission of Na^+ had a smaller effect. In the guinea pig, omission of Na^+ had almost no effect and the rate of glucose uptake by HRT was several fold greater than the highest measured values of Na^+-dependent glucose transported. Supported by NIH Grant AM-10696.

EFFECT OF RAPID PERIPHERAL TEMPERATURE CHANGE ON MEAN BODY TEMPERATURE AND GILL VENTILATION IN THE CARP. L.I.Crawshaw, J.B.Pierce Fndn. and Yale Univ.Sch. of Med.,New Haven,CT 06519.

Carp were transferred from 15°C water to a calorimeter at 25°C, or from 25°C water to a calorimeter at 15°C. Dorsal muscle temperature (T_{dm}) and mean body temperature ($\bar{T}_b$) were continuously monitored. In a 0.47 kg carp, warming increased $\bar{T}_b$ and T_{dm} to 1/3 of the difference between the initial temperature and the final temperature in 0.3 and 3.1 min and to 2/3 in 2.2 and 6.6 min. During cooling, 1/3 of the change took 0.5 and 4.2 min and 2/3 took 3.6 and 7.6 min for $\bar{T}_b$ and T_{dm} respectively. Carp heat faster than they cool. Carp were also placed in a device where ventilatory minute volume ($\dot{V}g$) could be continuously monitored while rapid shifts in the temperature of the inspired water (T_i) and/or body surface (T_{bs}) were effected. A given ΔT_i was more effective than a similar ΔT_{bs} in changing $\dot{V}g$. A rapid 7°C decrease in T_i was followed by a transient increase in $\dot{V}g$ which gave way to a 10% decrease which was maximal after 1.5 min and thereafter increased toward, but not to the initial value. The inverse of this response was obtained when T_i was rapidly increased by 7°C. In this case a transient decrease in $\dot{V}g$ gave way to a 17% increase which was maximal after 1.5 min and then decreased toward, but not to the initial value. The fish respiratory system is sensitive to dT_i/dt, which would cause more rapid heating than cooling and could be important in the regulation of arterial P_{O_2} under conditions of rapid temperature change. (Supported by NSF Grant GB 43453.)

THE GECKO VISUAL PIGMENTS: IONIC EFFECTS ON COLOR. **F. Crescitelli, Dept. Biology, University of California, Los Angeles, Calif. 90024**

The main visual pigment of Gekko gekko has an absorbance maximum close to 520nm. This is true for extracts at low temperatures (3°) and for the pigment in situ. When extracted into digitonin dissolved in chloride ion-deficient water the spectrum at 3°C is no longer at 520nm but is shifted hypsochromically by 20 to 25nm. Addition of chloride ions will restore the normal spectrum at 520nm, the shift being a quantitative one and related to the concentration of chloride ions. The effect is independent of the nature of the cation and is given also by bromide ions. Other common inorganic ions have no effect on the hypsochromic phase of the pigment, but iodide (not fluoride) will prevent or reverse the chloride and bromide bathochromic effects. The action of chloride is interpreted to be a perturbation of the electrical interaction between retinal and protein probably due to the chloride ion acting on the protonated nitrogen of the chromophoric group.

THERMOSENSITIVE NEURONS IN THE MIDBRAIN OF THE ANESTHETIZED CAT. M.J. Cronin* and M.A. Baker, Dept. of Physiology, University of Southern California School of Medicine, Los Angeles, Calif., 90033

Thermosensitive neurons have been found in the midbrain of the rabbit (Nakayama et al, J. Appl. Physiol., 27, 1969), although a thermoregulatory function for this area is controversial. We studied responses of neurons in the caudal midbrain tegmentum of the cat during changes in midbrain temperature. Eleven cats anesthetized with chloral hydrate were used. Midbrain temperature was controlled with bilateral water-perfused thermodes and deep body temperature was maintained with a water blanket. Thermode temperature and anterior hypothalamic temperatures were recorded continuously. Thermode and electrode positions were verified histologically. Seventy-three neurons were sampled during at least one midbrain heating-cooling cycle. Of these, 58 were warm-sensitive, 33 increasing their firing rates linearly and 25 increasing their rates nonlinearly with warming. Only one neuron appeared to be cold-sensitive. Fourteen neurons showed no clear change in firing rate or pattern during midbrain temperature changes. Q_{10}'s for the warm-sensitive neurons ranged from 1.8 to above 10. Slopes of frequency-temperature curves ranged from 0.4 to 3.3 impulses/second/degree Centigrade. In this study, a surprisingly high percentage (80%) of neurons sampled were sensitive to local brain temperature. It is possible that the midbrain plays a role in physiological thermoregulation in the cat. (Supported by NSF grant #BMS 74-14665)

RENAL EXTRACTION OF CIRCULATING SECRETIN IN DOGS. P.J.Curtis,* P.L.Rayford* and J.C.Thompson. Department of Surgery, University of Texas Medical Branch, Galveston, Texas 77550.

The kidney has been shown to extract about 40% of circulating gastrin and cholecystokinin in dogs. We have studied the effect of renal transit on circulating secretin levels measured by radioimmunoassay. Methods. Fifteen anesthetized dogs were prepared with catheters in the aorta, right renal vein and right ureter. Synchronous arterial and venous blood samples were collected periodically in tubes containing Trasylol, and urine was collected. Group I: Collections were made during a basal period and during and after infusion of secretin (1.5 U/kg over 30 min). Group II: After a basal period, endogenous release of secretin was secured by infusing 0.1 M hydrochloric acid (HCl) into the duodenum and proximal jejunum. Periodic blood samples were obtained. Results. Group I: Basal secretin levels were 88±22 pg/ml and 101±22 pg/ml in artery and vein, and rose to 1170±152 pg/ml and 778±114 pg/ml at the end of the infusion. The venous level was significantly lower than the arterial level (p <0.01). Group II: Basal secretin levels in the artery and vein were 86±35 pg/ml and 79±37 pg/ml and rose to peak levels of 457±137 pg/ml and 243±58 pg/ml during HCl irrigation of the duodenum. The venous level was again significantly lower than the arterial level (p <0.05). The mean recovery of secretin from the urine during the two studies was 1.8 ng/30 min. Conclusions: The kidney did not extract secretin from the circulation at basal levels but was able to remove a mean of 34% of endogenously released secretin and 43% of exogenous secretin. Less than 3% of secretin removed from the circulation by the kidney appeared in the urine. The kidney is an efficient organ for extracting secretin immunoreactivity from the circulation of the dog. (Supported by NIH grant AM 15241).

URINARY CORTICOSTEROID AND CATECHOLAMINE RESPONSES TO SIMULATED HIGH ALTITUDE. A. Cymerman*, R.P. Francesconi, J.W. Stokes*, L.E. Banderet* and S.M. Robinson. US Army Res Inst Env Med, Natick, MA 01760

Studies of man at high altitude indicate increases in urinary 17-OH corticosteroids (17-OHCS) and norepinephrine (NE) of 30 to 300%. Previously, we observed that training, motivation, and anticipation in test subjects undergoing a strict performance regimen may result in high control values which obscure the expected increases during altitude exposure. In the present study, serial 8 h urine samples were obtained from 6 subjects who underwent 4 sessions consisting of: 1) 48 h of normal activity (CONTROL); 2) 24 h of intensive performance training (IT); 3) a 48 h performance session at 457 m (PERF); and 4) a 48 h performance session at 4242 m (ALT). During CONTROL, normal diurnal rhythmicities were observed with nadirs occurring during the 2400-0800 h period. Mean 24 h excretory values (±SE) were: 17-OHCS, 4.89±0.34 mg; 11-OHCS, 600±75 µg; and NE, 37±3 µg. IT disrupted rhythmicities for all the measured hormones and increased the excretion (approximately 56%) of 17-OHCS and NE. Rhythmicities were re-established during PERF, while 17-OHCS and NE excretion increased 41% and 34%, respectively. ALT abolished NE and 11-OHCS rhythms but caused no change in excretory rate. 17-OHCS rhythm at ALT was not altered, while 24 h values increased approximately 83%. These results indicate that demanding task situations (IT) disrupt diurnal rhythms and increase steroid and catecholamine excretion. Performance at 457 m results in elevation of 17-OHCS, while performance at ALT is accompanied by a further increase in 17-OHCS. The increases in 17-OHCS in all situations, with no change in 11-OHCS excretion, may reflect increased turnover of cortisol.

ACTH TREATMENT DELAYS THE DEVELOPMENT OF COMPENSATORY ADRENAL GROWTH, Mary F. Dallman and W.C. Engeland*, Dept. of Physiology, U.C. San Francisco School of Medicine, San Francisco, CA 94143.

We showed previously that compensatory adrenal growth following unilateral adrenalectomy occurs in rats by 6 h only when ACTH secretion has been prevented by pretreatment with dexamethasone. To test the possibility that ACTH inhibits development of this growth, we pretreated young male rats with dexamethasone (100 µg/100 g BW, twice) to prevent ACTH secretion. After sham adrenalectomy (control) or left adrenalectomy, half of the latter were injected with 8 U long-acting ACTH. At 12 h right adrenals were removed, weighed and analyzed for nucleic acids. ACTH treatment prevented an increase in weight above control. Rats not treated with ACTH showed increased weight of the remaining gland ($p<0.05$). DNA and RNA contents were elevated above control in both adrenalectomy groups ($p<0.01$), however adrenal DNA in the ACTH treated group was less than that in the untreated group ($p<0.05$). Next development of compensatory adrenal growth was studied in rats treated with ACTH 4 U bid or saline after left adrenalectomy and control operations. Although the adrenals enlarged, significant differences in weight did not occur between the ACTH treated groups until 7 d ($p<0.05$). The increase in weight after adrenalectomy in the saline treated rats occurred by 1 d and persisted at 3 and 7 d ($p<0.1$). Adrenal DNA increased gradually in both groups treated with ACTH; RNA increased dramatically by 1 d and remained high. In contrast, in saline groups adrenal DNA and RNA of unilaterally adrenalectomized rats increased above control by 1 d and remained elevated at 3 and 7 d ($p<0.01$). We conclude from these studies that ACTH delays the development of normal compensatory adrenal growth although it produces dramatic changes in adrenal weight and RNA content.

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ADDITIVE EFFECT OF STEROID AND REPERFUSION IN REVERSING MYOCARDIAL ISCHEMIC DYSFUNCTION

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The hypothesis that methylprednisolone (MP-30 mg/kg) delays progression of ischemia and potentiates mechanical and metabolic response to reperfusion, was studied in 15 control and 13 treated dogs. Systolic shortening (SS) of ischemic myocardium was assessed by epicardial length gauges. An epicardial vein was cannulated for regional metabolic studies. MP was given 30-60 minutes after left anterior descending occlusion; reperfusion was at 3 hour post-occlusion. Following occlusion, SS decreased significantly and regional transmyocardial lactate (LAC) and potassium balance (K^+) became negative. At 3 hour ischemia, SS was greater in treated dogs (40.6% vs. 12%, $p<0.05$), LAC production reversed to extraction and K^+ became normal. LAC and K^+ became normal. Following reperfusion, recovery of SS was greater in the treated animals (75% vs. 32%, $p<0.05$).

Finally, while LAC remained negative among control dogs (-14.2± 10.5% SEM) it returned to normal levels (19.0±8.7%) in the treated dogs. In conclusion, early MP administration delays the progression of ischemia and has an additive effect to reperfusion in reversing regional myocardial dysfunction.

NEGATIVE FEEDBACK CONTROL OF LUTEINIZING HORMONE(LH) BY TESTOSTERONE(T) : A QUANTITATIVE STUDY IN MALE RATS.

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Adult male Long Evans rats were castrated and immediately given subcutaneous implants of T-filled polydimethylsiloxane (PDS) capsules of various sizes. Blood samples (1.0 ml) were obtained under ether anesthesia at 3 day intervals and plasma T and LH concentrations were determined by means of radioimmunoassay. The PDS capsules, incubated *in vitro* before implantation, produced plasma T levels that were constant over the 21 days of the experiment and proportional to the length of the implant. Suppression of plasma LH below intact levels was seen with 60 mm (plasma T = 3.1 ±.2 ng/ml: mean ±SE) and 30 mm (T= 1.8 ±.1) implants, while the 2 mm (T = 0.23 ±.02) and 5 mm (T = 0.47 ± .03) groups showed a post-castration LH rise that was indistinguishable from the castrate group (T < 0.1). Animals in the 10 mm (T = 0.68 ±.03) group, however, showed intact, castrate or intermediate plasma LH responses. These data indicated that the feedback effective range for PDS-administered T was between 0.5 ng/ml (castrate response) and 1.8 ng/ml (at or below intact LH levels). A further study was carried out to determine if individual rats had a more restricted range of feedback-effective T concentrations than was indicated by the group data. Implantation of five 5 mm T-filled or five empty PDS capsules at the time of castration was followed by blood sampling and the removal of one PDS capsule at weekly intervals. Preliminary results indicate that a change of about 0.5 ng/ml T may constitute the entire feedback range for individual animals.

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THE DEFORMITY OF CHEST WALL CAUSED BY DIAPHRAGMATIC OR STERNOMASTOID CONTRACTION. J. Danon*, W. S. Druz* and J. T. Sharp, VAH, Hines, Illinois 60141 and University of Illinois, Chicago.

The deformity of the chest wall caused by contraction of the diaphragm or sternomastoid alone and in combination during several supine respiratory maneuvers was studied in a C_1 quadriplegic patient in whom phrenic stimulating electrodes were implanted. Four pairs of linearized magnetometer sensors were used, a pair each for the anteroposterior (AP) and lateral (Lat) diameters of the rib-cage (RC) and abdomen (Abd). Volume, air flow and airway pressure were recorded together with EMG's from the sternocleidomastoid and diaphragm. Following are some of the findings: 1) Both sternomastoid and diaphragm generate less pressure as lung volume increases. 2) During diaphragmatic contraction the Abd AP leads the RC AP, and the RC AP leads both the RC Lat and Abd Lat. 3) The effects of contraction of the diaphragmatic halves differed: when only the right diaphragm contracted, the RC Lat led the Abd AP, the order being reversed when only the left phrenic nerve or both nerves were stimulated. 4) In diaphragmatic breathing the inspiratory pathways in AP vs lateral diameter oscilloscopic plots were different than during expiration. With sternomastoid breathing, however, active pathways were nearly superimposed upon curves inscribed during passive relaxation maneuvers. 5) The diaphragm deformed the chest wall in different ways depending on whether the airway was open or closed, whereas the deformity caused by sternomastoid contraction was nearly identical in the two instances. 6) Supplementing diaphragmatic breathing by sternomastoid effort increased the tidal volume in spite of decreased cross sectional areas of both Abd and RC, indicating that the sternomastoid's inspiratory action is by increasing the vertical dimensions of the chest.
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SUPERSATURATION DECAY RATES AS A FUNCTION OF CONCENTRATION, ENERGY INPUT AND SURFACE/VOLUME RATIO IN PHYSICAL AND PHYSIOLOGICAL SYSTEMS. B. G. D'Aoust and D. L. Beyer.* Virginia Mason Research Center, 1000 Seneca Street, Seattle, Wn., 98101, and Fisheries Research Institute, University of Washington, Seattle, Wn., 98195.

The demonstration of bubbles in the vascular system of divers using accepted decompression procedures has focused attention on the problem of predicting phase separation in supersaturated systems. Since phase separation can occur in macroscopic systems with minimal supersaturation and in some microscopic systems only at very high supersaturations, any one "critical" level for different tissues is only a conceptual convenience. Both extremes are used, one group assuming that supersaturations of 300% are necessary for gas elimination, while others propose a "no supersaturation" concept as a working model for design of decompression tables. In fact, both extremes are contradicted by field observations and laboratory experiments where supersaturation has been observed to remain for considerable periods of time. High supersaturations of 300% (i.e. decompression from saturation at 4 ATA to 1 ATA) have been completely relieved in 35 minutes upon decompression in a stirred system. However, supersaturations of only 30% (involving decompression from 1.3 ATA to 1 ATA) have persisted for 90 minutes in the same system with the same stirring rate. This demonstrates that in a stirred, aqueous system, supersaturations which are half of those "allowed" at the surface (in the Workman model) for a half-time ($t_{1/2}$) of 80 minutes could persist for approximately one such half time.

DIRECT VERSUS NERVE STIMULATION OF ANTERIOR TIBIAL ARTERY STRIPS.
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Helical strips approximately 0.5 mm wide and 1 cm long were cut from dog anterior tibial arteries. They were suspended in physiologic salt solution (PSS), buffered to 7.4 pH, and bubbled with 95% O_2 and 5% CO_2 at 37°C. Strips were allowed to equilibrate for 1-2 hrs. after storage overnight at 4°C. They were suspended in the PSS between platinum wire electrodes, connected to a stimulus isolation unit of a Grass S-88 stimulator. The top electrode was suspended from a Grass FTO 3C force transducer. Resting tension was set at approximately 1 g. Immediately before stimulation periods the PSS was drained from the bath, the strip was electrically stimulated, a short period of recovery was recorded, and new PSS returned to the bath. Ten minutes were allowed for recovery between successive stimulation periods. Data on strength of stimulus, stimulation frequency, and stimulus pulse duration versus isometric tension were obtained before and after treatment with phenoxybenzamine (PBA). Results showed that the strips could be stimulated via terminal nerve units at short pulse durations of 0.3-0.5 msec. Frequency response curves showed an increase up to 10-20 Hz, a plateau from 10-20 Hz, and a secondary increase at higher stimulation frequencies. Stimulus voltage versus response curves showed increases to 30-60 V, a plateau from 30-60 V, and secondary increases at higher voltages. After treatment with PBA, longer pulse durations and higher voltages were required for stimulation. After PBA, a clear tendency for increased response as stimulation frequency was increased over the 20-50 Hz range was noted. The results of this study indicate that the helical strip preparation could be stimulated via terminal nerves or directly after treatment with PBA. (Supported in part by a grant from the Florida Heart Association.

INFEROTEMPORAL CORTEX FUNCTION IN SELECTIVE ATTENTION AND MEMORY.
Benjamin M. Dawson* and Leo Ganz* (SPON: J. Dewson). Department of Psychology, Stanford University, Stanford, CA. 94305

To investigate inferotemporal cortex (IT) function and models of attention, we studied visual evoked potentials (VEPs) in macaque monkeys performing a difficult delayed match-from-sample task. In this task, a compound sample is tachistoscopically (.6 msec) presented on the middle of three response panels, and .5 sec later, possible matches consisting of elements of the compound sample are presented. For 40 trials the animal must attend to one class of elements in the compound stimuli, and in the next set of 40 trials to different elements (aspects) of the same compound stimuli. Thus under different sets of trials, the animal must extract and hold in memory different elements from an identical compound sample. Changes in the VEPs to the same compound sample under different sets can only be due to internal mechanisms of attention and memory (controls run for eye movements).

Of the 8 out of 50 electrodes showing marked changes, 6 were in middle and anterior IT (roughly A5 to A10). Other visual sites (LGB, pulvinar, striate, prestriate, posterior IT) showed no changes. Surprisingly, no changes occurred in frontal electrodes.

These results are consistent with the lesion work by Mishkin, et al. (see Brain and Human Behavior, 1972), suggesting a fractioning of IT into a posterior perceptual segment and an anterior mnemonic/attentional segment. They also support a hierarchical model of selective attention for this difficult task (mean trials to criterion = 60000), rather than an efferent or filter model.
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AORTIC COMPLIANCE IN THE YOUNG AND OLD DOG BY APPLICATION OF THE LINEAR ELASTIC RESERVOIR THEORY. S. Deavers, M. E. Valentinuzzi, and J. P. Rosborough*. Physiol. Dept., Baylor Coll. Med., Houston, TX 77025, and Laboratorio Bioingenieria, Universidad Nacional de Tucuman, Argentina.

Two groups of beagles from the same colony, anesthetized with morphine and pentobarbital, were studied. Group A consisted of 8 dogs, 5 months old; group B, 4 dogs, 8 years old. Aortic pressure and flow were measured by means of two miniature indwelling catheter-tip transducers (Millar Instruments and Carolina Velocity Probe) and recorded with a high speed recorder (Visicorder). The parameter α (1/sec), inverse of the time constant, and the aortic compliance, b (cm^3/mm Hg), were calculated from these records (selecting arbitrarily 5 cycles per dog) by applying the linear elastic reservoir theory (F. W. Cope, *Adv. Biol. & Med. Physics* 10: 277, 1965; N. Rashevsky, In: *Foundations Math. Biol.*, R. Rosen, ed., Chap. 2A, 1974, p. 97). The results are as follows:

		Mean	SD	SEM	Max	Min
Group A	α	.902	±.150	±.024	1.263	.558
	b	.159	±.042	±.007	.226	.063
Group B	α	.928	±.162	±.034	1.181	.637
	b	.105	±.043	±.009	.188	.039

The Student test for b yielded a highly significant difference between group A and group B ($p < 0.1\%$), indicating a definite stiffening of the aorta (lower compliance) in the older group. For α, the difference between the groups was not significant. This method, which utilizes the simple elastic reservoir theory combined with a faithful recording of physiological events, appears promising for making *in vivo* quantitative studies of aortic distensibility under different physiological or clinical conditions.

HISTAMINE RECEPTORS IN OPOSSUM ESOPHAGEAL SMOOTH MUSCLE. D. de Carle* and J. Christensen, Dept Int Med, Univ of Iowa, Iowa City, Ia, 52242

Histamine (hist), the hist analogs 4-methyl hist (4-MH) and 2-(2-pyridyl) ethylamine (PEA), the hist antagonists mepyramine (mep) and metiamide (met), and the hist releasing compound 48/80, were tested on opossum lower esophageal sphincter (LES) and esophageal body (EB) circular smooth muscle strips, suspended in an organ bath and perfused with Krebs solution at standard conditions. LES muscle had a high basal tension and responded to field stimulation with inhibition during the stimulus train, while EB muscle responded only with a twitch contraction at the end of the stimulus train, the "off response." The responses to drugs consisted of either increased LES basal tension and "off response" amplitude (stimulation) or a fall in both parameters (inhibition). Hist caused dose-related stimulation with a threshold concentration of 6×10^{-8}M in the LES and 3×10^{-7}M in the EB. The maximal increase occurred at 3×10^{-5}M in both tissues and was 187.5% of control in LES and 41.8% in EB. Mep 10^{-5}M alone had no effect, but it altered the response to hist to inhibition, with a threshold in both tissues of 3×10^{-7}M and a maximal fall of 89.3% in LES basal tension and 57% in "off response" amplitude at 3×10^{-5}M. 4-MH, a selective H_2 agonist, caused dose-related inhibition. Met 10^{-5}M alone had no effect but altered the response to 4-MH to weak stimulation. PEA, a selective H_1 agonist, caused dose-related stimulation, and its effects were abolished by mep 10^{-5}M. 48/80 had the same effects as hist, with marked tachyphylaxis. Mep 10^{-5} with met 10^{-5} abolished all responses to all agonists. It is concluded that the opossum LES and EB contain excitatory H_1 and inhibitory H_2 receptors as well as stored hist.
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VAGAL AFFERENT CONNECTIONS OF THE CEREBELLUM IN THE CAT AND RAT. D.L. Decktor* and M. Kalia* (SPON: J.C. Scott). Dept. of Physiol. and Biophys., Hahnemann Med. Col. and Hosp., Philadelphia, Pa. 19102

The retrograde marker, horseradish peroxidase (HRP), has been used to identify cells and nerve fibers in the cerebellum receiving a direct afferent input from the vagus nerves. In 3 cats and 4 rats, anesthetized with nembutal, the cut central end of the right vagus nerve was bathed in a 33% solution of HRP (Type VI, Sigma) for 1-24 hours. At the end of the experiment, the animals were perfused with Karnovsky's fixative and the brains removed, sectioned and processed so that the brown reaction product of HRP could be demonstrated in the nervous tissue by light and dark field microscopy. HRP positive neurons were found in the inferior cerebellar peduncle which is known to be primarily sensory. In addition, labelled fibers were identified in the deep white matter of the cerebellar hemisphere. Occasionally, small discrete areas showing HRP reaction were seen in the granule cell layer of the gray matter of the cerebellar cortex. Control animals without HRP were studied to exclude the presence of endogenous peroxidase activity in the cerebellum. These observations, taken together with physiological studies involving vagal afferents, e.g., pulmonary type J afferents, suggest that (1) a system for coordinating pulmonary-somatic reflexes, e.g., the J reflex, may include as a major component a vagal-cerebellar pathway; (2) there is a direct (monosynaptic) pathway for vagal afferents projecting to the cerebellum. (Supported by USPHS grants HL-00103 and HL-00178.)

KINETIC ANALYSIS OF POTASSIUM TRANSPORT IN THE BULLFROG KIDNEY. D. G. Deeds, L. P. Sullivan, and D. J. Welling. Univ. of Kans. Med. Ctr., Kansas City, Kans.

The movement of potassium in and out of cells in the perfused bullfrog kidney has been studied with the use of ^{42}K. Measurement of tissue uptake and washout of the tracer into the venous effluent and the urine were made using standard techniques. To permit control and experimental measurements in the same kidney, a "pulse-washout" technique was also developed. A one second pulse of ^{42}K is injected into the portal circulation and the urine and venous efflent are serially collected. The washout curves obtained with both techniques are quite similar. The curves for the venous effluent and the urine are parallel but the level of activity in the urine is much less. Other experimental evidence indicates that the curves are not influenced by exchange diffusion of K between tubular fluid and circulation or by backflux of ^{42}K into the cells during the washout procedure. Analysis of the data indicates that there are two major cellular pools of K with half-times of exchange of 5.2±.2 (pool a) and 1.6±.04 mins (pool b) (N=16). Both pools communicate with the urine and circulation. Pool b is smaller than pool a but contributes more K to the urine. In 10 experiments the efflux rate constants from pools a and b into the circulation (k_{ac}, k_{bc}) equaled 0.13±.01 and 0.43±.02 min^{-1}. The efflux rate constants from the pools into the urine (k_{au}, k_{bu}) were much smaller: .004±.001 and 0.13±.002 min^{-1}. With the pulse-washout technique an experimental/control ratio of the flux from the circulation into the pools (J_{ca}, J_{cb}) can be calculated. Acetazoleamide (5×10^{-4}M) increased J_{ca} and J_{cb} and k_{au} and k_{bu} but did not change k_{ac} and k_{bc}: portal perfusion with 10 mM K produced similar results. Ouabain (5×10^{-6}M) reduced J_{ca} and J_{cb} and the size of the two pools.

EFFECTS OF AN ANTI-LH-RH-SERUM IN GONADAL FUNCTION OF HAMSTERS. A. de la Cruz*, A. Arimura, K.G. de la Cruz*, and A.V. Schally, Tulane University School of Medicine and Veterans Administration Hospital, New Orleans, La. 70146

Sheep-anti-LH-RH-serum (antiserum # 772), 0.5 ml completely blocked ovulation when administered iv or sc at any stage of the estrous cycle in cycling hamsters. Intravenous administration of 0.2 ml of antiserum at noon of proestrous still inhibited preovulatory LH surge and ovulation. Serum estradiol (E_2) levels were not completely abolished after 0.5 ml of antiserum, but an arrest of follicular development was observed 3 days after antiserum injection. E_2 administered 22 hrs before the preovulatory LH surge improved significantly ($P < 0.05$) the LH response to LH-RH in antiserum-blocked animals. This suggests a direct modulation of pituitary responsiveness by E_2 in the absence of endogenous LH-RH. When the integrated levels of serum LH following an injection of a minimum effective dose of exogenous LH-RH to induce full ovulation, were compared with those during the physiological preovulatory LH surge, it was found that only 11% of the amount of LH released in the afternoon of proestrous was sufficient for inducing full ovulation in hamsters.

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EFFECT OF OUABAIN ON INTERCELLULAR COMMUNICATION IN HEART. W. C. De Mello, Dept. Pharmacology, Medical Sciences Campus, San Juan, Puerto Rico 00936.

Previous results from our laboratory have shown that intracellular Na injection produces uncoupling of myocardial cells, probably through an increase in the intracellular Ca concentration. In the present study the influence of ouabain on the electrical coupling of canine Purkinje cells was investigated. Dogs were anesthetized with sodium pentobarbital intravenously and the heart immediately removed. Short strands of Purkinje fibers were dissected from the left ventricle and immersed in oxygenated Tyrode's solution at 36°C. The input resistance was measured with a balance bridge circuit. Na was injected electrophoretically into the cell in absence and in presence of ouabain (2.5×10^{-7} M). It was found that the drug shortened the time required for the development of total uncoupling produced by Na injection from 500 sec. to 225 sec. The input resistance of the injected cell increased concomitantly with the decrease in cell communication. Stimulation at high rate (240/min.) in presence of ouabain and Na injection can lead to total uncoupling in two minutes. In fibers partially depolarized by ouabain, the injection of Na leads to total block of impulse conduction through a decrease in junctional conductance. The results support the view that the Na pump can have an important role on the control of junctional resistance in heart. (Supported by grant HL10897 from N.H.I., Bethesda, Md., P.R. Heart Association and General Research Support Grant).

THE APERIODIC CHARACTER OF THE ELECTROENCEPHALOGRAM (EEG): A NEW APPROACH TO DATA ANALYSIS AND CONDENSATION. M. Demetrescu, Dept. Physiology, Univ. of Calif. Irvine, CA., 92664.

EEG information is decoded and presented in a concentrated form while preserving individual characteristics of waves. Criteria for automatic recognition of EEG patterns have been developed starting from the classification initially derived from visual examination of analog EEG recording which, during the past decades has yielded the most efficient way of analyzing and communicating experimental as well as clinical EEG results. Each wave, isolated (e.g. "spike") or in a group (e.g. alpha spindle), is treated as an aperiodic transistory event and defined between two successive maxima (or minima); the reciprocal of the wave duration determines the equivalent frequency; the amplitude of each recognized wave is displayed as the height of an L-shaped character shown in a 3-dimensional reference system (similar to perspective drawing) where equivalent frequency (1-30Hz) is indicated on the horizontal, and time on the depth, axis. Automatic recognition is done by independent channels of analysis in the slow, medium-fast and spike wave ranges. Recordings of sleep sequences, of the effect of drugs (incl. general anesthesia) and of epileptic activity (experimental and clinical) show characteristic patterns due to preserving the temporal sequence and to concentrating up to 180 sec of EEG recording on a single page; averaging, with the inherent loss of information conveyed by single events such as occurring with Fourier-based analysis, is avoided.

CORONARY BLOOD FLOW IN THE CONSCIOUS, UNRESTRAINED PIG. M.J. Denn* and H.L. Stone (SPON: Stewart Wolf). Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

The present studies were designed to examine the roles of atrial pacing and isoproterenol on the left circumflex coronary circulation (LCC) in the conscious, unrestrained pig. LCC flow was also examined during moderate exercise and in response to β-adrenergic receptor blockade during exercise. Under sterile surgical conditions a Doppler flow probe was positioned around the LCC. A catheter was placed in the left atrium along with a solid state pressure cell in the apex of the left ventricle. Experimentation was begun four weeks subsequent to surgery. The average mean LCC flow velocity was 25 cm/sec; while the average mean heart rate was 84 beats/min. A change in heart rate of 150 beats/min by atrial pacing increased LCC flow by 18 cm/sec. dP/dt did not change with pacing. The infusion of isoproterenol at a rate of 0.2 μg/min/kg increased LCC flow by 22 cm/sec. Both flow and dP/dt increased with rates of isoproterenol infusion below this level but only dP/dt continued to increase as the rate of infusion was increased. Flow and maximum heart rate increased linearly with graded exercise. At one level of exercise, flow increased 40% and heart rate increased 134% above control. β-blockade with propranolol decreased both these responses. Body temperature rose slightly during these submaximal work loads. These results indicate that the pig demonstrates a linear relationship between flow and heart rate with pacing and that with exercise the increased flow is greater at similar heart rates. β-blockade eliminates most of the heart rate and flow response to graded exercise. This would mean a dominant role for the sympathetic nervous system in this animal's response to exercise. (Supported by USAF AFOSR 74 2622.)

SPECIFICITY OF NEURAL EFFECT ON RENAL TUBULAR SODIUM REABSORPTION. Gerald F. DiBona. Univ. Iowa Coll. Med. & VA Hosp., Iowa City, Iowa 52242.

To test the specificity of low level direct renal nerve stimulation to decrease sodium excretion ($U_{Na}V$) without changing glomerular filtration rate (GFR) or renal blood flow (RBF, flowmeter), studies were done in the same dog before (NaCl) and after left renal alpha adrenergic receptor blockade with phenoxybenzamine (POB, 0.2 µg/kg/min into left renal artery). Control (C) and recovery (R) periods bracketed stimulation (S) periods; left renal nerve stimulation was 0.5 msec, 10 V, 1.0 Hz. N=10; mean ± SE; † p<.01

	NaCl			POB		
	C	S	R	C	S	R
$U_{Na}V$, µEq/min	237±47	186±44†	235±47	233±46	234±46	231±46
GFR, ml/min	38±5	38±5	38±5	37±6	38±5	38±5
RBF, ml/min	194±24	203±21	192±28	202±21	201±21	202±21

Neither mean arterial pressure (125-130 mmHg) or E_{PAH} (.71-.77) changed significantly throughout. Using microspheres no significant changes in intrarenal distribution of blood flow were observed. Identical studies (N=9) using left renal adrenergic blockade via intrarenal guanethidine infusion (0.4 mg/min) showed similar results.

These studies show that low level direct renal nerve stimulation increases tubular sodium transport in the absence of changes in renal hemodynamics. This effect is specifically blocked by phenoxybenzamine and guanethidine, agents known to interrupt adrenergic neurotransmission.

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THE EFFECT OF LANTHANUM ON THE KINETICS OF THE SODIUM-SENSITIVE CALCIUM FLUX IN MYELINATED NERVE. F.P.J. Diecke and Marguerite A. Stout*, Dept. of Physiology, CMDNJ, New Jersey Medical School, Newark, NJ 07103

Calcium transport in myelinated nerve fibers of frog is mediated by a sodium-calcium countertransport (Diecke and Stout, 1974). In this preparation calcium transport as a function of extracellular calcium concentration follows unimolecular kinetics, while calcium transport as a function of extracellular sodium can be described best by bi-molecular kinetics with a second component resembling substrate activation. We have investigated the effect of lanthanum ions on this transport mechanism. The influx and efflux of 45-calcium were measured in desheathed bundles of myelinated nerve as a function of extracellular sodium or calcium concentrations in the presence and in the absence of lanthanum. Lanthanum ions increase the concentration at which half-maximal saturation of calcium influx occurs (K_M) without affecting the maximal transport (V_{max}). This effect is consistent with competitive inhibition. A similar competitive inhibition of the sodium stimulated and calcium stimulated calcium efflux is observed. In contrast, lanthanum reduces significantly the V_{max} of the activating component without affecting the K_M, thus resembling a non-competitive inhibition.

The dual effect of lanthanum on the kinetics of the sodium-calcium countertransport is compatible with the trivalent carrier model proposed by Baker et al. (1969) for this transport mechanism. The results suggest that lanthanum interacts competitively with the divalent site, but does not interact with the monovalent activating site.

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KINETIC PROPERTIES OF PIG ERYTHROCYTE HEXOKINASE. Earl Dixon. Dept. of Physiology & Pharmacology, Tuskegee Inst., AL 36088

Studies in our laboratory have been designed to determine the regulatory properties of erythrocyte hexokinases. Pig erythrocyte hexokinase has been partially-purified utilizing DEAE-Sephadex A-50, Ammonium sulfate precipitation, KCl elution from DEAE-Cellulose and gel-filtration on Sephadex G-100. The results of these studies indicate that pig mature erythrocytes possess Type III hexokinase. Additionally, the enzyme undergoes a change in both electrophoretic motility and requirements for glucose as the animal matures. The chronological age associated with these changes has been found to be between the ages of 3 to 6 months. While the Km value for glucose increases during this period, the biochemical properties related to $Mg\text{-}ATP^{-2}$ are not significantly altered. Other studies suggest that the activation of the enzyme by Mg^{+2} does not differ for the twc isoenzyme types. These findings suggest that factors involving the isoenzyme type must be taken into consideration in an analysis of metabolic regulation in the mature erythrocyte of the pig.

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CENTRALLY MEDIATED CARDIOVASCULAR EFFECTS OF SYSTEMICALLY ADMINISTERED E. COLI ENDOTOXIN. David E. Dobbins* and George J. Grega. Michigan State University, Dept. of Physiology, E. Lansing, MI 48824

A vascularly isolated, neurally intact canine head-trunk preparation was employed to determine if endotoxin exerts centrally mediated cardiovascular effects. The vascularly isolated head was perfused at constant flow with arterial blood supplied by a donor dog. Spectophotometric examination of the blood following injection of Evan's blue dye to the donor and/or recipient trunk confirmed that there was absolutely no circulatory leakage between the head and trunk of the recipient animal. The responses to various physiological maneuvers, denervations, and pharmacological agents indicated that the central nervous system and all afferents and the efferents involved in the regulation of the cardiovascular system were functioning normally. Endotoxin (1 or 5 mg/kg) infused into the donor animal or into the arterial circuit perfusing the vascularly isolated head produced marked hypotension within 30 minutes in the recipient trunk. This hypotension also occurred following carotid sinus denervation and, therefore, must represent a direct action of endotoxin or substance(s) released by endotoxin on the cardiovascular control centers. The infusion of endotoxin into the vascularly isolated recipient trunk, excluding the toxin from the central nervous system, also produced marked hypotension in the trunk of the recipient animal within 5 minutes. The time course of these responses suggests that the centrally mediated hypotension cannot account for the initial fall in blood pressure following the systemic administration of this substance, but rather that it may contribute significantly to the maintenance of the hypotension. (Supported by National Heart and Lung grant HL 12421).

IDENTIFICATION OF VASCULAR MUSCLE SERIES ELASTIC COMPONENT. Philip Dobrin. Departments of Physiology and Surgery, Loyola University of Chicago, Stritch School of Medicine, and Hines V.A. Hospital, Maywood, Illinois 60153.

Experiments were performed to identify the series elastic component (SEC) in isolated, pressurized dog carotid arteries held at in situ length. Vessels were studied during excitation of the muscle with norepinephrine and also after metabolic-poisoning of the muscle with cyanide-iodoacetate. Static stress-strain curves and stress-quick release dynamic stiffness curves were examined to evaluate Maxwell and Voigt model elements. Twenty-four vessels were treated with elastase, collagenase or hyaluronidase to differentially digest each of the connective tissue components of the wall. Both elastase and collagenase altered the connective tissue properties, but only elastase unequivocally altered SEC stiffness. Hyaluronidase had no detectable effect on vessel mechanics. These observations indicate that a portion of the SEC is located in elastin. Another group of twelve vessels was subjected to thermal variations between 33 and 39°C. This narrow temperature range altered both the muscle length-active stress relationship and the SEC stiffness, but not the connective tissue properties. This association indicates that another portion of the SEC probably is located in the active contractile system. Conclusion: the functional SEC is distributed over two locations. One portion is in the connective tissue elastin, and a second portion is within the active contractile apparatus.

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THE ROLE OF EXTERNAL CALCIUM IN MYOCARDIAL TENSION DEVELOPMENT AND GLYCOGEN PHOSPHORYLASE a FORMATION. James G. Dobson, Jr., Department of Physiology, University of Massachusetts Medical School, Worcester, Massachusetts, 01605.

Since myocardial contraction and glycogenolysis appear to be calcium dependent, this study was undertaken to investigate the role of external calcium in both tension development and phosphorylase a formation in cardiac muscle by removing external ionic calcium (Ca^{2+}). Guinea pig papillary muscles with a maximum diameter of 1.2 mm were continuously stimulated to contract isometrically at 12/min. The muscles were first bathed in normal physiological saline containing 2.5mM Ca^{2+} for 20 min. Both peak contractile force and the fraction of phosphorylase in the a form were determined at the end of an additional 30 min bathing period of either normal physiological saline or Ca^{2+} free physiological saline in which Ca^{2+} was replaced with Na^{+}. Peak contractile force (0.46 ± 0.08 gm) did not change in normal physiological saline, whereas in Ca^{2+}-free physiological saline peak contractile force declined to zero. The fraction of phosphorylase a was the same (0.12 ± 0.03) in muscles bathed with either normal or Ca^{2+} - free physiological saline. At the end of the 30 min bathing period isoproterenol (1×10^{-6}M, for 4 min) produced an increase in peak contractile force from 0.46 ± 0.09 to 1.19 ± 0.30 gm in normal physiological saline, but did not augment peak contractile force in Ca^{2+}- free physiological saline. Isoproterenol increased the fraction of phosphorylase a from 0.13 ± 0.02 to 0.29 ± .03 and 0.30 ± 0.04 in normal physiological saline and Ca^{2+}- free physiological saline, respectively. These results suggest that in cardiac muscle catecholamine induced phosphorylase a formation depends on internal Ca^{2+} and is independent of that external source of Ca^{2+} that appears to be involved in active tension development. Supported by GRS Grant RRO 5712.

EFFECTS OF A AND C FIBER INPUT ON CELLS IN THE THALAMIC POSTERIOR GROUP OF NUCLEI. W.K. Dong* and I.H. Wagman. Department of Animal Physiology, University of California, Davis, California 95616

An investigation was undertaken to determine the response characteristics of thalamic posterior group neurons (PO) elicited by stimulation of A and C fibers, together and separately, in the contralateral superficial radial nerve (RN) of cats lightly anesthetized with sodium thiopental. Three distinct discharge bursts, each followed by an inhibitory period were elicited and correlated to recruitment of Aβγ, Aδ, and C fiber groups respectively. Aβ or Aβγ fibers evoked a brief initial discharge burst of 5 to 15 msec latency followed by an inhibitory period with a duration of 80-100 msec. Recruitment of Aδ fibers evoked a second discharge burst lasting usually 100 msec followed by a second inhibitory period of variable duration. Addition of C fibers increased the discharge frequency of the second burst and also evoked a third discharge burst of 250-300 msec latency followed by another inhibitory period. The appearance of the third burst and inhibitory period was is invariably followed by a prolonged discharge decrementing in frequency over 1 sec or more. When A fibers were selectively blocked by d.c. polarization, C fiber activation elicited only that portion of the response beginning with the latter part of the second burst. Increased levels of anesthesia attenuated the response following the initial burst (i.e., that due to Aβγ input) and more clearly revealed the inhibitory periods; eventually the discharges to Aδ and C input were suppressed. Our results indicate that the response pattern of PO cells to radial nerve stimulation clearly shows a temporal separation due to Aδ and C fiber input. This is in contrast to the response of lumbar dorsal horn cells to sural nerve stimulation. (Supported in part by USPHS Grants NS07844 and RR00169, and A. P. Giannini Foundation.)

HEART RATE AND CONTRACTILITY CHANGES WITH CEREBELLAR STIMULATION. K.J. Dormer* and H.L. Stone. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550

Stimulation of the fastigial nucleus of the cerebellum causes a pressor response accompanied by tachycardia. Dogs were anesthetized with alpha-chloralose and the left ventricle catheterized retrograde. Heart rate, arterial pressure, left ventricular pressure and its derivative (dP/dt) were recorded in response to stimulation of the fastigial nucleus. Heart rate and contractility increased at 0.25 mA of stimulation and increased linearly to a maximum response at 1.5 mA. Heart rate increased 100 beats/min above control while dP/dt was elevated 150% over resting contractility for 1 mA stimulations. Maximally evoked heart rates and contractility exceeded 300 beats/min and 9000 mmHg/sec, respectively. Tachycardia began 1 second into stimulation and peaked after 5 seconds. Contractility began increasing 2 seconds into stimulation and peaked by 7 seconds. Contractility remained elevated throughout stimulation while heart rate often dropped below control levels due to the baroreceptor reflex. Maximal dP/dt dropped slightly during prolonged stimulation (30 sec). Neither response was obliterated by submaximal doses of barbiturates (30 mg/kg pentobarbital). Contractility changes were almost abolished by left stellate ganglionectomy. Frequency response curves were comparable with maximal increases resulting from stimulation frequencies of 80 pulses/sec, 0.1 msec duration. Responses decreased rapidly down to a threshold near 20 pulses/sec. Increases in either dP/dt of 2000 mmHg/sec or heart rates of 120 beats/min were still possible at stimulations of 200 pulses/sec. The results clearly demonstrate cardiac sympathetic activation affects both heart rate and dP/dt, and dP/dt was maintained despite a decrease in heart rate. (Supported by NASA NGR 44 088 002.)

FACTORS INFLUENCING THE ESOPHAGEAL PRESSURE GRADIENT IN UPRIGHT MAN. J. Dosman*, A. Grassino*, P.T. Macklem, and L.A. Engel, Meakins Christie Labs., McGill University Clinic, Royal Victoria Hospital, Montreal, Canada.

We measured the esophageal pressure gradient (EPG) in 5 seated subjects with 2 balloons placed in the mid-esophagus 7.5 ± 1.2 (mean ± 1SE) cm apart. At FRC, the EPG was 0.16 ± .02 cmH_2O/cm. Mueller maneuvers performed mainly with the ribcage (Mrc), as evidenced by only small rises in transdiaphragmatic pressure (Pdi), increased EPG by 0.24 ± .09 cmH_2O/cm for a 5 cmH_2O increase in Pdi (ΔPdi). When similar mouth pressures were reached by Mueller maneuvers performed mainly with the diaphragm (Mdi) EPG decreased by 0.03 ± .01 cmH_2O/cm/ΔPdi ($p < 0.001$). When a lung volume (ca 73%VC) was actively held mainly by contraction of the ribcage muscles (low Pdi) EPG increased by 0.12 cmH_2O/cm above the value at FRC. In contrast, when the same lung volume was maintained predominantly by diaphragmatic contraction (high Pdi) EPG decreased by 0.12 cmH_2O/cm. When subjects relaxed against an obstructed airway at a similar lung volume EPG generally decreased but full relaxation of the diaphragm was not always achieved. We conclude that if esophageal pressures reflect pleural pressures, the ribcage muscles act non-uniformly on the lung during inspiratory efforts, increasing the pleural pressure gradient. Diaphragmatic contraction opposes this increase, tends to decrease the pressure gradient, and helps to preserve homogeneous expansion of the lung.
(Supported by MRC of Canada).

ACTIVATION OF PROTEIN KINASE IN RENAL MEDULLARY SLICES BY VASOPRESSIN Thomas P. Dousa, Y. F. S. Hui* and L. D. Barnes*, Mayo Clinic and Foundation, Rochester, Minnesota 55901

Although protein kinase was implicated in the cellular action of vasopressin, and its presence in renal medullary tissue was described, the activation of protein kinase by vasopressin in unbroken cells was never demonstrated. Bovine renal medullary slices were incubated with or without 2.5 x 10^{-7}M [8-Arg]-vasopressin for 20 min at 30°C in modified Krebs-Ringer solution and at the end of the incubation period slices were homogenized in a medium containing 0.5 mM 1-methyl-3-isobutyl xanthine, 5 mM KH_2PO_4, 2 mM EDTA and 0.25 M sucrose (pH 7.0). The homogenate was centrifuged at 40,000 x g for 10 min and the supernatant was immediately assayed for protein kinase using histones as a substrate with or without addition of a maximal stimulatory dose of cyclic AMP. Protein kinase activation was assessed by the ratio of activity in absence of added cyclic AMP to activity after addition of 5 x 10^{-6}M cyclic AMP in vitro (-cAMP/+cAMP). In slices incubated with vasopressin a significant increase in (-cAMP/+cAMP) ratio was observed, and this was associated with a significant increase in tissue levels of cyclic AMP. Des-gly NH_2-oxytocin, a vasopressin analog which does not stimulate renal medullary adenylate cyclase and some other hormones, which are known not to stimulate renal medullary adenylate cyclase had no effect on protein kinase activity ratio. These observations indicate that cyclic AMP accumulated in renal medulla after addition of vasopressin activates the protein kinase in intact cells.
(Supported by NIH grant AM-16105 and AHA Grant-in-Aid #73689).

BINDING OF Tb3+ TO THE CALCIUM-BINDING SITES OF TROPONIN. R. M. Dowben, J. R. Bunting*, and C. C. Ford*, Depts. Biophysics & Physiology, Univ. Texas Health Sci. Cntr., Dallas, Texas 75235.

The interaction of Tb3+ with the regulatory protein troponin (TN), and with its calcium-binding subunit (TN-C) prepared from rabbit muscle was studied. Ca2+ was removed from the proteins by dialysis against EDTA, and in turn the EDTA was removed by chromatography on Sephadex. Addition of Tb3+ to apo-TN resulted in substantial enhancement of Tb3+ fluorescence. Titration of apo-TN with Tb3+ demonstrated three binding sites for the ion. Two types of sites resulted in strong enhancement of Tb3+ emission with association constants of 3.4×10^5 and 6.3×10^3 at pH 5.5. The third type of site possessed a higher Ka ($\sim 1 \times 10^6$), but gave less Tb3+ emission enhancement. Ca2+ ions strongly competed with Tb3+ binding to the two high affinity sites of apo-TN. Mg2+ ions at physiological concentrations inhibited or altered the binding constants of the highest and lowest affinity sites. Analysis of the Ca2+ concentration dependent inhibition of binding to the middle affinity site demonstrated its equivalence to the previously reported value of Ka = 5×10^6. Binding of Tb3+ to apo-TN-C showed enhancement of Tb3+ emission with one type of binding site, Ka = 1.25×10^5. Mg2+ at concentrations of 5 mM reduced this binding constant to Ka = 6.3×10^4. Ca2+ at 9×10^{-6} M strongly competes for binding reducing the apparent Ka for Tb3+ to 4.0×10^4. Supported by grants from the Muscular Dystrophy Associations and National Institutes of Health HL-16678.

LEFT VENTRICULAR VASCULARITY IN THE HYPERTROPHIED HEART. R.T. Dowell. Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77550.

Pressure-induced left ventricular hypertrophy was created in adult male rats by constricting the abdominal aorta. Three weeks after surgery, aortic constricted (AC) and sham-operated (S) animals were anesthetized and left ventricular pressure was measured in an open-chest preparation. The heart was excised, separated into right and left ventricular (LV) samples and weighed. The LV was further separated into epicardial (EPI) and endocardial (ENDO) portions. Tissue samples were analyzed for alkaline phosphatase (AP) activity. AP is localized in the endothelium of rat coronary vessels and thus served as a marker for total vascularity. AC animals had a significant elevation in LV pressure and approximately a 20% increase in LV mass. In S animals, AP activity (nmole/mg protein min^{-1}) was 6.27 ± 0.68 ($\bar{x}$ ± SE) and 7.56 ± 0.51 in EPI and ENDO, respectively. The ENDO/EPI ratio was 1.24 ± 0.09. In AC animals, AP activity was 7.03 ± 0.32 and 6.85 ± 0.48 in EPI and ENDO, respectively. The ENDO/EPI ratio was significantly reduced to 0.97 ± 0.04. The lower AP activity in ENDO and reduced ENDO/EPI ratio suggests that ENDO vascularity did not increase in proportion to the increase in myocardial mass. Reduced relative vascularity may be related to the reduction in coronary blood flow/gm tissue reported by others in the hypertrophied heart and could result in ENDO ischemia and/or hypoxia in the hypertrophied LV. (Supported by HL 16352 and Amer. Heart Asso. - Texas Affiliate.)

INTRAMYOCARDIAL COMPRESSION IN THE FIBRILLATING HEART. James M. Downey. Dept. Physiology, Univ. of So. Fla., Col. of Med., Tampa, Fla. 33620.

Evidence indicates that subendocardial ischemia is a complication of elective ventricular fibrillation (VF) during cardiac surgery. Experiments were performed to test whether this could be the result of muscle activity compressing the subendocardial vessels. The left coronary artery of the open chest anesthetized dog was cannulated and perfused with arterial blood through an extracorporeal circuit. Coronary inflow rate was held constant with a pump and the coronary vessels were maximally dilated with infusion of adenosine (0.62 mg/min). Thus any change in perfusion pressure or the transmural distribution of flow in these hearts would have been due to changes in compression. When the hearts were stopped in diastole by vagus nerve stimulation, 15μ microspheres revealed a subendocardial to subepicardial flow ratio (1/0) of 1.2. When the same hearts were then electrically fibrillated the 1/0 fell by 40% to 0.7. Coronary perfusion pressure was 74 mm Hg during VF and 70 during arrest indicating that VF elevated total coronary resistance by only 5%. When the contractile activity during VF was attenuated by intracoronary sodium pentobarbital (120 mg) the 1/0 rose by 25% toward that seen in arrest. Augmenting muscle activity with 0.4 μg of isoproterenol, however, failed to change the 1/0. It was concluded that the subendocardial vasculature is selectively compressed during VF. Assuming that compression reduces blood flow by reducing driving pressure (perfusion pressure minus tissue pressure) a mean tissue pressure of 30 mm Hg was calculated for the subendocardium during VF.
(Supported by American Heart grant 74-809 and funds from Palm Beach Heart Association.)

STIMULATION OF ADENYLATE CYCLASE FROM DOG GASTRIC MUCOSA BY HISTAMINE AND ITS BLOCKADE BY METIAMIDE. R.R. Dozois*, A. Wollin*, and R.D. Rettmann* (SPON: C.F. Code). Dept. Surgery & Physiology, Mayo Clinic, Rochester, Minn. 55901

The role of cAMP as an intracellular mediator of gastric acid secretion remains controversial in the dog. Our aim was to determine the effect of the gastric secretagogues histamine (H), N^{α}-dimethyl histamine (N^{α}-Me_2H) and 4(5)-methyl histamine (4(5)MeH) on the adenylate cyclase (AC) of canine gastric mucosa. Membrane fractions from dog gastric fundic mucosae (GFM) were prepared and assayed for AC activity without (basal activity) or with the additions of either H in graded doses, or N^{α}-Me_2H, 4(5)MeH and NaF. The effect of metiamide, a histamine H_2-receptor antagonist, on the AC activity of GFM was then examined. Finally, membrane preparations from gastric antral mucosae (GAM) were assayed for AC activity with and without the addition of H. In the GFM, H(10^{-4}M), N^{α}-Me_2H(10^{-4}M), 4(5)-MeH(10^{-4}M) and NaF(10^{-2}M) significantly ($P < 0.025$ or better) increased AC activity by (mean±SE) 43±7%, 41±8%, 36±11% and 514±95% respectively above basal activity. The H effect was dose-dependent in concentrations ranging from 10^{-6} to 10^{-3}M with maximal stimulation being observed with 10^{-4}M. Metiamide (10^{-3}M) completely blocked the stimulation of AC by H(10^{-4}M). The AC present in GAM was not affected by H but was stimulated by NaF. The findings that the AC of only the GFM is sensitive to H and that this effect can be antagonized by metiamide suggest that the canine gastric acid response to H may be mediated by cAMP.

THE RELATIVE IMPORTANCE OF NET CAPILLARY FILTRATION PRESSURE, TISSUE PRESSURE AND TISSUE FLUID COLLOID OSMOTIC PRESSURE IN OPPOSING PULMONARY EDEMA. R.E. Drake* and A.E. Taylor, Dept. Physiology & Biophysics, Univ. Mississippi Medical Center, Jackson, MS 39216.

To produce pulmonary edema in dogs, the left atrial pressure (P_{LA}) must be raised to 20-25 mmHg. Other tissue forces must change to reduce filtration when P_{LA} is elevated to values less than 20-25 mm Hg. These experiments were designed to demonstrate the relative importance of the net capillary filtration pressure (imbalance in Starling forces), changes in tissue hydrostatic pressure (P_T), and tissue fluid colloid osmotic pressure (π_T) in opposing capillary filtration caused by an increased capillary pressure (P_C). The lymphatic protein concentration was measured in isolated, perfused dog lungs, respired with humidified air and maintained at 37°C. To prevent evaporation from the lung surface, lungs were covered with a transparent plastic bag. In 15 lungs the average P_C was increased from 6.6 $\pm$ 0.9(S.E.M.) mm Hg to 21.2 $\pm$ 1.7 mm Hg and π_T decreased from 15.3 $\pm$ 4.9 mm Hg to 10.5 $\pm$ 2.6 mm Hg. The average lymph to plasma ratio of protein concentration decreased from 0.75 $\pm$ 0.09 to 0.50 $\pm$ 0.02, and lymph flow increased an average of 6.5 times normal. Assuming a reflection coefficient of 1, the permeability-surface area product for total protein was 1.7 x 10^{-3}(ml/sec/100 gm) at the low P_C state and increased to 3.7 x 10^{-3} at the high P_C state. The $K_{F,C}$ was 0.21 ml/min/mm Hg/100 gm, and a pressure drop of only 2 mm Hg across the capillary would cause a filtration rate equal to the higher lymph flow rate observed in edematous lungs. The present investigation indicates that the P_C in dog lungs can be increased 13 mm Hg before edema develops. The increase in P_C is partially balanced by 6 mm Hg increase in P_T, 5 mm Hg decrease in π_T, and 2 mm Hg pressure difference across the capillary membrane.(Supported by NIH grant HL 11477.)

SITE OF AIRWAY CONSTRICTION DETERMINED BY USE OF GASES OF VARYING PHYSICAL PROPERTIES. J.M. Drazen* S.H. Loring* and R.H. Ingram* (sponsored by J. Mead). Dept. of Physiology, Harvard School of Public Health, Dept. of Medicine, Peter Bent Brigham Hospital, Harvard Medical School, Boston, Mass. 02115

Density dependence of maximal expiratory flow rates has been used to analyze the relative contributions of large and small airways to flow limitation. We have performed studies on the use of submaximal flows with gases of varying physical properties as an alternate means of localizing airways obstruction. From fluid mechanical predictions central airway constriction should cause a larger percent change in resistance (R) when flow is turbulent, while peripheral constriction should cause a larger percent change under conditions of predominantly laminar flow.

In anesthetized intubated dogs resistance under predominantly laminar conditions was determined at .25 LPS while breathing an 80% Helium-20% oxygen mixture. Resistance under predominantly turbulent conditions was determined at 1.0 LPS while breathing an 80% SF_6-20% oxygen mixture. R under laminar flow conditions increased 200% during a histamine infusion, while R under turbulent flow conditions increased 60%. This suggested a peripheral site of airway constriction which was confirmed with a bronchial catheter. Tracheal constriction resulted in a 310% increase in R on SF_6 and a 120% increase in R on He. Thus the site of airway constriction can be localized by utilizing different submaximal flow regimes.
(Supported by NHLI grant #HL14580)

BLOOD FLOW IN THE ISOLATED, PERFUSED CANINE BRAIN: NORMAL OXYGENATION VS. ANOXIC ANOXIA. L.R. Drewes*, Lawrence Frazin*, and Allan Levin* (SPON: J.E. Kendrick). Division of Neurological Surgery, University Hospitals, Madison, WI 53706

The mechanisms which regulate cerebral blood flow (CBF) are known to respond to various physiological and chemical stimuli. In most studies of CBF, many of these stimuli are difficult to control or monitor. However, with the isolated, perfused dog brain preparation, a single variable may be altered while keeping others constant. This report evaluates the CBF in this preparation and describes the perfusion characteristics during anoxic, non-ischemic, anoxia. Blood flow distribution was determined by injecting radioactive microspheres (25±5 microns) into the arterial blood stream, fixing and sectioning the brain, and quantifying the radioactivity in brain samples with a gamma counter. During the studies of anoxic anoxia, differently labeled microspheres were injected before and at 5, 15, and 30 min. after the onset of anoxic (PO_2 10mmHg) perfusion. During perfusion at normal PO_2 levels regional blood flow rates varied from about 35 ml/100g per min in the brain stem to over 90 ml/100g per min in the cerebral cortex. Within five minutes of the onset of anoxic anoxia, blood flow to the cerebellum decreased by approximately 40% and remained depressed for the 30 min perfusion period. In contrast, blood flow to the brain stem increased by more than 60% after 5 min and remained elevated during the perfusion period. No evidence for arteriovenous anastomoses of 25 micron diameter or larger was obtained either before or during anoxic perfusion. It is concluded that the brain responds to anoxia by increasing the rate of blood flow to the brain stem and respiratory centers. (Supported by UW Surgical Assoc. and NIH NS05961).

EFFECT OF SINGLE TRIIODOTHYRONINE INJECTION ON GONADOTROPIN-TREATED RATS. N. H. Dubin* (SPON: W. M. Allen). University of Maryland, School of Medicine, Dept. of OB-GYN, Baltimore, Maryland 21201

Ovarian response to gonadotropin is known to be diminished in hyperthyroid rats. The present study considers the effect of a single injection of triiodothyronine (T_3) at various times and doses on the ovarian and uterine weight and serum progesterone response following gonadotropin administration. Immature female rats (26-28 days old) were injected with pregnant mare's serum gonadotropin (PMS) 10 iu/day on days 1-3 of the experimental period and autopsied on day 10. Comparing responses on day 10 to the initial control, increases were observed in ovarian weight (154.3 $\pm$ 16.7 vs. 25.7 $\pm$ 1.6 mg), serum progesterone (208.3 $\pm$ 32.4 vs. 2.5 $\pm$ 0.9 ng/ml) and uterine weight (159.5 $\pm$ 11.6 vs. 40.3 $\pm$ 2.6 mg). Other groups, in addition to PMS, received a single injection of 50 µg T_3 on day 2, 4, 6 or 8. Neither ovarian weight nor serum progesterone was affected by T_3 injection, however, uterine weight was significantly less ($P<.001$) on day 10 in rats receiving T_3 on day 2 (109.1 $\pm$ 4.9 mg) or 4 (117.9 $\pm$ 2.4 mg). In a subsequent experiment, PMS-treated rats received a dose of T_3 ranging from 5 to 200 µg on day 4 and were autopsied on day 10. Uterine weight was less in T_3-treated rats and was inversely proportional to the log of the dose for the range studied. A single properly-timed injection of T_3 interferes with the uterine response following PMS without affecting ovarian weight or serum progesterone. (Supported by the Lalor Foundation)

PHYSIOLOGICAL CHARACTERISTICS OF MOTOR UNITS IN TIBIALIS ANTERIOR AND EXTENSOR DIGITORUM LONGUS OF THE CAT. Richard P. Dum* and Thelma T. Kennedy. Dept. Physiology and Biophysics, University of Washington, Seattle, Wa. 98195

Intracellular stimulation and recording in motoneurons allows the properties of single motor units to be studied in isolation. Using the shape of unfused tetanus and a test of fatigue consisting of 13 stimuli at 40 Hz every second for 2-5 min (Burke, et al., J. Physiol. 234, 1973, 723-748), motor units in tibialis anterior (TA) and extensor digitorum longus (EDL) corresponded to the fast fatigue (FF), fast, fatigue-resistant (FR) and slow (S) categories defined by Burke for gastrocnemius. Few S units or exceptions were found. Three histochemical muscle fiber types have been seen in TA and EDL; it is not yet known if these correspond to the motor unit types. FR units in both TA and EDL tended to have lower tetanic tension than FF units. Distributions of conduction velocity, time to peak of single twitches, and twitch tension to tetanic ratio were coextensive for FF and FR units. In a small sample of the motoneurons having resting potentials greater than 55 mV, homonymous Group Ia EPSPs tended to be larger in EDL-FR units than EDL-FF units, but the population overlapped. Input from flexor reflex afferents from an antagonist (gastrocnemius) and a cutaneous nerve, (sural) tended to be stronger in TA units than in EDL units. The results suggest that the motor units in TA and EDL are similar to gastrocnemius motor units both in muscle unit properties and Group Ia input.
(Supported by PHS GM 00260.)

GLUCAGON SECRETION IN HAMSTERS WITH A TRANSPLANTABLE INSULOMA. J.C. Dunbar*, M. Walsh* and P.P. Foà (SPON: R.S. Shepard). Dept. of Research, Sinai Hospital of Detroit, Detroit, MI 48235.

Tumor-bearing hamsters (TH) had lower serum glucose (G) and higher insulin (IRI) than normal (NH) hamsters (G, 62 ± 8 vs 127 ± 8 mg/dl*; IRI, 36 ± 4 vs 17 ± 4 μU/ml*). Since glucose and insulin are believed to regulate A-cell activity, we studied the effect of the tumor on glucagon secretion in vitro and in vivo, using an antiglucagon serum that measures pancreatic glucagon (IRG) and one that measures IRG and gut or total glucagon (GLI). Pancreatic islets, isolated from NH and TH by collagenase digestion, were incubated for 2 h in Krebs-bicarbonate buffer containing different amounts of G. Islets of TH secreted less glucagon (IRG) and less insulin than islets of NH.

G mg/dl	IRG pg/islet/2 h		IRI μU/islet/2 h	
	NH	TH	NH	TH
30	323 ± 33	108 ± 22**	173 ± 23	27 ± 10**
100	229 ± 43	138 ± 23**	334 ± 37	132 ± 20*
300	203 ± 32	117 ± 25**	952 ± 74	588 ± 37*

Arginine (2 mg/ml) stimulated the secretion of glucagon by islets of NH (control, 164 ± 36; exp., 265 ± 29 pg/islet/2 h*), but not of TH (control, 75 ± 25; exp., 90 ± 26 pg/islet/2 h, n.s.). Although the islets of TH released less IRG in vitro their serum IRG level was normal (TH, 48.5 ± 6 vs NH, 35.6 ± 6 pg/ml, n.s.) and their serum GLI was elevated in the peripheral (TH, 446 ± 64 vs NH, 137 ± 37 pg/ml**) as well as in the portal (465 ± 47 vs 159 ± 40 pg/ml**) blood. Thus, hyperinsulinism may suppress A- as well as B-cell function in TH, while the gut may be a source of GLI in these animals. *=$p<0.05$; **=$p<0.01$; n.s. = not significant; ± = SEM (Aided by NIH Grant AM06034)

EFFECT OF LOADING CONDITIONS ON A TRANSMURAL LACTATE GRADIENT IN THE ISCHEMIC LEFT VENTRICLE. R.B. Dunn*, K.M. Hickey*, and D.M. Griggs, Jr. Dept. Physiology, University of Missouri, Columbia, Mo. 65201

We have previously shown that completely stopping right and left coronary flow in the open chest dog for 30 seconds produced a left ventricular transmural lactate gradient increasing from epicardium to endocardium. Additional studies suggested that the transmural lactate gradient might be indicative of regional differences in energy need within the ventricular wall. In order to test this hypothesis further the effect of altering ventricular loading conditions on the lactate gradient were studied. Experimental interventions included 1) infusing the animal with donor blood prior to stopping coronary flow to increase ventricular preload and afterload 2) excising the apex of the heart coincident with stopping coronary flow to unload the left ventricle and 3) removing blood from the left atrium during no coronary flow to maintain ventricular preload within normal limits. After varying periods of no flow a transmural left ventricular sample was taken and freeze clamped in <2 seconds. Analysis was performed on the outer, middle and inner thirds. Results revealed that during no coronary flow animals with increased preload and afterload had an accelerated rate of lactate production and an earlier appearance of the lactate gradient. Unloading the ventricle reduced the rate of lactate production and abolished the transmural lactate gradient. Maintaining the preload within a normal range did not eliminate the development of a lactate gradient. These results indicate that regional myocardial lactate production during no coronary flow is related to the ventricular loading conditions, and they support the hypothesis that the energy need of the normal left ventricle is uneven and greatest in the subendocardium. (Supported by Grant HL 11876 from NHLI).

MYOCARDIAL METABOLISM AND HEMODYNAMICS DURING EXPERIMENTAL NECROSIS. Beatrice C. Durham and Harvey I. Miller, Hahnemann Medical College, Philadelphia, PA and L.S.U. Medical Center, New Orleans, LA

Myocardial (myo) infarction or necrosis can be produced experimentally by coronary artery ligation, obstruction with microspheres (MS) or by large doses of catecholamines. Metabolic and hemodynamic effects of two experimental models for producing these kinds of lesions were studied in closed-chested, unanesthetized dogs. In one group, DL-isoproterenol (ISO) (2.5 mg/kg) was administered subcutaneously at 24 hr intervals and hourly samples drawn after the 2nd dose. In the other group, coronary occlusion was achieved by injecting plastic MS (400 microns) into a coronary artery and sampling was at 30 min intervals. Arterial FFA concentration did not change due to MS, but ISO caused a marked rise from 1.181 to 1.902 μEq/ml (mean change $p < .001$). Myo FFA extraction ratio (XR) decreased in both cases ($p < .001$ and $< .01$ respectively). Arterial glucose remained constant following MS but decreased 37% with ISO ($p < .001$). With ISO, myo glucose XR was unchanged but decreased significantly following MS ($p < .01$). In neither group did arterial lactate concentration, myo lactate XR or myo respiratory quotient change significantly. In both cases, coronary blood flow showed a tendency to increase greatly. Cardiac output decreased with MS by 70% but increased by 64% with ISO (both $p < .01$). Mean arterial pressure remained unchanged by MS but showed a decrease with ISO ($p < .001$). While both models produce areas of necrotic tissue, ISO's additional sympathomimetic effect might account for the contrasting results obtained. Diverse etiology might also contribute to differences seen in the human disease states.

INHIBITION AND DESTRUCTION OF PREOPTIC NEURONES BY IRON. R. G. Dyer* (SPON: A. L. Hodgkin). Institue of Animal Physiology, Babraham, Cambridge, England.

Female rats were anaesthetized with pentobarbitone (40mg/kg,I.P.) at 13.00 hours on proestrus. The tip of a microsyringe was stereotaxically lowered into the rostral hypothalamus and 1 µl of either 0.9% saline or 200 mMFe^{++} injected into the brain. The following morning no ova were collected from the fallopian tubes of the saline treated animals (N-8). However, a full complement of eggs (12.6 ± 0.5/rat) was recovered from all 8 rats injected with Fe^{++}. Microscopic examination of the brains injected with Fe^{++} revealed very few intact cells in the 100 µm.sq. surrounding the initial lesion caused by the tip of the syringe. At the periphery of this zone many of the cells contained iron, although there was none remaining in the extracellular space. The profiles of cells showing the strongest concentration of iron were indistinct and the histology showed that cells exposed to Fe^{++} were destroyed. In a final series of experiments minute quantities of ferrous ions were applied, by microiontophoresis, to single neurones, in the rostral hypothalamus. The spontaneous discharge of 14 out of 18 cells was markedly inhibited by Fe^{++} whereas, at the same current, Na^{+} was always without effect. Excitation was never observed with Fe^{++} It is unlikely, therefore, that electrochemical stimulation of the rostral hypothalamus triggers gonadotrophin secretion by excitation of neurones. Furthermore, if iron destroys cells their contents may then diffuse directly to the region of the median eminence and exert an effect independent of the electrical activity of preoptic and anterior hypothalamic neurones.

NOREPINEPHRINE BIOSYNTHESIS AND CHOLINE ACETYLTRANSFERASE ACTIVITY IN THE HEART CHAMBERS OF GUINEA PIGS. R.H. Dykstra*, H.E. Mayer*, R.P. Oda*, R. Roskoski, Jr.*, and P.G. Schmid. Dept. of Int. Med. and CV Center, Univ. of Iowa and VA Hosps., Iowa City, Ia. 52242

The concept that sympathetic-parasympathetic interactions are significantly involved in the overall autonomic regulation of cardiac function is based partially on the qualitative evidence that both types of innervation have corresponding distributions to the various regions of the heart. The present study was done to obtain a quantitative indication of the relationship of the sympathetic and parasympathetic innervation to the heart. Resting levels of sympathetic activity to the four heart chambers were assessed by quantitating the decay of tracer amounts of ^{3}H-l-norepinephrine in tissues from atria and ventricles of normal guinea pigs. Tissues were obtained 6, 18, and 27 hours after intravenous injection of the tracer. Synthesis rates were calculated as the product of the rate of decay (k_{NE}) and the endogenous level of norepinephrine. The synthesis rates of norepinephrine averaged 334±116 ng $gm^{-1}hr^{-1}$ (±SE) in the right atrial appendage, 187±81 ng $gm^{-1}hr^{-1}$ in the left atrial appendage, 111±48 ng $gm^{-1}hr^{-1}$ in the right ventricle, and 71±35 ng $gm^{-1}hr^{-1}$ in the left ventricle. These values suggest that resting sympathetic activity is greatest in right atrium and least in left ventricle. In a previous study, choline acetyltransferase, a marker of the parasympathetic innervation, was greatest in right atrium and right ventricle and lower in left atrium and left ventricle (4.05± 0.43, 2.33±0.14, 1.77±0.20 and 1.33±0.14 n moles $min^{-1}gm^{-1}$, respectively). Thus, the pattern of resting sympathetic activity and the distribution of the sympathetic innervation to heart chambers of the guinea pig appears to correspond to the distribution of the parasympathetic innervation.

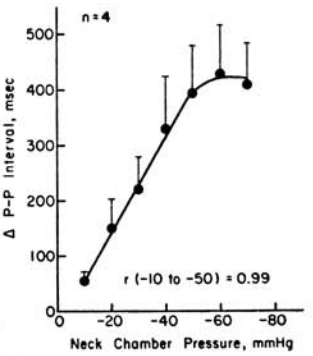
NUCLEAR TRIIDOTHRYONINE (T_3) RECEPTORS IN DEVELOPING RAT BRAIN AND LIVER. N.L. Eberhardt,* T. Valcana,* and P.S. Timiras, Dept. of Physiol.-Anat., Univ. of Cal., Berkeley, Ca. 94720

To understand the role of thyroid hormones in development we have examined binding characteristics of nuclear T_3 receptors in cerebral hemispheres and liver of the rat. Binding was monitored with a competitive binding assay over the concentration range 5-2000 pM. Scatchard analysis of the data revealed deviations from linearity at low concentrations for both cerebral and liver nuclear binding, evidence for cooperative binding and/or multiple hormone receptors. The apparent number of binding sites (n^{ap}) expressed as moles T_3 bound/μg DNA and apparent dissociation constants (k_d^{ap}) were extrapolated from the linear portion of the Scatchard plot. There was no significant change in n^{ap} with age in either liver or cerebrum, nor was there any significant change in the k_d^{ap} of liver nuclei with age. The k_d^{ap} of cerebral nuclear receptors(s) from newborns is similar to those of liver, however, the 13day and adult cerebral nuclei have lower k_d^{ap} than 13day and adult liver nuclei. The k_d^{ap} of adult cerebral nuclei is also lower than that of adult anterior pituitary nuclei. The decrease with age in k_d^{ap} of cerebral receptor(s) suggests that they may be modified, are uniquely different or that there is a change in the relative proportion of receptors with different k_d^{ap}. The decrease in k_d^{ap} indicates that the normal cerebrum is responsive to T_3 at lower levels in the adult, which could explain differences in response to exogenous T_3 treatment, e.g., the lack of increased O_2 consumption, between adult and developing brain and adult brain and liver, since the adult brain may be operating at maximum efficiency at normal hormonal levels.

(Supported by NIH grant HD 07340)

TRANSFER CHARACTERISTICS OF THE HUMAN CAROTID SINUS. Dwain L. Eckberg. Cardiovascular Center and Cardiovascular Division, Department of Medicine, University of Iowa College of Medicine and VA Hospital, Iowa City, Iowa 52242.

Carotid sinus nerve firing frequency, or pulse interval, has been recorded during step increases of endosinus pressure in experimental animals, but comparable studies have not been undertaken in man. In four healthy, young men, carotid stretch receptors were activated with transient (0.6 sec) reductions of pressure in a neck chamber, of from ten to 70 mm Hg, and carotid distending pressure was considered to be the absolute sum of neck chamber and peak systolic arterial pressures. Stimuli were delivered during held expiration, and were timed to occur 0.8 sec before the anticipated appearance of the P wave. Arterial pressure averaged 110/73 mm Hg. Average pulse interval (+SEM) responses are summarized in the figure.



These preliminary results suggest the following: 1) In the normal arterial pressure range, pulse interval is a linear function of carotid sinus distending pressure. 2) In the subjects studied, the average gain over the linear portion of the response was 8.7 msec/mm Hg. 3) Pulse interval prolongation reaches an asymptotic peak at carotid sinus distending pressures of about 165 mm Hg; distending pressures which exceed this limit do not evoke additional baroreceptor activity.

BRAIN MONAMINE DYNAMICS: POLYPEPTIDE HORMONE REFRACTORINESS TO LEVODOPA. R.L. Eddy and K.M. Parker*, Endocrinology Unit, Dept. Medicine, VAH & University Texas (Southwestern) Medical School, Dallas, Texas 75216

Much evidence has accumulated implicating dopamine as a CNS neurotransmittor involved in the regulation of trophic hormone secretion. We have previously shown a consistent HGH peak response (mean increment 28.2 ng/ml, $p < 0.001$) at 90 minutes following a single 0.5 gm oral levodopa (l-dopa) dose. To further examine the pharmacodynamics of l-dopa upon HGH secretion we studied 16 normal adults under basal conditions for their HGH responses to repeated 0.5 gm l-dopa doses. All subjects revealed a HGH response (mean 26.5 ng/ml) to the initial l-dopa dose. Four subjects then received a repeat l-dopa dose at 3 hrs; 4 subjects at 4 hrs; 4 subjects at 5 hrs; and 4 subjects at 6 hrs. No subjects (0%) responded to a repeat l-dopa dose at 3 hrs; 50% responded to a repeat l-dopa dose at 4 hrs; and, 100% of the subjects responded to a repeat l-dopa dose at 5 and 6 hrs. The same subjects were then re-studied utilizing higher (1.0 gm) l-dopa doses. Again, all subjects responded initially (mean increment 27.1 ng/ml) to l-dopa. No subjects (0%) responded to a repeat l-dopa dose at 3 hrs; 75% responded to a repeat l-dopa dose at 4 hrs; and, a 100% response occurred to repeat l-dopa doses at 5 and 6 hrs. The results indicate that the dopaminergic mechanism of HGH release is refractory to further stimulation for 4-5 hrs following the initial response to l-dopa. The significance of this refractory interval is unknown. We suspect an explanation involving a failure during this interval to acheive a sufficient central dopamine concentration rather than the unlikely depletion of HGH or growth hormone releasing factor (GRF).

THE ACTION OF PENTAGASTRIN ON INSULIN AND GLUCAGON RELEASE IN THE ANESTHETIZED DOG. L.E. Edwards and A.C. Brehme*, Department of Physiology, Medical College of Virginia, Richmond, Virginia 23298.

This investigation was designed to study the partial control of intermediary metabolism by the G.I. hormones. The fact that gastrin and the other G.I. hormones are involved in the release of insulin and glucagon must mean they have some control of intermediary metabolism. If one makes the assumption that insulin and glucagon are the dominating hormones in this regulation, then the portal levels of these hormones set the beginning stage for the further control of intermediary metabolism. Eight anesthetized dogs were prepared so that portal blood samples could be taken. Glucose, glucagon and insulin were measured over 3½ hour intervals. After two one half hour control periods, each animal was perfused with pentagastrin for one half hour period and then followed another 2 hours. Four dogs were treated as normal animals. Two dogs were treated the same way after their pancreases were removed. Two dogs were given the same treatment after their stomachs were removed. It was found that the normal animals produced as many as three peaks in the insulin and glucagon levels. The first and the most prominent occurred during the perfusion period. From the studies on the depancreatized and gastrectomized animals it was concluded that during pentagastrin stimulation the glucagon comes from pancreatic sources. Later peaks may come from non-pancreatic sources.

SELECTIVE IMPAIRMENT OF RED CELL FLOW THROUGH THE LUNGS. R.M. Effros and P. Silverman*, Div. of Resp. Physiol. and Med., Harbor Gen. Hosp.-UCLA School of Medicine, Torrance, CA 90509.

An isolated,perfused, ventilated rabbit-lung preparation was used to study factors which alter the relative rates of passage of labeled red cells and albumin through the pulmonary vasculature. A bolus containing rabbit red cells (labeled with ^{51}Cr or ^{99m}Tc) and ^{125}I-albumin was injected into the pulmonary artery and the venous outflow collected from the left atrium in 40 serial samples at 0.6 second intervals. The perfusion solution hematocrit remained less than 2%. The ratio (r) of the mean transit time of red cells to that of albumin averaged 0.84 $\pm$ 0.02 (SD) and red cell recovery averaged 100 $\pm$ 3% of albumin recovery. These control values were similar to those obtained in intact rabbits. In 19 studies of 5 lungs, r invariably increased as perfusion sodium chloride concentrations were raised, ranging from 0.75 at 220mosm/kg to 1.04 at 550 mosm/kg. This impairment of red cell passage occurred despite decreases in pulmonary vascular resistance observed with moderate increases of osmolality. Red cells hardened with acetaldehyde showed increased r values and decreased recovery. Increases in red cell size (from 70μ^3 for rabbit cells to 87 μ^3 for human cells), changes in vascular resistance, increases in left atrial pressure and pulmonary edema had minor or no effects on r. Of the factors studied, only those which alter red cell deformability were important in selectively slowing red cell transit through the pulmonary vessels.
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EFFECTS OF DISULFONIC STILBENES ON ANION AND CATION TRANSPORT IN THE TURTLE BLADDER. G. Ehrenspeck* and W.A. Brodsky. Dept. of Physiology & Biophysics, Mount Sinai School of Medicine, N.Y., N.Y. 10029.

Cabantchik and Rothstein (1972) showed that disulfonic stilbenes bind to the outer surface of erythrocytes to block the Cl efflux component of a Cl:Cl exchange across this membrane. We have found that 4-Acetamido-4'-iso-thiocyanato-stilbene-2,2'-disulfonic acid (SITS), at concentrations of 10^{-6} to 10^{-4}M inhibits the active transport of anions (Cl and HCO_3) from mucosal to serosal fluid in the turtle bladder. This inhibition was complete and occurred with little or no delay, having half-times of about 5 min (10^{-4}M) to 30 min (10^{-6}M). Compared to erythrocytes, SITS inhibition of anion movement in the turtle bladder is 10^2 to 10^3 more potent, and cannot be reversed by washing with albumin. Evidence for sidedness of this effect is the following: (i) Inhibition of anion transport is elicited only after adding SITS to the serosal fluid. Even when added to the mucosal fluid at much higher concentrations (10^{-3} M), SITS had no effect whatsoever for 20-30 min, then induced a slow and sometimes partial inhibition with a half-time of about 30 min. (ii) Although SITS is as strong an inhibitor of in-vitro (Na + K)·ATPase as is ouabain, Na transport in vivo is not inhibited by SITS either in the serosal or in the mucosal fluid. This suggests that: (i) the inhibitory sites for SITS are located on the cytoplasmic-facing surface of the basal-lateral membrane, and that (ii) little or no SITS crosses the apical or basal-lateral membrane to reach the cytoplasmic compartment. Nevertheless, the inhibitory actions of SITS parallel those of acetazolamide on anion transport and on carbonic anhydrase activity. These findings suggest that the flow of anions across the basal-lateral membrane (from cell to serosal fluid) is mediated by a carrier which is related to or identical with carbonic anhydrase. (Supported by grant GB-34062 from NSF and grant 1 ROI AM 16928-01 from NIH.)

ROLE OF DORSAL FUNICULI IN POSITIONAL CONTROL OF SKILLED MOVEMENTS IN MONKEYS. E. Eidelberg, B. Woolf* and C. J. Kreinick*. Division of Neurobiology, Barrow Neurological Institute, Phoenix, AZ. 85013.

Monkeys (M. speciosa) were trained in a visuomotor pursuit tracking task where indirect visual control of forelimb position could be introduced or excluded. Performance was assessed by analysis of the tracking error signal. Section of the corresponding dorsal funiculus (F. cuneatus) produced only a transient deficit in the performance of this task. Subsequent ablation of postcentral cortex (SI) produced a more persistent deficit, which was reduced by introducing visual feedback. We suggest that sensory feedback is required for accurate control of forelimb movement, but that the dorsal funiculi are not the only routes for the proprioceptive data. Cortical SI lesions could interfere with sensory feedback, with corollary discharge mechanisms, or both.
(Supported by General Research Support Grant RR05575 from the National Institutes of Health).

REGIONAL MYOCARDIAL BLOOD FLOW (RMF) IN CLOSED-CHESTED DOGS WITH LEFT VENTRICULAR HYPERTROPHY (LVH). S. Einzig, J.J. Leonard, M.R. Tripp, H.B. Burchell and I.J. Fox. Univ. of Minn., Minneapolis, MN 55455.

LVH was produced by supravalvar aortic banding in 6-10 week puppies. 6-8 months later, under morphine-chloralose, catheters were placed in R. atrium (RA), pulmonary artery, LA (transeptally) and retrogradely into LV of 6 dogs (mean weight: 12 kg) which met our criterion of LVH: Heart weight/body weight (H/B) ratio > 9.9×10^{-3}. Control LV pressure averaged 237 $\pm$ 21/11 $\pm$ 3 (SEM) mm Hg, aortic pressure, 98 $\pm$ 5/72 $\pm$ 7 mm Hg and heart rate 92 $\pm$ 20. RMF was measured by successive LA injections of ^{85}Sr, ^{46}Sc and ^{141}Ce-labeled 8μ microspheres. For RMF studies, the entire LV was divided into 3 coronal slices comprising 9 different regions (4 in each of both the basal and midventricular slices plus the apical remainder) which were subdivided into sixty 0.5-2.5 gm samples taken from the endocardial (endo) midwall and epicardial (epi) areas. The control endo:epi flow ratio of 0.89 $\pm$ 0.05 in the 6 dogs with LVH (mean H/B ratio 14.1×10^{-3}) was significantly ($P < 0.05$) lower than that of 1.11 $\pm$ 0.03 found in our lab and in the literature in normal dogs. In 5 operated dogs which did not develop LVH (mean H/B ratio 7.9×10^{-3}) the control endo:epi flow ratio was 1.14 $\pm$ 0.05 ($P < 0.01$). Nitroglycerin (TNG)(2 μg/kg) was injected i.v. as a bolus in 4 LVH dogs and microspheres injected immediately after the systemic pressure returned to near control level (at 2 min) showed no change in mean LV endo:epi ratio (0.99 $\pm$ 0.05, $P > 0.05$). Of the 9 regions only the posterior papillary muscle showed a significant change, a decrease in the endo:epi ratio after TNG to 0.83 $\pm$ 0.05, $P < 0.01$. Preventing the systemic pressure fall and reflex tachycardia after TNG by thoracic aorta balloon inflation in 2 dogs increased the endo:epi flow ratio to 1.16, supporting data previously reported from this lab in open-chested dogs without LVH.

EFFECT OF ENDOTOXIN ON GLUCOSE KINETICS AND CARDIOVASCULAR RESPONSE IN THE CONSCIOUS DOG. D. Elahi, R.R. Wolfe, and J.J. Spitzer, Dept. of Physiology, L.S.U. Medical Center, New Orleans, La. 70112

The rate of appearance of glucose (Ra) was measured in unanesthetized, unrestrained dogs with indwelling arterial and venous catheters, according to the primed constant rate infusion technique, using 6-^{3}H-glucose as the tracer. After establishing steady state, E. coli endotoxin (0.8-1 mg/kg, Difco Laboratories, Detroit) was administered intravenously and glucose turnover was measured until the animal died, or for 6 hours. In all dogs plasma glucose (GLU) decreased in the early part of the experiment. In the survivors GLU then increased towards the pre-endotoxin level, whereas in the nonsurvivors GLU continued to fall to about 20 mg per cent. Although GLU frequently decreased to 50 mg per cent, Ra did not decrease and in some cases it increased. Only preterminally did Ra exhibit lower than control values. The metabolic clearance rate increased in all dogs following endotoxin but the increase in the nonsurvivors was greater than that of the survivors. The plasma insulin levels tended to decrease. Cardiac output and mean arterial pressure both decreased transiently, but returned towards normal by 30 minutes. We concluded that death appeared to be due to severe hypoglycemia rather than cardiovascular failure. Endotoxin greatly increased the ability of the tissues to remove glucose from the plasma independent of changes in Ra or insulin levels. (Supported by NIH grant HL 16850)

THE EFFECT OF PARADOXICAL SYSTOLIC EXPANSION ON THE DERIVATIVE OF LEFT VENTRICULAR PRESSURE. Virgil B. Elings,* George E. Jahn,* William W. Parmley, John V. Tyberg and John H. K. Vogel, Physics Dept., Univ. of Calif., Santa Barbara, Calif. 93106

The effect of paradoxical systolic expansion of ischemic myocardium on the derivative of left-ventricular (LV) pressure was studied both experimentally and theoretically. Simultaneous high-fidelity pressure and segment lengths were measured from left ventricles of 6 open-chested dogs in which the LAD coronary artery was occluded for periods from 2 to 5 minutes. The onset of stretching of the ischemic segment was accompanied by a dip in the time derivative of the LV pressure, both of which moved to earlier points in the cardiac cycle as the occlusion progressed. In the portion of the cardiac cycle up to the onset of stretching, the contraction of the ischemic segment was essentially normal and, therefore, isometric indices of contractility such as V_{max} were not affected until the ischemic region became completely passive. A theoretical model of regionally ischemic cardiac muscle was analyzed and the results indicate that the dip would not occur if the ischemic region were replaced by a stiff, scarred region or a passive aneurysm. Clinically the appearance of the dip in the derivative may aid in the discrimination between salvageable ischemic myocardium and irreversibly-damaged myocardium in the intact heart.

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A SIMPLE MODEL FOR PREDICTION OF RISK OF HEART ATTACK.
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Coronary atherosclerosis is the main cause for heart attack. The degree of coronary sclerosis can be used as a risk index. Over the last two decades we have been especially interested in the mechanism of atherosclerosis and we have reached the conclusion that the narrowing process of the arterial lumen is primarily dependent upon two basic factors. One is a physical factor, namely blood pressure (p) which drives lipid material into the arterial wall. The other is a chemical one, namely the concentration of lipid (c) in the plasma. The so-called secondary contributing factors, such as diabetes, coffee drinking etc. are essentially comprised in the two basic factors. Hence the risk value can be simplified by the following equation.

$$I/E = \text{degree of atherosclerosis} = 1 - e^{-kcpt}$$

where k is a constant, a focal factor in any particular artery, p is the blood pressure, c is the concentration of cholesterol in the plasma and t is the age in years of the subject. The risk values are computed through a computer at different concentration of cholesterol, blood pressure and age. The tables are very useful for the general practitioners as well as researchers to get a general idea of the patient without the expensive clinical tests once the blood pressure and cholesterol value are known.

INFLUENCE OF IN VIVO DEXAMETHASONE ON CANINE PULMONARY LAVAGE FLUID SIALIC ACID, PROTEIN, AND GLYCOPROTEINS. R. L. Engen and Y. Intraraksa*, College of Veterinary Medicine, Iowa State University, Ames, Iowa 50010

The right lung was lavaged on six dogs. After a six week recovery period, the dogs were treated for five days with Dexamethasone (0.22/kg) and the right lung lavaged. Two thousand mls of lavaged fluid were collected from each dog for the control and treatment periods. Dexamethasone decreased the quantity of lyophilized surfactant fraction from 72.9 $\pm$ 9.30 ($\bar{X} \pm$ SEM) to 50.45 $\pm$ 6.74 mg (P, .10-.20) and decreased the quantity of lyophilized supernatant fraction from 189.1 $\pm$ 13.42 to 124.38 $\pm$ 14.49 mg (P, 0.02). Sialic acid concentration in the lyophilized surfactant fraction increased from 7.89 $\pm$ 0.91 to 11.90 $\pm$ 0.84 mg/gm (P, 0.02). Sialic acid in the supernatant fraction increased from 15.97 $\pm$ 1.06 to 18.33 $\pm$ 1.76 mg/gm (P, NS.) Because of a decreased quantity of both lyophilized surfactant and supernatant fractions after Dexamethasone treatment, the total amount of sialic acid decreased. The plasma sialic acid concentration increased from 53.52 $\pm$ 2.45 to 69.06 $\pm$ 4.93 mg/100 ml (P, 0.02). Electrophoretic gel separations of the plasma, lyophilized surfactant and supernatant fractions were conducted for protein and glycoproteins. Thin-layer chromatography was used to identify the phospholipids in the surfactant fraction. (This work was supported by GRSG # 430-23-45-00-0204.)

LOCAL RELEASE OF AUTONOMIC MEDIATORS FROM VENTRICULAR EPICARDIUM BY FIELD STIMULATION. D. E. Euler* and W. C. Randall. (SPON: A. R. Dawe) Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Field stimulation was used to release autonomic mediators from the epicardial surface of the ventricles in anesthetized dogs. The stimulations were performed through a unipolar electrode embedded in one foot of a modified Walton-Brodie strain gauge arch. The gauges were sutured to four different regions of the ventricular epicardium. Pulse trains of 5-40 ma intensity were applied through the strain gauge electrodes during the absolute refractory phase of the cardiac cycle. The trains were applied for a total duration of one minute. Local changes in contractility were measured as changes in amplitude of the strain gauge recordings. The trains caused local increases in contractility as great at 100% of control. IV administration of atropine (1 mg/Kg) caused an increase in magnitude of the positive inotropic response to the pulse trains while bilateral vagal stimulation (8V, .5 ms, 20 Hz) during ventricular pacing caused a decrease. β-adrenergic blockade with Tolamolol (2-3 mg/Kg) completely eliminated the positive inotropic response during the pulse trains. After total autonomic blockade the pulse trains exerted a slight direct negative inotropic effect on the ventricular epicardium which was followed by a positive rebound. The results suggest that there are sympathetic and parasympathetic plexuses in the ventricular epicardium which are activated during field stimulation. The simultaneous release of the two autonomic mediators results in predominately a sympathetic response which is slightly attenuated by the parasympathetic influence. (Supported by NHLI/NIH Grant HL 08682.)

OSMOTIC TRANSFER OF WATER IN THE PLACENTA OF THE SHEEP. J. Job Faber and Kent L. Thornburg, Dept. of Physiology, Medical School, University of Oregon Health Sciences Center, Portland, Ore. 97201

The sheep placenta has a high diffusional permeability to isotopically labelled water although, unlike the hemochorial placenta, its diffusional permeability to solutes such as Na^+, Cl^-, mannitol, and urea is low. In chronically prepared fetal lambs, we measured umbilical blood flow, arterial and venous osmolarities, and maternal placental blood flow and arterial and venous osmolarities. Maternal plasma osmolarity was raised by an intravenous infusion of mannitol to about 60 mOsm/L above its control value. Fetal osmolarity increased, due to the withdrawal of fetal water. Arteriovenous differences in osmolarity were small in both placental circulations, but the blood flow in these circulations is large. We estimate the osmotic water permeability of the sheep placenta at about 0.0025 $ml \cdot min^{-1} \cdot mm\ Hg^{-1} \cdot kg\ fetus^{-1}$. The permeability, if expressed per gram placental weight would be about 200 times smaller. There is essentially complete osmotic equilibration of fetal and maternal plasma osmolarity during gestation. If fetal water acquisition is by way of the placenta, we must conclude that the transfer of an osmotically active solute must accompany and may regulate the transfer of water.

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VENTILATORY EFFECTS ACCOMPANYING BODY MOVEMENT IN SUCKLING OPOSSUMS.
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While ventilatory effects of induced and spontaneous body movement have been studied in adult mammals, little is known about the potential for similar responses during development. We assessed ventilation during spontaneous body movement in suckling opossums between 20 and 60 days of age. The youngest animals of this group are capable of rhythmic ventilation, but only the oldest of these animals are comparable in development to the placental mammal newborn. Ventilation breathing air as well as hypoxic and asphyxiant gas mixtures was measured using pressure plethysmography. Spontaneous movements, most often consisting of wriggling, were observed visually and measured electromyographically from the phasic activity of neck muscles. Periods of body movement could occur breathing any test gas, but were most regularly observed during hypoxia. Ventilatory responses with spontaneous movement were variable. In some cases, tidal volume (V_T) and breathing rate (f) became highly irregular; and episodes of apnea were observed. However, opossums retaining a generally regular ventilation pattern showed characteristic responses with movement. The youngest animals increased V_T but changes in f were variable. With increasing age, f as well as V_T was increased; and increases in f dominated the response by the 30-40th day. These data suggest that spontaneous body movement is associated with ventilatory effects early in the course of development. The observed increases in f, contrast with the predominantly V_T response of 20 to 60 day old opossums during ventilatory chemostimulation with hypercapnic and asphyxiant gas mixtures (The Physiologist 17:219, 1974). (Supported by NIH grant HL-15311.)

METABOLIC ACTIVITY DIFFERENCES BETWEEN BEHAVIORAL TYPES OF DEER MICE.
L. Farr*, M. Kline* and R.V. Andrews, Creighton U., Omaha, Nb. 68178.

A study designed to determine whether there are differences in metabolism and energy expenditure between different behavioral cohort types. Male deer mice were reared both in single cages and within a multi-cage habitat in which a heterosexual population was allowed to interact and breed freely. Metabolic measurements were made by isolating unrestrained mice in a closed circuit metabolism chamber. Oxygen usage was monitored simultaneously with microswitch recording of running and feeding activity. All ranks of isolated animals have higher daily oxygen consumption and activity than do habitat-reared animals. Habitat dominants have higher metabolic rates than subordinates, and the metabolic rates of isolated males are higher than those of either intermediates or subordinates. Isolated dominants eat more than do isolated intermediate and subordinate mice or than all three habitat types. Isolated dominants also lose weight under conditions of exposure to the metabolic chamber while subordinate and intermediates gain. All habitat ranks gain; however, dominants show the smallest increase. Habitat subordinates make more trips to the food hopper than do dominants and confine much of their eating to periods during which dominants are inactive. Dominant habitat-reared males show more running activity than do habitat subordinates. Metabolic rates of both isolated and habitat-reared animals show that dominant animals use more energy. Food consumption and body weight changes by dominants support this conclusion. Utilization of food by habitat subordinates during periods of dominate inactivity and lower running wheel usage by habitat than isolation subordinates suggest avoidance resulting from dominate-subordinate interactions during rearing. Differences observed in daily metabolism become more pronounced when the daily rhythm of oxygen consumption and activity is analyzed. (Supported in part by NSF Grant GB25450)

FLOW RESERVE AND LARGE ARTERY HEMODYNAMICS DURING GRADED STENOSIS
D.J. Farrar*, G.S. Malindzak, Jr., and G. Johnson, Jr.*, Department of Surgery, University of North Carolina, Chapel Hill, N.C. 27514

Large artery resistance (R_L), total resistance (R_T), flow ($\dot{Q}$), and stenosis pressure differential (ΔP) were determined in the femoral arteries of 12 anesthetized mongrel dogs during graded arterial stenosis. At each level of stenosis maximum flow response was produced by reactive hyperemia (RH), following 2 minute total occlusion of the artery, and by 0.3 mg intra-arterial bolus nitroglycerine (NG). Pressure was measured approximately 5 cm proximal (P_P) and distal (P_D) to the graded stenosis which was produced by a snare placed around the artery. R_L was determined for each fixed stenosis from the slope of the relationship $\Delta(P_P-P_D)/\Delta\dot{Q}$. R_T was computed from the ratio $P_P/\dot{Q}$, and an estimate of the % diameter reduction (% D) from the unstenosed artery was computed from the data for each level of stenosis. The mean results for all the animals are summarized in the following table for baseline (no stenosis) and two levels of increasing stenosis. [Units: R_L and R_T in 10^3 dyne · sec/cm^5, $\dot{Q}$ in ml/min, $\Delta P=P_P-P_D$ in mmHg; SS = steady state before RH and NG.]

	% D	R_L	R_T			$\dot{Q}$			ΔP	
			SS	RH	NG	SS	RH	NG	SS	NG
BASELINE	0	2	130	70	25	93	194	505	2	10
STENOSIS A	58	15	144	100	43	79	126	212	7	45
STENOSIS B	65	45	174	136	75	64	74	112	15	67

Conclusions: Maximum flow reserve is greater with NG than RH, possibly due to cutaneous shunts; both responses are substantially reduced by increases in R_L. Large increases in R_L due to stenosis also produce large increases in ΔP with NG compared to relatively small changes in steady state R_T, $\dot{Q}$, and ΔP.

EFFECT OF INDOMETHACIN ON RENAL HEMODYNAMICS AND SALT AND WATER EXCRETION. L. P. Feigen*, E. Klainer*, B. M. Chapnick*, and P. J. Kadowitz* (Spon: J. Pisano). Tulane Medical Center, N.O. La. 70112.

The effect of indomethacin (In, 2.5 mg/kg i.v.) on glomerular filtration rate (GFR), renal blood flow (RBF), filtration fraction (FF), renal vascular resistance (RVR), fractional values of osmolar clearance (FC_{osm}), free water clearance (FC_{H_2O}), urine flow rate ($F\dot{V}$), and excretion rates of Na (FE_{Na}) and K (FE_K) was studied in 10 dogs under pentobarbital anesthesia (30 mg/kg i.v.). Blood and urine samples were obtained before and then 15, 45, and 75 min after In. Fifteen min after In, mean aortic pressure had increased by 15% and then remained elevated. RBF fell by 1/3, RVR had doubled, and since GFR remained unchanged, FF increased 33%. FC_{osm} fell to 50% of control while FC_{H_2O} remained at control levels. $F\dot{V}$ fell by 50%. FE_{Na} and FE_K both fell 50%. The 45 min data paralleled that of 15 min while the 75 min values showed that RVR increased still further while FC_{osm}, $F\dot{V}$, FE_{Na}, and FE_K had returned to near control values. These results indicate that In caused a transient Na, K and total osmolar retention, but not free water retention. GFR was not affected while RVR was markedly increased. The decrease in $F\dot{V}$ and FC_{osm}, as well as FE_{Na} at 15 min in contrast to the maintenance of constant FC_{H_2O} indicates the presence of enhanced reabsorption in more proximal nephron sites than the ascending limb of Henle's Loop.

REGULATION OF LOCAL CEREBRAL OXYGEN EXTRACTION RATES. J.M. Fein and R. Eastman, Dept. Neurosurgery, Albert Einstein College of Medicine, New York, N.Y. 10461

The factors influencing the rates of local oxygen extraction in cortex, white matter and putamen was investigated in seven adult cats. Oxygen sensitive polarographic electrodes were placed stereotactically and after recording the level of oxygen availability transient occlusion of both common carotid arteries produced a decay whose slope was related to the oxygen extraction rate. The resting values for oxygen extraction in cortex and putamen differed significantly from those obtained in white matter and correlated with the difference in blood flow values in these regions of interest. Changes in arterial blood pCO_2 values known to effect the cerebral blood flow rates did not significantly change oxygen extraction rates between pCO_2 values of 18 - 60 mm Hg. Larger doses of barbiturate anesthesia depressed the extraction rates significantly. Metrazol, 50 mg i.v. produced a significant increase in mean extraction rates in cortical recording in all animals studied. The data indicate that measurement of local oxygen extraction rates in vivo, utilizing polarographic techniques, is practical and provides an indication of the oxidative metabolic rate of small volumes of brain tissue. The rates of oxidative metabolism are regulated between narrow limits despite large changes in blood flow, but quickly adapt to changes in pharmacologically induced neuronal stimulation and depression.

EFFECTS OF PULMONARY AFFERENTS (PA) ON BRAIN STEM RESPIRATORY NEURONS IN RELATION TO INSPIRATORY CUTOFF. J.L. Feldman*, M.I. Cohen, and P. Wolotsky*. Dept. Physiol., Albert Einstein Col. Med., New York, N.Y.

The mechanism of inspiratory cutoff was studied by observing the effects of cycle-triggered inflations on brain stem respiratory neuron discharge in decerebrate, paralyzed cats. Phrenic nerve discharge served as an indicator of respiratory center output. Lung inflation at constant flow was applied coincidentally with phrenic discharge during control cycles by means of a phrenic-triggered pressure system; and during test cycles (every 10th cycle), no inflation was applied. This procedure allowed observation of changes in neuronal activity associated with the Breuer-Hering reflex, which consisted of prolongation of the inspiratory phase with no change in the slope of the directly integrated phrenic discharge. In the region of the nucleus tractus solitarius (NTS), two types of inspiratory neuronal responses were observed: a) Some neurons showed changes in discharge pattern similar to those of phrenic discharge. b) Other neurons showed a decreased rate of rise of frequency when there was no inflation; these might be identified as the $R\beta$ neurons described by others, and which are thought to function as inspiratory cutoff neurons.

Dorsolateral rostral pontine (pneumotaxic center, PC) neuronal activity showed dramatic changes during test cycles; many units which had tonic activity, not respiratory-modulated, during the control cycles became strongly inspiratory-modulated when inflation was absent. This strong ascending inhibitory influence from the PA to the PC inspiratory-modulated neurons suggests that the Breuer-Hering reflex may be mediated through pontine neuronal as well as medullary neuronal circuits. (Supported by NS 03970.)

EFFECT OF BOMBESIN ON GASTRIN AND SECRETIN AND ON GASTRIC AND PANCREATIC SECRETION. H.R.Fender,* P.J.Curtis,* P.L.Rayford,* D.D.Reeder and J.C.Thompson, Department of Surgery, University of Texas Medical Branch, Galveston, Texas 77550.

Bombesin, a 14-amino acid polypeptide purified by Erspamer from extracts of the skin of certain frogs, is known to release gastrin in dogs. We have tested the effects of bombesin infusion on gastrin and secretin and on gastric and pancreatic secretion. Methods: Five mongrel dogs were prepared with pancreatic fistulas and Heidenhain pouches (HP). Venous catheters were later placed for blood sampling and for bombesin infusion. Samples of pancreatic juice (PJ) and of peripheral blood were obtained before, during and after a 1-hr infusion of bombesin (1 µg/kg/hr). Gastrin and secretin were measured by radioimmunoassay; molecular forms of gastrin were separated by Sephadex gel filtration. PJ was collected in 10-minute aliquots for volume, bicarbonate output, and protein output determinations. HP secretions were collected at 30-minute intervals. Results: Gastrin increased significantly from 45±7 pg/ml to 254±64 pg/ml at 15 minutes (p <0.02) and was significantly elevated at 5, 10, 30 and 60 minutes. Elevated levels of gastrin were chiefly the G-34 and G-17 forms. HP acid output increased from 0.94±0.51 mEq/30 min to 2.67±0.45 mEq/30 min (p <0.05). Secretin levels declined significantly at 5, 10, 15, 30 and 120 minutes after beginning the infusion. Volume of PJ was insignificantly elevated, but both bicarbonate and protein levels increased significantly. Conclusions: Bombesin releases significant quantities of serum gastrin and augments HP acid secretion in the dog. Bombesin directly or indirectly depresses serum secretin levels, but significant elevations in pancreatic juice bicarbonate and protein were noted.
(Supported by NIH grant AM 15241.)

RES-INSULIN INTERACTIONS IN ENDOTOXIN SHOCK. James P. Filkins and Bernard J. Buchanan. Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Lethal endotoxin shock in rats is characterized by profound hypoglycemia and a depression of the reticuloendothelial system (RES). In addition, inhibition of insulin secretion protects against endotoxin shock (The Physiologist 17: 189, 1974). The present study evaluated select interactions of RES and insulin functions in endotoxin shock in rats. Hypoglycemia induced by insulin ip depressed the intravascular clearances of both colloidal carbon and endotoxin. Depression of the RES by carbon blockade sensitized rats both to endotoxin shock as well as fatal insulin-induced hypoglycemic convulsions. Endotoxin sensitized rats to lethal insulin convulsions; insulin, in turn, sensitized rats to fatal endotoxin shock. RES depression concomitant with endotoxin treatment resulted in enhanced insulin sensitivity as compared to either carbon blockade or endotoxin treatments alone. Carbon blockade increased glucose tolerance as reflected in a depression of the zenith of the blood glucose response to 400 mg glucose iv; in addition, the hyperglycemic response was abbreviated. Glucose catabolism as reflected by increased expiration of $^{14}CO_2$ after ^{14}C-glucose ip was enhanced by RES depression. These data support a novel role for the RES in the altered insulin sensitivity and the concomitant changes in carbohydrate homeostasis which characterize endotoxin shock.

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CHARACTERIZATION OF ADRENERGIC RECEPTORS MEDIATING DEPOLARIZATION IN BROWN ADIPOSE OF NEWBORN RATS. S.A. Fink* and J.A. Williams (SPON: E. Mayeri). Dept. of Physiology, U. of California, San Francisco, CA. 94143.

The effect of catecholamines on the transmembrane potential (Vm) of brown adipocytes was studied in vitro using interscapular brown fat pads from reserpinized, 7-12 day old rats. L-phenylephrine (PH), L-isoproterenol (IP) and L-norepinephrine (NE) when added to the superfusion medium induced dose-dependent depolarizations over the range of 10^{-8} to 10^{-6}M. Maximal depolarizations in response to all three agonists was 22 to 27 mV while control Vm was normally -55 to -63 mV. These adrenergic agonists also all produced similar transient depolarizations when bolus-injected into the superfusion chamber while continuously recording from one cell. D-NE was 300 times less potent than L-NE. The PH-induced depolarization was antagonized by phentolamine (10^{-7}M), but not by propranolol (3×10^{-6}M). IP was antagonized by propranolol, and to a lesser extent by phentolamine. Phenoxybenzamine (10^{-8}M)acted similarly to phentolamine, but was observed to act in a non-competitive manner. Dopamine was 100 times less potent than PH and was antagonized by phentolamine. Acetylcholine (10^{-4}M) and serotonin (10^{-5}M) had no significant effect on Vm. Tyramine (10^{-5}M) and DMPP (100 μ gm/ml) depolarized the brown adipocytes in untreated rats comparably to exogenous catecholamines but had no effect when tested on brown fat from reserpinized rats. These results indicate that both alpha and beta-like receptors mediate catecholamine-induced depolarization of brown fat cells; neither acetylcholine nor serotonin affect Vm, and tyramine and DMPP depolarize by causing release of endogenous catecholamines (supported by NIH grant GM-19998).

MUSCLE FIBER COMPOSITION AND ENZYME ACTIVITIES IN MALE AND FEMALE ATHLETES. W. J. Fink*, D. L. Costill, J. Daniels*, M. Pollock* and B. Saltin*. (SPON: T. Lesh). Human Performance Laboratory, Ball State University, Muncie, Indiana 47306

Muscle samples were obtained from the gastrocnemius of 17 female and 46 male track athletes, and 11 untrained men. Portions of the specimen were analyzed for total phosphorylase, lactic dehydrogenase (LDH), and succinic dehydrogenase (SDH) activities. Sections of the muscle were stained for myosin adenosine triphosphatase (ATP-ase), $NADH_2$ tetrazolium reductase, and alpha-glycerophosphate dehydrogenase. Maximal oxygen uptake ($\dot{V}o_2$ max) was measured at exhaustion on a treadmill. Significant differences were found between the fiber composition of sprint, middle distance, and long distance runners. Slow twitch fiber composition (% ST) averaged 25.7, 56.3, and 79.9% for these runners, respectively. Athletes who demonstrated successful performance in jumping and throwing events were found to have 38.6 to 56.2% ST fibers. Untrained men showed a wide range in fiber composition, 38 to 73.2% ST. Enzyme data demonstrate that endurance training significantly increases ($P < 0.05$) SDH activity. Distance runners, for example, were found to have SDH activities in excess of 25 μmoles/g x min, whereas the untrained and sprint trained men averaged 7.4 and 10.4 μmoles/g x min, respectively. LDH activity was found to be a function of muscle fiber composition ($r = -0.70$). It was concluded that the adaptability of fibers for oxidative and glycolytic metabolism may be of greater importance to performance than the relative composition of slow and fast twitch fibers in muscle.

SODIUM REQUIREMENT FOR THE CHLORIDE TRANSPORT STIMULATION BY EPINEPHRINE IN THE RABBIT CORNEAL EPITHELIUM. F. H. Fischer* and J. A. Zadunaisky (Spon: W.J.Sullivan), NYU Medical Center, New York, N. Y. 10016

Potential difference (PD) and short-circuit current (SCC) were measured in isolated rabbit corneas mounted in Ussing-Zerahn type chambers. After stimulation by $5 \cdot 10^{-5}$M epinephrine the SCC increased 80% to 16.3 ± 1.6 (SEM) $\mu A \cdot cm^{-2}$. This response of the SCC to epinephrine was modified by the sodium content of the bathing solution. There was no increase at zero sodium, and a full response at 100 mM sodium and over. The SCC remained low between 2-3 $\mu A \cdot cm^{-2}$ at low sodium concentration and increased suddenly between 100 and 144 sodium to 9.5 ± 0.9 (SEM) $\mu A \cdot cm^{-2}$. The low current may represent the chloride fraction of the SCC in rabbit corneas, thus confirming previous findings. There was an inverse relationship between initial SCC and SCC after epinephrine: % increase of SCC after epinephrine was higher at low initial SCC and lower at high initial SCC. This relationship was found at 75, 100 and 144 mM sodium. There was no such relationship at zero and 40 mM sodium. The sodium ion was required on the endothelial side of the cornea. Low sodium on the epithelial side did not modify the epinephrine response, whereas low sodium on the endothelial side caused a decrease of SCC after epinephrine. Ouabain $5 \cdot 10^{-5}$M inhibits after 3 hours 59% of the epinephrine response.

The findings confirm the hypothesis that the ATPase system is involved in the stimulation of the active chloride transport by epinephrine in the rabbit corneal epithelium.

PROGESTERONE AND THE CAROTID BODY. R. Fitzgerald and J.W.C. Johnson*, Departments of Environmental Medicine and Obstetrics-Gynecology, Johns Hopkins University, Baltimore, Maryland 21205.

Progesterone has been used to stimulate ventilation in subjects hypoventilating due to obesity. It has not been clear how progesterone promotes the increase in ventilation observed either in these patients or in pregnancy. The purpose of these experiments was to test the possibility that progesterone changes the sensitivity of the carotid body to CO_2 under normoxic conditions. Cats were prepared so that single or few fiber recordings of carotid body chemoreceptor activity could be made. Under control conditions with the mean PaO_2 = 90.5 torr the $PaCO_2$ was raised from 22.3 torr to 45.0 torr. The slope of the response was 0.26 counts/sec/torr CO_2. A solution of progesterone (1 µgm/1ml saline-Emulphor) was administered into the femoral vein or thyroid artery just caudad to the carotid body at a rate of 1 µgm/3 minutes. This represents a concentration of 6-13 µgm/100 ml plasma. Though progesterone is rapidly cleared from the blood, we allowed one hour to pass before repeating the response curve. At a mean PaO_2 = 95.0 torr $PaCO_2$ was increased from 18.0 torr to 47.7 torr. The slope was somewhat elevated (0.31 counts/second/torr CO_2). From these data we conclude that under normoxic conditions physiological levels of progesterone seem to have little immediate effect on the carotid chemoreceptor response to moderate degrees of hypocapnia or hypercapnia. (PHS Grants HL-10342, ES-00454.)

DUODENAL-JEJUNAL LOOP DIALYSIS WITH CHOLERA TOXIN IN ANURIC DOGS. Christopher Fletcher*, Stephen Kimbrough*, Ralph A. Nelson and Charles F. Code. Mayo Medical School, and Mayo Clinic and Mayo Foundation, Rochester, MN 55901 (Spon: D. T. Cody)

The effect of cholera toxin on duodenal-jejunal loop dialysis was investigated in nine anuric dogs. A Thiry-Vella loop was constructed in each dog, following which the dogs were fed a low protein, low water diet which reduced blood urea level 50% prior to surgical induction of acute renal failure. The dogs were divided into three groups for intestinal loop dialysis. Group I was dialyzed with sodium sulfate or mannitol solution 6 L/8 hr; Group II with cholera toxin alone; and Group III with a combination of cholera toxin and sodium sulfate solution 6 L/8 hr. In Group I, urea, Na, Cl, K moved from blood to dialysate readily while P, Ca, and creatinine were slow in movement. About 1.4 gm urea and 2.3 mEq of K were removed/day. Cholera toxin in Group II produced a continuous hypertonic fluid loss into the gut lumen from blood. Concentrations of Na, K, Cl were significantly higher, P, Ca, creatinine lower and urea slightly higher than respective blood concentrations. About 0.5 gm urea and 2.0 mEq of K were removed/8 hr. Group III dialysis revealed enhanced removal of urea and potassium over Groups I and II, but no effect on P, Ca, creatinine. About 2.2 gm urea and 4.5 mEq K were removed/8 hr. It was concluded that under the conditions of this study the effect of cholera toxin was selective, enhancing movement from blood to gut lumen of urea, K, Na, Cl, while producing no change in that of P, Ca, and creatinine.
(Supported by Northwest Area Foundation grant 8469.) (Cholera toxin supplied by NIH cholera program.)

DECREASE OF MAXIMUM OXYGEN UPTAKE FOLLOWING EXPOSURE TO OZONE. L.J. Folinsbee, F. Silverman*, and R.J. Shephard. Gage Research Institute, Toronto, Canada.

We have measured the maximum oxygen uptake ($\dot{V}O2$ max), using a bicycle ergometer, of 13 adult males following two hours of intermittent bicycle exercise (15 min work at ~ 50 W alternated with 15 min rest) in an environmental chamber. Two maximum exercise tests were performed; the chamber was ventilated once with filtered air (FA test) and once with filtered air plus 0.75 ppm ozone (PO test). Two subjects were unable to perform maximum exercise following ozone exposure. When the two maximum tests were compared, the $\dot{V}O2$ max declined 11% ($P<.01$) following ozone exposure. In addition, the maximum workload attained was reduced by 12% ($P<.01$), maximum ventilation decreased 16% ($P<.01$) and maximum heart rate decreased by 6% ($P<.05$) in the PO test. At the highest workload attained in both maximum exercise tests, heart rate and oxygen consumption were similar although ventilation tended to be slightly higher in the PO test ($P<.05$). However, in the PO test, the frequency of respiration increased 45% ($P<.01$) and tidal volume fell 29% ($P<.01$) relative to the FA test at the same workload. At maximum exercise, the respiratory frequency was similar in both the FA and PO tests but the tidal volume was 21% lower ($P<.01$) in the PO test. A decrease in vital capacity and $FEV_{1.0}$ as well as cough and discomfort on taking a deep breath were noted following ozone exposure. We conclude that the reduction in $\dot{V}O2$ max is a result of a limitation of maximum ventilation due to discomfort at the high level of ventilation demanded by maximum effort.
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ISCHEMIC-LIKE CHANGES INDUCED BY ATRACTYLOSIDE. J. D. Folts, A. L. Shug,* J. R. Koke,* and N. Bittar,* Dept. of Medicine, University of Wisconsin, Madison, Wisconsin 53706.

Experiments were conducted on 8 open chest anesthetized dogs to determine the cardiac effects of the glycoside, atractyloside, a specific inhibitor of adenine nucleotide translocase (ANT), the mitochondrial nucleotide carrier whose activity has been shown to be inhibited when myocardial ischemia is produced by coronary artery ligation. The dogs were instrumented with electromagnetic flowprobes on the aorta and a branch of the left coronary artery, as well as with epicardial ECG leads, and an aortic pressure catheter. With an infusion rate of 75nmoles/ml/min directly into the coronary artery for 10 min, ST segment elevation (5-7 mm) was noted within 30 sec. Coronary flow increased from an average of 43 ml/min to 88 ml/min ($p < 0.001$). Aortic blood pressure decreased from an average of 106 mm Hg to 96 mm Hg ($p < 0.01$), and contractility in the perfused bed was visibly impaired. Heart rate and cardiac output did not change significantly. Ultrastructural studies of biopsy specimens obtained during the infusion showed mitochondrial changes similar to those seen in the ischemic myocardium. The ST segment deviation, with increased coronary flow and unchanged cardiac work indicates that atractyloside may produce changes similar to ischemia, without an actual decrease in oxygen delivery to the myocardium. These studies suggest that inhibition of the mitochondrial nucleotide carrier may be an important initial event in the changes noted in myocardial ischemia.

INHIBITION OF ARTERIAL ACTOMYOSIN SUPERPRECIPITATION BY SUBCELLULAR FRACTIONS FROM BOVINE AORTA by G.D. Ford*, J. A. Davis* and R.Z. Litten* (Spon. J. Poland). Dept. of Physiology, Medical College of Virginia, Richmond, Virginia 23298.

Two subcellular organelles, mitochondria and sarcoplasmic reticulum, of vascular smooth muscle have been implicated as possible sequestration sites for activator calcium on the basis of their ability to sequester divalent cations. To further verify this implication, we have prepared a calcium-sensitive actomyosin from bovine aorta by a modification of the method of Sparrow, et al. (Am. J. Physiol. 219: 1366 (1970)) and monitored its superprecipitation by following absorbance changes at 550 nm upon addition of ATP. Under conditions chosen to maximize the superprecipitation reaction (I = 0.1 M, pH 7.0 and T = 37 C), a mon-mitochondrial, vesicular fraction also prepared from bovine aorta was able to completely inhibit the superprecipitation reaction when the ratio of vesicular material to actomyosin was as low as 1:1000 on a mg protein basis provided a calcium-precipitating anion such as oxalate was present. A mitochondrial-enriched fraction also prepared from bovine aorta was unable to inhibit the arterial actomyosin superprecipitation reaction under the same conditions even when the ratio of mitochondrial material to actomyosin was 3:4 on a mg protein basis. These results correlate with a diminished ability of the mitochondrial to take up ^{45}Ca under the conditions in which the superprecipitation was monitored. In so far as these conditions apply, these results suggest that the mitochondria may not play a major role in the calcium sequestration producing relaxation in vascular smooth muscle.

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THE EFFECT OF PERIPHERAL CHEMORECEPTOR DENERVATION ON VENTILATORY ACCLIMATIZATION TO HYPOXIA IN PONIES. H.V. Forster, G.E. Bisgard, B. Rasmussen,* D.D. Buss*, J.A. Orr* and M. Manohar*, Dept. of Vet. Science, Univ. of Wisconsin, Madison, 53706 and Dept. of Env. Med., Medical Coll. of Wis., Milwaukee, 53226

Six ponies were studied under normal conditions and then were subjected to surgical denervation of their carotid and aortic chemoreceptors (CD). CD resulted in: 1) hypoventilation during sea level conditions (Pa_{CO_2} +6.3, Pa_{O_2} -5.0 mmHg, $P<.05$) and 2) elimination of the ventilatory response to intravenous injections of NaCN. Four weeks after CD the ponies were studied in a hypo/hyperbaric chamber after 2 days at 740 mmHg and then repeatedly during 4 days at 570 mmHg. Pa_{CO_2} did not change during the first 1.5 hr of hypoxia (H) (Pa_{O_2} = 42 mmHg) which suggests that $\dot{V}_E$ remained at control levels. Between the 2nd and 6th hr of H, Pa_{CO_2} fell 2.6 mmHg ($P<.05$), and decreased an additional 1.9 mmHg between the 6th and 12th hr ($P<.05$). $\dot{V}_E$ and $\dot{V}_A$ measured at 5 hrs were above normal ($\dot{V}_A$ significant at $P<.05$). This coupled with Pa_{CO_2} data suggests ventilatory acclimatization to H equal to that of normal ponies. Our measured values of arterial and cerebrospinal fluid pH could not account for this change. Acclimatization was transient, however, as by 18 hrs Pa_{CO_2} was only 1.5 mmHg below control ($P>.05$) and after 44 hrs $\dot{V}_E$, $\dot{V}_A$ and Pa_{CO_2} remained at control levels. Prior to chronic H, hyperoxygenation had no effect on $\dot{V}_E$ but after 92 hrs of H, it induced hyperventilation (ΔPa_{CO_2} = -8.4 after 45 min at Pa_{O_2} = 160 mmHg). Our data may reflect hypoxic induced changes in facilitation and inhibition of the ventilatory control centers in various CNS structures. It is concluded that the peripheral chemoreceptors are vital for the normal process of ventilatory acclimatization to H in ponies. (Supported by PHS grant HL15473).

THERMOREGULATORY EFFECTS OF MONOAMINE INHIBITION AND POTENTIATION. R. P. Francesconi and M. Mager. U. S. Army Research Institute of Environmental Medicine, Natick, MA 01760

We have previously reported hypothermic effects of L-tryptophan and L-tyrosine when these monoamine precursors were administered peripherally. These studies have been extended to investigate further the relationship between central monoamines and thermoregulation. Thus, rats were equipped with permanent indwelling cannulae to permit direct intraventricular administration of effector substances. Large doses (20 µg) of serotonin (S) and norepinephrine (NE) resulted in significant hypothermia ($p< .001$, $p< .005$ respectively) when rats were housed at 22°C. However, intraventricular administration of parachlorophenylalanine (CPA) and alpha-methyltyrosine (MT), inhibitors of S and NE biosynthesis respectively, produced no thermoregulatory effects. Interestingly, both chlorimipramine (C) and imipramine (I), drugs which potentiate the effects of S and NE in a more physiological manner by preventing their reuptake into nerve endings, elicited significant ($p< .001$) hyperthermic responses. Even when endogenous levels of S and NE were reduced by chronic intraperitoneal administration of CPA and MT, treatment with C and I consistently evoked marked hyperthermia ($p< .001$). Results of these investigations indicate that hypothermic responses, elicited by peripheral administration of monoamine precursors and inhibitors, are produced peripherally by action on the sites of heat production. Further, hypothermic responses to pharmacological dosages of S and NE are possibly induced by synaptic blockade, while synaptic stimulation, effected by the prevention of reuptake of either S or NE, results in marked hyperthermia even when hypothalamic levels of endogenous monoamines are reduced by chronic CPA and MT administration.

MATURATION OF THYROID RESPONSES TO COLD EXPOSURE IN RATS. S.Frankel* and G. Lange, Dept. Physiology, Downstate Medical Center, Brooklyn. New York 11203

Maturation of the response to cold exposure stress was studied by assaying the quick thyroid reaction to acute exposure of 4,5,7 and 10 week old male rats to cold (5°C. for 30 min.). The degree of response was assayed by counting P.A.S. stained colloid droplets (CD) within follicular cells (Shishiba, et al,Endocrinology 80:957, 1967). Plasma T_4 levels were likewise determined. Fifteen minutes prior to exposure, three groups of animals were given I.V. injections: 0.2 ml saline (normal reaction group), TSH (10mU), TRF (10μg) in 0.2 ml volumes of saline. In the 4 and 5 week old rats cold exposure elicited no thyroid response (no increase in CD) in normal, TSH or TRF injected animals. In the 5 week old rats cold exposure actually diminished the CD count below that of the controls which was, however, unexpectedly high. In the 7 week old rats there was a significant thyroid reaction but the 10 week old animals showed a markedly greater response to cold. TSH and TRF did augment CD formation indicating an ability of the pituitary and thyroid to respond in all age groups but the responses of the 4 week olds were minimal. Histological evidence of thyroid activation indicated immaturity of the hypothalamic or central mechanisms responsible for reaction to cold stress in 4 and 5 week old rats. Even in 7 week old animals the response was not as great as in 10 week old animals. Plasma T_4 levels were increased by exposure to cold in all animals, even those injected with TSH and TRF and those showing no CD indication of thyroid response. The early response to brief periods of cold exposure is therefore complex, involving a release of T_4 not readily detected by observation of CD formation.

REGIONAL VENTRICULAR WALL DYNAMICS DURING ACUTE CORONARY ARTERY OCCLUSION AND REPERFUSION IN CONSCIOUS DOGS. D. Franklin, S. Sasayama*, D. McKown*, S. Kemper* and J. Ross, Jr., Scripps Clinic and University of California, San Diego, La Jolla, California 92037

Dimensions i.e., wall thickness (WTh) and circumferential endocardial segment length (SL), of perfused and ischemic elements of myocardium were measured using miniature (<2 mm) implanted ultrasonic dimension gauges. In 5 conscious dogs prior to CO, WTh increased during systole by 2.3 ± 0.3 mm (SEM) (22 ± 3%). During 2 min. circumflex coronary artery occlusion (CO) by inflation of hydraulic occluder, end-diastolic ischemic WTh decreased with a further systolic thinning totalling 1.5 ± 0.5 (15 ± 5%) as SL elongated. A transient (15-20 sec.) protodiastolic elongation and thickening appeared in the perfused element at onset of CO. On reperfusion, ischemic wall thickening increased within 40 sec. to 49 ± 13% greater than control with a systolic component related to reactive hyperemia (3-4 min. elevation over control of circumflex coronary artery blood flow and systolic WTh to SL ratio) and a protodiastolic component which persisted for 20-40 min. This protodiastolic thickening occurred simultaneously with the previously reported protodiastolic shortening of ischemic SL following reperfusion. Thus, ischemic WTh changes correlated with abnormalities in contraction, anomalous protodiastolic wall thickening was associated with ischemic events and wall thinning during systole identified completely ischemic areas. Also, ischemic wall stress was elevated due to wall thinning and the normal reduction in wall stress during systole due to wall thickening was eliminated in completely ischemic elements.

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ADDITIONAL EVIDENCE OF TRAPPED AIR HAVING OPEN AIRWAYS IN EXCISED RAT LUNGS. D. G. Frazer* and K. C. Weber. ALFORD, NIOSH, USPHS, DHEW, & Dept. of Physiology & Biophysics, WVU Med. Ctr., Morgantown, WV 26506.

Rat lungs were ventilated in a liquid filled plethysmograph in which tracheal pressure, P_{ao}, could be altered while holding lung volume, V_L, constant (Physiologist, 17:3;74). The level of the carina was chosen as the zero transpulmonary pressure, P_L, reference. Prior studies show that the amount of trapped air in the lungs increased as the inflation-deflation rate decreases (Fed. Proc., 33:303;74) and that air is trapped during inflation (Fed. Proc., 33:1494;74). In this study control curves were recorded for 10 continuous cycles as lungs were inflated-deflated at 3.82 cc/min from an initial atelectatic state and with P_{ao} equal to ambient pressure. The lungs were then degassed and a second ventilation pattern was used consisting of the following cycles: (1) inflation at 3.82 cc/min, a PVSA (Pressure, Vacuum, Stress Adaptation) maneuver, deflation at 3.82 cc/min, (2) inflation at 38.2 cc/min, a PVSA maneuver, deflation at 1.91 cc/min, and (3) inflation at 1.91 cc/min, PVSA maneuver, and deflation at 38.2 cc/min. The PVSA maneuver was performed at maximum lung volume (P_L = 30cm H_2O) and consisted of the following: (a) an 8 minute stress-adaptation period (SAP), (b) P_{ao} was increased to P_{amb} + 350 torr followed by a 3 min. SAP, (c) P_{ao} was allowed to assume P_{amb} at a controlled rate and the lung underwent another 8 min. SAP, (d) procedures (b) and (c) were repeated with P_{ao} = P_{amb} - 350 torr. A third ventilation pattern identical to the second except cycles (2) and (3) were reversed was performed to show that the results were not cycle dependent. The maximum P_L response recorded as P_{ao} approached P_{amb} in the PVSA maneuver was proportional to the amount of trapped gas at the end of each cycle indicating that: (1) air was trapped prior to lung deflation, and (2) air was trapped at maximum lung volume where all airways would be expected to be open.

THE EFFECT OF PARATHYROID HORMONE ON H^+ AND NH_4^+ EXCRETION IN TOAD URINARY BLADDER. L.W. Frazier, Dept. of Physiology, Baylor Col. of Dent., Dallas, Texas 75226.

The urinary bladder of Bufo marinus excretes H^+ and NH_4^+ and the H^+ excretion is increased by a metabolic acidosis (Biochim. Biophys. Acta, 241, 20-29, 1971). This study was done to determine if parathyroid hormone (PTH) could stimulate the bladder to increase excretion of H^+ and/or NH_4^+. Paired hemibladders from normal toads were used as the in vitro assay system, one hemibladder serving as a control and the other as experimental. The mucosal and serosal solutions were a PO_4 buffered Ringer solution. PTH was added to the serosal solution in a final concentration of 10 µg/ml in the experimental bladder. Net H^+ and NH_4^+ excretion into the mucosal medium in (n moles)(100 mg bladder)$^{-1}$(min)$^{-1}$ were measured. The addition of PTH to the serosal medium resulted in an increased H^+ excretion from 8.38 to 12.71 (mean difference=4.33 ± 0.75; $p<0.025$) in a series of 10 hemibladders. While NH_4^+ excretion was not affected by PTH addition to the serosal medium (control=1.02; PTH=1.04; mean difference=0.03 ± 0.19; $p>0.50$). Theophylline (10^{-3}M) also stimulated H^+ excretion from 7.39 to 11.57 (mean difference=4.18 ± 0.84; $p<0.05$) in a series of ten hemibladders, suggesting that the effect of PTH is mediated by cyclic AMP. In addition, theophylline also stimulated NH_4^+ excretion from 1.08 to 1.50(mean difference=0.42 ± 0.28; $p<0.05$). In another series of 10 hemibladders, from toads in metabolic acidosis, PTH had no effect on H^+ excretion ($P>0.10$) or NH_4^+ excretion ($p<0.05$). We conclude that PTH can stimulate H^+ excretion in the toad urinary bladder. It is not apparent from this study if PTH plays a role in the physiological response to metabolic acidosis by the toad. (Supported by NIH Grant AM 18689).

PRODUCTION OF SUSTAINED PERINEPHRITIC HYPERTENSION IN CHRONICALLY SODIUM-DEPLETED DOGS. R.H. Freeman* and J.O. Davis. (SPON: D.H. York). Dept. Physiology, University of Missouri, Columbia, Mo. 65201

Dogs were made hypertensive by wrapping the left kidney in cellophane and performing a contralateral nephrectomy 3 weeks later. One week prior to right nephrectomy, the dogs were sodium-depleted by a combination of a low sodium diet (<3 mEq Na daily) and mercuhydrin; cumulative, negative sodium balance averaged 173±22 mEq. The dogs were fed the low sodium diet throughout the duration of the study. Arterial pressures were determined at least 3 times weekly by puncture of the femoral artery. Blood samples for plasma renin activity (PRA) and plasma electrolytes were obtained by venipuncture of the external jugular. Also, 24 hour measurements of renal sodium excretion and water turnover were made throughout the study. Mean arterial blood pressure began to rise during the first week following right nephrectomy and was significantly elevated by the eleventh day and remained elevated thereafter. Mean arterial pressure averaged 104±2 mmHg during the control period and reached 151±15 mmHg ($P<.05$) on the eleventh day post-nephrectomy. Four weeks after nephrectomy, mean arterial pressure averaged 153±3 mmHg ($P<.05$). PRA averaged 7.1±0.8 ng/ml per 3 hrs. during the control period and was elevated to 37.5±4.1 ng/ml per 3 hrs. ($P<.01$) during sodium depletion. PRA did not change significantly from this high level following nephrectomy and the development of hypertension until the animals were Na-repleted; then, PRA decreased to normal but arterial pressure remained at the high level. The dogs were not in positive water balance during the study. These data suggest strongly that additional factors other than the renin-angiotensin system or volume expansion are critically involved during the pathogenesis of hypertension in this experimental model.

FACE IMMERSION BRADYCARDIA--THE ROLES OF SWIMMING TRAINING AND AGE M.A.B.Frey*and R.A.Kenney, Department of Physiology, The George Washington University Medical Center, Washington, D.C.

The bradycardial response to face immersion (FI) or apnea has been investigated in 3 groups of male & female subjects (Ss): (1) 8 rigorously training competitive swimmers 15-20 yrs; (2) 8 moderately active Ss 15-22 yrs; and (3) 5 moderately active Ss 32-41 yrs. Apnea with or without FI was initiated at end inspiration while prone. Heart rate (HR) was determined from ECG. Measures of bradycardia were: longest beat interval (L.INT.) during apnea; longest mean 5 consecutive beats (5 INT.); and mean INT. 2d half of apneic period less mean 1st half (ΔINT.). Appearance of cardiac arrhythmias was also considered a response parameter. A significant ($P \leq .05$) difference existed between control (resting) HR for Groups 1 and 3. A wide range existed in Group 2, however; and its resting rate did not differ significantly from the other groups. Comparisons are presented below as value first group/value second group/P value for difference.

COMPARISON	MANEUVER	L.INT.(msec)	5 INT. (msec)	Δ INT. (msec)
PHYS.TNG.				
Grp 1/Grp 2	FI	1536/1140/.01	1394/1088/.01	237/75.6/.05
	Apnea	1371/1128/.05	1274/1068/.05	81.1/7.25/.10
AGE				
Grp 2/Grp 3	FI	1140/1061/n.s.	1088/ 990/n.s.	75.6/98.6/n.s.
	Apnea	1128/ 910/.10	1068/ 880/.10	7.25/-27.6/n.s.

Arrhythmias occurred exclusively in the highly trained Ss. Evidence suggests that FI bradycardia and arrhythmias both involve vagal dominance; thus, these results suggest an increased vagal tone in the swimmers. Modification of vagal tone with age remains equivocal.

REGIONAL ACID-BASE CHANGES IN ACUTE RESPIRATORY ACIDOSIS. M.J.Frumin, Y.O.Youn* & Y.T.Lin*, Dept Anesthesiology, A. Einstein College Med., Yeshiva U., Bronx, N.Y.10461

10 dogs were anesthetized with pentobarbital IV, immobilized with succinylcholine IV, intubated & respired with 100% O_2 with a time cycled, volume controlled ventilator. V_T & f were adjusted so $PaCO_2$=35.6±1.2 torr & was maintained for at least 30 min. A continuously increasing respiratory acidosis was induced by rebreathing, i.e., interposing a 600 ml deadspace between dog and ventilator so V_{DS}=3V_T. Blood was drawn from catheters in the femoral artery(a), femoral vein(fv), right ventricle(v̄)& saggital sinus(ss) at 1 min before & 1,2,3 & 5 min after V_{DS} was increased & were analyzed with electrodes for PCO_2,pH & PO_2 & the base deficit (BD) was calculated.

Torr	Min Rebreathing 0	1	5
$PaCO_2$	36	47	70
$P\bar{f}vCO_2$ - "	6	-4	-12
$P\bar{v}CO_2$ - "	6	-1	-1
$PssCO_2$ - "	13	6	6

These differences can be understood in terms of the CO_2 production and particularly its storage in each bed, i.e. its buffer capacity for CO_2. The lungs produce little CO_2 and also are a poor buffer - hence $PaCO_2 \cong P\bar{v}CO_2$. However, the limb & particularly its muscle has a relatively high storage capacity for CO_2(in H_2O & protien) & so stores CO_2 produced elsewhere by more actively metabolizing beds like brain where $PssCO_2 > PaCO_2$. The rise in BD is roughly proportional to the rise in PCO2.

INFLUENCE OF FASTING ON THE LUNG. D.B. Gail,* C.A. Gregorio,* M.A. Nirdlinger,* G.D. Massaro and D. Massaro. Pulmonary Division, V.A. Hospital, Department of Medicine, George Washington University Medical Center, Washington, D. C. 20422.

We measured the oxygen consumption ($\dot{Q}O_2$) of lung slices from rats and rabbits, and the respiratory quotient (RQ) of lung slices from fed and fasted rats. The $\dot{Q}O_2$ of lung slices is lowered within 24 hrs after the onset of food deprivation; this decrease in $\dot{Q}O_2$ lasts during at least 2 additional days of fasting and is not eliminated by adding glucose to the reaction medium. In fed rats the RQ of lung slices after 30 min of incubation without glucose is 0.75 ± 0.01 (mean ± SEM) and 0.96 ± 0.02 with glucose present. Fasting for 72 hrs lowers the RQ of lung slices after 30 min of incubation without glucose to 0.68 ± 0.03; addition of glucose raises the RQ of lung slices from 72 hr fasted rats to 0.76 ± 0.02. We conclude that fasting depresses lung oxidative metabolism. In the fed rat glucose is a major substrate for oxidative processes but in the fasting rat the oxidation of glucose is impaired, and lipids are an important source of lung energy. (Supported by PHS Grant HL 16031).

URINARY PROTEIN EXCRETION IN THE RAT: STRAIN AND AGE DEPENDENCE.
R. G. Galaske*, J. B. Van Liew, and J. W. Boylan. Depts. Medicine and Physiology, SUNY and Veterans Administration Hospital, Buffalo, N. Y. 14215.

Using gel filtration technique followed by gradient gel electrophoresis (1-40%) we have identified the major protein constituents in normal urine of immature and mature rats of 4 strains: brown Norway (BN), Wistar (W), spontaneous hypertensive (SH), and normotensive Wistar Kyoto (NWK) strains. 24-hr. urines were first concentrated by ultrafiltration. In Sephadex G75, albumin and globulins appear as peak 1 and separate by gradient gel electrophoresis into the typical serum patterns. Fractionation peaks 2-5 contain in order, proteins of mol wt 45-50, 18-23, 10-14 and $1\text{-}3\text{x}10^3$. These proteins occur in urines of all strains and ages investigated. Electrophoretic patterns of each peak vary with age and strain; sex differences were not examined. Low and middle molecular weight (L-MMW) proteins of mol wt $10\text{-}50\text{x}10^3$ comprise 49-63% of total in all strains before maturation and increase markedly (from 49 to 91%) during and after maturation in W, NWK and SH rats; in NWK the % of globulins falls (39 to 4%) during maturation. In BN's the % globulin (20-26%) and L-MMW proteins (60-63%) remain constant except for a transient increase during maturation. L-MMW protein patterns are identical in ureteral, bladder and voided urine so do not derive from the genital tract. L-MMW proteins are below detectable concentrations in serum or filtrate, by present analytical methods. How their individual reabsorptive mechanisms determine the important contribution of these proteins to total urinary protein must await definition of their concentration in capsular fluid.

ANALYSIS OF CONTRACTILE THEORIES BASED ON TRANSVERSE REPULSIVE FORCES.
H.H. Gale and K.M. Davies.* Dept. of Physiology and Dept. of Physics, Creighton University, Omaha, Nebraska 68178.

We have previously analyzed theories based on attractive interactions between side by side filaments - the cross-bridge theory belongs to this class - and shown fundamental inconsistencies inherent in all such theories (Fed. Proc. 32(3): 374, 1973). It is possible to construct theories based on repulsive filamentary interaction. Since muscle is a constant volume system, transverse expansion can cause longitudinal shortening. How can the force produced by the laterally expanding filament lattice be transferred to the tendons? Direct filamentary connection between the force generating elements, myosin rods, and the tendons is ruled out by ultrastructural evidence. Actin filaments and Z discs do not move in the way required by this model. The sarcolemma cannot be invoked because skinned fibers also contract. This leaves intracellular liquid as the force-transmitting agent. Surface tension forces are only 1.5% of the required magnitude. Although liquids have tensile strength (which just might be sufficient to bear contractile forces in the conditions inside of muscle cells), they have little resistance to shearing forces, accounting for easy change of shape. Thus, in a skinned fiber, a myosin rod feeling an outward repulsive force would simply move through and out of the sarcoplasm and fall to the floor. Some force can be transmitted because of liquid viscosity, but reasonable estimates of the required sarcoplasmic viscosity are 10^6 times larger than observed. Also, isometric contraction is impossible by this mechanism since viscous forces only occur in moving liquids. Therefore, models based on the repulsion of side by side filaments are also untenable.

EFFECTS OF CEREBROSPINAL FLUID CATIONS ON THE PLASMA CORTISOL LEVELS OF CONSCIOUS CATS. A.M. Garcy* and S.F. Marotta, Dept. Physiology and Research Resources Laboratory, University of Illinois at the Medical Center, Chicago, IL. 60680

Previous work from our laboratory has shown that cerebroventricular perfusion with mock cerebrospinal fluid (CSF) of various [H^+] altered the activity of the hypothalamo-hypophyseal-adrenocortical(HHA) system. The present study was undertaken to determine whether varying the CSF concentrations of Na^+, K^+, Li^+, Ca^{2+} and Mg^{2+}would affect the function of the HHA system. Adult cats were prepared with left lateral ventricular and external jugular cannulae and allowed to recover for at least 7 days before use. The lateral ventricles of cats(5-7/grp.) were perfused with normal CSF for 30 min.(control period) and then for 60 min. with CSF containing an excess or deficiency of the above-mentioned cations. Jugular plasma cortisol levels were measured at 30, 60, 90 and 110(20 min. after IV ACTH) min. after ventricular perfusion. These studies showed that: 1)perfusion of both conscious and nembutalized cats with normal CSF for 90 min. caused modest fluctuations in cortisol levels, 2)increasing or decreasing CSF [Na^+] and [K^+] in conscious cats elevated cortisol levels 8-29% above control values, whereas the addition of 1 mEq Li^+/l caused a marked(@40%) increase in cortisol levels, 3)the removal of Ca^{2+} from CSF caused a twofold increase in cortisol levels within 60 min., whereas lowering or elevating CSF [Mg^{2+}] gradually increased(@50%) plasma cortisol, and 4)the IV infusion of ACTH, while the animals were perfused with various CSF cations, approximately doubled cortisol levels. These data suggest that altering the concentrations of CSF cations elevates the plasma cortisol levels by affecting the activity of the hypothalamo-hypophyseal complex. (Supported by the Office of Naval Research Contract NR 201-020.)

THE EFFECT OF HYPERCAPNIA, HYPOXIA AND HYPEROXIA ON FRC AND THE $P_{0.1}$ IN HUMANS. F. Garfinkel* & R. Fitzgerald (SPON:R.L. Riley). Gerontology Res. Ctr., NIA, NIH, Baltimore, MD.; Dept. of Environ. Med., Johns Hopkins University, Baltimore, MD. 21205.

In attempting to evaluate the regulation of respiration clinically Whitelaw et al. (Resp. Physiol. 23:181-199, 1975) have proposed the $P_{0.1}$ method as a measure of central respiratory neuronal discharge (CRND). This method requires that the FRC remain constant during the application of the stimulus which in their experiments was CO_2. The purpose of our experiments was to determine if at equal increases in $\dot{V}_E$ due to hypercapnia and to hypoxia the increases in CRND were equal; i.e., equal increases in $P_{0.1}$. Our first tests were to see if in the same subject 4% CO_2 in air, and 12% O_2 changed the FRC from the air-breathing values. We also used 100% O_2 since hypoxia and hyperoxia have been reported to change the FRC in anesthetized and unanesthetized dogs (Resp. Physiol. 7:203-215, 1969). Seven subjects were seated in an air-conditioned volume body plethysmograph breathing room air. After 10 minutes the subject took 3 deep breaths of the gas, and breathed normally for the next minute. During the following three minutes 4 determinations of FRC were made. Three determinations of the mouth pressure at 0.1 sec after the initiation of inspiration were also made. The mean ($\pm$ S.E.) FRC (L.) for the seven subjects on air was 3.1 ($\pm$ 0.3). All seven subjects decreased FRC on hyperoxia (2.5 $\pm$ 0.2), and increased FRC with both hypoxia (3.8 $\pm$ 0.3) and hypercapnia (4.1 $\pm$ 0.4). Mean ($\pm$ S.E.) $P_{0.1}$ measurements (cm H_2O) were: Air = 1.38 $\pm$ 0.19; hyperoxia = 0.98 $\pm$ 0.13; hypoxia = 1.73 $\pm$ 0.23; hypercapnia = 1.81 $\pm$ 0.34. We conclude that under these experimental conditions: (1) both CO_2 and O_2 affect the FRC; (2) $P_{0.1}$ measurements do not measure only CRND but also the effect of lung volume changes on $P_{0.1}$. (PHS Grants HL-10342, ES-00454.)

THE HEMODYNAMIC EFFECTS OF LONG TERM SUBHYPERTENSIVE INFUSION OF NOREPINEPHRINE (NE) IN THE CONSCIOUS DOG. Dan Garner* and Michael M. Laks, Dept. of Medicine, Harbor General Hospital and UCLA School of Medicine, Torrance, California 90509

We have reported that acute infusion of a low dose of NE produces systemic vasodilatation in the conscious dog. The purpose of this study was to determine the effects of a subhypertensive dose of NE on cardiac and systemic hemodynamics. Long term indwelling catheters were placed in the aorta via the carotid artery for measurement of blood pressure, in the left atrium and/or ventricle via the right atrium through the atrial septum for the measurements of pressures and the performance of cineangiograms, and in the right atrium via the jugular vein for infusion of NE (J.Appl.Physiol.38:934, 1975). The initial subhypertensive dose of NE (.18 μg/kg/min) was infused into the right atrium using a micro infusion pump housed in a specially designed jacket for the conscious dog. Infusion rates were increased with maintenance of subhypertensive doses for a period of 16 weeks. The hemodynamic studies including cineangiography were performed in the conscious dog. In comparison with the control, long-term NE infusion increased the cardiac output from 3.7 ± 0.16* to 6.7 ± 0.44 L/min ($P<.005$), stroke volume from 38 ± 3.3 to 67 ± 8.0 ml ($P<.01$), end-diastolic volume from 72 ± 6.4 to 89 ± 12.9 ml ($P<.05$), ejection fractions from 52 ± 3.6 to 76 ± 3.6% ($P<.005$); while total systemic resistance decreased from 27 ± 1.2 to 15 ± 1.6 mmHg/L/min ($P<.01$); however, the heart rate from 100 ± 11 to 103 ± 11 beats/min (P=NS+) and aortic pressure from 120/88 ± 6.8/5.2 to 129/84 8.9/5.4 mmHg (P=NS) did not change. We postulate that chronic infusion of a subhypertensive dose of NE produces systemic peripheral arteriolar vasodilation and an increased force of myocardial contraction.
(Supported by NIH grant HL 14717-03A1 (CVB)).
* Mean ± SEM +Not statistically significant

ARTERIAL PRESSURE, CARDIAC OUTPUT, PLASMA VOLUME AND L-LACTATE CHANGES IN EQUINE LAMINITIS. H.E. Garner, J.R. Coffman*, A.W. Hahn, C. Salem* and J.A. Johnson, Dalton Research Center, Dept. Veterinary Medicine and Surgery, V.A. Hospital, University of Missouri, Columbia, Mo. 65201.

Specific objectives of this investigation included measurement of cardiovascular and biochemical blood changes during the onset of acute alimentary laminitis and arterial hypertension. Acute laminitis and arterial hypertension were experimentally induced in mature horses via carbohydrate (cornstarch) overload of the gastrointestinal tract. Changes in heart rate, rectal temperature and arterial blood pressure were consistent during the onset of laminitis. A marked decrease in central venous pressure and moderate arterial hypotension occurred during the early onset phase of laminitis. Arterial blood pressure and lameness severity simultaneously increased in the final prodromal phase of laminitis. Significant ($P<0.05$) increases in cardiac output and arterial pressure were concomitant with decreased plasma volume and severe lameness. Plasma L-lactate levels increased during the onset of laminitis and in retrospect could have been used to predict severity of lameness. Decreases in blood bicarbonate were concurrent with increases in plasma L-lactate levels. The results imply that lactic acidosis is responsible for the compartmental fluid shifts and the triggering of an acute hypertensive state.
(Supported by grants from the American Quarter Horse Association and Hoechst-Roussel Pharmaceuticals Inc.)

LATE EXPIRATORY SPINAL INHIBITION OF PHRENIC NERVE DISCHARGE. G.L. Gebber and A.T. Zielinski*. Dept. of Pharmacology, Michigan State Univ., East Lansing, Michigan, 48824.

The relationship between spinal inhibition of phrenic nerve activity and thoracic expiratory motoneuronal discharge was studied in chloralose-anesthetized and unanesthetized decerebrate cats with bilateral vagotomy. The amplitude of the phrenic nerve response elicited by single shocks applied to descending tracts in the second cervical spinal segment progressively fell during the late expiratory phase of the central respiratory cycle. The depression resulted, at least in part, from active spinal inhibition since the spinal-to-phrenic evoked response was smaller in late expiration than after C_1 spinal transection. C_1, but not T_1 spinal transection eliminated inhibition of the spinal-to-phrenic response. This observation indicated that spinal inhibition of phrenic nerve discharge was of supraspinal rather than of proprioceptive reflex origin. Inhibition of the spinal-to-phrenic evoked response was time-locked to the spontaneous burst of activity recorded from the eighth internal intercostal nerve. The degree of inhibition of the spinal-to-phrenic discharge was directly related to the amplitude of spontaneously occurring internal intercostal nerve activity. A similar relationship was observed when internal intercostal nerve activity and spinal inhibition of phrenic nerve discharge were evoked by stimulation of the superior laryngeal nerve. It is concluded that late expiratory spinal inhibition of phrenic nerve discharge was dependent on those neural events responsible for the activation of thoracic expiratory motoneurons. (Supported by USPHS Grant HL-13187.)

BULK FLOW OF FLUID AND PROTEIN FROM AIRWAYS TO LUNG INTERSTITIUM IN ISOLATED DOG LUNG LOBES. M.H. Gee and N.C. Staub. Dept. Physiol., Jefferson Medical College, Philadelphia, PA 19107 and Cardiovasc. Res. Inst. and Dept. Physiol., University of California, San Francisco CA 94143.

In each of 10 degassed dog lung lobes, we tied a Y-tube into the main bronchus. We attached the tube to a reservoir filled with 500 ml of Krebs-Henseleit buffer containing 125-radioiodinated serum albumin (RISA) and to a water manometer. We filled each lobe with fluid at a constant pressure of 10, 20 or 30 cm H_2O. After time intervals ranging from 10 to 120 minutes, we clamped the lobar cannula and rapidly froze the lobe in liquid nitrogen. We microsampled free interstitial fluid in perivascular cuffs and the fluid in small airways in the frozen lung lobes and measured the 125-RISA activity in these samples. We also estimated the interstitial fluid volume by point counting in photographs of frozen lung tissue. The cuff free interstitial fluid RISA concentration averaged .90 $\pm$ .04 (SD) of the airway fluid concentration and there was no significant change in the ratio with pressure or time to freeze. In four lung lobes filled to 10 cm H_2O pressure for 30, 60 and 120 minutes and 20 cm H_2O for 15 minutes before freezing, there was a linear increase in interstitial fluid volume with time reaching 2.8 ml/g dry lung. The pulmonary interstitium fills with fluid and protein by bulk flow from the fluid-filled airspace along a hydrostatic pressure gradient between the lobe fluid and interstitium. We suggest that pathways large enough for passage of protein molecules are part of the normal structure of the epithelial lining layer. These pathways are probably not in the alveoli but may be at the level of the terminal bronchioles.

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GASTRIN RELEASE BY VAGAL STIMULATION, URECHOLINE AND BOMBESIN. R. G. Gibson,*A. A. Mihas*, B. I. Hirschowitz. Division of Gastroenterology, University of Alabama in Birmingham, Birmingham, Alabama 35294.

Serum gastrin levels and gastric H^+ and pepsin were studied in 4 fistula dogs with intact vagus and in three dogs 3 years after highly selective vagotomy (HSV). Each dog was given constant 4 1/2 hour infusions of urecholine (20 & 120 µg/kg.hr), or bombesin (0.1 & 0.5 µg/kg.hr), and single injections of 2-deoxyglucose (2-DG) (50 & 100 mg/kg), and insulin (0.2 & 0.6 U/kg). Serum gastrin levels were consistently (3-7 X) greater in the HSV dogs with each stimulus (table).

	Drug (Dose)	Basal	30	60	90	180	270 min.
Intact	2-DG (100)	32	53	61	55	62	63
	Insulin (.2)	38	67	80	77	66	45
	Urech. (120)	56	83	84	85	101	124
	Bomb. (0.5)	33	136	153	135	168	64
HSV	2-DG (100)	46	413	428	320	312	-
	Insulin (.2)	64	190	279	191	172	86
	Urech. (120)	72	172	134	135	168	101
	Bomb. (0.5)	25	233	259	272	273	182

Though H^+ secretion was lower with 2-DG and insulin after HSV, it was essentially similar following the illustrated doses of urecholine and bombesin. Therefore the gastrin differences between the intact and HSV dogs can be explained on differences in H^+ output and more likely is due to loss of a gastrin-release inhibitory mechanism after vagal denervation of the fundus. Also atropine (100 µg/kg) eliminated both the gastric H^+ and the serum gastrin responses to 2-DG and to insulin, showing that the vagal release of gastrin is cholinergically mediated. NIH support, AM09260, TIAM 05286.

KINETICS OF UPTAKE AND ADRENERGIC RESPONSE TO NOREPINEPHRINE IN THE CEREBRAL VASCULATURE. D.D. Gilboe and M.S. Saffitz*, Dept. Surgery, University of Wisconsin, Madison, Wisconsin 53706

The indicator dilution method was used to investigate the kinetics of unidirectional norepinephrine (Norepi) uptake in the isolated canine brain. These studies revealed that Norepi is not transported across the cerebral capillary endothelium but rather it passes into the brain by simple diffusion. The extraction of Norepi from the blood during a single capillary pass was 7.2±SE 0.4% (N=40). Although unidirectional uptake of Norepi exhibited the kinetics of simple diffusion, the Norepi-induced response as measured by an increase in cerebral vascular resistance following Norepi doses ranging from 0.01-100 µg, are best described by the Michaelis-Menten equation. The maximum response (R_{max}) was 0.84±SE0.12 mmHg/(mls/min per 100g) and the dose at half maximum response ($D_{½}$) was 5.9±SE4.0 µg (N=92). Norepi dose-responses in the presence of phenoxybenzamine, a non-competitive α-blocker, displayed an R_{max} of 0.14±SE0.03 and $D_{½}$ of 2.1±SE2.9 (N=57). Norepi dose-responses in the presence of phentolamine, a competitive α-blocker had an R_{max} of 0.82±SE0.59 and $D_{½}$ of 67.0±SE102.0 (N=28). The Norepi response with each of the α-blocking drugs is consistent with their stated mode of inhibition. These response kinetics follow from a reaction scheme in which agonist and receptor bind reversibly. There is a significant ($p<.0025$) difference between the time required for the Norepi bolus to exit from the brain (11.7±SE0.2 sec) and the time for maximum vasoconstriction (44.5±SE3.0 sec). This lag period in adrenergic response may be due to the time required for movement of agonist from capillary to receptor or a delay in receptor activation. (Supported by Grant NS-05961 from NINDS).

BREATHING RESPONSES OF AWAKE GUINEA PIGS AND MAN TO INCREASED TRANSRESPIRATORY PRESSURE. J. Gillespie, E. Bruce* and J. Mead, Dept. Physiology, Harvard School of Public Health, Boston, Mass. 02115, and School of Veterinary Medicine, University of Calif., Davis, CA. 95616

We measured the breathing frequency (f), tidal volume (V_t) and minute volume (V_{min}) in 10 guinea pigs and 3 human subjects prior to, during, and following their exposure to steady negative pressure around the body and with mouth pressure at atmospheric [transrespiratory pressure (P_{RS}) = 10 cm H_2O in guinea pigs; P_{RS} = 15 cm H_2O in human subjects]. We also measured arterial CO_2 tension (P_{aCO_2}) in the guinea pigs and end-tidal CO_2 tension (P_{ACO_2}) in the human subjects. Both species were awake, breathing through a mask or mouth piece. The human subjects were not aware of the objectives of the experiment. The guinea pigs' f, V_t and V_{min} decreased and the P_{aCO_2} increased significantly during increased P_{RS}. The P_{aCO_2} increased a mean of 5 mm Hg at 3 min. after increasing P_{RS} to 10 cm H_2O, but tended back toward control by 10 min. In contrast, there were no consistent or significant changes in comparable values during increased P_{RS} in the human subjects. We think the differences between these species reflect the difference in the balance between vagal (Hering-Breuer) inflation reflexes and mechanisms compensating for changes in operating length of muscles. The former dominates in guinea pigs whose muscle length is probably tightly coupled to metabolism, and the latter in man, in whom muscle length is uncoupled substantially from metabolism by postural change.

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PLASMA CATECHOLAMINES IN HUMANS DURING HELIUM BREATHING. N. Gledhill*, A.K. Chin*, and A.C. Bryan. York University and The Hospital for Sick Children, Toronto, Ontario Canada.

The antiarrhythmic property of Helium originally reported by Piffare (J. Thorac. Cardiov. Surg. 60, 1970) has been substantiated by several workers and from observations on animals it has been suggested that this effect is mediated through decreased plasma epinepherine and norepinepherine. In this study, the time course of plasma catecholamine changes in man were examined during inhalation of (a) 20% He, 40% O_2 and 40% N_2 and (b) 75% He and 25% O_2. Eight healthy male subjects inhaled mixtures a and b while seated and resting. Arterialized venous blood samples were taken from an indwelling catheter and analyzed fluorometrically for epinepherine and norepinepherine (J. Appl. Physiol. 30: 205, 1971). After ten minutes of Helium inhalation, both epinepherine and norepinepherine had decreased significantly (38% and 31% respectively; ($p < .01$) and this decrease was equal for mixtures a and b. Following 30 minutes of 75% Helium inhalation, epinepherine had decreased a further 25% ($p < .01$), but there was no additional significant change in norepinepherine. No progressive decrease in epinepherine or norepinepherine was observed with continued 20% Helium inhalation, and ten minutes after cessation of Helium breathing, both epinepherine and norepinepherine had returned to resting levels. We conclude that Helium inhalation alters catecholamine activity in man.

EFFECT OF STARVATION ON RENAL HANDLING OF CITRATE.
Armand Gold and Leslie Costello. Department of Physiology and Biophysics, Howard University College of Medicine, Washington, D. C. 20059.

Plasma, renal cortex, and urine citrate levels were determined in two groups of rats after seven days under the following dietary conditions: (control) provided standard diet and tap water ad libitum; (starvation) provided only tap water ad libitum. Mean citrate values (± SE) obtained from 4 experiments are tabulated below:

	Renal Cortex (nmoles/g)	Art. (nM)	Renal Vein (nM)	A-V / A	C_{citr} (ml/24 hr)	C_{citr}/C_{creat}
C	419 ± 68	116 ± 7	71 ± 7	0.39 ± 0.04	460 ± 15	0.74 ± 0.09
S	118 ± 70	49 ± 6	28 ± 4	0.43 ± 0.04	30 ± 10	0.06 ± 0.01

Starvation resulted in marked hypocitricemia, reduced renal cortex citrate, and hypocitraturia. However, the coefficient of citrate utilization in the kidney was unchanged. It is therefore evident that, despite a decline in circulating citrate during starvation, the kidneys continued to utilize citrate to the same extent as under control dietary conditions. That urinary excretion was reduced nearly to zero also suggests a renal mechanism for the conservation of plasma citrate. (Supported by NIH GRS Grant No. 5 S01 RR 05361-14)

Evidence Indicating the Presumed Site for the Acclimation of Brain (Na^++ K^+)-ATPase during Hibernation. Stephen S. Goldman and R. Wayne Albers* Laboratory of Neurochemistry, N.I.H., Bethesda, Md. 20014.

Brain(Na^++K^+)- ATPase acclimates prior to the onset of hibernation in the hamster(Cryobiology 10:218,1973). The acclimation occurs as a qualitative change in its kinetic properties. To deduce the site(s) of the acclimation a kinetic analysis of the (Na^++K^+)-ATPase was undertaken in both the warm-adapted and hibernating hamster. The enzymatic cycle consists of a number of sequentially ordered partial reactions: (1) a (Na^++Mg^{++}) dependent ATP-ADP exchange step associated with E_1P formation, (2) a Mg^{++} dependent isomerization of E_1P to E_2P, (3) a K^+ dependent hydrolysis of E_2P to E_2 and (4) an isomerization of E_2 to E_1 thus completing the enzymatic cycle. It was found that the acclimation was only observed for the overall ATPase reaction and not reactions (1) and (3). Reaction (2) is manifest as an inhibition of (1) by Mg^{++}. The apparent Keq of (2) is relatively less affected by temperature in the hibernating hamster. It was concluded that reaction (4) becomes the most temperature sensitive step within the catalytic cycle: this step is apparently dependent upon the dissociation of either or both Mg^{++} and K^+ from the E_2 form of the enzyme. The dissociation of these cations occurs with greater efficacy at low temperature in the case of the enzyme from the hibernating hamster. Thus it was concluded that this step is the primary site involved with the acclimation of the (Na^++K^+)-ATPase. In reactions (2) and (4) major conformational changes within the enzyme are presumed to occur. The efficacy by which these conformational changes occur are apparently governed by the fluidity of the lipid matrix. The acclimation of the enzyme may in part be dependent upon the reported lipid adaptation that also occurs in brain during hibernation (Am. J. Physiol. 228: 834, 1975).

ULTRASTRUCTURAL LOCALIZATION OF SOMATOSTATIN (GIF) IN PANCREATIC ISLETS OF THE RAT. P.C. Goldsmith*, J.C. Rose*, A. Arimura, J.E. Gerich*, and W.F. Ganong. Dept of Physiology and Metabolic Research Unit, University of California, San Francisco, CA and Veterans Administration Hospital and Tulane University School of Medicine, New Orleans, LA.

The hypothalamic tetradecapeptide somatostatin or growth hormone-release inhibiting factor (GIF) has been shown to inhibit insulin and glucagon secretion, and to be present in the pancreas and stomach by immunoassay (Arimura et al., Fed. Proc. 34:273, 1975). In order to determine the precise localization of GIF in the pancreas, electron microscopic immunocytochemistry was performed on thin sections of whole pancreas and isolated pancreatic islets of the rat. Rabbit anti-GIF (#103) diluted 1:100 and absorbed with 1% human α-globulin was applied in the peroxidase anti-peroxidase (PAP) technique. PAP complexes indicating the presence of GIF were localized over secretory granules concentrated away from the nucleus in cells sparsely distributed near the periphery of the islet. Positive granules were closely applied to their limiting membrane, exhibited moderate electron density, and were smaller than those in other islet cells. The morphology of the granules as well as the location and relative number of positive cells suggests that GIF is present in a subgroup of delta cells or in a separate cell type. Beta cell granules did not show a positive reaction, but a few PAP complexes observed over alpha cell granules imply that rabbit anti-GIF may partially cross react with glucagon. Controls utilizing 1:100 rabbit anti-GIF absorbed with 10 μl GIF/ml or 1:100 rabbit anti-bovine serum albumin failed to give a positive reaction. These results provide further evidence for the presence of GIF within islet cells of the pancreas and indicate that the hormone is present in a discrete granule fraction in a specific cell type.

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AMINO ACIDS AS PRECURSORS OF ALANINE IN SKELETAL MUSCLE. Leon Goldstein and Eric A. Newsholme*, Department of Biochemistry, Oxford University, England.

The aim of this study was to determine whether glucogenic amino acids can be converted via pyruvate to alanine in the absence of glucose in skeletal muscle. Rat hemidiaphragms were incubated in Krebs-Ringer bicarbonate solution w/ or w/o amino acids. In the absence of added amino acid 2.20 ± .12 (mean ± S.E.) and 3.00 ± .12 nmoles alanine/mg tissue were produced after 1 and 2 h incubation, respectively. Addition of 3 mM isoleucine (isoleu) or glutamate (glu) to the medium increased alanine production to 2.96 ± .12 and 3.83 ± .24 (after 1 and 2 h w/isoleu) and 2.96 ± .11 and 3.79 ± .28 (w/glu). In the presence of these amino acids, the content of pyruvate in the diaphragm was increased. In diaphragms that had been incubated for 1 h and then freeze-clamped, the pyruvate contents were: 0.078 ± .007, 0.128 ± .014 and 0.129 ± .019 μmoles/g tissue without added amino acid, with isoleu and with glu, respectively ($P < 0.01$ and < 0.05, isoleu and glu vs. control). The stimulation of alanine production by isoleu or glu was not reduced by NaF (.01 M), which was added to minimize the possibility that pyruvate was being produced from endogenous glycogen. These results suggest that alanine can act as a carrier of carbon and nitrogen in the transport of amino acids from the muscle to the liver. (This work was supported by USPHS grant AM12443.)

ALTERATION INDUCED BY PHOSPHATIDYL SERINE IN TENSION RESPONSES AND ^{45}Ca FLUXES IN RABBIT AORTIC SMOOTH MUSCLE. Frank R. Goodman*, George B. Weiss and Andres Goth* (SPON: John C. Vanatta). Department of Pharmacology, University of Texas Southwestern Medical School, Dallas, Texas 75235

The effects of different concentrations of phosphatidyl serine (PS) on ^{45}Ca distribution, ^{45}Ca movements and contractile responses induced by different stimulatory agents were examined in isolated rabbit aortic smooth muscle. Contractile responses obtained with submaximal concentrations of either norepinephrine or histamine were potentiated by prior exposure to PS, but equipotent responses to elevated potassium ion were unaffected. However, PS did not potentiate maximum tension responses and had no effect when calcium ion (Ca^{++}) was removed from the bathing solution. In media-intimal preparations dissected from rabbit aortic strips, addition of PS to the incubation solution decreased ^{45}Ca uptake in solutions containing no added Ca^{++}. Exposure to PS during ^{45}Ca washout produced a sustained and reversible increase in ^{45}Ca efflux. Furthermore, the presence of PS during the washout significantly reduced the increase in ^{45}Ca efflux rate obtained with 0.05 mM concentrations of either Ca^{++} or ethylenediamine tetraacetic acid. Addition of PS also elicited a sustained increase in the efflux rate of promethium (^{147}Pm), a radioactive trivalent ion which does not penetrate the cell membrane. Thus, in rabbit aortic smooth muscle, PS alters the availability and/or exchangeability of membrane-bound ^{45}Ca. In this manner, PS may play a significant role in the membrane retention and regulation of calcium ion important for cellular responsiveness. (Supported by USPHS grant HL-14775.)

SUDDEN INTERRUPTION OF LEAFLET OPENING BY VENTRICULAR CONTRACTIONS: A MECHANISM OF MITRAL REGURGITATION. Douglas A. Gordon*, Yves Mathieu*, Ramesh Padiyar*, Claude Labrosse* and Anastasios G. Tsakiris. University of Sherbrooke Medical School, Sherbrooke, Quebec, Canada

The mechanism of mitral regurgitation, following isolated ventricular contractions, in the normal heart is not entirely clear. In order to investigate this, the motion of both mitral cusps and the presence of valvular regurgitation were studied in seven experiments on intact dogs in which radiopaque markers had been sutured to the cusps and the valve annulus 1 to 32 weeks before the studies. Cineangiograms of the left ventricle (100-120 f/sec) were obtained during isolated or recurrent ventricular ectopic beats, interposed throughout the cardiac cycle (20-99% of total cycle length) and during induced variations in the P-R interval (0-200 msecs). Mitral regurgitation was observed only during a) very weak, early occuring ectopic beats (peak pressure below 34 mmHg) which were incapable of closing the cusps and b) when the ventricular contraction suddenly interrupted normal leaflet motion towards the ventricle, during three well defined diastolic periods (diastolic valve opening, diastolic rebound and atrial opening). Valve closure following this sudden reversal of cusp motion was slow and the cusps often did not arrive sinultaneously at their closed positions. These findings suggest that the sudden interruption of leaflet opening by a ventricular contraction is an important mechanism of transient mitral regurgitation in the normal heart.

CAN PULMONARY REFLEXES CONTRIBUTE TO HYPERCAPNIA? B. Gothe*, D.H. Simmons, R.L. Waymost*, and A. Osher*, Dept. Medicine & Pediatrics, UCLA School of Medicine, Los Angeles, CA 90024.

To test the hypothesis that pulmonary reflexes can play a role in causing hypercapnia under certain conditions, severe lung injury was induced by I.V. oleic acid (O.A.) (0.2 mg/kg) in 9 anesthetized spontaneously breathing dogs with and without application of 15 cm H_2O of continuous positive airway pressure (CPAP) while breathing 100% O_2. Steel coils were placed surgically around both cervical vagi to permit reversible blockade by cooling the nerves to 2°C. As a result of O.A., mean PaO_2 fell from 458.8±16.5 (SE) to 75.9±18.4 mmHg and pH from 7.39±0.01 to 7.242±0.04. Measurements were then made after 30 minute periods of spontaneous breathing with and without CPAP and with the vagi at body temperature or 2°C. Changes were calculated from the immediate preceding period (O.A. values were compared with controls before O.A.):

Effect of:	Δf	ΔV_T	$\Delta \dot{V}_E$	$\Delta PaCO_2$
Oleic acid	+46.0±9.2	-241.0±77.8	+13.5±3.4	+5.7±3.6
+ Blockade	-36.5±7.5	+702.5±213.2	+0.1±2.2	-4.4±1.4
CPAP (after O.A.)	-10.0±2.5	-79.4±30.8	-7.3±1.4	+10.8±3.2
+ Blockade	-33.4±3.8	+330.3±45.2	-6.0±1.3	-7.0±2.3

O.A. lung damage caused hypercapnia which was increased by loading with CPAP. Vagal blockade partially corrected the hypercapnia with or without CPAP. f decreased with vagal blockade. The drop in $PaCO_2$ with blockade during CPAP was associated with a decrease in $\dot{V}_E$, suggesting that dead space ventilation decreased markedly as f decreased. There was a significant correlation between changes in $PaCO_2$ and changes in f or V_T. These data are consistent with the hypothesis that excessive stimulation of pulmonary reflexes contributes to hypercapnia in this model because of excessively rapid breathing.

AN ISOLATED TRACHEAL SEGMENT TO STUDY AIRWAY REFLEXES IN CONSCIOUS DOGS. P.D. Graf*, S.P. Fischer*, M. Nisam*, J.A. Nadel and W.M. Gold. Univ. of California, Cardiovascular Research Institute and Department of Medicine, San Francisco, California 94143.

Airway reflexes are difficult to study in conscious animals, because associated changes in ventilation alter intrathoracic airway dimensions. By studying a by-passed segment of extrathoracic trachea, we have overcome this problem. In each of 2 dogs, we created surgically a by-passed tracheal segment just below the larynx, sealed at one end, tapered at the other to a 3 mm opening via a skin fistula. We also created a chronic tracheostomy near the thoracic outlet. During studies, we introduced a catheter into the orifice of the segment to monitor pressure (Ps) as an indication of changes in tracheal smooth muscle tone. During pentobarbital anesthesia (30 mg/kg, iv), gentle mechanical stimulation of the carina with a catheter, deflation of the lungs 500 ml below FRC, or 1-2 min of asphyxia increased Ps(range, 5-10 cm H_2O); concomitantly, the diameter of the lower trachea outlined with tantalum decreased 20-27%. Lung inflation or artificial hyperventilation decreased Ps (9-16 cm H_2O). Five breaths of 2% histamine aerosol increased Ps (4-5 cm H_2O). Atropine sulfate (0.2 mg/kg, iv) abolished all constrictor and dilator responses. In the conscious dog, lung inflation resulted in decreased Ps; the degree of relaxation of the segment was proportional to inflation volume. Gentle carinal stimulation increased Ps. Dilator and constrictor responses and resting tone were decreased by 0.1 mg/kg and abolished by 0.2 mg/kg atropine sulfate, i.v.

We conclude that an innervated extrathoracic tracheal segment constricts and dilates reflexly via cholinergic pathways and is suitable for the study of airway reflexes in conscious dogs. (Supported by NIH grants HL-14201 and HL-06285).

SITES OF ALBUMIN LEAKAGE IN DOG ILEUM: CRYPTS OR TIPS? D.N. Granger,* B.H. Cook,* and A.E. Taylor (SPON: M.D. Turner). Dept. Physiology & Biophysics, Univ. Mississippi Med. Center, Jackson, MS 39216.

The serosal to mucosal flux of albumin has been shown to increase following elevations of venous pressure. This increased mucosal membrane permeability could be due to either widening of tight junctions between tip epithelial cells or a physical opening of other leakage sites. Cook et al.(A.J.P.221:1491,1971) have shown that villus tips are denuded of epithelial cells in post-shock intestine, which results in large, nonspecific leak sites. When venous pressure is elevated, the site of albumin leakage has not been established since the epithelial cells are not pushed off the villi. The purpose of this study was to determine the site of albumin leakage into the intestinal lumen using the fluorescence properties of Evans-blue dye(T-1824). Evans-blue dye has a high affinity for albumin and emits an orange-red fluorescence at a wavelength of 720 nm. Evans-blue was mixed with a solution of bovine serum albumin (EB-albumin) at concentrations which yield negligible amounts of free dye. Control ileal samples were obtained in order to visualize the natural tissue fluorescence. The EB-albumin was injected and tissue samples were obtained at 60 min. post injection, then venous outflow was occluded and after 60 min. the tissues were sampled. The samples were immediately frozen (-180°C), freeze-dried, embedded in paraffin and 7μ sections were made. The EB-albumin was demonstrated histologically using a fluorescence microscope. After elevation of venous pressure, EB-albumin streaming was observed between the epithelial cells of the villi and no EB-albumin was observed in the crypts. This data supports Hakim and Lifson's theory(A.J.P.216: 276,1969) that elevation of venous pressure disrupts the tight junctions in the villus tips creating large channels which can accommodate the albumin molecules. (Supported by NIH grant HL 15680.)

NEGATIVE INOTROPIC EFFECTS OF GLUCAGON-CALCIUM INTERACTION. R.L. Green* (Spon.: F.W. Kinard), Dept. of Physiology, Medical University of South Carolina, Charleston, S.C. 29401

The tension produced by glucagon depends on the concentration of Ca++ in the medium. This interrelationship between glucagon and Ca++ has been studied in spontaneous and paced guinea pig isometric atria. Glucagon-induced increments in contractility of non-paced atria were increased with the Ca++ level in the range of .95-3.8 mM Ca++, and tension increased as glucagon dose was increased from .05 to 5.0 μg/ml. If $[Ca^{++}]_o$ were high enough one would expect that the additional inotropic response to another agent such as glucagon would be diminished because the excitation-contraction mechanism would saturate. This condition was approached at 7.6 mM Ca++, since non-paced inotropic responses were uniformly positive but small (<10%Δ) with glucagon (.05-5.0 μg/ml). When Ca++ was increased to 10 mM, glucagon (5.0 μg/ml) paradoxically produced a negative inotropic response in both paced and spontaneously beating atria. Isoproterenol was found to produce a positive inotropic response in 10 mM Ca++ medium in both atrial preparations, indicating that further increase in tension was possible in 10 mM $[Ca^{++}]_o$ and therefore excitation-contraction mechanism was not saturated. In both paced and non-paced atria glucagon-induced time to max. positive contractile state was found to decrease with increased Ca++ concn. or with increased pace rate. One would conclude that more Ca++ ions were at active sites contributing to the active state of the muscle. However at high extracellular Ca++ levels, glucagon could uncouple these active sites and produce a negative inotropic response.

EXCESS Ca^{++} IN CEREBROSPINAL FLUID LOWERS RECTAL TEMPERATURE DURING EXERCISE IN DOGS. J. E. Greenleaf and J. Sobocinska* Dept. of Applied Physiology, Medical Research Centre, Polish Academy of Sciences, 00-730 Warsaw, Poland

Rectal temperature (Tre) was measured in five dogs, during 1 hr of rest and 1 hr of moderate treadmill exercise (1.2 m/sec up to 12° slope), with no perfusion and with continuous perfusion (40 µl/min) of normocalcic (1.3 mM/ℓ Ca^{++}, 151.5 mM/ℓ Na^{+}) and hypercalcic (2.6 mM/ℓ Ca^{++}, 149.6 mM/ℓ Na^{+}) concentrations of artificial cerebrospinal fluids into the left lateral cerebral ventricle. There was no effect of the normo- or hypercalcic perfusions on resting Tre. Compared with the post-exercise Tre level of 39.9°C (ΔTre = +1.4°C) with no perfusion and 40.0°C (ΔTre = +1.4°C) with normocalcic perfusion (n.s.), there was a significantly smaller ($p < 0.01$) rise in Tre to 39.2°C (ΔTre = +0.8°C) with hypercalcic perfusion. The hypothermic response to excess Ca^{++} perfusion was not due to plasma fluid or electrolyte shifts. During exercise the mean (± SE) body wt loss was greater with hypercalcic perfusion (-2.7 ± 0.6%) compared with normocalcic (-1.0 ± 0.3%) and no perfusion (-1.4 ± 0.3%) values. The results suggest that Ca^{++} ions affect the sensitivity of the central thermoreceptor to thermal stimuli and cause an increased heat loss.

RESPONSE OF PRIMATE JOINT AFFERENT NEURONS TO PASSIVE AND ACTIVE MOVEMENTS OF THE KNEE. Peter Grigg, Dept. of Physiology, University of Massachusetts Medical School, Worcester, Massachusetts, 01605.

130 joint afferent neurons from the knee were studied in a primate, Macaca Fasiculata. Afferents were recorded in dorsal root filaments, and identified by electrical stimulation of the posterior articular nerve (PAN). 60% of the neurons recorded were activated when the knee was displaced into the limit of extension of the knee; activation angles were from 165° to 180°. It was necessary to apply torque to the knee to activate extension neurons. The response was related to the level of applied torque, and therefore presumably to the degree of capsullar stretching. One third of the neurons activated in extension could also be activated by flexing the knee. Activation angles in flexion were from 45° to 30° and in general high torques were required to initiate discharge. 6% of the population responded only to flexion of the knee. 7% could be activated by passively moving the knee through angles intermediate between extreme flexion and extension. 17% of the population could not be activated with mechanical stimulation of the knee. In some preparations, joint afferents were tested for the effect of activation of quadriceps, gastrocnemius, or semimembranosus muscles. Muscle nerves were stimulated, through implanted electrodes, while joint angle was fixed by clamping tibia and femur. Of the neurons tested, about 15% could be activated by contracting the quadriceps muscles, 29% could be activated by contracting or stretching the gastrocnemius muscles, and 20% could be activated by contracting semimembranosus.

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ANALOG DISPLACEMENT OF TRITIATED ANGIOTENSIN II BOUND TO ZONA GLOMERULOSA CELLS FROM RABBIT ADRENALS. Steve Gurchinoff* and Philip A. Khairallah. Research Division, Cleveland Clinic, Cleveland, Ohio 44106.

The myotropic and steroidogenic responses to various analogs of angiotensin II (AII) have been well documented. To better understand the activity of some of these analogs, studies of their binding to zona glomerulosa cells would be very useful. However, since they are not available as tritiated compounds, their displacement of bound tritiated AII was studied. Approximately equimolar concentrations (10^{-8}) of unlabelled analogs were added to determine the displacement of the bound radioactive hormone. Displacement by unlabelled angiotensin II was 20%. Heptapeptide analogs (desAsp^1 AII, desAsp^1 Thr^8, and desAsp^1 Ala^8) displaced approximately the same amount as the unlabelled octapeptide with desAsp^1 Ile^8 displacing 51%. Analogs with sarcosine substituted in position one all displaced more than 50% of the bound ligand (Sar^1 Ala^8, 55%; Sar^1 Thr^8, 59%; Sar^1 Ile^8, 68%; and Sar^1 AII, 62%). Additions of other octapeptide analogs (Ile^8 AII, β-thienyl Ala^8, MeAla^1 Ile^8, and Me$_2$Gly^1 AII) displaced 30-40% of the unlabelled hormone while OMeTyr AII and poly(OAc)Ser displaced 10% or less. These results seem to correlate well with reports that show sarcosine substituted analogs to be the best antagonists of aldosterone biosynthesis or release. They also provide further evidence that angiotensin II must be bound to membranes in order to elicit a response. (Supported in part by NIH training grant HL-5126 and grant HL-6835.)

FIBRINOGEN HETEROGENEITY IN HEALTHY SUBJECTS AND IN CANCER, OCCLUSIVE VASCULAR DISEASE AND AFTER SURGERY. V. Gurewich, I. Lipinska*, B. Lipinski*, Vascular Laboratory, Lemuel Shattuck Hospital, Tufts University School of Medicine, Boston, MA 02130.

A method was developed using electrophoresis in 3.5% polyacrylamide gels which permits direct visualization and quantitation of fibrinogen heterogeneity in blood. Two major and one minor fractions were identified. In 50 healthy subjects, a high molecular weight (HMW) fibrinogen constituted 60-70% of the total. In 34 patients with occlusive vascular disease, the HMW fraction was identical to normal but the concentration of a lower molecular weight (LMW) fibrinogen was twice as great ($p < 0.001$). A third fraction (LMW^1) was found in 80% of vascular patients compared to 20% of normal ($p < 0.001$). In 32 cancer patients, the concentrations of both HMW and LMW fibrinogen were significantly ($p < 0.001$) increased, the ratio being comparable to normal. Postoperative fibrinogen synthesis was accompanied by a 2-3 fold increase in the concentration of the HMW fraction ($p < 0.001$) without significant change in LMW or LMW^1 fibrinogen. The HMW fraction is believed therefore to represent native fibrinogen and the LMW and LMW^1 fractions its derivatives. The concentration of LMW fibrinogen was not correlated with blood fibrinolytic activity or FDP concentration. Serial determinations in normals and vascular patients demonstrated little variation in the concentration of the LMW fraction. The mechanism by which limited degradation of HMW fibrinogen occurs is not known, but a steady process which is accelerated in vascular disease is implicated. HMW fibrinogen has a low solubility and forms a sticky fibrous precipitate. These biological properties may favor its intravascular precipitation and subsequent degradation.

SATURATION KINETICS FOR PLACENTAL CO TRANSFER. G. Gurtner, J. Bissonnette and B. Burns. The Johns Hopkins University, Baltimore, Maryland and University of Oregon, Portland, Oregon.

We have previously reported evidence consistent with the presence of carrier mediated transport for O_2 in the placenta (Nature 240:473-475, 1973; Drug Metabolism and Disposition 1:368-379, 1973; Fed. Proc. 34:417, 1975). We think that the carrier may be Cytochrome P-450 because compounds which bind to the cytochrome markedly reduce transplacental O_2 transfer without affecting transfer of inert gases. If Cytochrome P-450 is the carrier, CO transfer should also be carrier mediated; furthermore there should be interactions between O_2 and CO transfer. Using a closed recirculating system we perfused the fetal side of the placenta with blood which had different COHb contents and observed the rate of CO disappearance. Rates of gain or loss for O_2, Ar, urea, inulin and ^3H_2O were also measured. We found that the rate of disappearance of CO always decreased as COHb increased. This decrease was not due to back pressure of CO in the ewe since this always remained at low levels. O_2 transfer also decreased as COHb increased. This effect occurred at CO levels as low as 10% COHb. The rates of transfer of the other substances were not systematically related to the COHb content. The decrease in rate of disappearance of CO as the COHb content increased may be due to saturation of the placental CO carrier. The decrease in O_2 transfer may represent competition between O_2 and CO for the carrier binding sites. The lack of effect of CO on the rate of transfer of the other substances indicates that CO did not cause non-specific changes in placental permeability. (Supported in part by PHS Grants HL-10342 and ES-00454.)

REVERSAL POTENTIAL FOR EPSPs IN FROG PURKINJE CELLS EVOKED BY CLIMBING FIBER STIMULATION. J. T. Hackett, Dept. Physiology, Univ. of Virginia, Charlottesville, VA 22901

Determination of the reversal potential for central nervous system EPSPs is hampered by diffuse distribution of synaptic inputs and contamination by inhibitory synapses. A central synapse where these properties appear not to affect EPSP reversal potentials is the climbing fiber-Purkinje cell (CF-PC) synapse of the frog cerebellar cortex. Experiments were done in isolated frog cerebella maintained in vitro (Hackett, Brain Res. 48, 385, 1972). Climbing fibers were selectively activated by fine bipolar electrodes placed in the ipsilateral brain stem. CF-EPSPs with a latency of 6.8 to 13.8 msec were recorded intracellularly with 2 M K citrate electrodes with beveled tips. A bridge circuit was used to pass current through the impaled cell. Depolarization of PC by current of 0.14×10^{-8} ampere (average of 7 cells) through the recording microelectrodes brought the membrane potential to near zero and nulled the CF-EPSPs. In deteriorated cells whose membrane potentials were about zero, the reversal potential was found at a more negative value. Further depolarization reversed the direction of CF-EPSPs. Hyperpolarizing current injections increased the amplitude of CF-EPSPs. Unlike other central EPSPs, the CF-EPSP was reversed uniformly over its whole wave form as judged by measurements of peak amplitude, amplitude at 1/2 decay, duration at 1/2 peak amplitude and time to peak. Spontaneous EPSPs which were about 5 times smaller than evoked CF-EPSPs also reversed at near zero membrane potentials. These results indicate that PC-subsynaptic membranes innervated by CF can be uniformly polarized by current injections from microelectrode tips in the cell soma, and that the reversal potential for CF-EPSPs is zero.

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ABSENCE OF SUPERSENSITIVITY TO ACETYLCHOLINE IN THE EXTRINSICALLY DENERVATED CANINE SINUS NODE. Gilbert R. Hageman, Ferdinand Urthaler*, and Thomas N. James*. Cardiovascular Research and Training Center, University of Alabama, Birmingham, Alabama 35294.

Supersensitivity to neurotransmitters in denervated organs has been investigated since Cannon's 1939 Law of Denervation. Sympathetically denervated hearts become supersensitive to catecholamines but it is not known whether parasympathetic denervation causes cardiac supersensitivity to acetylcholine (ACh). This investigation determines the chronotropic effect of ACh administered selectively into the canine sinus node artery after cardiac denervation. Thirty-one dogs were anesthetized with I.V. pentobarbital. Using aseptic techniques the cervical vagosympathetic trunks were isolated and the heart exposed through a thoracotomy. Stimulations of the vagi and right stellate ganglion were made before and after total external parasympathectomy and partial sympathectomy of the sinus node or a sham procedure. Four to 16 days later the dogs were reanesthetized and blood pressure, heart rate, ECG, His bundle and local electrograms were recorded. The vagi and right stellate were stimulated and the effectiveness of the parasympathectomy verified in 8 dogs. The sinus node artery was selectively perfused with 10^{-9} to 10^{-6} g doses of ACh or norepinephrine. The response to ACh in the denervated or sham-operated dogs was not significantly different ($p > .05$), but the sinus node was supersensitive to norepinephrine. Pharmacological separation with intranodal pentolinium of the nicotinic and muscarinic receptors did not alter the parasympathectomized sinus node response to ACh. We conclude after external denervation the canine sinus node develops a differential response to neurotransmitters which in turn may disrupt electrical stability of denervated and reinnervating hearts. (Supported by NHLI Grant HL11,310.)

EFFECT OF VAGAL TONE ON AIRWAY DIAMETERS AND ON LUNG VOLUME IN ANESTHETIZED DOGS. H.L. Hahn*, P.D. Graf*, and J.A. Nadel. Cardiovascular Research Institute, San Francisco, California 94143.

In 18 open-chest dogs we obtained static pressure-diameter (P-D) curves from tantalum bronchograms and static lung pressure-volume (P-V) curves with a body plethysmograph. When the vagi were cut, diameters decreased only slightly as transpulmonary pressure (P_{TP}) was lowered from 30 cm H_2O; most of the change occurred below 10 cm H_2O, and diameters during inflation were the same as during deflation (no hysteresis). With vagi intact, diameters were smaller at all P_{TP} compared to vagotomy, and diameters were slightly smaller during inflation than during deflation (mild hysteresis). Vagal stimulation narrowed airways further at all P_{TP}, narrowing was least at 30 cm H_2O, and hysteresis was marked. Smaller airways (3-8 mm) narrowed more than larger ones, and the slopes of the P-D curves of different generations became similar with increasing tone. Lung P-V curves were the same with vagi cut or intact. During vagal stimulation, the deflation limb of the P-V curves was not changed significantly; during inflation, the curve was shifted to slightly lower lung volumes at a given P_{TP}. We conclude that: (1) the physical properties of airways (but not of lungs) are affected markedly by the presence of vagal smooth muscle tone, varying with the state of inflation and volume history; (2) airways show remarkable independence from lung parenchyma, since the airways narrowed as much as 35% at a given lung volume; (3) vagal stimulation constricts the smaller airways more than larger ones, making airway compliances of different generations similar. (Supported by NIH grant HL-06285 and North Foundation fellowship).

LYMPHOCYTE SURFACE MODULATION FOR THE RELEASE OF THE MIGRATION INHIBITION FACTOR. Anwar A. Hakim. Depts. Surgery & Physiology. University of Illinois at the Medical Center. Chicago. Ill. 60680.

Release of the migration inhibition factor (MIF) from sensitized peripheral blood or spleen lymphocytes occurs as a result of the reaction of the sensitizing antigen with sensitized lymphocytes. To reveal the physiological events which occur leading to the release of MIF, the effects of colchicine, vincristine and vinblastine were investigated by: (a)Non-specific stimulation with phytohaemagglutinin(PHA) or Concanavalin A(Con A) by spleen lymphocytes from normal(NSpL) and adenocarcinoma-bearing(AfCaSpL) BALB/c mice, and (b) specific stimulation with an adenocarcinoma cell surface specific glycoprotein(AdCaGP) by NSpL and AdCaSpL. When cultured in presence of PHA and Con A, NSpL and AdCaSpL yielded supernatants which inhibited migration of guinea pig peritoneal cells. If added with the mitogens, colchicine, vincristine and vinblastine increased the inhibitory effects of the supernatant fluids. Although, supernatants of lymphocytes from normal mice cultured in presence of AdCaGP had no effect, supernatants of lymphocytes from immune mice cultured in presence of AdCaGP inhibited migration of normal guinea pig peritoneal cells. The magnitude of inhibition was increased if colchicine, vincristine or vinblastine were added with AdCaGP to the culture medium. PHA non-specifically and AdCaGP specifically released MIF into the cell free medium. In both cases, colchicine or vincristine enhanced the release of MIF. MIF was heat-stable at 56°C for 30 min, it was non-dialyzable and not influenced by freeze-thawing and freeze-drying. It was eluted from Sephadex G-100 after albumin peak, with Mw of 13000. Colchicine and vincristine are known to interfere with the microtubular system of several cell type. The release of MIF is modulated by the interaction of the microfilaments and microtubules of the lymphocytes surface.

HEMOLYSIS AND HEMOGLOBINURIA FOLLOWING ORAL WATER ADMINISTRATION TO RATS. C.E. Hall, S. Ayachi* and O. Hall.* Dept. of Physiology & Biophysics, The Univ. of Texas Medical Branch, Galveston, Texas 77550

Adult female rats given distilled water by stomach tube (5ml/100g body wt.) after an overnight fast, invariably display significant and often severe hemoglobinuria within 30 minutes. Lesser quantities of Hb occur in urine over the next 30 min, but later samples are usually clear. Since these effects are not seen following administration of either isotonic saline or glucose solution, osmotic hemolysis is indicated. Peripheral blood samples reveal that hemolysis occurs within 5 min of water administration, but that blood osmolality continues to decline for at least 15 min. Furthermore, the levels of hemodilution are insufficient to account for the observed hemolysis, since even after 15 min the plasma osmolality falls from about 307 mOsm/L to 289 mOsm/L. The latter figure is equivalent to about 0.85% NaCl, whereas there is little hemolysis until 220 mOsm/L, corresponding to about 0.65% NaCl solution, is reached. It is therefore probable that hemolysis occurs not in peripheral blood vessels, but in a more restricted vascular bed. The extreme rapidity of hemolysis, its limited duration and other characteristics, suggest that perhaps it occurs within capillaries draining the intestinal tract, into which the water is resorbed. These are of limited capacity and, given the rapidity with which free water moves, here intravascular osmolality might well fall to levels that would precipitate hemolytic disruption of red-blood cell integrity. The gut can probably transfer water into the bloodstream almost as rapidly as can the lungs, from which, as in freshwater drowning, water resorption is rapid enough to cause massive intravascular hemolysis.

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EFFECTS OF INCREASED PLASMA COLLOID OSMOTIC PRESSURE ON RENAL HEMODYNAMICS AND RENIN SECRETION. J.E. Hall*, A.C. Guyton, and T.E. Jackson*, Dept. Physiol. & Biophy., Univ. Miss. Med. Ctr., Jackson, MS 39216

The effect of increased plasma colloid osmotic pressure (PCOP) on renal blood flow (RBF), glomerular filtration rate (GFR), electrolyte excretion, and renin secretion rate (RSR) was studied in dogs anesthetized with sodium pentobarbital. After a control period and a 5 min. vehicle (0.9% NaCl) infusion period, either dextran (20%, MW = 83,000; N=13) or human serum albumin (25%;N=5) was infused into the left renal artery (5-12 ml/min.) for 3-5 min. Dextran infusion increased renal venous PCOP from 17.4 ± 0.4 mmHg during saline infusion to 24.3 ± 0.7 mmHg, increased RBF (ml/min.) and RSR(ng $ml^{-1}min.^{-1}$) from 237 ± 21 and 63 ± 9 to 296 ± 20 and 185 ± 38 while decreasing urine flow rate (V;ml/min.), sodium ($U_{Na}V$) and potassium ($U_{K}V$) excretion rates (uEq/min.) from 0.42 ± 0.06, 89.5 ± 15.8, and 53.5 ± 3.6 to 0.16 ± 0.02, 33.0 ± 4.9, and 22.8 ± 2.6, respectively, after 3 min. of infusion. Dextran infusion elicited a transient fall in GFR, but after 3 min., mean GFR was not significantly different from control. A sustained decrease in GFR was observed only when PCOP was increased 11-14 mmHg above control. Albumin infusion produced similar changes in all variables studied. In contrast to direct renal vasodilators, dextran or albumin infusion does not increase RBF at perfusion pressures below the autoregulatory range. Also, the time course of renal vasodilation associated with increased PCOP is slower than during infusion of direct vasodilators. These observations suggest that GFR autoregulation during increased PCOP is due to alterations in tubular fluid dynamics sensed at the macula densa (MD). The stimulation of renin secretion by increased PCOP is also consistent with an MD mechanism since V, and Na^+ and K^+ delivery to the MD were probably reduced during colloid infusion. Supported by NIH grant HL 11678.

HUMAN DRINKING: ORBICULARIS ORIS EMG PATTERNS AND LIQUID CONTACT DURATIONS. B.P. Halpern & T.L. Nichols*, Dept. of Psych. & Sec. of Neurobiol. & Behav., Cornell Univ., Ithaca, NY, 14853, & Behav. Sci. Div., Food Sci. Lab., U.S. Army Natick Devel. Ctr., Natick, MA 01760.

Male and female adults took single sips of a liquid from a 296 ml drinking glass after receiving a "ready" signal (separated by >1 min). EMG was recorded with bipolar electrodes on the right upper lip; contact with the liquid, a drinkometer(<1 μa); swallows, a sound-shielded microphone on the anterior surface of the throat. Volume ingested was measured by refilling the glass to 174 ml. Each subject sipped 3 liquids 6-9 times each, in random order. Lifting the glass produced a signal which triggered A/D conversion of EMG and contact voltages. Subsequent averaging was done from 1450 msec before contact to 6000 msec after the beginning of contact. Results were that EMG increased steadily before contact and during initial (450 msec) contact, independent of liquid sipped (p>.025). Maximum EMG occurred 500-700 msec after contact start. Liquid dependent (p<.001) differences in late contact (500-1051 msec) and postcontact EMG did occur.

Liquid Ingested	Contact Duration msec		Time After Contact to 1st Swallow msec	
	Dyed	Colorless	Dyed	Colorless
1. Cherry Kool-Aid	1051	943	262	703
2. 1 + 100mM NaCl	----	1032	---	885
3. 309 MM sucrose	973	933	512	727
4. Distilled Water	964	973	650	806

Stimulus triads: 1,2,&4 or 1,3,&4. Dyed solutions were matched with Red #40. All swallows occurred postcontact.

It appears that precontact and early contact EMG is taste-independent, while later upper lip EMG is taste related. (Supported in part by US Army R.O. Contract DACO-72-0001, T.O. 72-468, and NSF Grant GB-43557.

THE TIME COURSE OF THE FORCE-VELOCITY(FV) RELATIONSHIP AND SERIES ELASTICITY(SE), AND PARALLEL ELASTICITY(PE) IN NORMAL(N) AND HYPERTROPHY(H) RABBIT RIGHT VENTRICULAR PAPILLARY MUSCLES(RVPM) Burt B. Hamrell* and Norman R. Alpert, Department of Physiology & Biophysics, University of Vermont, Burlington, Vt. 05401

The FV relationship was depressed in H as compared with N RVPM studied with isotonic quick-release(QR) at 30 to 33% of time-to-peak-tension(TPT)(Circ. Res. 34 & 35(Suppl. II): 71-82, 1974). The extrapolated estimate of shortening velocity at zero load (Vmax) was less in H than in N, and was independent of resting muscle length from 96 to 100% Lmax(resting length at maximal peak active twitch tension). In order to determine whether Vmax was independent of time RVPM from N rabbits (n=7) and rabbits with H (n=8) following pulmonary artery banding were studied with QR at 10%, 15%, 20%, 25% and 30% TPT. Curvilinear regression analyses were used to extrapolate the FV curve to the velocity axis in order to estimate Vmax at each %TPT. H Vmax was constant from 10% to 30% TPT (0.9 muscle lengths(ML)/sec) but was 56% of N Vmax (1.6 ML/sec) which also was constant over the same %TPT range. Therefore there was a rapid onset and a plateau of mechanical activity in N and H RVPM but with evidence of intrinsic depression of H contractile apparatus shortening capacity. SE was obtained from the initial rapid force and length changes in QR at each %TPT, and was the same at each %TPT and in H and N. PE, measured with quick stretches between twitches, was significantly stiffer in H (stress/strain/stress slope=$25(\Delta 1/1)^{-1}$) than in N (slope=$12(\Delta 1/1)^{-1}$). A stiffer PE with no change in SE suggests an analogue model containing a Voigt-like element and this model was used in these analyses.

ELEVATIONS OF BLOOD PRESSURE AND HEART RATE DURING CLASSICAL CONDITIONING PROCEDURES IN THE SQUIRREL MONKEY. T. R. Hansen and J. A. Herd. Dept. Physiology and Psychiatry, Harvard Medical School, Boston, MA and New Engl. Reg. Primate Res. Ctr., Southborough, MA.

Squirrel monkeys isolated in a chamber maintained at 32°C were exposed to pairs of stimuli which consisted of an auditory tone (1000 hz, 80 db) followed immediately by an electric shock (8 ma, 200 msec). A 60-minute period in which these pairs were presented at time intervals of 1, 2, 3, 5, or 15 minutes was followed by a period of 30 minutes in which the tone without electric shock was presented under the same schedule. Transient elevations followed each presentation of tone and shock and sustained elevations occurred during the entire 90-minute session. The greatest increases in mean blood pressure and heart rate occurred when the tone-shock pairs were presented at two-minute intervals. During the first 30 minutes of sessions in which tone-shock pairs were presented at two-minute intervals, blood pressure rose 11 $\pm$ 2 mm Hg (mean $\pm$ SEM) and heart rate rose 96 $\pm$ 11 beats/min. During the next 30 minutes under the same schedule, blood pressure was 7 $\pm$ 3 mm Hg and heart rate was 76 $\pm$ 11 beats/min above values recorded before each session began. During the final 30-minute period, presentations of the tone alone at two-minute intervals produced transient elevations but little sustained increase in average blood pressure (3 $\pm$ 3 mm Hg) or heart rate (21 $\pm$ 6 beats/min). Presentations of shock alone produced greater elevations in blood pressure and heart rate than presentations of tone-shock pairs under the same schedule. The results of these experiments indicate that presentations of conditional stimuli may decrease the cardiovascular response to unconditional stimuli. (Supported by USPHS Grants Nos. HL 14150 and HL 09154).

MEASUREMENT OF LEFT VENTRICULAR WALL THICKNESS AND CHAMBER VOLUME USING THREE-DIMENSIONAL RECONSTRUCTION. L.D. Harris*, R. A. Robb, E. H. Wood, and E. L. Ritman. Mayo Foundation, Rochester, Minnesota 55901.

Left ventricular chamber volume, myocardial volume and thickness are determined from images of computer determined cross section reconstructions of the distribution of x-ray attenuation coefficients generated over the entire anatomic extent of opacified isolated beating left ventricles and urethane casts of left ventricles. The reconstructed cross sections are displayed, the outlines of the epicardial and endocardial borders are traced, and the coordinates stored in a digital computer using a light pen and computer generated cursor. The areas enclosed by both the epicardial and endocardial contours, the regional wall thickness within the plane of the reconstructed cross section, true three-dimensional wall thickness, and chamber volume are then calculated. The urethane casts of isolated left ventricles are sliced transversely at the levels of the ventricle corresponding to the levels of the reconstructed cross sections to measure the accuracy of the method. Results show that left ventricular chamber and total volume can be measured to within 5% of true dimensions. The ability to determine the dynamic changes in true three-dimensional geometry of complex moving objects is necessary for computation of myocardial mechanical function in the working intact heart. (Supported in part by NIH grants HL04664 and RR-7; NASA-NGR-24003-001, and AHA CI-10).

RESPONSE OF SUPRAOPTIC NEUROENDOCRINE CELL FIRING PATTERN TYPES TO MEASURED CHANGES IN PLASMA OSMOLALITY. J.T. Haskins*, D.P. Jennings*, and J.M. Rogers* (SPON: C.G. Beames). Department of Physiological Sciences, Oklahoma State University, Stillwater, Oklahoma 74074.

Southdown ewes were prepared under general anesthesia with a cranial platform-cylinder arrangement, pituitary stimulating electrodes, and cannulae in both jugular veins. Following recovery from surgery, microelectrodes were hydraulically driven into the unanesthetized sheeps' hypothalamus; neuroendocrine cells were identified by antidromic and collision techniques; activity of all identified units were categorized as silent (10%), continuously active (CA) (65%), and low frequency bursting (LFB) (25%). Once control firing patterns were established a slow intrajugular infusion of 1.2 M NaCl solution was used to force a 15 mOsm/kg increase in plasma osmolality (posm) over a period of 10 min. Blood samples were drawn periodically for posm determinations during the hypertonic forcing and ensuing return of posm to control levels. All LFB cells responded initially by increased burst mean firing rate (MFR) and subsequent decreased interburst intervals and increased burst durations. Most silent and CA cells responded with variable increases in MFR and were not recruited into a bursting pattern of discharge. A few CA slow cells responded by progressing through LFB discharges to a CA fast pattern of firing. Neurons most responsive to osmotic forcing decreased their MFR during recovery more rapidly than the posm returned to control levels, implying a dynamic sensitivity to changing osmolalities. The functional significance of each firing pattern type was not related exclusively to thresholds of posm [Arnauld et al, 1974] or to functional cell types [Hayward and Jennings, 1973]; they may be related to a combination of these principles and to dynamic properties of the appropriate neuroendocrine control system. (Supported in part by USPHS GRS RR05567, NIH NS11978, & Dept. of Physiol. Sci.)

ELECTROCARDIOGRAPHIC CHANGES IN ISOLATED PERFUSED HEARTS EXPOSED TO CADMIUM IONS. P.L.Hawley and S.J. Kopp*. Dept. Physiology Univ. Illinois Medical Center, Chicago, Ill. 60680

Rat hearts were cannulated for retrograde Langendorff perfusion with oxygenated, Tris-buffered Ringer-Locke's solution at 35oC. ECGs from the isolated hearts were recorded by silver electrodes located on the walss of atemperature controlled Lucite chamber. Recrodings were made with a Grass Model 79 polygraph. Coronary overflow of the perfusion medium served as the volume conductor. Perfusion pressure was maintained by oxygen gassing pressure and monitored with a Staham P23 transducer in the perfusion line. The addition of Cd^{++} to the perfusiop medium increased the PR interval at a concentration as low as 10^{-5} mM. As the Cd^{++} was increased, PR interval extended and A-V blocking occurred when the concentration was 10^{-3} mM. Complete, irreversible A-V block occurred in less than ten minutes of exposure to 10^{-2} mM Cd^{++}. Sensitivity of the heart to Cd^{++} was pH dependent, having the least sensitivity at pH 7.6 and the greatest at pH 7.0. Further lowering of the pH had no significant additional effect. Following A-V block, the presence of rhythmical P waves indicated a continuation of atrial electrical activity. Other changes observed were an increase in P wave voltage, broadening and notching of the QRS complex prior to blocking, and depression of the ST segment. Whole animals given Cd^{++} in drinking water (0.089 mM or 1.15 mM Cd^{++} in 0.5% saline) showed similar changes in ECG patterns over a period of ten weeks. These observations are consistent with the hypothesis that the conductile system shows a specific sensitivity to Cd^{++} in the mammalian heart.

QUANTITATIVE DIFFERENCES IN AIRWAY MORPHOLOGY OF MALE AND FEMALE RATS. M. Hayashi*, P. Phelps* and G. Huber. Dept. of Medicine and Thorndike Laboratory, Harvard Medical School and Beth Israel Hospital, Boston, Massachusetts 02215

In man, males appear to be more susceptible to airway injury from tobacco inhalation, air pollutants and other factors. The cause of higher morbidity rates in human males than females from diseases of the respiratory tract may be a complex one involving several factors. To study this experimentally, 13 male and 45 female (15 each in proestrus, estrus and diestrus) CD rats weighing around 250 g were evaluated. Tracheas were fixed in situ by injection of a mixture of formaldehyde and glutaraldehyde. Longitudinal sections cut from paraffin blocks were stained with combined alcian blue (pH 2.6) and periodic acid Schiff (PAS) to count goblet cells or with H & E to determine epithelial thickness. In the normal rat trachea, cells containing PAS-positive granules at their apexes constituted a major population of goblet cells. The presence of these goblet cells in the trachea was greater in females than in males. Proestrus and estrus females contained significantly more goblet cells of this type than did males. However, diestrus females did not differ significantly from males. In females, estrus rats contained significantly more of these goblet cells than did diestrus animals. The tracheal epithelium of male rats was significantly thicker than that of estrus females, but did not always differ significantly from proestrus and diestrus females. These studies demonstrate that airway morphology differs in males and females and varies in the female as a function of hormonal cycles. These results raise the question that similar differences may be important in the pathogenesis of human disease and deserve further clarification in man.

ELECTRICALLY ELICITED RELEASE OF NEUROHORMONE FROM ISOLATED CRAB SINUS GLAND AND ITS DEPENDENCE ON CA^{++}. Beverley A. Haylett*, Tina M. Weatherby*, and Ian M. Cooke, Lab. of Sensory Sciences, Univ. of Hawaii, Honolulu, Hi. 96822

A sinus gland (s.g.) and its nerve were isolated from Portunus sanguinolentus and arranged for extracellular stimulation and recording. Stimuli (0.3 msec. pulses), adjusted for maximal propagated electrical response, were given at rates of 4-10/sec. repetitively or in trains of 4-6 at 0.2/sec. For assay of released hormone, perfusion of physiological saline is halted during the control (5 min. unstimulated) or test (electrically stimulated, 1-3 min.) period. The saline is collected from the chamber and the total volume adjusted to 0.2 or 0.4 ml. 0.2 ml. is injected into an isolated meropodite of Ocypode laevis which has its red chromatophores (chroms.) fully expanded (state 5 on 1-5 scale). The state of contraction of at least 5 chroms. is staged and the average change (Δ) after 2 min. taken as a measure of hormone present. If undamaged in dissection, saline from controls produces insignificant chrom. changes ($\Delta < 1$). If propagated electrical activity in response to stimulation is observable, then hormone is released. As few as 50 stimuli release significant amounts (chrom. $\Delta > 1$) of hormone. Repeated tests result in exhaustion of releasable hormone; 'rest' (no stim. for 1/2 hr.) results in partial recovery. As many as five tests over a period of 4 1/2 hrs. giving significant release have been obtained from a single s.g. In low Ca^{++}, stimulation does not result in hormone release although the electrical response is usually increased. These observations add the s.g. to the systems in which neurohormone release has been shown to be mediated by propagated electrical activity of the neurosecretory cells themselves and in which Ca^{++} appears to couple electrical to secretory activity. (Supported by NSF grant BMS72-02521 A01.)

ADAPTATION TO EXERCISE: LEUCINE METABOLISM IN SKELETAL MUSCLE. A.L. Hecker*, G.J. Klain, E.W. Askew* and W.R. Wise, Jr.*. Biochemistry Division, Dept. Nutrition, Letterman Army Institute of Research, Presidio of San Francisco, CA 94129

Male carworth CFN rats were subjected to a 12 week treadmill training regimen culminating in a performance rate of 35 m/minute, 2 hours/day, 5 days/week at an 8^{o} incline. The animals were sacrificed in a rested condition at 2 week intervals beginning at the conclusion of the 4th week of training. Corresponding groups of sedentary ad lib and sedentary pair fed animals were used as controls. Oxidative capacity was determined by monitoring $^{14}CO_2$ production in muscle slices (gastrocnemius) using ^{14}C-U-leucine as the substrate. Leucine oxidation was significantly ($P<.01$) increased following approximately 8 weeks of treadmill running. The adaptation became more pronounced with continued training. The oxidative rate of the untrained pair fed group did not differ from the ad lib controls. This supported the conclusion that the observed effects were exercise induced and did not result from a lowered caloric intake due to the anorexigenic effect of training. The incorporation of leucine into the TCA precipitable protein portion of the microsomal cell fraction did not display any significant adaptation during the training program. These data indicate that physical training significantly increases the catabolism of leucine in skeletal muscle but has only marginal effects on the anabolic processes.

MODULATION OF VASCULAR RESPONSE TO CHEMORECEPTOR STIMULATION BY BARORECEPTOR ACTIVITY IN SPONTANEOUSLY BREATHING DOGS. Donald D. Heistad, Francois M. Abboud and James L. Prochaska*, Dept. Med. & Cardiovascular Center, Univ. of Iowa and VA Hosp., Iowa City, Iowa.

Activation of the baroreceptor reflex by hypotension potentiates vasoconstrictor responses (VCR) to chemoreceptor stimulation (CRS) in paralyzed dogs and potentiates hyperventilation during CRS in spontaneously breathing dogs. Since hyperventilation activates pulmonary stretch receptors which, in turn, inhibit VCR during CRS, we have examined the possibility that activation of pulmonary stretch receptors by hyperventilation might override or mask the potentiating effect of hypotension on VCR during CRS. VCR during CRS with nicotine were measured in anesthetized ventilated and spontaneously breathing dogs. VCR are shown below as increases in perfusion pressure (Mean±SE) in innervated gracilis muscle and kidney perfused at constant flow. Carotid sinus pressure (CSP) was reduced by bleeding (systemic hypotension) and raised by perfusing a carotid sinus at high pressure. I, II, and III represent responses to CRS during fixed ventilation, before vagotomy in breathing dogs, and after vagotomy in breathing dogs, respectively.

CSP	Muscle			Kidney		
mmHg	I	II	III	I	II	III
35	48±7	34±12	43±12	85±43	33+14	34±16
110	16±3	17±5	29±13	12±7	5±2	14±7
175	---	6±2	8±2	---	1+1	3+2

In muscle, responses during CRS were often diphasic in II; CSP appeared to modulate vasodilator as well as VCR during CRS. We conclude that baroreceptor activity modulates VCR during CRS in spontaneously breathing dogs and that hyperventilation does not mask this interaction.

CHANGES IN THE CHARACTERISTICS OF POH THERMOSENSITIVITY DURING SLEEP AND HIBERNATION. H.C. Heller, S.F. Glotzbach* and R. Benster* Dept. of Biological Sciences, Stanford University, Stanford, Ca. 94305.

Responses in rate of metabolic heat production to manipulations of POH temperature were measured in kangaroo rats (Dipodomys) and ground squirrels (Citellus) as a function of ambient temperature and stage of torpor, sleep, and wakefulness. Changes in the threshold POH temperature and the proportionality constant (α_{MHP}) for this thermoregulator response were measured. In the kangaroo rat the transition from wakefulness to slow-wave sleep was accompanied by a reduction in α_{MHP} and/or a reduction in the threshold T_{hy} for this response. POH thermosensitivity was not demonstrable during REM sleep. Transitions from REM sleep to slow wave or wakefulness were accompanied by an immediate return of POH thermosensitivity. Collaborative studies with J. Walker and R. Berger at the University of California, Santa Cruz showed that ground squirrels enter hibernation through slow-wave sleep. Brief returns to wakefulness are associated with simultaneous increases in metabolic rate and plateaus or rises in T_b. Experiments in which the POH was heated and cooled during entrance into hibernation demonstrated a slowly declining threshold T_{hy} for the metabolic heat production response. Over the 30°C range of body temperatures from euthermia to deep torpor the average decrease in α_{MHP} was 15 to 16-fold. We believe that these results demonstrate the continuity of the CNS regulation of body temperature in the hibernating mammal and support the hypothesis that hibernation is an extension of the physiological changes normally occurring in the thermoregulatory system during sleep. (Supported by NIH Grant 5 R01-NS10367.

ISOMETRIC PROPERTIES OF CARDIAC MUSCLE FROM AGING SPONTANEOUS HYPERTENSIVE RATS. L.J. Heller and J. G. Hartmann*, Dept. Physiology, University of Minnesota, School of Medicine, Duluth; Duluth, Minn. 55812

Cardiac muscle from the Spontaneous Hypertensive Rat (SHR) has previously been shown to have a propensity to develop aftercontractions (small, slow, spontaneous contractions not associated with propagated action potentials) in response to paired pulse stimulation, a property not as evident in normotensive controls. These and other isometric mechanical properties of the SHR papillary muscle were studied to determine if an age-dependent relationship exists.

Three groups of SHR preparations were tested: Group A=84±19 days, Group B=353± 19 days and Group C=556±13 days. Group C animals were not always "hypertensive" (arterial pressure>150 mmHg) at the time of death but an elevated heart weight/body weight ratio ($p<.001$) indicated a previous persistent overload.

Aftercontractions associated with paired pulse stimulation were evident in all age groups. The delay between paired stimuli which elicited the largest aftercontractions increased with age as did the amplitude of the aftercontractions. At L_o, resting tension, active tension and dT/dt did not differ between age groups while time-to-peak-tension-development and ½ relaxation time increased significantly with each age group. Mechanical refractory period (the minimum delay between paired stimuli required to elicit a second coupled mechanical response) did not change significantly with age. Rapid stimulation rates tended to depressed tension development in all groups but Group A was more depressed and took longer to recover than Group B or C.

Results are consistent with the hypothesis that aging may be associated with decrease in the rate of processes associated with deactivation of the contractile system.

DISTRIBUTION OF NA AND K IN SPLIT SKIN PREPARATIONS OF ISOLATED FROG SKIN. S. I. Helman, Dept. of Physiology & Biophysics, University of Illinois, Urbana, Illinois 61801

Sheets of split skins (6.4 cm^2) consisting of stratified epithelium (E) and outer cornified cells (C) were prepared according to methods of others where intact skins were incubated in Ringer solution (2-3 hours) containing collagenase (inside only) and subsequently exposed to hydrostatic pressure. Analysis by flame photometry showed that total Na and K averaged near 0.13 and 0.60 $\mu Eq/cm^2$ split skin, respectively. These values were similar regardless of whether the intact skins were incubated overnight with aldosterone-Ringer or studied acutely. In 9 of 18 separate studies, samples of C alone could be separated away from aldosterone-treated skins, and their values of Na and K compared with total Na and K of the split skins (C+E). C was found to contain a mean of .073 and .019 $\mu Eq/cm^2$ of Na and K, respectively. Accordingly, the Na and K of E was calculated to average .061 and .616 $\mu Eq/cm^2$ respectively, and thus 56% of total Na and 3.1% of total K of split skins could be attributed to the existence of the stratum corneum. With the idea that Amiloride inhibits sodium entry into E, studies were done to determine what fraction of E was sensitive to 10^{-5} M Amiloride. Total Na of (C+E) fell by a mean of .083 $\mu Eq/cm^2$ (with little or no change of K) to levels observed before for C alone (.07 $\mu Eq/cm^2$). Thus, it is thought that the quantity of sodium in the sodium transport pools can be determined directly after subtraction of the significant contribution of C to the total sodium of the split skin. (Supported by USPHS AM 16663.)

EFFECT OF INHIBITION OF GABA UTILIZATION ON THE DOG EEG RECOVERY FROM ANOXIA. F.G. Hempel* and A.P. Sanders* (SPON: H.A. Saltzman). Duke University Medical Center, Durham, N.C. 27710

In the brain, part of the succinate providing reducing equivalents to the mitochondrial respiratory chain may be derived from GABA (Roberts and Baxter, 1958). We have investigated the effect which blockage of this shunt with the GABA-transaminase inhibitor amino-oxyacetic acid (AOAA) has on the EEG response of the dog to transient anoxia. Pyridine nucleotide (NADH) fluorescence was monitored as an index of oxygen replenishment to the cortex following anoxia. Our results indicate that the time to abrupt EEG shutdown, 160-200 sec. after ventilation with nitrogen begins, is not appreciably affected by succinate (10mM/kg/hour, infused continuously), or by AOAA (0.5mM per kg, injected 2 hours prior). The abrupt recovery of the EEG from its flat anoxic level is retarded two-fold, however, by AOAA. A mean EEG recovery time, measured from the onset of cortical NADH oxidation, was found to be 9 seconds in controls. If AOAA had been administered, the mean recovery period was extended to 22 seconds. Succinate infusion restored normal recovery times to the AOAA-treated animals. We interpret these data as evidence that the substrate supply and subsequent energy production provided by the GABA to succinate shunt is important in reestablishing neuronal function after an anoxic insult, and that exogenous succinate replaces the pathway blocked by AOAA. (Supported by grant HL07896 from the NHLI.)

EFFECT OF ALTITUDE ON THYROID FUNCTION IN THE UINTAH GROUND SQUIRREL (Citellus armatus). R.W. Heninger, S.K. Ware* and W.L. Wells.* Brigham Young U., Provo, Utah 84602

Thyroid function in the Uintah Ground Squirrel (Citellus armatus) collected at two different altitudes (5400 and 9000 ft) was studied. Parameters selected to evaluate overall thyroid activity were: thyroid 125-I uptake, thyroid thyroxine (T4) and triiodothyronine (T3) content, serum T4 and T3, urinary T3 and T4, pituitary and serum TSH, plasma half-life of injected T4-125I, T4 distribution space, metabolic clearance rate, T4-derived urinary excretion of 125-I and *in vitro* deiodination of T4-125I by cardiac tissue. Animals from the higher elevation had a depressed thyroidal 125-I uptake and lower serum T4. Pituitary TSH was significantly higher in these animals. Plasma half-life of injected T4-125I was shorter in the high elevation animals and the T4 distribution space, metabolic clearance and T4 secretion rate were lower. Urinary excretion of iodide-125 at various times following injection of T4-125I was not different between the two groups except during the 44-70 hour post-injection interval. During this interval there was an increased excretion rate in the high elevation animals. Although all parameters studied did not unequivocally give a clear-cut indication of relative thyroid function as affected by altitude stress, there was sufficient consistency to conclude that ground squirrels native to a high elevation exhibit thyroid hypofunction when compared with squirrels inhabiting a lower elevation.

SPONTANEOUS CONTRACTIONS AND NOREPINEPHRINE SENSITIVITY OF CULTURED VASCULAR MUSCLE CELLS. Kent Hermsmeyer. Dept. of Pharmacology and The Cardiovascular Center, University of Iowa, Iowa City 52242

A method for culturing vascular muscle cells has been developed in this laboratory which maintains contractile function, to allow physiological investigations of isolated cells. Omphalomesenteric artery and vein of 13-day embryos were used for these experiments. Trypsin dispersed muscle cells attached to glass culture flasks and showed spontaneous contractions for as much as 12 days. Single cells and most of the contracting cell groups, which consisted of 3-30 cells, contracted 2-5 times per min. No movement of the ends of the cells was possible because of their attachment, but identified regions of the cell moved from one-twentieth up to one-half the cell length during contractions. Cinemicrographic analysis revealed that commonly, the shortening phase of contraction took 2-3 sec, but the most rapid shortening-relaxation cycles occurred in less than 1 sec. Cultured vascular muscle cells responded to low norepinephrine concentrations (< 3 nM) by an initial contraction of 5-60 sec duration and/or an increase in the rate of the spontaneous contractions. Shortening in the presence of norepinephrine was increased up to 50% in some of the cells. These experiments demonstrate that isolated vascular muscle cells show pacemaker activity, contractions much quicker than a segment of the intact vessel, and high norepinephrine sensitivity.
(Supported by grants HL 16328 and HL 14388 from the National Institutes of Health.)

COMPARISON OF EFFECTS OF IONOPHORES AND PROSTAGLANDIN E ON GROWTH HORMONE SECRETION AND CYCLIC NUCLEOTIDE LEVELS IN RAT PITUITARIES. F. Hertelendy*, R. J. Narconis*, M. S. Yeh*, and J. A. Ferrendelli*. (SPON: A. R. Lind). St. Louis Univ. Sch. Med., St. Louis, MO 63104 and Washington Univ. Sch. Med., St. Louis, MO 63110

Incubation of rat anterior pituitaries in KRB in the presence of the ionophores A23187 and X537A resulted in a dose dependent increase of GH secretion. However, whereas prostaglandins E1 and E2 (PGE) induced a very pronounced rise in tissue levels of cyclic AMP which preceded GH release, the ionophores did not cause significant changes in the concentration of either cyclic AMP or cyclic GMP, both of which nucleotides have been implicated in GH secretion. Omission of Ca from the incubation medium abolished GH responses to both ionophores and to PGE although PGE-induced cyclic AMP accumulation was not prevented in Ca-free medium with or without EGTA. Metabolic inhibitors such as DNP, rotenone, and valinomycin inhibited GH responses to all three stimuli. Pre-incubation of pituitaries with A23187 or X537A in a Ca-free EGTA medium inhibited subsequent responses in Ca containing medium to both ionophores (expecially that to X537A) as well as to PGE. This inhibition was not observed in the absence of ionophores or when PGE was present alone during a 60-min. pre-incubation. Ionophores accelerated Ca efflux from pituitaries preloaded with Ca^{45} while PGE caused a significant initial inhibition. Electron microscopic examination of tissues after a 60-min. incubation with X537A (10^{-5}M) revealed extensive and generalized vacuolization in all cell types which was not observed with X23187, PGE, or controls. Apparently, ionophores stimulate GH secretion by a mechanism different in some respects from that activated by PGE, although Ca and energy are essential for both.

THE EFFECTS OF AIRWAY PRESSURE (P_A), BOTH WITH AND WITHOUT LUNG EXPANSION, ON THE PULMONARY VASCULATURE (PV) OF FLUID FILLED FETAL LUNGS (FL) AND AIR FILLED NEWBORN LUNGS (AL). J.R. HESSLER* (Intr. by C. Cornelius) Div. of Comparative Med., Col. of Med., & Col. of Veterinary Medicine, U. of Fla., Gainesville, Fla. 32610.

Studies were conducted on the left lower lung lobe of 15 near term fetal and 15 newborn goats. P_A without lung expansion was elevated from 10 to 20 mm Hg in AL and 0 to 10 mm Hg in FL by external pressure on the chest with the airway closed and to the same pressures with lung expansion by filling the airway with equivalent volumes of air or isotonic saline. A Starting Resistor (SR) model was used to analyze the PV. Use of this model permits the calculation of resistances proximal (R_p) and distal (R_d) to the vessels behaving as SRs as well as the SR surrounding pressure (P_s). Pulmonary artery pressure (P_{pa}), P_s, R_p & R_d were all determined while pulmonary artery blood flow was held constant. The following table shows the % change from control produced by 10 mm Hg increases in P_A. * = $P < .05$

	WITHOUT LUNG EXPANSION				WITH LUNG EXPANSION			
	P_{pa}	P_s	R_p	R_d	P_{pa}	P_s	R_p	R_d
FL	26*	37*	19*	49	20*	7	28*	35
AL	34*	57*	9	92*	15*	29*	2	50

From this data it is concluded that: 1) Lung expansion more effectively reduced the influence of P_A on the PV in the AL than in the FL. 2) Since R_p increased in response to elevated P_A in the FL and R_d in the AL, the SR site must be further down stream in the FL than AL. 3) Since P_s in the expanded FL is not significantly elevated by the increased P_A, the SR site must be in extralveolar vessels not influenced by P_A, very likely on the venous side of the PV and accordingly, in the AL the SR site must be in alveolar vessels which are influenced by P_A, very likely on the arterial side. (Supported by N.I.H. HL 13749)

TRANSMURAL DIFFERENCES IN CELLULAR CONSTITUENTS OF THE NORMAL CANINE MYOCARDIUM. K.M. Hickey*, R.B. Dunn*, and D.M. Griggs, Jr. (SPON: A.W. Hahn). Dept. Physiology, Univ. of Missouri, Columbia, Mo. 65201

Evidence for the nonhomogeneity of the left ventricular myocardium has been obtained by a number of laboratories with reference to several different variables. Capillary permeability and sarcomere length have been reported to vary across the normal ventricular wall. Studies of enzymes and several elements (Fe,Cu,K) have also been reported to show transmural differences. A greater accumulation of lactate in the subendocardium during no coronary flow has been interpreted by this laboratory as an indication of transmural differences in energy utilization and tension development in the left ventricle. To further characterize regional variations of the canine left ventricle, tissue samples were taken and divided into inner, middle and outer thirds for the analysis of total protein nitrogen, glycogen, tissue lipids and myoglobin. Tissue for glycogen analysis was obtained by a quick freezing method whereas analysis for the other substances was performed on freshly excised tissue. Total protein nitrogen showed no transmural differences; however, glycogen and triglycerides showed gradients in reverse directions-glycogen decreasing from inner to outer regions and triglycerides increasing from inner to outer regions. The variation in these two metabolites might be indicative of differences in the energy producing pathways across the ventricle. Although myoglobin did not show a gradient in all animals studied, a greater concentration was consistently found in the inner region as compared to the outer region. Since myoglobin can serve as a store for oxygen and may be involved in facilitated diffusion of oxygen, this greater subendocardial concentration may be a compensatory mechanism for a greater oxygen utilization in this region. (Supported by Grant HL 11876 from NHLI.)

ON THE MODE OF ACTION OF METHYL MERCURY: THE BARNACLE MUSCLE FIBER AS A PREPARATION. Helen Hift and R. Schultz*, Departments of Medicine and Physiology, Univ. of Wisconsin, Madison, WI. 53706

External application of 10^{-4}M-methyl mercury (MeHg) produced a multiphasic effect on Na efflux. First, there was a decline followed by a transitory new steady state (the 'trough' period). This in turn was followed by a drastic rise and fall in the Na efflux. The inhibitory effect was in the order of 31.84±5.61% (SEM)(n=9), while the terminal rise was in the order of 975.0±114.63% (n=9). MeHg(10^{-4}M) when applied to fibers pretreated with 10^{-4}M-ouabain promptly caused only stimulation, whereas ouabain when applied after MeHg caused a further fall in Na efflux. Fibers treated with 10^{-4}M-MeHg contracted slowly after some 15-25 min of exposure, reaching a maximum (~30% of original length) about the time of onset of the stimulatory response. Although the resting membrane potential showed only a decline of 3 mv over the first 30 min, its decline became more rapid and reached zero during the period of terminal rise in the Na efflux. Ultrastructural studies carried out on fibers treated with 10^{-4}M-MeHg showed that during the first 25 min there was progressive deterioration of the plasmalemma, mitochondria and SR, and that during the 'trough' period the mitochondria were typically in phase 3 (dense configuration), and that there was extensive fluid retention in the subsarcolemmal region and pinhole formation in the plasmalemma. During the terminal rise and fall in the Na efflux gaps in the plasmalemma and cleft walls were common, and the myofilaments were in disarray. The fiber as a whole assumed a granular appearance, and the surface and cleft walls fragmented into vesicles. These results suggest that the early fall in the Na efflux is the result of reduced membrane Na^+-K^+ ATPase activity or reduced ATP supply, and that the stimulatory response represents release of radiosodium following destruction of the sarcolemma.

CARBON MONOXIDE CONCENTRATIONS IN MATERNAL AND FETAL BLOOD: A MATHEMATICAL MODEL. E. P. Hill*, J. R. Hill*, G. G. Power, & L. D. Longo, Dept. of Medicine, Univ. Calif. San Diego, La Jolla, Ca. 92037 and Dept. of Physiology, Loma Linda Univ., Loma Linda, Ca. 92354.

We have developed a mathematical model that calculates the time course of changes in maternal and fetal carboxyhemoglobin levels following inspiration of various CO concentrations. The calculations include effects of endogenous production of CO in mother and fetus, alveolar ventilation, pulmonary and placental diffusing capacities, and interactions with oxygen. During steady-state, resting conditions in humans, fetal HbCO levels exceed maternal HbCO levels by about 10%, principally because of the leftward shift of the fetal oxyhemoglobin dissociation curve. At 50 parts per million inspired CO, steady-state fetal and maternal HbCO are 9% and 8% respectively. After the initiation of CO breathing, the maternal HbCO reaches half its final steady-state value in about 3 hours. In contrast, the fetal HbCO requires about 7 1/2 hours to reach half its steady-state value. Final equilibrium occurs at about 48 hours. During both uptake and elimination of CO, fetal HbCO levels lag behind maternal values and may attain higher peak values. The effects of elevated $HbCO_f$ on tissue oxygenation were investigated by calculating the equivalent changes in fetal placental flow, $\dot{Q}_f$, and fetal arterial P_{O2} necessary to maintain placental O_2 exchange. For instance, at 10% $HbCO_f$, $\dot{Q}_f$ must increase about 63% or umbilical arterial P_{O2} decrease 31% to maintain fetal oxygenation. (Supported in part by grant HD 04394.)

ROLE OF BLOOD IN THE HYPOGLYCEMIC RESPONSE TO ENDOTOXIN. L.B. Hinshaw B. K. Beller*, L. T. Archer*, C. Bridges*, and B. Benjamin*. V.A. Hosp. and U. Okla. Hlth. Sci. Ctr., Okla. City, Okla. 73104

Progressively developing lethal hypoglycemia in dogs and baboons subjected to endotoxin or live E. coli shock, has recently been reported by this laboratory. The purpose of the present study was to explore the possibility that accelerated glycolysis in blood might contribute to the elicitation of the hypoglycemia of shock. Experiments were carried out on human and canine heparinized blood maintained in vitro under controlled temperature conditions. Plasma glucose was determined with a Beckman Glucose Analyzer. Endotoxin was added to the blood in concentrations estimated to be below and above the LD_{100} in vivo dose. Glucose concentration, pH, and in some instances pCO_2 and pO_2, were monitored up to 7 hours post endotoxin. Paired control blood samples received equal volumes of saline in place of endotoxin. Results demonstrated consistent accelerated glucose disappearance in human and canine blood at concentrations of endotoxin 1 mg/10ml blood or greater. The average period of greatest rate of disappearance was between 1 and 4 hours in both species, and following this time, glucose utilization slopes were equal in experimental and control groups. At values of 5-11mg%, glucose concentrations remained relatively constant in all samples. A positive correlation was observed between the decreases in glucose and pH, with endotoxin addition yielding greater depressions in both parameters. Alterations in pO_2 and pCO_2 were inconstant. Findings are extrapolated to suggest in the in vivo state, a significant quantity of glucose may be used by the blood after endotoxin administration with a concomitant depression of pH. (Supported by V.A. Hosp. and U.S. Navy Contract N00014-68-A-0496).

AN ACTION OF INSULIN ON FEEDBACK REGULATOR LEVELS. R.J. Ho, T.R. Russell* and T. Asakawa*. E.W. Sutherland Research Labs, Dept. of Biochemistry, Univ. of Miami School of Medicine, Miami, Florida 33136.

Direct evidence showing the cellular formation and subsequent release of a potent inhibitor (FR) of adenylate cyclase by adipocytes has been obtained. The appearance of FR in adipocytes preceded its release into the medium. Insulin inhibited the epinephrine-stimulated formation and release of the feedback regulator (FR) when adipocytes of rat epididymal adipose tissue were incubated with epinephrine (0.6, uM) and caffeine (1 mM) and/or insulin, 50-500 uU/ml indicating a new action for insulin. FR formation and release was increased 5 fold 30 minutes after stimulation by epinephrine and caffeine, however, this stimulated level of FR was gradually decreased by the addition of various concentrations of insulin. FR was partially purified and its content was determined by its ability to inhibit epinephrine-stimulated adenylate cyclase of adipocyte plasma membrane. Insulin, 50 uU/ml, inhibited FR release from 110 U/g to 80 U/g. Insulin, 500 uU/ml, inhibited FR release to 30 U/g. ACTH-stimulated FR formation in adipocytes of hamster was also inhibited by insulin. When fresh adipocytes of rat were incubated in the presence of epinephrine and caffeine, insulin, 200 uU/ml, inhibited cAMP formation by 18% at 10 minutes of incubation. FR, 0.8 U/ml, inhibited cAMP formation 32% at 10 minutes. The combination of insulin and FR inhibited about 45%. The effect of insulin on FR formation and the combined effect of insulin and FR on cyclic AMP levels may reveal some yet unexplained discrepancy in the literature concerning the mechanism of action of insulin. (Supported by grants from NIH (HL 16671) NSF (GB 04671) and the AHA).

CARDIOVASCULAR AND METABOLIC RESPONSES OF EXERCISING MEN IMMERSED IN 25.5°C WATER BREATHING COMPRESSED AIR OR HELIUM TRI-MIX. P.F. Hoar‡ L.W. Raymond, H.C. Langworthy‡ R.E. Johnsonbaugh‡ and J. Sode* Naval Medical Research Institute, Bethesda, Maryland 20014.

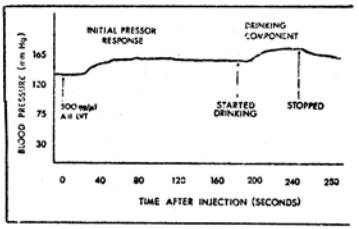
Efforts have been directed at identifying mechanisms by which exposure of normal men to hyperbaric helium atmospheres, under conditions of thermal stress and underwater exercise, alters cardiovascular and metabolic functions. Fourteen unprotected scuba divers performed ergometric work at 3 meters in 25.5°C water. They were stressed by work and cold. Exercise produced increases in heart rate, minute ventilation ($\dot{V}E$), oxygen consumption ($\dot{V}O_2$) and catecholamine excretion (CE). Cold lowered core temperature (T_r) despite exercise, and accentuated the increase in $\dot{V}O_2$ and CE. Immersion, cold-induced vasoconstriction and scuba breathing contributed to a brisk diuresis; since such factors all tend to centralize blood volume, thereby stimulating central vascular stretch receptors (Gauer-Henry reflex, GHR). Similar exercise in 25.5°C water, breathing helium tri-mix (gas density less than air), produced higher $\dot{V}E$ but lower $\dot{V}O_2$ when compared to air breathing. Thus, tri-mix scuba breathing may stimulate the GHR to a less degree than air scuba breathing, since its lower density should cause less stretch receptor distension during exercise hyperpnea, resulting in decreased diuresis. The fall in T_r during work in 25.5°C water was identical whether air or helium tri-mix was respired, as helium does not accentuate respiratory convective heat loss.

PALLIDO-ENTOPEDUNCULAR MODULATION OF REFLEX DEGLUTITION. C. H. Hockman and D. Bieger*, Dept. of Physiology and Biophysics, and Sch. Basic Med. Sci., University of Illinois, Urbana, Ill. 61801.

In anesthetized cats, reflex deglutition elicited by electrical stimulation of the superior laryngeal nerve (SLN) was markedly facilitated by electrical stimulation of points distributed along a trajectory coextensive with fiber tracts connecting the brain stem with the corpus striatum. The responsive sites were located in the pallidal and entopeduncular region, the lateral hypothalamus, and in and above the lateral portion of the substantia nigra. Facilitation could be obtained when the brain and SLN were stimulated simultaneously or successively, or with subliminal SLN stimulation. Chronic bilateral ablation of the cortical field representing mastication and swallowing had no effect on reflex modulation. In a number of animals, systemic administration of L-DOPA and L-5-HTP not only induced spontaneous swallowing but also markedly facilitated the reflex response. Work is in progress to define the role of the nigrostriatal dopamine pathway in this modulation. Our findings may provide useful leads for an experimental study of pathogenetic mechanisms underlying human bulbar motor disabilities. (Supported by a grant from the Illinois Department of Mental Health.)

A TWO COMPONENT BLOOD PRESSURE RESPONSE WITH DRINKING TO INTRACRANIAL ANGIOTENSIN II (AII) INJECTIONS. W.E. Hoffman* and M. Ian Phillips (SPON: D.C. Dawson). Department of Physiology & Biophysics, University of Iowa, Iowa City, Iowa 52242

Intracerebroventricular (IVT) injections of AII in unanesthetized rats will produce a short latency pressor response and drinking. The site of action of IVT AII for both the drinking and pressor responses was found to be the anterior ventral third ventricle in rats (Hoffman and Phillips, Fed. Proc. 1975). We now report that there is a double pressor response to IVT AII microinjections related to the act of drinking. This drinking associated pressor response usually appears as an additive component to the initial pressor response seen with IVT AII injections. We have separated out this drinking associated pressor response by withholding access of water. In 21 rats, the pressor response to 500ng AII IVT decreased from 30.33 mmHg with drinking to 19.71 mmHg with no water available ($p<.001$). For 50 ng AII IVT tests the pressor response was 26.16 mmHg with drinking and 17.25 mmHg without ($p<.001$, n=12). The drinking-associated pressor response is not due to arterial catheter placement, changes in head position, or hypoxia. Both the initial and the drinking associated pressor responses were shown to decrease hypophysectomy (24% and 43% respectively). The pituitary is therefore necessary for the maximum response for both pressor components and ADH release is probably involved. (Supported by NSF GB 27704, NINDS, NIMH RSDA II.)



^{45}Ca FLUXES INDUCED BY A23187 IN GUINEA PIG LEFT ATRIA. D. R. Holland*, W. McD. Armstrong and M. I. Steinberg*. Dept. Physiol., Indiana Univ. Sch. Med., Indianapolis, IN 46202 and Lilly Res. Labs., Indianapolis, IN 46206

The Ca^{2+} ionophore A23187 directly increases myocardial contractility by a mechanism dependent on extracellular calcium concentration. The mechanism of this positive inotropic effect was further investigated by studying the effect of A23187 on ^{45}Ca uptake and efflux in paired atrial strips incubated in Mg^{2+} free Chenoweth-Koelle buffer at 35° C. Uptake was investigated by incubating the tissue for 3 minutes with ^{45}Ca in the presence and absence of A23187 (10^{-5} M). In resting atria, the ionophore increased relative specific activity (RSA) from 0.262 ± 0.014 to 0.328 ± 0.021 ($P < 0.01$). In tissue stimulated at 2Hz A23187 increased the RSA from $0.365 \pm .015$ to 0.405 ± 0.022 ($P < 0.05$). Thus A23187 increases Ca^{2+} exchange by a mechanism not dependent on membrane excitation. In other studies, Ca^{2+} efflux in the presence or absence of A23187 (10^{-5} M) was investigated following a 3 hour equilibration in a buffer containing ^{45}Ca. The loss of ^{45}Ca from the tissue was more rapid in the presence than in the absence of A23187. After 3 hours, the percent of initial ^{45}Ca retained by the tissue was 2.78 ± 0.41 in control experiments and 2.17 ± 0.50 in the presence of A23187 ($P < 0.05$, paired t test). The increased efflux induced by A23187 cannot be fully explained by an enhanced permeability of the myocardial cell membrane to Ca^{2+}. These results suggest two actions of A23187 on guinea pig left atria: an increase in Ca^{2+} influx and an enhanced release of tissue Ca^{2+}. (Supported in part by NIH grants HL06308 and AM12715).

A THEORETIC AND EXPERIMENTAL ANALYSIS OF ISCHEMIA-INDUCED QRS ALTERATIONS IN THE PORCINE HEART. Roger Holland, and Harold Brooks.* (SPON: L. Dexter). The University of Chicago, Chicago, Il. 60637

In previous work it has been shown that the pig, unlike the dog, has an extensive ventricular intramural Purkinje network and hence a tangential (TAN) pathway of ventricular activation. A formal theoretical analysis of the Tan pathway through normal (N) and ischemic (I) myocardium was made and suggested that a close relationship existed between 1) R wave height (R), 2) time from base-to-peak of R wave (CT) and, 3) depth of the ischemic process (DIP). With ischemia, CTI/CTN is increased at the same values of RI/RN. Thus the actual curve RI/RN vs CTI/CTN will be shifted to the right or left with increasing or decreasing DIP. These theoretical findings were tested in 10 chloralose-anesthetized pigs in which small and large branches of the anterior descending artery (LAD) were temporarily occluded. Confirmation of change in DIP with small and large occlusions was obtained by intravenous injection of 4% Thioflavin S which localizes myocardial perfusion by post-mortem fluorescence. In addition, after control LAD occlusions, isoproterenol, propranolol or $CaCl_2$ was administered in pharmacologic doses intravenously. The EpiECG was recorded from the heart's surface using a newly designed atraumatic electrode. The following experiments confirmed the theoretic predictions. Large occlusions as well as $CaCl_2$ and isoproterenol were found to significantly shift the curve to the right indicating an increase in DIP. Propranolol on the other hand, when it was accompanied by a decrease in heart rate, shifted the curve to the left. It is concluded that surface QRS alterations in the porcine heart are specific in detailing relative changes in ischemic size. They can therefore be useful in assessing the efficacy or detriment of various pharmacologic interventions.

THE EFFECT OF DRY SWALLOWS, WET SWALLOWS, AND BALLOON DISTENTION ON ESOPHAGEAL PERISTALSIS. J. B. Hollis*, M. S. LeVine* and D. O. Castell. Naval Hospitals, Portsmouth, Virginia and Bethesda, Maryland

The effect of dry swallows (DS), wet swallows (WS), and balloon distention on esophageal function was studied in normal subjects using intraesophageal transducers positioned 5 and 10 cm above the lower esophageal sphincter (LES). A balloon was attached to the assembly 20 cm above the LES and momentarily inflated with air to stimulate secondary peristalsis (2°P). Subjects were randomly asked to swallow without water (DS) or given a water bolus (WS) ranging from 1 ml to 20 ml to stimulate primary peristalsis (1°P). Amplitude of esophageal contraction as measured 10 cm above LES following a 1 ml liquid bolus (61±7.5 mmHg, ±SE) was similar to that following a DS (62±12.7 mmHg) but was significantly less than that following a WS of a larger volume. There was no difference in strength of esophageal contraction following swallows ranging from 2 ml to 20 ml (2 ml, 106±20.3 mmHg; 5 ml, 123±14.2 mm Hg; 10 ml, 130±17.3 mmHg, 20 ml, 127±15.7 mmHg). Amplitude of 2°P from balloon distention (31±9.8 mmHg) was significantly less than amplitude of 1°P either from a DS or WS. In addition, the percent response of 2°P from balloon distention (35±5.2%) was significantly less than 1°P. However, the prevalence of 1°P was significantly greater with a WS (97±0 .75%) than a DS (71±4.5%). Furthermore, 2°P was associated with faster wave speed, lesser duration of the contraction wave, and shorter time of appearance of the peristaltic wave in the distal esophagus than 1°P either from a DS or WS. The results of our studies indicate that: 1) although the act of swallowing alone in man initiates peristalsis, afferent information from proprioceptors stimulated by a bolus contributes to the regulation of 1°P; 2) these receptors appear to respond in an all or non-fashion to a liquid bolus; and 3) 1°P and 2°P differ in their modes of esophageal propagation.

TRANSMURAL GRADIENTS OF GLYCOLYTIC INTERMEDIATES AFTER TRANSIENT CORONARY ARTERY LIGATION AND BLOOD REFLOW IN DOGS. James W. Holsinger, Jr. and Craig A. Ramey*, Veterans Administration Hosp., Newington, CT 06111

The subendocardium of the left ventricle may be the layer of the heart which is most susceptible to ischemic changes. After 20 minutes of ischemia, there is a shift from aerobic to anaerobic metabolism demonstrated by the accumulation of glucose-6-phosphate (G-6-P) and lactate with little change in pyruvate levels with the subendocardium more sensitive to ischemia. Since ischemic injury is reversible if coronary blood flow is restored within 20 minutes, glycolytic intermediates were examined to test the hypothesis that transient ischemia may affect transmural gradients. After a midline sternotomy the left circumflex artery (LCA) was either ligated (4 dogs) or left patent in controls (4 dogs). Following 20 minutes of ligation and 20 minutes of blood reflow transmural tissue samples were obtained from the ischemic zone and placed in liquid N_2. The frozen sample was divided into epicardial (EPI), midmyocardial (MID) and endocardial (ENDO) portions. Glycolytic intermediates were determined by standardized techniques; values are μmol/g dry wt. Values are expressed as EPI→MID→ENDO. Control values. G-6-P: 0.31±0.15→0.53±0.08→0.64±0.13; Pyruvate: 0.98±0.06→1.03±0.09→0.97±0.13; Lactate: 6.90±0.70→8.77±1.25→9.28±1.46; Lactate/Pyruvate Ratio: 7.15±0.96→8.40±0.57→10.00±1.70. Experimental values. G-6-P: 0.28±0.07→0.42±0.18→0.58±0.24; Pyruvate: 0.98±0.16→1.21±0.13→1.26±0.13; Lactate: 7.55±1.56→8.12±0.96→7.75±0.43; Lactate/Pyruvate Ratio: 7.73±0.79→6.80±0.70→6.26±0.40. No significant difference was noted between controls and experimentals in G-6-P and lactate transmurally. Pyruvate demonstrated a 31% increase in the subendocardium while lactate/pyruvate ratio was decreased 37% in the subendocardium. This data supports the restoration of aerobic metabolism and suggests the subendocardium is more vulnerable to ischemia.

INDOCYANINE GREEN CLEARANCE IN THE SPLENECTOMIZED EXERCISING DOG. D. Horstman, D. Wolfe*, D. Castignetti*, V. Forte*. US Army Research Institute of Environmental Medicine, Natick, MA 01760

It has been observed that while exercise results in a marked depression of hepatic blood flow (HBF) in man, the converse occurs in normal dog. We postulated that the splenectomized dog would exhibit a pattern of exercise HBF similar to that of man and thus provide a more adequate model for exercising man. To test this hypothesis we measured the clearance of Indocyanine Green (ICG) in a series of dogs during rest, moderate exercise (7.0 mph, 5% grade), and heavy exercise (7.0 mph, 10% grade) both pre-and post-splenectomy. Some additional cardiovascular and metabolic measures were also included for a more complete description of the responses to exercise. There were no differences in the time to clear one-half the initial concentration of ICG (t 1/2) between rest and exercise in either the non-splectomized or splenectomized conditions. There were also no differences in t 1/2 between the non-splenectomized and splenectomized conditions despite the fact that total blood volume was reduced about 20% (as a result of reductions of both plasma volume and red cell volume) with splenectomy. Splenectomized dogs did not differ from non-splenectomized in resting or exercise ventilatory minute volume, oxygen consumption, arterial-mixed venous oxygen difference, cardiac output, and arterial lactate concentration. With splenectomy there was a tendency for increased heart rate and decreased stroke volume during both rest and exercise. It was concluded that, with few exceptions, splenectomy does not alter the dog's physiological responses to exercise.

EFFECTS OF INTRAVENOUS ANESTHETIC AGENTS ON CARDIAC DYNAMICS. L.D. Horwitz, Dept. Medicine, The Univ. of Texas Health Science Center at San Antonio and the Veterans Administration Hospital, San Antonio, Tx. 78284

The cardiovascular response to intravenous boluses of ketamine hydrochloride (K) (4 mg/kg) and sodium thiopental (T) (1 mg/kg) was studied in 8 dogs with and without beta adrenergic blockade with propranolol (1 mg/kg i.v.). The boluses were administered while the dogs were conscious and resting in a sling. At the time hemodynamic measurements were obtained, between 30 seconds and 3 minutes after the injection, light anesthesia was present during which there was no reaction to painful stimuli. Left ventricular pressure was measured with a solid state transducer, cardiac output with an electromagnetic flow probe on the ascending aorta and aortic pressure with a catheter. At 30 seconds, without beta block, mean heart rate increased (77 b/min, $p < 0.01$, for K and 50 b/min, $p < 0.01$, for T). The maximum first derivative of the left ventricular pressure (dP/dt max) was not changed significantly by K but fell by 514 mm Hg/sec (19%) ($p < 0.01$) with T. Both drugs increased cardiac output and mean aortic pressure, with the changes in response to K exceeding those to T. With beta block, both drugs resulted in significant reductions in dP/dt max: increases in heart rate were again noted but the increment were substantially less than occurred in studies without propranolol. It is concluded that both K and T increase sympathetic tone and directly depress myocardial contractility. Because K is associated with greater sympathetic stimulation there is less apparent myocardial depression in the absence of beta block.

THE LABORATORY RAT AS A MODEL FOR HEAT AND WORK INDUCED FATALITIES. R. Hubbard, G. Angoff*, W. Bowers*, I. Leav* and M. Mager. U. S. Army Res. Instit. of Environ. Med., Natick, MA 01760

The primary goal of this research was the development of a rat model for the study of heat and exertion induced heatstroke. In order to separate the effects of heat from those related to work and other predisposing factors, rats were exposed to one of three conditions: running to exhaustion at low temperatures (5 or 15C), running to exhaustion at or near room temperature (26C) and sedentary heating at 41.5C. The data from untrained, control rats (450 - 500 g), when plotted as % mortality versus core temperature at exhaustion, generated a dose response curve with an L.D. 50 equivalent to a core temperature at exhaustion of 41.5 ± 0.1C. The results indicate a continuum of increasing risk with increasing levels of hyperthermia across a core temperature range of 40.4 to 43C. Rats run to exhaustion at or near room temperature and sedentary heated rats showed pathological and biochemical manifestations which were similar to those of heatstroke in man. Potassium depletion, through dietary restriction, produced performance decrements and additional abnormalities.

STATISTICAL FEATURES OF NEURONAL OUTPUT POPULATIONS IN THE ARM AREA OF PRIMATE MOTOR CORTEX. D. R. Humphrey, W. S. Corrie* and R. Rietz*, Lab. Neurophysiology, Emory Univ., Atlanta, GA., 30322.

To obtain data that will be useful in planning future functional studies of the primate motor cortex, microelectrode techniques were used to examine the statistical properties of pyramidal tract (PT), corticorubral and corticoreticular neuron populations within the precentral gyrus of the anesthetized rhesus monkey. The cells were identified antidromically, and the investigation was confined to a small cortical column, 1.5 - 2.0 mm in dia., whose major motor effects are exerted upon the flexor and extensor muscles of the contralateral wrist. Each cell system was studied with regard to intracortical location, neuronal packing density, distribution of axonal conduction velocities, and major axonal destination. Recordings were obtained from over 1600 neurons, and the unit samples were corrected numerically for sampling errors. The results show that, on a numerical basis, the major outflow from the cortical arm area comes not from the population of widely studied, large PT cells, but instead from: (i) a much larger population of small, slowly conducting PT cells, 75 % of which send their axons to the cervical cord; and (ii) a separate population of small, non-PT, corticorubral neurons, that exert excitatory synaptic actions upon cervically projecting rubrospinal tract cells. Together, these two populations appear to account for 88 % of the cortical neurons that one might expect to participate in any reasonably direct way in the control of wrist movements. These findings are of considerable significance for the design of future studies of the cortical control of movement, for many of our current concepts of motor cortex function are based principally upon the observed activities of the comparatively small population of large PT cells. (Supported by NIH Grant NS-10183).

EVIDENCE FOR A VERY SMALL PARTIAL PRESSURE GRADIENT FOR AMMONIA GAS ACROSS THE BLOOD BRAIN BARRIER. R. D. Hunt* and A. B. Otis, Dept. of Physiology, Univ. of Florida, Gainesville, Florida 32610.

Plasma, saline and cerebrospinal fluid (CSF) were equilibrated with gas mixtures in tonometers. Measurements were made of pH and total ammonia, [Am], in the liquid phases and of ammonia partial pressure, PNH_3, in the gas phases. From the results of these measurements on each fluid the ratio K_A'/α for the chemical equilibrium $NH_3 + H^+ = NH_4^+$ was derived using the relationship $[H^+] = K_A'/\alpha \cdot [Am]/PNH_3 + K_A'$; where: α is the solubility coefficient of ammonia gas in solution, $K_A' = [NH_3] \cdot [H^+]/[NH_4^+]$ at equilibrium, $[NH_3] = \alpha \cdot PNH_3$, and $[H^+]$ is 10^{-pH}. Experiments conducted at temperatures of 36.7°C yielded values for K_A'/α of 11.8 for plasma, 10.46 for saline and 17.6 x 10^{-9} L(STPD) mmHg/Equiv. for CSF. The plasma and saline values compare with the value of 10.43 at 37°C which may be calculated from the data of Jacquez et al. (J. Appl. Physiol. 14:255-258, 1959). The CSF value is significantly different for reasons that are not known at this time. If the pH and [Am] are known, the ratio K_A'/α can be used to estimate the PNH_3 from the equilibrium relationship $PNH_3 = K_A'/\alpha \cdot [NH_4^+]/[H^+]$; where $[NH_4^+]$ is approximated by [Am] at physiological pH. Using this relation and assuming that plasma and CSF PNH_3's are equal, one may calculate the partition -- CSF [Am]/plasma[Am] -- as a function of the difference in pH between the two fluids. At zero pH difference a partition of 67% is arrived at. A similar value can be calculated from results of direct analyses of [Am] reported in the literature. This is consistent with the assumption that PNH_3 in CSF is essentially identical to that in plasma. (This work was supported by NIH Training Grant HL05979 and NIH GM 20237-01.)

COMPARATIVE STUDY OF THE THIOUREA CARRIER IN ERYTHROCYTES. F.R.Hunter, Carl Wong*, Luis Carlos Gomezjurado D.* and Ramon Fayad*. Dept. of Biological Sciences, University of the Pacific, Stockton, CA 95211 and Depts. of Biology and Physics, The Pontificia Univ. Javeriana, Bogotá, Colombia.

Using a densimeter technique, studies were made of the rate of exit of thiourea from erythrocytes of several species of mammals. The values for half-saturation of the carrier in millimoles and for maximum transport rate in isotones per minute respectively are: Mouse - 46, 3.2; Pig - 110, 1.6; Human - 60, 1.2; Rabbit - 46, 0.8; Ox - 107, 0.6; Sheep - 56, 0.9; and Rat - 65, 6.1. There is no obvious relationship between these two parameters nor is there any obvious evolutionary correlation.

LIGHT-DEPENDENT PROTON TRANSPORT BY BACTERIAL RHODOPSIN AT AIR-WATER AND DECANE-WATER INTERFACES. S.B. Hwang*, J.I. Korenbrot*, J. Goerke & W. Stoeckenius*, (SPON: J. Botts) Depts. of Physiology & Biochemistry, & Cardiovasc. Res. Inst., U. of Calif. San Francisco 94143

Sonicated fragments of the "purple membrane" of Halobacterium halobium suspended in a solution of purified soya phosphatidylcholine in hexane have been spread at the air-water interface. Both surface potential and surface tension measurements indicate that the membrane fragments and lipids organize at the interface as a monolayer. Freeze-etch and shadow-cast replicas of the monolayer reveal that under appropriate conditions the fragments of purple membrane do not overlap at the interface and that over 85% orient with their intracellular surface towards the aqueous phase. The spectrophotometric characteristics of the fragments at the interface are identical to those of aqueous suspensions of the same fragments or of intact cells: the absorption spectrum in the visible range is typical of bacterial rhodopsin with a single absorption band with 570 nm λ_{max}. Further, upon flash illumination the 570 nm peak undergoes a cyclic decrease in absorbance with the transient appearance of a blue-shifted photoproduct. Rapid positive changes in the monolayer surface potential have been detected following illumination. The measured potential is dramatically increased when the monolayer is overlaid with a thin layer (<0.3mm thick) of decane containing the hydrophobic proton acceptor DNP (up to 70mV at 10^{-6}M). This indicates that the purple membrane fragments are acting as light-driven proton pumps, transferring H^+ from the aqueous into the organic phase. Measurements of aqueous phase pH changes upon illumination support this conclusion. The surface potential action spectrum matches the absorption spectrum of the bacterial rhodopsin in the purple membrane. Supported by UCSF Academic Senate and Medical School grants, NASA grant NGL 05-025-014 and HL-06285 (USPHS).

METABOLIC POTENTIAL OF HYPERTROPHIED NORMAL AND DIABETIC SKELETAL MUSCLE. C.D. Ianuzzo[1] and R.B. Armstrong*, Depts. Biology and Health Sciences, Boston University, Boston, MA 02215

Previous histochemical findings from hypertrophied normal and diabetic skeletal muscle suggest the metabolic potential of the enlarged muscle has been altered. The purpose of this study was to biochemically investigate the metabolic adaptations that possibly accompany compensatory growth of normal and diabetic skeletal muscle. Compensatory hypertrophy of the plantaris muscle was induced by surgical myectomy of the synergistic gastrocnemius muscle. Streptozotocin-diabetes resulted from a single intravenous injection (70mg/kg body weight). Animals were sacrificed 60-75 days post-surgery by exsanguination while under pentobarbital anesthesia. The plantaris muscles were excised, weighed, and then homogenized in phosphate buffer at pH 7.4. Phosphofructokinase(PFK) and succinate dehydrogenase(SDH) activities were spectrophotometrically determined by following the rate of reduction of nicotinamide adenine dinucleotide and cytochrome c, respectively. Muscle wet weights increased significantly($P<.001$) in the normal(82%) and diabetic(64%) animals. PFK and SDH activities of the hypertrophied normal and diabetic muscles were similar to those of the respective control muscles. Both the control and hypertrophied diabetic muscles contained lower than normal enzyme activities. The findings demonstrate that the biochemical determination of PFK and SDH activities of whole muscle homogenates do not reflect the metabolic alterations observed histochemically.

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TRANSFER OF COBALT IONS ACROSS ELECTROTONIC JUNCTIONS OF THE CHICK CILIARY GANGLION. M. Ichiki,* D. Johnson,* and G. Pilar. Biol. Sciences Group, Univ. of Connecticut, Storrs, Conn. 06268.

The ciliary cells in adult birds are electrically as well as chemically synaptically coupled. Of the total junctional area of each cell, .2% is occupied by gap junctions (Cantino & Mugnaini, J. Neurocytol., 1975, in press). The present study was undertaken to further characterize these low-resistance pathways across the junctional membranes, using cobalt (Co) ions as a marker. Both whole mounts and paraffin serially-sectioned ganglia reacted according to the method of Tyrer & Bell (Brain Res. 73: 151-155, 1974) were used. Isolated ciliary ganglia from 1-10 day old chicks were incubated in Tyrode at different temperatures and in 2,4-dinitrophenol (DNP) solution (500μM). When ciliary and choroid nerves were immersed in a droplet of 3% Co chloride, both ciliary and choroid cells were stained. When similar procedures were applied to the oculomotor nerve, only the ciliary population was stained. Temperatures below 6°C and soaking the ganglion in DNP blocked orthodromic Co transport across synapses in the ciliary cells and calyces were clearly seen. The transport of Co ions in the nerves is interrupted by Ca^{++}-free solution and 15 min. local application of 2% colchicine solution. The speed of the axonal transport is 12-20mm per day at 10°C. These findings suggest that (1) Co may be transferred across ciliary cells through hydrophilic channels and that this process is energy-dependent; and (2) that Co ions in the axons may be transported by a mechanism similar to axonal flow.

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CHANGES IN VENTILATION IN RESPONSE TO ALTERATIONS OF AIRWAY AND ALVEOLAR PCO_2. F.O. Igler*, E.J. Zuperku*, S.R. Peters*, R.V. Purtock†, R.L. Coon*, and J.P. Kampine*. (SPON: L.H. Hamilton). Med. Col. of Wisc. and Wood V.A. Center, Milwaukee, Wisconsin 53226.

Recently, changes in CO_2 concentration in the airways and alveoli have been shown to alter ventilation by utilizing cardiopulmonary bypass techniques in the intact dog (Bartoli A., B.A. Cross, A. Guz, S.K. Jain, M.I.M. Noble, and D.W. Trenchard. J. Physiol. (London)240:91-109, 1974). The purpose of this research was to further define this response. Open-chested dogs anesthetized with halothane (0.5-1%) were placed on total heart-lung bypass. Blood was drained from the left ventricle to assure that no ejection of blood into the aorta occurred. Ventilation of the lungs was accomplished by a square flow respirator which delivered a constant, predetermined V_T. Phrenic nerve activity obtained from the C_5 root was used to trigger the respirator. Inspired CO_2 was systematically manipulated in steps, between 0-70 mmHg. Inspired O_2 and systemic blood gasses and pH were held constant during each manipulation at a P_AO_2 of 147-175 mmHg, $PaCO_2$ of 35-47 mmHg, PaO_2 of 300-650 mmHg, and pH of 7.31-7.43. Breathing frequency increases up to seven fold were observed when inspired PCO_2 was increased from 0 mmHg to 35 mmHg. Increases of up to two fold were observed when inspired PCO_2 was increased from 35 to 70 mmHg. Bilateral vagotomy abolished these responses. Compliance of the lungs increased with each increase in inspired CO_2. This study confirms that changes in CO_2 in alveoli and airways change the frequency of breathing. These reflex changes may play an important role in regulation of respiration.

CENTRAL GENERATION OF A RHYTHMIC LOCOMOTOR BEHAVIOR IN APLYSIA. D. Impelman* and H. Wachtel (SPON: G.J. Somjen). Department Physiology and Pharmacology, Duke University, Durham, N.C. 27710

We have made en passant recordings from pedal nerves in Aplysia during the performance of a rhythmic locomotor output, the gallop escape response. Simultaneous cinematographic records of the cyclic movement components of the gallop step were used to make behavioral correlations. The peripheral contribution to the motor program was evaluated in a deafferented preparation. The essential central ganglia were delimited by severing central inputs to the pedal ganglia and noting the gallop deficits associated with the lesions. These studies showed that (1) the basic timing of the response is generated in the pleural-pedal ganglia and (2) that alternate bursts of activity on the anterior and posterior pedal nerves lead the anterior and posterior phases of the stepping cycle by 100-200 msec.

We have also recorded in situ with intracellular electrodes from endogenously bursting neurons in the pleural pedal ganglia. The timing of their bursting pattern (2-3 cpm) is strikingly similar to the timing of the gallop stepping cycles (1-5 cpm). The susceptibility of their burst pattern to peripheral modulation and their peripheral connectivity are indicative of a cell that drives rhythmic behavior. We conclude that the pleural-pedal cellular oscillators display functional properties consistent with those of the presumed pedal oscillators but definitive proof is as yet unavailable. (Supported by the NIMH)

LEFT VENTRICULAR MYOCARDIAL FIBER ANGLE DYNAMICS.
E. Ino-Oka*, L.D. Harris*, P.A. Chevalier, and E.L. Ritman, Mayo Foundation, Rochester, Minnesota 55901.

Changes in myocardial fiber orientation in the beating heart were estimated from stereo roentgenographic images of a grid pattern of lead beads sewn onto the left ventricular myocardium of dogs. Left ventricular angiography was used for computation of left ventricular chamber volume. Changes in fiber angles were calculated for each 1/30 second throughout the cardiac cycle assuming that fibers contract along their longitudinal axes and move circumferentially by contraction of "equatorially" oriented fibers. Changes in fiber angle throughout the cardiac cycle were calculated from the dynamic geometric distortion of triangles formed by sets of three closely oriented beads. Absolute fiber angles were computed by adding the roentgenologically determined change of fiber angle to the absolute fiber angle measured histologically at postmortem at each bead. Angles calculated in models were correct to within 5° of the true angle. Epicardial fiber angle relative to equatorial circumferential planes perpendicular to axis through apex and base decreased about 5 to 10° during diastole and increased during systole. Different rates and amounts of change in fiber angle occur in the apex to base regions. These differences were accentuated in the presence of increased peripheral arterial resistance. (Supported in part by NIH grants HL 4664 and RR-0007; AF-44620; NASA-NGR-24-003-001; and AHA CI-10.)

THE TRANSPORT OF PROTEIN THROUGH THE BASOLATERAL MEMBRANE OF THE PANCREATIC ACINAR CELL. L.D. Isenman* and S.S. Rothman, Dept. of Physiology, Univ. of California, San Francisco, CA. 94143

It has been shown recently that digestive enzyme enters the pancreatic acinar cell across its basolateral membrane (C. Liebow and S.S. Rothman Science, 1975). To examine the permeability of this surface to digestive enzymes, the cell to bath flux of amylase was measured from the whole rabbit pancreas in vitro. The initial flux, approx. 6 x 10^{-8} moles/h, was in the same range as the unstimulated cell to duct secretory flux. The amylase concentration in the bathing medium reached an apparent steady-state value of approx. 3.5 x 10^{-7}M with a $t_{\frac{1}{2}}$ of about 70 min. In contrast, the net cell to duct secretory flux remained relatively constant over the course of the experiment. Cholecystokinin-pancreozymin, a duodenal hormone that stimulates protein secretion, did not alter the steady-state concentration of amylase in the bathing medium, while a cholinergic drug, acetyl-β-methycholine chloride, increased steady-state amylase concentration by about 2.5x. When exogenous porcine α-amylase was added to the bathing medium (2.2 x 10^{-5}M), the net amylase cell to duct secretory flux was increased, while the output of endogenous (previously labeled) amylase was greatly inhibited (as much as 90%). This inhibition was preceded by an unexpected transient increase in the secretion of endogenous amylase (approx. 2x). There is a range of evidence which indicates that digestive enzyme secretion across the apical surface of the pancreatic acinar cell is derived, at least in part, directly from the cytoplasm and that the enzyme contents of the cytoplasm are in "equilibrium" with enzyme in zymogen granules. The present results indicate a similar "equilibrium" across the basolateral face of the acinar cell produced by the movement of amylase in both directions through the cell membrane. (Supported by grant AM16990 and GM00927 from NIH).

ESTIMATION OF cAMP TURNOVER IN METHYLPREDNISOLONE (MP) TREATED DOGS, EFFECTS OF EPINEPHRINE (E) AND NOREPINEPHRINE (NE). T.B. Issekutz* (SPON: B. Issekutz, Jr.). Department of Physiology and Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada, B3H 4H7

A simple method was developed to measure the rate of appearance (Ra) of plasma cAMP in the unanesthetized dog with 8-^{3}H-cAMP as tracer. The determination of the specific activity was based on the saturation of a specific binding protein, thus bypassing the need to know the plasma level of cAMP. In the controls infusion of "E" increased plasma glucose by 33% and both the plasma level and Ra of cAMP by 2 1/2 fold. MP treatment decreased the concentration as well as Ra of cAMP by 50%, and it greatly potentiated not only the hyperglycemic effect (4 fold) of "E", but also the rise of plasma cAMP (8 1/2 fold) and that of Ra (6.8 fold). NE increased Ra only by 50%, this effect was not potentiated by MP. The immunoreactive insulin (IRI) is increased by MP (by 40%), "NE" causes a further rise while "E" does not. There was a linear correlation between the plasma concentration and the turnover rate of cAMP. Conclusions: a) the increase of hepatic glycogenolysis is accompanied by a rise of the cAMP output, while that of lipolysis is not. b) Glucocorticoid treatment decreases cAMP turnover, but greatly increases its sensitivity to "E". These effects can best be explained by a glucocorticoid-insulin interaction. c) The plasma level of cAMP is controlled by Ra, whereas the rate of disappearance is the result of the mass-action effect of the concentration.

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HABITUATION AT THE GILL TERMINALS OF CENTRAL NEURONS L7 AND LDG, IN THE GILL WITHDRAWAL REFLEX OF APLYSIA. Jon W. Jacklet and Jasper Rine*. Dept. Biology, SUNYA, Albany, N.Y. 12222.

Tactile stimulation of the siphon sufficient to evoke the gill withdrawal reflex produces spiking in central neurons L7 and LDG, at rates comparable to those observed by others (Kupfermann et al. 1970-74). Repeated tactile stimulation led to a decrease in the rate of spiking in these neurons but this decrease in rate was much slower than the rapid decline in gill withdrawal. This suggested that the decline in spike rate in these neurons was accounting for a small portion of the habituation of the reflex and that other mechanisms must be contributing to habituation in this reflex. We tested this idea by direct selective intracellular stimulation of these neurons to produce gill withdrawal. A 2 sec pulse of current, sufficient to produce constant spiking at 12-15/sec in either of these neurons was administered every 30 sec in a run. The preparation was allowed to rest 30 min prior to a run and 30 min between runs. Stimulation of either of these neurons in this habituation paradigm showed that the gill withdrawal habituated to 30% of the initial amplitude in 10 trials in response to a constant number of spikes (±5%) evoked by current at each trial. The prepara - tion recovered with rest and could be dishabituated by tactile stimulation of the siphon or mantle. The dishabituating stimulus produced a recovery of the gill amplitude to 80% of its initial value without producing a significant change in the spike rate evoked by the next current injection trial. These experiments show that the terminals of the central neurons L7 and LDG, in the gill are a site of habituation and dishabituation of equal importance and in addition to presynaptic changes at these neurons. This peripheral site of habituation could be at the neuromuscular junction or at a peripheral neural circuit in the gill. (Supported by NIH grant 0844 3 to J.W.J.)

CHARACTERISTICS OF THE ELECTRORETINOGRAM OF THE FLYING SQUIRREL. Gerald H. Jacobs and Martin S. Silverman,* Dept. Psychology, University of California, Santa Barbara, California 93106

The flying squirrel (Glaucomys volans) is a prototypical nocturnal mammal. We have examined several aspects of the ERGs recorded intravitreally from this animal. The waveform of this ERG is similar to that recorded from other nocturnal species. It includes a very prominent PIII component that is particularly pronounced in the responses to high intensity stimuli. The total dynamic range of the ERG of the flying squirrel from threshold to saturation spans about 5.5 log units of stimulus intensity. The spectral sensitivity of the dark-adapted eye as assessed by single-flash ERG techniques reveals the presence of a typical mammalian rhodopsin. No shift in spectral sensitivity could be seen in any of the ERG components elicited by single flashes in the light-adapted eye. However, the ERG response to square-wave flicker does clearly reveal the occurrence of a Purkinje shift in this eye--spectral sensitivity measured for high-frequency flicker is higher through the long wavelengths than that predicted by rhodopsin alone. In conjunction with anatomical observations it appears that, like other nocturnal species, the flying squirrel has some viable cone-based vision. (Supported by NEI Grant EY-00105.)

TEMPERATURE INFLUENCES ON ELECTRICAL AND MECHANICAL EVENTS OF HIBERNATING MYOCARDIUM. H.K. Jacobs. Dept. of Anesthesiology, Cook County Hospital, Chicago, Ill. 60612 and Dept. of Physiology, Loyola U. Med. Sch., Maywood, Ill. 60153.

This study, undertaken to test the hypothesis that a membrane modification may occur in hibernating species that allows continued function at low temperatures, used left ventricular papillary muscle isolated from hibernating thirteen-lined ground squirrels. These muscles were isometrically mounted in a controlled temperature bath and superfused with oxygenated Krebs solution at pH 7.4 at 38,30, 20,12 and 5C.

The resting membrane potential declined slowly to about 20C below which temperature the decline became more rapid though still not as severe as the drop seen for non-hibernators. Action potential (AP) magnitudes were even less altered by low temperatures holding at 85.7±23mV at 12C and at about 65mV (roughly the resting membrane potential) at 5C. Rates of rise of the AP declined from 225.6V/sec at 38C to about 1V/sec at 5C. Stimulating currents required increased 4X at 5C when compared to those required at 30C. Mechanical parameters were similarly adequate at low temperature. Peak tension production at 5C approximated that seen at 38C. The temperature optimum for tension development was between 20 and 12C. Times to peak tension increased from about 50msec at 38C to over 1sec at 5C. Rates of tension production declined from about 5g/sec at 38C and 30C to about 200mg/sec at 5C. These data are consistant with the hypothesis that an altered membrane makeup exists in the hibernating state. (Supported by NHLI grant HE08682)

CONTROL OF THE RENAL COUNTER CURRENT CONCENTRATING MECHANISM. INPUT-OUTPUT STUDIES ON A MODEL. J.A. Jacquez and D.M. Foster*. Dept. Physiology, The Univ. of Michigan, Ann Arbor, Michigan 48104.

Simulation studies on a central core model of the renal medulla show that increase in inflow to the descending limb of Henle (DHL) increases the concentration gradients attained up to an optimal value for inflow; further increase in inflow then decreases the gradients. Increase in inflow to collecting ducts markedly increases urine flow and decreases urine solute concentration. For a model of the renal medulla which includes the vasa recta, increasing inflow to vasa recta tends to wash out the gradients in the interstitium. Consideration of these results have led us to propose two new hypotheses about the control of urine concentration. Hypothesis 1: One of the immediate mechanisms of control of medullary concentration gradients involves control of medullary blood flow and of inflow to DHL, and these two are linked aspects of one mechanism, the control of the resistance of the efferent arterioles of the juxtamedullary glomeruli. We call this the juxtamedullary pressor control mechanism. (The other mechanism is the control of the water permeability of distal tubules and collecting ducts by ADH.) Hypothesis 2: There may be states in which the efferent arterioles of the juxtamedullary glomeruli become unusually sensitive to the pressor effects of ADH. In such states, ADH would serve as the common signal for integrating the action of the two mechanisms.

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PULMONARY ARTERIAL BLOOD VELOCITY SIGNALS BY PULSED, RANGE-GATED DIRECTIONAL DOPPLER METHOD IN NORMAL SUBJECTS. G.J. Jahn*, S.P. Creekmore*, M.M. Graham* and M.B. McIlroy, Cardiovascular Research Institute, Univ of California, San Francisco 94143

A new, pulsed, range-gated, directional Doppler blood velocity meter has been constructed and used to record transcutaneous signals originating from blood flow in the main pulmonary artery of four normal subjects. A standard 2.25 mHz echocardiographic transducer was held in a plastic probe holder secured by straps around the chest. The most satisfactory signals were obtained from the 3rd or 4th left intercostal space with the probe pointing about 10° to the left of the sagittal plane and about 25° superior to the horizontal plane. The range gate was set to 3-4 cm depth and the instrument recorded flow away from the probe. Audio Doppler shifted signals could be heard to increase in frequency with inspiration. Blood velocity increased in an almost linear manner during the early phase of systole reaching a peak of >50 cm/sec. The period of constant acceleration lasted an average of 140 m sec, which is about three times the length of a comparable measurement in the aorta.

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EFFECTS OF CEREBROVENTRICULAR PERFUSION WITH ENDOTOXIN IN THE ANESTHETIZED ADULT DOG. H. F. Janssen*, J. R. Hillman*, M. J. Hughes and L. S. Holloway. Departments of Physiology and Anatomy, Texas Tech University School of Medicine, Lubbock, Texas 79409.

Anesthetized dogs were bilaterally perfused with artificial cerebrospinal fluid (CSF) containing 0.1 mg of E. Coli endotoxin per ml at 250 µl/min through the cerebroventricular system from the lateral ventricles to the cisterna magna. Over a 6-hour period, arterial blood pressure slowly decreased to a point 20% below control volume. This is contrasted to the effect seen with IV endotoxin where there is an initial rapid decrease in blood pressure, a recovery phase and a secondary slow decline. There was no initial rapid decrease in arterial blood pressure when endotoxin was given centrally but rather a continued decrease having the same magnitude and time course as the secondary decrease seen in IV endotoxin shock. Control perfusion for the same time period showed no change in blood pressure. Mean CSF production rate was measured as 75 ± 13 µl/min and did not significantly change during the 6 hours of endotoxin perfusion nor did the clearance of PAH and Inulin. However, ultrastructural examination indicated large numbers of polymorphonuclear leukocytes (PMNs) migrating from the vascular system through the epithelial layer of the CP and into the CSF space. The basal lamina of the CP epithelium was intact except in areas where PMNs were observed moving through the epithelium. Areas of smooth oval cells interspersed between the apices of cells with microvillous borders when observed with the scanning electron microscope. These studies indicate a massive migration of PMNs from the capillaries into the CSF while the surface cells are still capable of maintaining normal physiological function. Identification of the mechanism by which these changes occur await further study. (Supported by NIH Grant #HL16244-02).

DECREASE IN CARDIAC OUTPUT RELATIVE TO OXYGEN CONSUMPTION IN PANTING AND NON-PANTING DOGS DURING EXERCISE AT 1 MPH. D.B. Jennings, Dept. Physiology, Queen's University, Kingston, Ontario, Canada.

We have previously described the relationship between circulatory function and ventilation ($\dot{V}_E$) in conscious panting and non-panting resting dogs (Amer. J. Physiol. 224: 1059, 1973). Resting dogs in a steady-state and cool environment (20°C) have $\dot{V}_E$ ranging from 2.5 to 35 l/min. In resting dogs, cardiac output (CO), heart rate (HR) and mean arterial pressure (MAP) increase with increased $\dot{V}_E$ and total peripheral resistance (TPR) decreases. During exercise at 1 mph (jogging gait) $\dot{V}_E$ in dogs ranged from 7.5 to 40 l/min, widely overlapping the spectrum of resting $\dot{V}_E$. At this exercise level CO, MAP and TPR were not different from the measurements made at the same level of $\dot{V}_E$ in dogs at rest. However, CO was delivered at a higher HR during exercise. The oxygen consumption ($\dot{V}_{O_2}$) was increased relative to $\dot{V}_E$ during exercise, associated with an increase in alveolar ventilation relative to $\dot{V}_E$. Therefore, surprisingly this meant that CO was lower relative to $\dot{V}_{O_2}$. Although oxygen delivery was maintained by increased extraction from the blood, the mixed venous oxygen tension was within the lower limits of rest. This new finding of a relative decrease in CO in relation to oxygen demand during mild exercise in dogs raises interesting questions of probable redistribution of blood flow to skeletal muscle at this level of activity and questions concerning the mechanisms underlying these readjustments.
(Supported by the Ontario Heart Foundation.)

CARDIAC OUTPUT DURING TRANSCENDENTAL MEDITATION. Ron Jevning, A. F. Wilson, and Richard Smith. Department of Medicine, University of California, Irvine, Irvine, CA 92664. (intr. by: A. A. Buerger)

Transcendental meditation (TM), a widely practiced mental technique which is reported to be relaxing, has been well investigated. For example, the associated EEG, characterized by increased central and frontal alpha activity, seems to be different from that of sleep (Amer. J. Physiol. 221:795, 1971). The cardiac output (c.o.) of clinically normal young adult subjects, divided into a meditation (n=6 regular practitioners of TM with 3 to 5 years of experience) and a control (n=5) group, was measured using the Stewart-Hamilton dye dilution technique. Following a 2 and 1/2 hour wait after the placement of a venous and an a terial catheter in the arm, the c.o. was measured twice in each of three consecutive 40-minute periods, consisting of a baseline, an experimental and a post-experimental period respectively. During the experimental period, the control group was instructed to relax with the eyes closed whereas the meditation group was instructed to close the eyes and meditate. The data in liters/min (means $\pm$ S.E. for the three respective periods) with significant differences (t-test at $p<0.05$) denoted by arrows were:

	Baseline	Experimental	Post-Experimental
Control	5.13 $\pm$ .36	5.17 $\pm$ .15	5.70 $\pm$ .47
Meditation	5.65 $\pm$ .39	6.50 $\pm$ .40	5.64 $\pm$ .42

The significant rise in c.o. (15%) observed during the meditation period is additional evidence that the physiology of TM is different from that of sleep in which c.o. declines.

TRANSPORT STUDIES UTILIZING ANTIPYRINE AND UREA TO EVALUATE THE SIEVING EFFECT OF THE CHOROID PLEXUS. Conrad E. Johanson* and Dixon Woodbury* (SPON: Donal Reed). Dept. Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, Utah 84132.

Urea and some other non-electrolytes are not transported by carrier-like mechanisms in the cerebrospinal fluid (CSF) system; the fractional values for the distribution ratios (CSF/plasma) are probably best explained by a sieve-like mechanism in the choroidal membrane. To understand better the sieving effect, we injected rats with solutions containing ^{14}C-antipyrine or ^{14}C-urea and analyzed the distribution of these tracers between plexus, CSF and brain. Antipyrine equilibrates very rapidly between plasma and the extravascular compartments of the plexus. Three minutes after administration antipyrine distributed in the total water of the plexus (79%). However, antipyrine in plasma H_2O takes longer to equilibrate with cerebral cortex (3-6 min) and with CSF (12 min). In marked contrast, the steady-state achievement times for ^{14}C-urea are considerably longer (several hours). For example, 1,2, 5 and 11 hrs after IP administration, respectively, the following ratios (tissue/plasma H_2O) for urea were found: choroid plexus (0.28, 0.43, 0.56 and 0.67); CSF (0.32, 0.48, 0.62 and 0.69); cerebral cortex (0.29, 0.40,0.60 and 0.69). These results and our additional studies of the kinetics of distribution of tritiated H_2O, as well as ventriculo-cisternal perfusion experiments with urea and antipyrine, suggest that there is a diffusion barrier to these solutes located at the apical part of the choroid cell.

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PREGANGLIONIC EFFECTS OF POSTGANGLIONIC NERVE SECTION. E.W. Johnson* and H.R. Brenner*(SPON: M.C. Neville), Univ. of Colorado Medical School, Denver, CO 80220.

Electrophysiological studies were performed on ciliary ganglion preparations isolated from 3-6 day old chicks. When perfused with oxygenated saline solution, preparations were viable for periods up to 6-12 hours. The ciliary nerves of some of the chicks had been sectioned on the day of hatching at a point approximately 6 mm distal to the ganglion. This post-ganglionic axotomy was done under ether anesthesia with aseptic surgical techinques. Using conventional electrophysiological techniques, it was observed that both the electrical and chemical components of synaptic transmission failed 5-6 days after axotomy. Studies on 3-4 day chicks indicated that there was no significant difference between control and axotomized groups in the ganglion cell resting membrane potential, input resistance, time constant or action potential threshold. The presynaptic action potential amplitude, recorded intracellularly from the calciform terminal, was also unchanged. However, there was a significant decrease in the amplitude of both the ganglion cell coupling potential and synaptic potential. In addition, at a stimulation frequency of 1/sec, depression of the synaptic potential amplitude was significantly greater in the axotomized cells than in the controls. These results suggest that post-ganglionic nerve section may alter the transmission release characteristics of the preganglionic nerve terminal.

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EFFECT OF 1-SARCOSINE-8-ALANINE ANGIOTENSIN II ON ARTERIAL PRESSURE IN CELLOPHANE-HYPERTENSIVE DOGS. J. Alan Johnson, James O. Davis, David Stubbs*, and W. Ford Keitzer*. V. A. Hospital and Depts. of Physiology and Surgery, University of Missouri, Columbia, Mo. 65201

Hypertension was produced in 4 dogs by wrapping the left kidney in cellophane and 2 weeks later removing the right kidney. Mean arterial pressure averaged 170 ±11 (SEM) mm Hg for the hypertensive dogs while the mean arterial pressure in 5 normal dogs averaged 100 ±10 mm Hg. In the 2 groups of dogs there were no differences in plasma renin activity (PRA), serum urea nitrogen, or plasma concentrations of Na and K. Each dog received an infusion of the angiotensin II (A-II) analog 1-sarcosine-8-alanine angiotensin II, a competitive antagonist of A-II, at a rate of 6 µg/min. per kg. of body weight for 45 minutes; during these experiments the dogs were conscious and mean arterial pressure was recorded continuously through a chronic arterial catheter. Blood samples for PRA were obtained prior to analog infusion, after 15, 30, and 45 min. of analog infusion, and 60 min. after stopping the infusion. The effect of the analog infusion on arterial pressure in these 2 groups of dogs is shown in the following table:

		min. of analog infusion			
	control	15	30	45	recovery
hypertensive dogs	170 ±11	184 ±14	175 ±14	171 ±15	169 ±10
normotensive dogs	100 ±10	99 ±10	100 ±10	98 ±10	100 ±10

The PRA values in each group were not altered during infusion of the A-II analog. These studies failed to demonstrate a role for A-II in the maintenance of the elevated arterial pressure in dogs with cellophane perinephritis hypertension.

MECHANISM OF PENTAGASTRIN STIMULATION OF GASTRIN MUCOSAL GROWTH. L.R. Johnson and M.R. Enochs, Dept. Physiology, University of Texas Medical School, Houston, TX 77025.

The mechanism of gastrin induced mucosal growth in the stomach was investigated by studying the temporal sequence of stimulation of macromolecular species. Previous results showed maximal protein synthesis at 6 hours, and DNA synthesis at 16 hours following injection with pentagastrin. To determine if the increase in protein synthesis depended on RNA synthesis, rats were injected with saline or pentagastrin. Half the pentagastrin injected rats received Actinomycin D while the remaining rats received vehicle. Gastric mucosa was incubated *in vitro* with C^{14} amino acids. Pentagastrin alone stimulated incorporation by 37%. Act. D decreased incorporation to 64% of control. These results indicated that stimulation of protein synthesis was dependent on prior RNA synthesis. To determine the nature of the RNA synthesized, rats were injected with pentagastrin at various times 1 to 18 hours prior to sacrifice. Two hours before sacrifice all rats received 200 µCi of ^{3}H-orotic acid IP. Gastric mucosal RNA was extracted with phenol and applied to oligo(dT)-cellulose to separate mRNA from rRNA. The incorporation of label was compared in messenger and ribosomal fractions at each time point. A significant increase in mRNA occurred 1 to 2 hours after pentagastrin. Total RNA was significantly elevated at 4 and 12 hours, and rRNA gradually increased, reaching significant elevation at 12 hours. Stimulation of all fractions had disappeared by 18 hours. These results suggest that the primary effect of pentagastrin is stimulation of mRNA synthesis. Stimulation of protein synthesis at the transcriptional level is further sustained by later increases in ribosomal and transfer RNA. (Supported by NIH Grant AM-16505.)

AUTOREGULATION IN ARTERIOLES OF SARTORIUS MUSCLE. P. C. Johnson and M. Intaglietta, Dept. of Physiol., University of Arizona and AMES-Bioengineering, University of Calif., San Diego.

We have studied the mechanism of blood flow autoregulation in isolated cat sartorius muscle by simultaneous measurement of vessel diameter and red cell velocity in single arterioles. Local reduction of arterial pressure in a stepwise manner from 100 mm Hg to 40 mm Hg produced a graded increase in arteriolar diameter, with the greatest change occurring when pressure was reduced from 60 mm Hg to 40 mm Hg. At 40 mm Hg, arteriolar diameter was about 35 percent greater than control. Similar responses were seen in arterioles having initial internal diameters of 10 to 100 microns. Volume flow was calculated from internal diameter and red cell velocity. Volume flow increased with reduced arterial pressure in about 75 percent of the vessels. Red cell velocity in some capillary networks also showed an increase at reduced arterial pressure. These findings suggest that the mechanism of autoregulation in sartorius muscle may not be flow-dependent.

(Supported by NIH Grants HL 12493, HL 17421 and HL AM 15390).

TRANSCAPILLARY FLUID MOVEMENT IN THE RAT RENAL MEDULLA. P.A. Johnston*, V.M. Sanjana*, C.R. Robertson*, and R.L. Jamison. Depts. of Medicine and Chemical Engineering, Stanford University, Stanford, Calif. 94305.

We recently found that net fluid uptake occurs in the vasa recta capillary system in the inner medulla. To define the site of fluid uptake, protein concentrations were determined in descending vasa recta (DVR) plasma at the base and tip of the exposed papilla in Munich-Wistar rats. Results (mean ± standard error) were:

	Protein concentrations (g/dl)[1]	VR/P[2]	Oncotic Pressure (mm Hg)
DVR (base)	5.6 ± 0.4	1.43 ± 0.09	17.7 ± 1.9
DVR (tip)	6.4 ± 0.4[3]	1.66 ± 0.09[3]	21.8 ± 1.9
Femoral artery	3.9 ± 0.1		

[1]N (rats) = 17; [2]VR/P, vasa recta protein to systemic plasma protein concentration ratio; [3]p <0.01.

These results indicate that fluid is removed from DVR. In 3 rats, in which plasma protein concentration was also determined in ascending vasa recta (AVR) at the base, the results indicated fluid addition to AVR. Transcapillary osmotic pressure differences due to small (non-protein) solutes secondary to an increase in interstitial osmolality from the base to tip of papilla may provide a force for fluid removal from DVR. DVR plasma osmolality at tip exceeded DVR osmolality at base by 72 ± 30 mOsm/kg H_2O ($p < 0.05$). If this increase in DVR plasma osmolality lags behind the interstitial rise in osmolality, a driving force for water loss will exist. We conclude: 1) Fluid uptake by the medullary circulation occurs in AVR. 2) Transcapillary fluid movement in the inner medulla is influenced by differences in osmotic as well as in oncotic and hydraulic pressures. (Supported by Bay Area Heart Association and grant NIH 9 ROI AM-18077.)

ONE POSSIBLE MECHANISM CONTRIBUTING TO THE PROTHROMBINOGENIC EFFECT OF ESTROGEN. D.W. Jolly* and T.E. Nelson, Jr., Dept. Pharmacology, School of Dental Medicine, Southern Il. University, Edwardsville, Il. 62025.

The prothrombinogenic effects of estrogen have received more attention recently as a result of widespread use of oral contraceptives and the apparent attendant increase in thromboembolic tendency. Of several plausible hypothetical explanations investigated in our laboratory, an estrogen-facilitated absorption of vitamin K from the intestine does indeed appear to have some experimental support. Male or female, 300-400 gram albino rats, castrated six days earlier, were given 3 cc whipping cream by stomach tube and anesthetized 60 minutes later with Nembutal. The thoracic lymph ducts were catheterized at the level of the cisterna chyli and lymph was collected throughout the experiment. Dehydration was reduced by repeated (1 ml hourly) intragastric injections of water. As soon as control lymph flow was established, 10 mg of vitamin K_1 (Aquamephyton) were injected intragastrically. Estrogen-treated animals received 100 µg of estradiol (Gothrogen) i.p., immediately following castration and again five days later, 24 hrs before canulation. Lymph samples were lyophilized, extracted with ether, evaporated to dryness and reextracted in ethyl alcohol. Vitamin K was assayed colorimetrically. No vitamin K was detectable in the thoracic duct lymph of control castrated male or female rats within 180 minutes, in contrast to the estrogen-treated animals in which vitamin K appeared in 90-120 minutes, with a total accumulative amount reaching 3-4 µg in 180 minutes and 5-10 µg in 240 minutes. The greatest contrast was observed between control and estrogen-treated, castrated male animals.

This work was supported by N.I.C.H.D. contract 72-2791, N.I.H., and SIU Research and Projects Institutional Grant 00-43-7-91702.

EFFECT OF ACUTE ADMINISTRATION OF CORTISOL ON THE ADH RESPONSE TO HEMORRHAGE IN ADRENALECTOMIZED DOGS. H. Jones, Jr.*, L. Share and R.E. Shade. UTCHS, Memphis, TN 38163.

A study was conducted to compare the ADH response to hemorrhage under conditions of low and elevated plasma glucocorticoid levels. A hemorrhage of 12 ml/kg at steps of 2.0 ml/kg was made in 8 anesthetized, adrenalectomized dogs. The adrenalectomized dogs were maintained by a daily intramuscular injection of 0.5 mg DOCA and 15 mg cortisone acetate. The experiments were performed 48 hours after the last cortisone acetate injection and 24 hours after the last DOCA injection. All the dogs were included in the four protocols which were as follows: time control, cortisol control, hemorrhage-vehicle and hemorrhage-cortisol. At zero time minus 30 minutes, the cortisol infused group received an intravenous injection of 0.5 mg cortisol/kg that was followed by an infusion of 19.0 µg cortisol/kg.min in 0.9% NaCl at 0.388 ml/min. In the non-cortisol treated groups, an equal volume of isotonic saline was injected and infused. Neither mean arterial blood pressure (MABP) nor the plasma ADH concentration (P_{ADH}) changed with time in the control groups. With reduction in blood volume, MABP decreased in both hemorrhage groups, but this effect was statistically significant only in the hemorrhage-vehicle group. There was a twofold increase in P_{ADH} in the hemorrhage-cortisol group which was not statistically significant (one way analysis of variance); the hemorrhage-vehicle group showed a sevenfold increase in P_{ADH} that was significant. Linear regression analysis of the increase in P_{ADH} with volume of blood removed indicated that the rate of increase of P_{ADH} was greater in the hemorrhage-vehicle group. Therefore, an acute administration of cortisol can abate the ADH response to hemorrhage in adrenalectomized dogs.

THE EFFECT OF HIGH SODIUM (Na) INTAKE ON MEAN BLOOD PRESSURE (MBP) AND ON PLASMA RENIN ACTIVITY (PRA) IN RABBITS WITH TWO-KIDNEY GOLDBLATT HYPERTENSION (2KGH). J. Jones*, J.C. Romero, and C.G. Strong, Div. of Neph. & Dept. of Physiol., Mayo Medical School, Rochester, MN. 55901.

This study was undertaken to determine if renin-dependent 2KGH could be rendered Na-dependent by high Na intake. Our hypothesis was that a decrease in PRA induced in 2KGH by high Na intake (82 $\pm$ 6 mEq/day, normal = 20 mEq Na/day) should not be followed by a reduction in MBP. Varying degrees of hypertension were induced in 11 rabbits by constricting the left renal artery. Six normotensive rabbits (3 unoperated and 3 in which the constriction of the renal artery failed to induce hypertension) were used as controls. Changes in MBP were measured with a Grant-Rothschild capsule and PRA by radioimmunoassay. Two to four weeks after surgery when MBP stabilized, all rabbits were put on high Na intake for 7 days. On the 7th day, PRA in all rabbits decreased from pre-high salt level of 15.4 $\pm$ 4 to 7.5 $\pm$ 2 ng/ml/hr ($p = <0.001$). This decrease was accompanied by a decrease in MBP (118 $\pm$ 3 to 96 $\pm$ 6 mm Hg, $p = <0.001$) in those animals (n=6) whose MBP was 108 mm Hg or greater before high salt intake. The decrease in PRA was accompanied by no change in MBP (104 $\pm$ 2 to 99 $\pm$ 6 mm Hg) in rabbits with initial MBP between 95 and 108 mm Hg (n=5) or in normotensive rabbits with MBP less than 95 mm Hg (85 $\pm$ 2 to 82 $\pm$ 4 mm Hg). Inspite of the changes in PRA and MBP cited above, there was no significant increase in body weight in any of the 17 rabbits. The data imply that in rabbits with MBP 108 mm Hg or more, decrease in PRA secondary to high Na intake was accompanied by a decrease in MBP. The high Na intake caused no change in MBP of rabbits whose MBP was less than 108 mm Hg, despite their similarly observed fall in PRA.

SYMPATHETIC CONTROL OF LOCAL MYOCARDIAL AUTOMATICITY AND CONTRACTILE FORCE. S. B. Jones*, W. C. Randall and D. E. Euler*. (SPON: R. D. Wurster) Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Sympathetic control of myocardial automaticity and contractile force during atrioventricular dissociation was studied in anesthetized dogs. Stimulation of the cervical vagi or formalin injection into the A-V node were used to establish idioventricular pacemakers. Changes in atrial and ventricular contractile force were measured with Walton-Brodie strain gauge arches sutured to each chamber. Electrical activity was monitored by means of a lead II ECG and bipolar plunge electrodes placed in the right atrium and ventricle. Under vagal block, idioventricular rates of greater than 185/min resulted from stellate stimulation in 7 out of 11 animals whereas in the other 4 animals the ventricular rate could not be driven above 100. The rapid idioventricular rates (greater than 185/min) could be overdriven or reestablished by modulating the vagal inhibition of the sinus rate. Beat to beat shifts of the idioventricular pacemaker site (less than 100/min) were frequently observed during simultaneous vagal-stellate stimulation. Stellate stimulation during vagal block also resulted in a marked and independent increase in contractile force of both atria and ventricles. Increases in contractile force with stellate stimulation were also observed following formalin block. These results suggest that: 1) idioventricular pacemakers are capable of faster rates than previously reported with vagal-stellate interactions (Vassalle et al., Circ. Res. 28: 249-258, 1968), and 2) sympathetic nerves can augment contractile force in discrete areas of the heart during idioventricular rhythms. (Supported by NHLI/NIH Grant HL 08682.)

HIGH RESOLUTION MICROPERFUSION TECHNIQUES FOR TRANSMEMBRANE IONIC FLUX MEASUREMENTS, D.F. Juncker*, E.A. Greene*, and V. Lorber, Dept. of Physiology, Univ. of MN., Minneapolis, MN 55455

In an attempt to directly measure cardiac transmembrane ionic fluxes during the contraction cycle, previously inconclusive tracer efflux and influx techniques were re-designed. The newly developed methods have been used to obtain an efflux profile for ^{42}K (Circ. Res. 30:350, 1972) and more recently a characteristic ^{42}K influx profile. It is the purpose of this paper to describe the rapid microperfusion techniques developed in terms of theory, resolution, and definitive results. Both methods have a resolution of approximately 30 mSec. and are based on specific attention to simple test chamber geometry and minimal fluid boundary layer thickness within the test chamber. Both the homogeneous tissue isolated for examination (amphibian atrial fibers) and the test environment are confined to cylindrical geometry. The region of perfusate flow thus formed is annular, and its description and manipulation are well understood. Boundary layer stability is maintained by damping or blocking the cardiac contraction with high flow velocity, or perfusion with 5 mM $NiCl_2$-Ringer's, or "zero"-Ca^{++} Ringer's. In addition, Ni^{++} and "zero"-Ca^{++} perfusates prolong the plateau of the action potential to different degrees, thus providing two additional test states for comparison of the action potentials with corresponding flux profiles. Some of the working details of the method, its versatility, and limitations will be presented and discussed.
(Supported by grants from the American and Minnesota Heart Associations, and the Minnesota Medical Foundation.)

EFFECTS OF SURGICAL AND CHEMICAL DENERVATION ON FHE PRODUCTION OF PULMONARY HYPERTENSION (PH) ASSOCIATED WITH DISTENTION OF THE MAIN PULMONARY ARTERY (MPA) IN THE DOG. C.E. Juratsch*, J.A. Jengo*, J.T. Castagna*, and M.M. Laks (SPON: J.P. Meehan). Dept. of Medicine Harbor General Hospital, UCLA, Torrance, California 90509

We have shown that pulmonary artery balloon inflation (PABI) results in a significant elevation of MPA pressure distal to the balloon. This PH occurs in the absence of significant change in right ventricular end diastolic pressure, aortic pressure and cardiac output. The purpose of the present study is to strengthen the hypothesis that the observed PH is part of a neural reflex. Using a Laks balloon catheter the hemodynamic responses to PABI were studied before and after: 100% O_2 breathing, pulmonary artery (PA) adventitial dissection, lidocaine infiltration of the PA wall, and 6-hydroxydopamine (6-OHDA) infusion. In 2 conscious dogs the magnitude of the PH produced by PABI did not decrease after steady state breathing of 100% O_2: Before PABI (B) 55%, during (D) 66%. In 5 dogs PABI caused an increase in PA pressure from 16 to 24 mmHg ($P<0.005$). After surgical denervation the PABI PH was abolished: (B) 17 mmHg, (D) 16 mmHg ($P>0.5$). Lidocaine infiltration abolished or significantly reduced the PABI PH in 3 of 4 dogs studied. Before lidocaine PA pressure increased from 14 to 25 mmHg ($P<0.01$); after lidocaine PA pressure did not change: (B) 18 mmHg, (D) 20 mmHg ($P>0.1$). In 4 conscious dogs PABI caused an increase in PA pressure from 19/4 to 29/11 mmHg ($P<0.02$). At 18 hours after infusion of 6-OHDA, PABI did not cause PH: (B) 19/6 mmHg, (D) 23/0 mmHg ($P>0.2$). We conclude that the PH associated with PABI is produced by excitation of stretch receptors located in the adventitia of the PA and that the efferent limb of this reflex is mediated in part via adrenergic pathways. Further, hypoxia is probably not involved in the production of PH by PABI.
(Supported by L.A. Affiliate AHA Grant #511.)

VASOPRESSIN-INDUCED CHANGES IN EPITHELIAL MEMBRANE MORPHOLOGY AND FUNCTION IN TOAD BLADDER. W.A. Kachadorian, J.B. Wade*, and V.A. DiScala*, Renal Service, USPHS Hospital, Staten Island, N.Y. 10304

Isolated urinary hemibladders (n=14) from female Dominican toads (Bufo marinus) were studied by freeze-fracture electron microscopy to evaluate the effect of vasopressin stimulation on membrane morphology. Vasopressin stimulation was associated with a reorganization of intramembranous particles in the luminal membrane of granular type cells only. This reorganization was characterized by aggregations of intramembranous particles at multiple sites on the inner membrane fracture face (fracture face A). At these sites intramembranous particles consistently appeared to be organized in parallel linear arrays. The relationship between the frequency of aggregation sites per standard area of membrane and corresponding rates of vasopressin-stimulated osmotic flow was linear ($r = 0.88$; $P < .005$). This relationship suggests that vasopressin-induced particle aggregation in granular cell luminal membranes may be of functional significance in the mechanism of action of vasopressin on transport phenomena across the toad bladder.
(Supported by grant SI-74-26 from the Central Clinical Investigations Committee, USPHS, Bureau of Medical Services, Division of Hospitals and Clinics.)

MEDULLARY PROJECTIONS OF VAGAL AFFERENTS - A STUDY INVOLVING AXONAL TRANSPORT OF HORSERADISH PEROXIDASE. Madhu Kalia* (SPON: R.E. Forster). Dept. of Physiol. and Biophys., Hahnemann Med. Col. and Hosp., Philadelphia, Pa. 19102

This study was undertaken to evaluate the use of the technique of retrograde axonal transport of horseradish peroxidase (HRP) in demonstrating central brain stem connections of vagal sensory fibers. So far in peripheral nerves, this technique has been limited to motor nerves only. In 15 adult cats and 4 kittens (1-3 weeks old), the cut central end of the right cervical vagus was submerged in a 33% solution of HRP in saline for 7-28 hours. The nodose and jugular ganglia of both sides and the brain stem were processed and examined for the presence of the HRP reaction product under light and dark field microscopy. In all animals, labelling was found in the motor nuclei of the vagus, i.e., the dorsal motor nucleus (DMN) and the nucleus ambiguus; in addition, very marked labelling of the nucleus of the solitary tract (ST) was found. This indicates that HRP moves in the anterograde direction from the nodose ganglion towards the second order neurons in the medulla. This marker was found in the ST as early as 18 hours after the nerve was exposed to HRP. The quantity of enzyme transported did not appear to be different in newborn and adult animals. There was no evidence of continuous transport along the axons even though the nerve remained in the HRP solution over the entire period. It is apparent from these experiments that HRP moves in both retrograde and anterograde directions in vagal sensory nerve fibers and labels the synaptic connections in the nucleus of the solitary tract, thus providing us with a neuroanatomical tool for studying central projections of specific vagal afferents, e.g., the different pulmonary afferents. (Supported by USPHS grants HL-00103 and HL-00178)

CHANGE IN RATE OF ELECTRICAL SELF-STIMULATION OF THE POSTERIOR HYPOTHALAMUS AFTER LESIONS IN THE AMYGDALA. Kenneth J. Kant, School of Nursing, University of Tennessee, Knoxville, Knoxville, Tennessee 37916.

Earlier work has shown that rats exhibit an increase in the rate of electrical self-stimulation (S-S) in the septum following bilateral electrolytic destruction of the amygdalae (AMY). This experiment was performed to determine if similar effects would result after damage to AMY when the stimulating electrodes were in the posterior medial forebrain bundle (MFB), the hypothalamic site that usually yields very high rates of S-S. Bipolar electrodes were stereotactically implanted into the posterior MFB of male, Long-Evans hooded rats. The rats received 6 days of training for S-S followed by 6 test days. The bar-pressing scores for S-S were recorded for each minute of the session and were also traced for the full session by an accumulative recorder. Following the test sessions the rats were randomly assigned to either control (sham-op) or AMY lesion groups. After recovery from surgery the rats were trained and tested as before. Pre- and post-op scores were compared. The results show that additional training produces an increase in S-S but an even greater increase in MFB S-S occurs as a result of destruction of AMY. The conclusions are that either AMY has an "inhibitory" influence on MFB neurons to which AMY cells project, resulting in less reactivity to MFB stimulation, or AMY has a generalized role of reducing the effectiveness of positive reinforcement, a view already offered by others.

THE EFFECT OF CALCIUM ON RNA AND PROTEIN SYNTHESIS IN ISOLATED AND PERFUSED HEART. Eli Kaplan* and H.G. Richman. V.A. Hospital, Minneapolis, Minn. 55417 and Department of Medicine, University of Minnesota, Minneapolis, Minn. 55455.

The effect of exogenous calcium on RNA and protein metabolism was investigated in the isolated and perfused rat heart. The hearts were perfused by the Langendorf procedure with Krebs Henseleit buffer, pH 7.4 containing 11.1 mM glucose, and all twenty amino acids at the normal serum concentration. The hearts were allowed to equilibrate for 10 min. with 1.5 mM Ca^{2+} in Krebs Henseleit buffer prior to a perfusion with either 0.1 mM Ca^{2+} or 1.5 mM Ca^{2+}. The final perfusion media contained 0.2 μc/ml uridine 5,6 ^{3}H plus 0.2 μc/ml leucine ^{14}C. The heart was perfused for 10, 20 or 30 min., and the rate of contraction was maintained at 240/min. Although the rate of incorporation of leucine into protein was linear over a 30 minute perfusion period, there were no differences between 0.1 mM and 1.5 mM Ca^{2+} in the rate of labeling of protein. The incorporation of uridine was increased 2-fold by 1.5 mM Ca^{2+} as compared to 0.1 mM Ca^{2+}. The rate of incorporation into RNA was linear with both concentrations of Ca^{2+}. The data suggest that extracellular Ca^{2+} may influence RNA synthesis but has no effect on protein synthesis.

RELATIONSHIP OF RETICULOENDOTHELIAL SYSTEMIC DEFENSE TO BACTERIAL CHALLENGE FOLLOWING TRAUMA. J.E. Kaplan*, H.R. Bernard*, W.A. Scovill*, T.M. Saba and V.C. Gray*. Sponsored by R.S. Alexander. Departments of Physiology & Surgery, Albany Medical College, Albany, New York 12208.

The host response to intravenous and intraperitoneal bacterial challenge during periods of post-traumatic reticuloendothelial (R.E.) depression as well as the influence of bacteremia on R.E. capacity were evaluated. The traumatic shock model utilized was anesthetized (2mg/100g) male rats subjected to 300 revolutions (non-lethal) of Noble-Collip drum trauma. R.E.S. phagocytic activity was evaluated by clearance of systemically injected ^{131}I colloid and opsonic activity was evaluated by bioassay. During post-trauma R.E. depression (60 min. post-injury) rats were challenged intravenously or intraperitoneally with Escherichia coli (1.68×10^{10}). The clearance half-time of the bacterial load (I.V.) was 1.23±0.10 min. in controls in contrast to 3.62±0.69 min. after trauma ($p<.005$) and associated with prolonged blood bacterial retention at the 5-15 min. ($p<.05$) post-injection period (Residual Viable Bacteria/extrapolated blood volume = 1.70×10^{6} in controls and 3.27×10^{8} in trauma). Pulmonary localization of E. coli (I.V. or I.P.) was elevated in traumatized rats at the 5-15 min. interval. Comparison of I.P. and I.V. models with respect to blood levels of viable bacteria at 24 hr. suggested lower host bacterial resistance to the I.P. route of administration. Production of experimental bacteremia in normal rats led to a 35% depression ($p<.01$) of hepatic phagocytosis accompanied by 77% increase ($p<.02$) in pulmonary colloid localization without an associated acute opsonic depletion. The data indicate that depressed systemic R.E.S. function following trauma may be associated with septicemia following severe traumatic shock. Additionally, bacteremia can lead to the development of R.E.S. impairment. (GM-21447).

DETERMINANTS OF PEAK LEFT VENTRICULAR RELAXATION IN THE NORMAL CONSCIOUS DOG. J.S. Karliner,* M.M. LeWinter,* F. Mahler * and R.A. O'Rourke* (SPON: J.W. Covell). University of California, San Diego, Ca 92037.

To assess factors influencing the peak rate of left ventricular relaxation (-dP/dt max) we studied the effects of atrial pacing, volume, phenylephrine, isoproterenol and calcium infusions in 13 normal conscious dogs using micromanometer tip catheters. Volume infusion and incremental pacing from 110 to 160 beats/min had no significant effect on -dP/dt max. In 15 studies of the first post-pacing beat -dP/dt max decreased by an average of 498 $\pm$ 90 ($\pm$SE) mmHg/sec ($p<.0001$), regardless of the level of +dP/dt max, and was associated with a mean decrease in left ventricular pressure of 12.5 mmHg ($p<.004$). In 10 studies phenylephrine infusion increased left ventricular pressure to 220 mmHg; +dP/dt max decreased by 209 $\pm$94 mmHg/sec ($p<.01$) but -dP/dt max increased by 712 $\pm$94 mmHg/sec ($p<.001$). During isoproterenol infusion (5 studies) +dP/dt max increased by 1862 $\pm$332 mmHg/sec ($p<.005$) but -dP/dt max decreased by 620 $\pm$149 mmHg ($p<.02$); addition of phenylephrine during isoproterenol infusion abolished the decrease in -dP/dt max. Calcium infusion (5 studies) increased +dP/dt max by 851 $\pm$135 mmHg/sec ($p<.04$), but had no effect on -dP/dt max when left ventricular pressure was constant. In 7 studies changes in -dP/dt max were unrelated to changes in cardiac dimensions measured by endocardial ultrasound crystals. We conclude that -dP/dt max is unrelated to left ventricular inotropic state, is affected primarily by the level of left ventricular systolic pressure and that left ventricular contraction and relaxation are independent phenomena.

RESPIRATORY MECHANICAL PARAMETER CHANGES IN SQUIRREL MONKEY DUE TO OZONE EXPOSURE. S. K. Karuza*, S. M. Yamashiro, H. L. Greenberg*, and J. D. Hackney (SPON: C. R. Collier). Rancho Los Amigos Hospital/USC School of Biomedical Engineering, Downey, CA 90242.

Previous studies have shown alterations of pulmonary mechanics in humans exposed to low concentrations of ozone, and pathological changes in lungs of animals similarly exposed. We have applied tests of pulmonary mechanics in unanesthetized squirrel monkeys for the purpose of determining possible relationships between structural and functional changes. The studies consisted of multiple breath N_2 washout and total respiratory resistance measurements before and after exposure to low concentrations of ozone. Two groups of 5 intermittently exercising male squirrel monkeys were tested after 4 hours of sham, .6 or 1.5 ppm ozone exposures on different days. Total respiratory resistance was determined by applying flow perturbations at the mouth and measuring the resultant mouth pressure changes at peak flow times. Resistance was measured at 10 and 20 Hz. FRC was determined by multiple breath N_2 washout. From this latter test we also determined respiratory frequency, tidal volume, expired minute ventilation and LCI (lung N_2 clearance index). Both groups of monkeys exhibited a significant decrease in specific conductance from sham levels at both levels of ozone exposure (mean decrease: 42% ($P<.005$) at .6 ppm for 4 days and 35% ($P<.01$) at 1.5 ppm ozone for one day). There was a significant increase in FRC at the higher ozone exposure (mean increase: 32% ($P<.05$)). The data indicate that respiratory mechanical parameter changes are present in squirrel monkeys following exposure to low concentrations of ozone.
(Supported by SCOR Grant No. HL 15098, NHLI)

SUBSTRATE UTILIZATION FOR IN VITRO GASTRIC ACID SECRETION- AN OBLIGATORY DEPENDENCE ON SECRETAGOGUES. Dinkar K. Kasbekar
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Free fatty acids (FFA) have been proposed to support H^+ secretion by the isolated amphibian gastric mucosa in the absence of secretagogue mediation (Alonso et al, Am. J. Physiol. 212: 992, 1967; Hersey, Biochim. Biophys. Acta 344: 157, 1974). This role of FFA and other substrates was examined vis a vis the secretagogue requirement for acid secretion in the present studies. Gastric mucosae depleted of endogenous substrate(s) and secretagogue(s) in the absence of exogenous sources of both by preincubation for 18 hrs. do not respond to addition either of histamine or of an appropriate substrate alone. Addition of FFA without a secretagogue to such mucosae is ineffective in eliciting H^+ secretion. Similarly, spontaneously secreting epithelia in which the secretion is brought to a resting state with burimamide, an H-2 histamine receptor antagonist, do not secrete in response to FFA. Secretion can be elicited in both groups of mucosae, however, in the presence of FFA, glucose or pyruvate, provided an exogenous secretagogue is also added. These observations suggest that the presence of secretagogues is obligatory to utilization of FFA and other substrates for supporting acid secretion and are inconsistent with the possibility that with the mobilization of FFA, the secretagogue requirement of the mucosae for H^+ secretion is obviated.

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ALDOSTERONE AND CORTISOL RESPONSE TO ANGIOTENSIN II, ACTH, AND SODIUM INTAKE IN A HIBERNATOR, MARMOTA FLAVIVENTRIS. P.R. Kastner*, M.L. Zatzman, and J. Alan Johnson. Dept. Physiology, Univ. of Missouri, Columbia, Mo. 65201

Peripheral levels of aldosterone and cortisol were measured in normothermic marmots by radioimmunoassay following sodium loading, sodium depletion, ACTH infusion and angiotensin II (AII) infusion. Infusion of AII at 1 μg/min. for 30 min. caused a significant increase in aldosterone levels from 3.96±1.29 to 26.54±6.35 ng%; there was no significant change in cortisol levels. ACTH infusion for 30 min. at .05 U/min. caused a significant increase in both aldosterone (7.83±3.02 to 47.21±18.39 ng%) and cortisol levels (94.3±17.06 to 189.7±3.7 ng/cc). Sodium depletion did not effect cortisol levels but resulted in more than a tripling of peripheral aldosterone levels from 4.67± .82 to 16.48±4.21 ng%. Sodium loading caused a variable but insignificant change in cortisol levels while aldosterone levels decreased significantly from 4.1±1.99 to 1.1±.49 ng%. Preliminary data indicate reduced plasma levels of aldosterone and cortisol during hibernation. In the marmot, the aldosterone response to ACTH, AII and sodium intake appears to be similar to other mammals.

VAGAL TACHYCARDIA: A COMPONENT OF THE RESPONSE TO HYPOXIA. D. B. Katzin* and E. H. Rubinstein. Department of Physiology and Anesthesiology, UCLA, Los Angeles, Ca. 90024.

Cats with cervical spinal section and beta-adrenergic blockade were decerebrated electrolytically at the midcollicular level, or, alternatively, were exposed to anesthetic concentrations of halothane for periods of 30-60 min. (Both of these procedures abolish the short latency--10-20 sec--bradycardia following hypoxic stimulation.) When cats subjected to either of these two procedures were ventilated with 100% N_2 for two or four breaths, tachycardia, reversible by atropine, was observed. The magnitude of the tachycardia varied directly with the level of the arterial pressure just prior to the hypoxic episode. (Different levels of arterial pressure, and of initial heart rate, were established by infusing graded doses of phenylephrine.) It was concluded that the vagal tachycardia in response to hypoxia is integrated at the bulbar level and is related to inhibition of that portion of vagal tone associated with input from the arterial baroreceptors. A further implication is that halothane acts in a manner functionally equivalent to midcollicular decerebration. (Supported by NIH Grants HL 5157-12 & HL 5696-08, and AHA-LA Grant 437IG6.)

ACUTE HYPOXIA FAILS TO AFFECT FRC IN MAN. R.H. Kellogg and A.H. Mines, Dept. of Physiology, University of California, San Francisco, CA 94143

Several authors have reported a large increase in functional residual capacity (FRC) within a few seconds of onset of severe hypoxia (8-16% O_2) in experimental animals. Bouverot and Fitzgerald (*Resp. Physiol.* 7:203, 1969) attributed the 20% increase in FRC in their dogs to a reflex from the arterial chemoreceptors. Evidence concerning such a response in man has been unsatisfactory because of possible artifacts. With a thermally-stabilized volume-displacement body plethysmograph, we have continuously recorded the end-expiratory level in 50 hypoxic exposures in 20 experiments on 7 men and 1 woman, using O_2-N_2 mixtures that quickly lowered $P_{A_{O_2}}$ to 42-50 mm Hg and held it there for a few minutes. Hypoxic chemoreceptor stimulation was evidenced by increased breathing despite the subject's complete ignorance of when gas was changed. As an alternative to exposing subjects to more severe hypoxia, we tried potentiating hypoxic stimulation by simultaneous hypercapnia. Because increased tidal volume sometimes encroached on FRC, this was controlled in 2 subjects by switching between equally stimulatory hypercapnic and hypoxic mixtures. We tried switching from hypoxia to 100% O_2 to make any effects more obvious. Effects of restricted posture (sitting in plethysmograph with fixed mouthpiece) were checked in 2 experiments with subjects recumbent outside the plethysmograph, which was used as a twin-bag-box system. In no case could we detect any increase in FRC with hypoxia. We conclude that such a response does not occur in most normal subjects at this level of hypoxia, corresponding to about 12-15,000 feet altitude. (Supported by grant HL-13841 from NHLI.)

BLOOD FLOW DISTRIBUTION IN UNIFORMLY COOLED DOGS. Barbara Kent and E. Converse Peirce II. Depts Surgery, Mount Sinai School of Medicine and Bronx Veterans Administration Hospital, New York, 10468.

Since hypothermia lowers regional blood flow requirements by decreasing tissue metabolism, possible redistribution of blood flow with cooling has been investigated using the isotopically labelled microsphere technique. Twenty-eight mongrel dogs (14±2kg), anesthetized (-chlorolose, 80 mg/kg), heparinized (200u/kg) and cannulated for total cardio-pulmonary bypass following ventricular fibrillation were perfused by an extracorporeal circuit which included a 1 M^2 G.E.-Peirce membrane lung. The dogs were cooled by total body perfusion with cold blood and by simultaneous surface cooling with a cold water spray to 30, 25, 20, 15 and 10°C (1 hour at each level). Fifty micron diameter isotopically labelled (Sc^{46}, or I^{125}) microspheres (5uCi) were injected into the left atrium through a previously implanted catheter at 37°C or into the arterial perfusion catheter at lower body temperatures. After injection, the animals were sacrificed and the organs weighed and sampled for radioactivity. The radioactivity of each organ was calculated as a per cent of the total dose and this was considered equal to the portion of cardiac output to that organ. The per cent cardiac output to the liver increased from 30±3% at 37°C to 45±5% at 25°C and fell again to 29±4% at 10°C. The per cent to the kidneys fell steadily from 24±3% at 37°C to 7±2% at 10°C while the portion to the heart increased from 8±1% to 21±7% respectively. The per cent cardiac output to the brain was between 2 and 3% for all temperatures. Since total body blood flow fell from 137ml/kg/min at 37°C to 48ml/kg/min at 10°C actual tissue perfusion decreased in all organs studied as body temperature was lowered.

EFFECT OF AORTIC BALLOON COUNTERPULSATION ON THE MOTION AND PERFUSION OF ACUTELY ISCHEMIC MYOCARDIUM. R.E. Kerber, M.L. Marcus*, J. Ehrhardt* and F.M. Abboud, C.V. Div., Dept. of Med. and Cardiov. Center, Univ. of Iowa Coll. of Med. and VA Hosp., Iowa City, Iowa 52242.

The effect of intra-aortic balloon counterpulsation (IABC) on the motion and perfusion of ischemic left ventricular posterior myocardium was studied in 15 open-chest dogs, using ultrasound and (9μ) radioactive microspheres. Circumflex coronary artery ligation produced acute aneurysmal bulging during isovolumetric contraction and diminished ischemic wall velocity during systolic ejection. This was accompanied by a fall in myocardial perfusion of the area supplied by the ligated artery, from 72.9±SE13.8 to 30.0±2.3 cc/100g/min ($p<.01$). IABC was then administered for one hour, with a fall in aortic systolic pressure (112±6 to 105±7 mmHg $p<.05$) and a rise in peak aortic diastolic pressure (94±6 to 103±7 mmHg $p<.05$). Despite this the ischemic area showed no change in perfusion (measured at the same time): 30.0±2.3 to 28.0±2.4 cc/100g/min, p=NS. Improvement in wall motion did occur: aneurysmal bulging decreased significantly (4.5±0.3 to 3.6±0.3 mm [$p<.05$]), and ischemic wall velocity tended to increase: 12.2±1.4 to 17.4±1.5 mm/sec, p=NS, but this increase was not significant. Conclusion: IABC reduces the aneurysmal bulging secondary to acute coronary occlusion, but does not improve the perfusion of the acutely ischemic area. The beneficial effects on dyskinesis may be due to reduction in afterload.

EFFECTS OF REDUCED TISSUE TEMPERATURE ON REACTIVE HYPEREMIA IN RED AND WHITE MUSCLE OF THE CHICKEN. R. E. Klabunde* and P. C. Johnson (SPON: G. A. Hedge). Department Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724.

An earlier study on reactive hyperemia in red and white skeletal muscle demonstrated that metabolic control mechanisms were dominant. Furthermore, there were no significant differences in the capillary red cell velocity responses following ischemia in the two muscle types when the data were normalized to the control capillary velocities. The present study was undertaken to determine if tissue temperature reduction would differentially affect the metabolic control mechanisms of red and white muscle such that differences in reactive hyperemia would be observed between the two muscle types. Reactive hyperemia was studied in individual capillaries of the red anterior and white posterior latissimus dorsi muscles of the chicken by measuring changes in capillary red cell velocity. Simultaneous arterial-venous occlusions of 15 and 60 seconds duration were performed while the muscle temperatures were maintained at 30 ± 1° C (normal temperature is 40 ± 1° C). Compared to normal temperature values, the mean capillary red cell velocities decreased 26% in the red and 39% in the white muscle. Reactive hyperemia duration, excess flow, and percent flow debt repayment values were comparably reduced in both muscle types at the lower temperature. These data indicate that the metabolically linked mechanisms which are presumably responsible for reactive hyperemia in this preparation have the same sensitivity to temperature reduction in both muscle types. (Supported by NIH grants HL 05884, HL 15390, and Grant-in-aid from American Heart Association).

THE AVIAN FEBRILE RESPONSE AND ITS IMPLICATIONS CONCERNING THE EVOLUTION OF FEVER. M.J. Kluger and L.G. D'Alecy. Dept. Physiology, Univ. of Michigan Medical School, Ann Arbor, Michigan 48104

In studying the evolution and adaptive value of fever, our laboratory has previously demonstrated that reptiles develop a fever in response to bacterial infection and that this fever increases the host survival. A clarification of the evolutionary relationships of the phenomenon of fever among the terrestrial vertebrates could help to define the role of fever in the higher vertebrates. As little was known about the febrile responses of birds, we have attempted to characterize the thermal responses of pigeons (Columba livia) to bacterial infection. The normal circadian pattern of body temperature was continuously recorded in 22 birds and resulted in a mean temperature of 40.72 ± 0.04°C SEM during the day and 39.70 ± 0.09°C SEM during the night. Injection (i.p.) with a known avian pathogen, Pasteurella multocida, produced a fever and eventually killed each bird (n=7). Injection of a 1 ml solution of dead bacteria (containing the endotoxin) in concentrations from $5x10^7$ to $5x10^{10}$ organisms/ml produced a dose-dependent complex febrile response with an average 24 hr increase in body temperature ranging from 0.09 to 1.06°C. Sodium salicylate attenuated the fever produced by injection with dead bacteria.

These results indicate a similarity in avian, reptilian, and mammalian fever which, although not definitive, is highly suggestive of a common origin for the febrile mechanism. If terrestrial vertebrates did have a common origin (i.e. did not evolve independently) then the function of fever might be expected to be similar in each class. Since fever in response to bacterial infection has been shown to increase host survival in reptiles, these data might suggest a similar adaptive value for fever in birds and mammals. Supported by Grant NSF GB 42749X.

EFFECT OF CARBONIC ANHYDRASE INHIBITION ON THE PHOSPHATURIC EFFECT OF PARATHYROID HORMONE (PTH). Franklyn G. Knox, John A. Haas* and Claude Lechene , Depts. Physiol., Mayo Med. School, Rochester, MN 55901 and Harvard Med. School, Boston, MA 02115.

The present studies evaluate the effect of parathyroid hormone on phosphate transport in the proximal tubule and phosphate excretion in the urine in the presence of carbonic anhydrase inhibition. Seven dogs were thyroparathyroidectomized (TPTX) and administered acetazolamide, 15 mg/kg prime and 15 mg/kg/hr with replacement of urinary losses. Following control measurements, bovine PTH extract, 3.3 μ/kg prime and 0.1 μ/kg/min was infused and recollections obtained. Control studies were performed in the absence of carbonic anhydrase inhibition. In 10 control studies in TPTX dogs, PTH increased fractional delivery of phosphate from the proximal tubule from 34 ± 3% to 42 ± 3%, $P < .025$, and increased fractional phosphate excretion from 3.9 ± .9% to 27.0 ± 2.2%, $P < .001$. In the presence of carbonic anhydrase inhibition, PTH did not change fractional delivery of phosphate from the proximal tubule, 49 ± 3% and 54 ± 3% respectively. In contrast, in the presence of carbonic anhydrase inhibition, fractional excretion of phosphate was 9.6 ± 3.2% before and 35.8 ± 5.1% after PTH, $P < .025$. Fractional excretion of bicarbonate was high in the presence of carbonic anhydrase inhibition, 24.2 ± 3.6%, and unchanged following PTH, 24.4 ± 3.4%, indicating little role of urinary pH in the phosphaturic effect of PTH. In conclusion, carbonic anhydrase inhibition mimicked the effect of PTH on proximal phosphate reabsorption but did not reproduce the effects of PTH on urinary phosphate excretion. In the presence of carbonic anhydrase inhibition, the phosphaturic response to PTH was similar to that seen in the absence of carbonic anhydrase inhibition.

EFFECT OF HEMORRHAGE ON RENAL FUNCTION IN THE DOMESTIC FOWL. T. I. Koike, G. C. Bond, and R. S. Venable*, Dept. of Physiology, Univ. of Ark. Med. Ctr., Little Rock, AR 72201.

Experiments were conducted to characterize the renal response of the domestic fowl to a reduction in circulating blood volume. Roosters of the Red Rock strain (n = 7) were anesthetized with sodium pentobarbital and appropriate catheters were inserted for monitoring central venous pressure, arterial pressure, and for the collection of urine. After stabilization of urine flow, 20% of the rooster's blood volume was withdrawn over a five min. period from the venous catheter. Hemodynamics and renal function were monitored for an additional six 30 min. clearance periods. A second group of roosters (n = 7) which was subjected to the same protocol but not hemorrhaged served as controls. When compared to the controls, roosters subjected to hemorrhage showed statistically significant decreases in sodium excretion ($p < .001$) and urine flow ($p < .01$) 30 min. after hemorrhage. The percent of filtered sodium reabsorbed increased significantly ($p < .01$) during the same period. Hematocrit in the hemorrhaged roosters was significantly reduced at 75 min. ($p < .05$) and 135 min. ($p < .05$) subsequent to hemorrhage. There were no statistically significant changes at any time after hemorrhage in potassium excretion, effective renal plasma flow, and glomerular filtration rate. These data suggest that the change in urine flow and sodium excretion occurred independently of any measurable changes in renal hemodynamics. (Supported by a grant from the Arkansas Heart Assoc.)

PERCUTANEOUS ELECTROMAGNETIC OBSERVATION OF BLOOD FLOW AND VASOMOTION. Alexander Kolin and Rex N. MacAlpin*, School of Medicine, University of California, Los Angeles, California, 90024

The objective of this study is to measure and record the volume rate of blood flow and variations of vascular diameter in superficial and deep-seated visceral arteries as well as aorta without surgical exposure of the blood vessel under study. The probe is a resilient fine wire loop (made of a 0.1 mm diameter wire pair). It is introduced into a branch artery through a skin puncture via an angiographic catheter (#5 to 7 French) which terminates in the aorta with its opening entering the ostium of the selected artery. The probe loop springs open as it enters the artery from the catheter. Two diametrically opposed electrodes on the loop, pick up the flow signal induced in the blood stream by the magnetic field established by an extracorporeal magnet. The loop also acts as a transformer secondary in the above magnetic field. The induced transformer e.m.f.(electromotive force) measures the vascular diameter, detecting changes as small as 0.1%. Flow zero is established reliably by switching off the magnet. Blood flow has been measured in the aorta, iliac, carotid, femoral, renal and superior mesenteric arteries and effects of various vasoconstrictors and dilators have been studied in intact animals, and observations have been extended to the aorta and iliac arteries of conscious human subjects. Phasic changes in vascular diameters have been recorded in the aorta and its branches in intact animals and in conscious patients undergoing angiographic diagnostic procedures. This new methodology offers a way to study peripheral and visceral circulation and vasomotion without surgical intervention and, in human subjects, without general anesthesia.

EFFECTS OF HYDROSTATIC COMPRESSION ON GAS EXCHANGE IN THE SEASNAKE, *Pelamis platurus*. G. L. Kooyman, Physiological Research Laboratory, Scripps Institution of Oceanography, La Jolla, CA 92037

Seasnakes were held at a simulated depth of 20 and 40 meters in a small compression chamber. The amount of gas diffusing from the lung to the blood and tissues was determined by measuring the amount of water injected into the chamber to maintain pressure. Multivariate analysis shows that there is a highly significant positive correlation among gas absorption rate and diving lung volume and water temperature. The correlation is negative between gas absorption rate and pressure. The total absorption rate considering all variables could raise the blood and tissue gas tensions several atmospheres if the snake remained at depth long. During immersion there is also cutaneous gas exchange that can be as much as 33% of resting metabolism (Graham, 1974). Snakes will voluntarily remain submerged indefinitely if the water is aerated with 100% O_2. When *Pelamis* dives to depth tissue and blood gas tensions rise and the amount depends on several factors. Antagonistic to this elevation is gas exchange through the skin to the water which results in a lowering of tensions. This exchange may be important in preventing bubbles forming in the blood and tissues when the animal returns to the surface.

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EVOKED POTENTIAL MAPPING OF UPPER THORACIC SPINAL CARDIAC EFFERENTS. D.R. Kostreva*, E.J. Zuperku*, J.F. Cusick*, and J.P. Kampine*. (SPON: G.B. Theil). Medical College of Wisconsin, Milwaukee, Wisconsin 53226.

Sympathetic efferent innervation of the heart and lungs has been shown to traverse the upper thoracic white rami communicantes. The neuroanatomy of mammalian close cardiac nerves has been described. To date, no one has described the primary efferent pathways of the thoracic cardiac efferents arising from the ventral roots. Efferent pathways of close cardiac nerves were studied by electrically stimulating thoracic ventral roots and recording evoked potentials from the close cardiac nerves. Ten mongrel dogs were anesthetized with sodium pentobarbital (35 mg/kg I.V.). A thoracotomy was done on the left side by removing ribs 1-5. A thoracic laminectomy was performed between T_1 and T_5. Left ventral roots $T_{2,3}$, and 4 were cut centrally and stimulated with a supramaximal stimulus. Evoked potentials were recorded from the left sympathetic chain, the anterior and posterior ansae subclavia, the cardiac stellate nerve, the ventrolateral and ventromedial cervical cardiac nerves and the vagosympathetic trunk. 128 evoked potentials were averaged at each of the stimulating and recording sites by an averaging computer. The range of conduction velocities for each evoked potential was computed along with the mean conduction velocity, the maximum amplitude of each component, and its corresponding conduction velocity and the area of each evoked potential. In this study three separate components of the evoked potentials were observed in the close cardiac nerves. A slow component with a small area and amplitude having a mean conduction velocity range of 1.0-1.8 m/s, a component with a large area and amplitude having a mean range of 2-3 m/s, and a small fast component with a range of 20-45 m/s. The fast components may be preganglionic efferents passing directly to the heart and lungs. T_2 and T3 yeilded potentials having the largest areas.

INTERACTION OF COOLING RATE, WARMING RATE AND CONCENTRATION OF DMSO ON SURVIVAL OF THE FROZEN CANINE KIDNEYS. S. Kubota, Bo Crabo and R. Lillehei, Dept. Surgery & Animal Sciences, University of Minnesota, Minneapolis, Minnesota 55455

Canine kidneys, frozen solid in liquid nitrogen ($-22^{o}C$),and then thawed, were capable of sustaining life following contralateral nephrectomy. Success or failure of this technique was dependent upon cooling rate, warming rate and concentration of dimethylsulfoxide (DMSO). The canine kidneys were perfused with 800 ml cryoprecipitated plasma containing various concentration of DMSO (7.5, 12.5 and 15.0%) frozen to $-22^{o}C$ at rates ranging from 0.1 to $10.0^{o}C$/min and thawed rapidly (70^{o} - $110^{o}C$/min) or slowly (20^{o} - $30^{o}C$/min). Eleven kidneys of 14 cooled at rates 2 to $4^{o}C$/min and thawed rapidly after perfused with 12.5% DMSO were viable following contralateral nephrectomy. Two of these dogs were allowed to survive for over 3 months. Average survival time for the other 9 was two weeks. Renal cell damage following thawing, evidenced by venous effluent, was less in the rapidly thawing group, LDH, 5.7 ± 2.7 IU/ml/g, GOT, 1.7 ± 0.6 IU/ml/g, compared to slowly thawing group, LDH, 11 ± 1.5 ($P<0.01$), GOT 6.2 ± 1.2 ($P<0.01$). The deleterious cooling rate were 0.1 and $10.0^{o}C$/min. None of the kidneys frozen at any cooling rates after perfused 7.5% DMSO survived following reimplantation. Four kidneys out of 6 cooled at rates 2 to 4 C/min and thawed rapidly after perfused with 15.0% DMSO produced urine. Urine output, however, gradually decreased and average survival time after contralateral nephrectomy was 5 days. These results suggest that viable kidneys frozen to $-22^{o}C$ can be achieved with the optimum cooling rate of 2 to 4 C/min and rapidly thawed of 70-110 C/min after perfused with 12.5% DMSO.

LABORATORY EVALUATION OF PERMISSIBLE EXPOSURE LIMITS (PEL) FOR FEMALES IN HOT ENVIRONMENTS. K.V. Kuhlemeier* and J.M. Miller* (SPON: L.H. Schneyer). University of Alabama Medical Center, Birmingham, AL 35294

Fully clothed female industrial workers aged 18 to 48 years walked on a treadmill in a controlled environment chamber at three metabolic rates averaging from 176 to 297 Kcal/hr in wet bulb globe temperatures ranging from 20.5 to 32.7°C for one hour or until a predetermined safety criterion was reached. Rectal temperatures (RT) and pulse rates (PR) were determined at the end of each work bout. The number of subjects with RT $\leq$ 38.0°C and the number of subjects with RT > 38.0°C were recorded for environments above and below or at the PEL as defined in the ASHRAE J. 15:57, 1973, and were found to be as follows:

	Below PEL	Above PEL
RT $\leq$ 38.0°	N=93	N=63
RT > 38.0°	N=41	N=66

Similarly the number of subjects with PR $\leq$ 150 beats per minute and the number of subjects with PR > 150 beats per minute above and below the PEL were:

	Below PEL	Above PEL
PR $\leq$ 150	N=128	N=99
PR > 150	N=8	N=20

We conclude that in laboratory situations the current PEL are such that RT frequently exceed 38.0°C in females during prolonged work in environments below the PEL but that high PR are much less frequent in the same environments. Supported by National Institute of Occupational Safety and Health Contract No. CDC-90-OSH-50.

LIPID COMPOSITION OF PLASMA MEMBRANE OF CHICK EMBRYO HEART AT VARIOUS STAGES OF DEVELOPMENT. H. Kutchai, T.F. Ross*, S.L. King*, and D. Dunning*, Dept. of Physiol., Univ. of Va. Med. Sch., Charlottesville, Virginia 22901.

We have previously reported that the plasma membrane fluidity of chick heart increases over the course of embryonic development and increases still further with development to adulthood. In this study we are asking whether changes in the lipid composition of the plasma membrane are responsible for the changes in membrane fluidity during development. A fraction of chick heart enriched in plasma membrane marker enzymes is obtained by sucrose density gradient centrifugation. Lipids are extracted from this fraction by the method of Bligh and Dyer. Cholesterol is assayed by the $FeCl_3$ method. Fatty acids are saponified and converted to fatty acid methyl esters (FAME) by treatment with methanolic HCl and the FAME extracted into pentane. FAME are quantified by gas-liquid chromatography. The cholesterol/phospholipid molar ratio remains near 1 throughout embryonic life, so that changes in cholesterol level do not account for the changes in membrane fluidity observed. There are no significant changes in the average chain length of membrane fatty acids during development, but the average number of double bonds per fatty acid molecule increases substantially as development proceeds principally via increases in the amount of the polyunsaturated fatty acids 18:2 and 20:4 at the expense of the saturated fatty acid 16:0. The results support the idea that increases in the degree of unsaturation in plasma membrane fatty acids during development contribute to the increase in plasma membrane fluidity that occurs. The possible role of changes in membrane fluidity in causing developmental changes in membrane transport activities is considered. (Supported by Grant HL-15716)

THE EFFECT OF BODY POSITION UPON POWER OUTPUT IN CYCLING. C.R. Kyle* and J. Mastropaolo, California State University, Long Beach 90840.

Recently new human powered vehicles are being tested which permit pedaling in the supine and prone positions. The purpose of these vehicles is to lower the projected frontal area of the rider, and thus decrease the total wind resistance which is the major retarding force in cycling on a level course. If the power output of a cyclist on a standard racing bicycle traveling at 25 MPH, is taken as a base of 100%, then the same cyclist in the supine and prone pedaling positions would require respectively about 76% and as little as 44% of this power output. Obviously, it would be possible for cyclists to achieve much higher average speeds if their power output were not decreased too greatly by assuming alternate pedaling positions. The current paper presents experimental data in graphical and tabular form comparing human power output in the supine, prone and standard cycling positions. The study includes extensive ergometer tests, as well as data taken from experiments with two new human powered vehicles. Test periods varied from six seconds to twenty minutes, spanning the range from short term anaerobic exercise to long term aerobic exercise. If the average power output in the standard cycling position is 100%, then the power output in the supine position is 96% while the prone position is 94%. Therefore, if practical vehicles can be built utilizing these alternate pedaling positions, they will be much faster than the standard bicycle.

EFFECT ON TRANQUILIZING DRUGS ON DETRUSOR CONTRACTILITY. P.C. Labay and M.S. Roussan*, Dept. of Physical Medicine & Rehabilitation, The Albert Einstein College of Medicine, Bronx, N.Y. 10461

The effect of tranquilizers on the detrusor contractility was studied in-vitro. Strip of rabbit or human detrusor muscles, 1 X 2 cm was placed in a bath containing 70 cc Locke's solution at 37° with oxygen bubbling through. One end of the strip was fixed to the bottom of the bath and the other end to a force displacement transducer. A Grass Polygraph monitored the detrusor tone, strength and frequency of contraction. Diazepam, Chlordiazepoxide and Phenobarbital in concentrations from 10 to 100 μg/ml were tested. Diazepam, 10 to 20 μg/ml decreased the detrusor tone, force and frequency of contraction within 20 minutes with complete cessation in 30 minutes. Above 30 μg/ml, decreased tone and contractile activity occurred followed by cessation of all activity within 10 minutes. 5 μg/ml had a lesser depressive effect without actual cessation. Mechanical restoration of tension after Diazepam depression caused some return of bladder contraction. Diazepam was found to be four times more effective than Chlordiazepoxide and Phenobarbital. The study suggests: 1) Diazepam can inhibit involuntary detrusor contraction; therefore, capable of increasing bladder capacity without necessarily precipitating acute urinary retention. 2) The effect is reversible and dose-dependent. 3) Diazepam is more effective in depressing bladder activity than Chlordiazepoxide and Phenobarbital.
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DIGITAL COMPUTER PROGRAM FOR CEREBRAL BLOOD FLOW. D. Laffin*, W. Hayward*, & G. Austin. Section of Neurological Surgery, Loma Linda University School of Medicine, Loma Linda, Calif 92354

Cerebral blood flow may be measured by the intravenous injection of the radioisotope ^{133}Xenon. This technique involves the external monitoring of the concentration of the isotope against time in the had and the expired air, the latter being proportional to the concentration of the isotope in the arterial blood. The analysis is based on a model of 3-compartments in parallel and in normal subjects represent the gray matter, white matter, and extracerebral tissue. The concentration of the isotope against time in each compartment is determined by the Fick equation. This necessitates a simultaneous solution of three convolution compartments. The flow terms enter the equations non-lineally.

A visual computer program has been developed to perform the analysis. To test this method a typical expired air curve recording was selected and an envelope drawn through the peaks and digitized at 18 points/min. Head curves were then generated by computer using selected values of flow and relative weight. Resulting head curves were normalized to a predetermined number of counts per minute and normally distributed noise at each point. The generated curves were first normalized to 60,000 counts/min and analyzed for 49' and then 30'. It was then repeated for curves normalized at 30,000 counts/min. A slight modification was made and a 2-compartment 10' analysis of the type suggested by W. Obrist carried out on the same set of curves (49', 60,000 counts/min) used previously. Though results indicate the parameters are identified more accurately in 49' curves,the degree of accuracy obtained is thought sufficient for use in the clinical environment. The 10' analysis has the advantage of being about five times faster and requires a test lasting 10'; however, the price paid is loss of information on parameters other than gray matter flow and decrease in resolution of gray matterflow.

THE COMBINED EFFECTS OF RENAL ARTERY CONSTRICTION AND ANGIOTENSIN II BLOCKADE ON RENAL FUNCTIONAL PARAMETERS. R.G. La Grange* and H.E. Schmid. South Alabama Coll. Med., Mobile, Ala. and Bowman Gray Sch. Med., Winston-Salem, N.C.

Renal artery pressure & flow, glomerular filtration (GFR), Na^+ and K^+ excretion, urine excretion and renin production were measured before and during continuous blockade of angiotensin II (AII) receptors with saralasin (P-113, Norwich). The effectiveness of renal arterial infusion of P-113 (5 ug/kg/min) was determined by the absence of response to renal arterial injection of a 10 ug bolus of AII. The usual autoregulatory phenomena were observed prior to P-113 infusion. During P-113 infusion, renal blood flow autoregulated at significantly higher flow values, GFR was slightly increased, K^+ excretion was depressed and renin production was considerably elevated. These effects were more prominent at renal arterial pressure levels below 100 mmHg. Na^+ and urine excretion were not significantly affected. These data are consistent with intrarenal AII effects on the resistance vessels associated with the autoregulatory process as well as a direct feedback action of AII on renin release. A decrease in PAH extraction during P-113 infusion suggests the diversion of flow away from the tubular secretory sites (since flow increased) indicating that AII may influence the distribution of intrarenal blood flow during low pressure states when renin release is augmented.

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ROLE OF CAROTID BODY, ARTERIAL AND CISTERNAL FLUID pH IN THE ACCLIMATIZATION TO CHRONIC HYPOXIA. S. Lahiri, N.S. Cherniack, N.H. Edelman and A.P. Fishman, Cardiovascular-Pulmonary Div., Dept. of Med. and Physiol., University of Pennsylvania, Philadelphia, Pa. 19104

Previously we reported (Lahiri et al., Respir. Physiol. 12:388, 1971) that chronic exposure of anesthetized goats to 5000 m was followed by a sustained decrease in arterial P_{CO_2} and $[HCO_3^-]$ and a slightly elevated arterial pH even when arterial P_{O_2} was acutely raised to normal sea level value. The lowered arterial P_{CO_2} and $[H^+]$ was attributed to persistent hyperventilation, the stimulus for which has been thought to partially reside in changes in cerebral spinal fluid $[H^+]$. In the present study we measured the effect of chronic exposure to hypoxia on cisternal fluid (CF) and arterial blood acid base status in unanesthetized goats before and after bilateral sections of carotid sinus nerves. All measurements were made after the chamber pressure was brought back to sea level. In intact animals ventilation increased promptly with altitude exposure. This increase in ventilation persisted even though animals were studied under euoxic conditions and was associated with a decrease in arterial CF P_{CO_2} and a normal CF pH. With deacclimatization at sea level, arterial and CF P_{CO_2} returned to 90% of the normal values within a day or two while arterial and CF pH remained unchanged. In the denervated animals exposure to 5000 m caused a smaller and slower decrease in arterial and CF P_{CO_2} with no significant change in blood or CF pH. Deacclimatization also caused a smaller and slower change. We conclude: 1) that intact carotid sinus nerves are important for prompt ventilatory responses to altitude hyperoxia; and 2) the euoxic hyperventilation occurring with chronic exposure to altitude are not explained by pH changes in the CF or arterial blood. (Supported in part by grant HL-08805 from NHLI).

RELATIONSHIP OF INSPIRED OXYGEN, REDOX LEVEL OF CYTOCHROME a AND ECoG IN CATS. J. LaManna,* G. Watkins* and M. Rosenthal. Dept. of Physiology and Pharmacology and Center for Aging, Duke University Medical School, Durham, N.C. 27710.

Changes in the redox level of cytochrome a were monitored in intact cerebral cortex of cats (cerveau isole preparations) by dual wavelength reflectance spectrophotometry. ECoG was monitored simultaneously and recorded on tape for spectral analysis. Blood gases were sampled throughout. When the level of inspired O_2 was increased from room air to 50% in 50% N_2, there was an increase in the oxidation level of cyt a accompanied by a slight increase in mean ECoG frequency. The increase in cyt a oxidation level and ECoG mean frequency were larger when 100% O_2 was inspired and larger still when 95% O_2 was given with 5% CO_2. When inxpired O_2 was increased from normoxia, the cyt and ECoG changes appeared nearly coincidently but when O_2 was switched from the high levels, ECoG lagged the return of cyt a to normoxic condition. Decreased O_2 levels below normoxia were accompanied by increasing levels of cyt a reduction and nearly coincident small decreases in mean ECoG frequency. When inspired O_2 was increased to room air levels, cyt a redox level returned to baseline before ECoG frequency shifted to normoxic values. On-line integration of total ECoG shows a peak value around room air with decreased total integral both at higher and lower O_2 pressures. It appears that this is due to increased fast and slow wave activities respectively in the two conditions. This study indicates that both cyt a and ECoG activity are labile with changes from normoxic conditions. It indicats that there is a continuum of dependency of cyt a redox state and ECoG activity on O_2 availability and that cytochrome redox levels and ECoG are interdependent. (This work supported by PHS grants NS-06233 and NS-10384).

ARE THE BASAL GANGLIA ONLY MOTOR STRUCTURES? Maryse C. Lassonde*, Maurice Ptito*, Karl H. Pribram, and Michael Fossel*. Departments of Psychology and of Psychiatry and Behavioral Sciences, Stanford University, Stanford, Ca. 94305.

Several studies on cats (Kadobayashi et al., Exp. Neurol., 33: 578, 1971) and on monkeys (Reitz and Pribram, Exp. Neurol., 25: 632, 1969; Buerger et al., J.C.C.P., 86(3): 440, 1974) have involved the basal ganglia in visual processing. The present study was undertaken to provide further evidence on the role of these structures in vision.

The responses of single units in the visual cortex (VC) were recorded with extracellular tungsten microelectrodes from paralyzed unanesthetized cats. Visual stimuli consisted of moving lines displayed on an oscilloscope by a computer (PDP-8) which also recorded the responses to the stimuli. The effects of bipolar electrical stimulation of the caudate nucleus (CN) or the putamen (P) on the response properties of a unit visually stimulated with a) one line moving in each of 36 directions in 10° increments; or b) two parallel lines moving in the preferred direction and orientation with various separations, were measured. In condition a), the cell's firing level dropped drastically during electrical stimulation of P but didn't change significantly during electrical stimulation of CN. In condition b), the size of the visual receptive fields of the units increased during CN stimulation and decreased during P stimulation. In the latter condition, the influence of P and CN was reciprocal. Moreover, even though the cells' responses were drastically affected by the electrical stimulation of P and CN, their original visual properties (i.e., orientation, velocity and direction) remained the same. These results support the conception that the basal ganglia influence visual inputs.

THE CORONARY BLOOD FLOW RESERVE OF THE HYPERTROPHIED DOG HEART. H. Laughlin*, J. Diana, Dept. of Physiology and Biophysics and Cardiovascular Center, University of Iowa, Iowa City, Iowa 52242

Measurements were made of the ability of the coronary circulation of normal and hypertrophied myocardium to increase flow during a reactive hyperemia produced by occluding the coronary artery for a 10 second period. These measurements of flow were made with an electromagnetic flow meter. Isoproterenol (1 μg/kg/min, i.v.) was used as an additional stress and regional distribution of flow was measured with radioactive microspheres. Cardiac hypertrophy was produced with exercise training (EH) and chronic tricuspid insufficiency (RHH). Mean values for peak reactive hyperemic flow were: Control, 260% (% resting flow); EH, 306%; and RHH, 180%. Mean values for resting coronary vascular resistance were the same in control and EH, but were lower in the right ventricle of RHH. Resting Endo/Epi flow ratios for the left ventricles were: Control, 1.08; EH, 1.06; and RHH, 0.99. Right ventricular values were: Control, 1.13; EH, 1.12; and RHH, 0.89. After the typical hemodynamic response to isoproterenol coronary vascular resistance was decreased in all animals with the RHH decrease being less pronounced. The left ventricular Endo/Epi ratio values were: Control, 0.67; EH, 0.68; and RHH, 0.66 while the right ventricular values were 0.86, 0.93, and 0.94 respectively. It is concluded that hearts of EH dogs have a coronary flow reserve capacity which is equal to control but the reserve of the RHH dogs is decreased. (Supported by Grants HL 16997 and HL 14388.)

NEURAL INFLUENCES ON MUSCLES OF NORMAL AND DYSTROPHIC MICE IN PARABIOSIS. Peter K. Law* and Ethel Cosmos, McMaster University Medical Centre, Hamilton, Ontario, Canada.

Dystrophic (D) mice and normal (N) littermates were parabiosed in pairs at 2-3 weeks ex utero to facilitate a cross of the "fast" tibial nerve of one partner onto the slow soleus muscle of the other. This model allows us a) to monitor the "neurotrophic" influences of a "fast" nerve on a slow muscle; b) to assess the influence of the nerve on the expression of dystrophy. Twelve parabiotic pairs examined at 3-6 months post-operatively indicated that the donor nerve, either N or D, successfully decreased the peak contraction time and the half-relaxation time of the cross-reinnervated muscle. Furthermore, the cross-reinnervated muscles, unlike the self-reinnervated solei, demonstrated post-tetanic potentiation which is a characteristic of fast muscles. Histochemical analyses of the cross-reinnervated muscles confirmed the presence and fibre type-grouping of fast twitch fibres. Although the fast and slow twitch characteristics of the cross-reinnervated muscles were altered, the donor nerves (N and D) did not seem to affect the normal and dystrophic properties of the cross-innervated muscles in terms of twitch and tetanic tensions and histochemical characteristics. Dystrophic muscle remained dystrophic under the influence of a normal nerve and the normal muscle retained normal characteristics when re-innervated by a dystrophic nerve.

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CHLORIDE TRANSPORT IN THE RAT NEPHRON. C. Lechene, R. Warner*, E. Abraham* and K. Blouch*. Biotechnology Resource in Electron Probe Microanalysis, Laboratory of Human Reproduction and Reproductive Biology, and Department of Physiology, Harvard Medical School, Boston, Mass. 02115

Micropuncture and electron probe analysis were performed to study the effect of an impermeant anion on nephron chloride reabsorption. Jugular vein perfusion with .2M $Na_2 SO_4$ (96 µl/min) was used to load the glomerular filtrate with sulfate. In a first series of 8 rats, in the proximal tubule mean TF/P_{Cl} = .88 and TF/P_{Na} = .92. In the distal tubule, mean TF/P_{Cl} = .27 (for a mean TF/P_{Inulin} = 6.79) and in some distal samples, chloride was undetectable; on the other hand, Na was high (TF/P_{Na} = 1.03). In the urine, chloride concentration was low (U/P_{Cl} = .26) whereas Na reached a high concentration (U/P_{Na} = 2.60). The fractional excretion of Na was 15.7%; that of Cl 1.42%. In another experimental series (6 rats) after a control period of sulfate loading, furosemide was perfused (5 mg prime, sustaining .3 mg/min). Before furosemide, in the urine: Cl was practically not detectable, U/P Na = 2.50, FE% Cl = .07, FE% Na = 10.2, UV_{Na} = 13.3 µm/min., UV_{Cl} = .115 µm/min. After furosemide U/P_{Na} decreased (1.23), FE% Na increased to 30%, UV Na did not change. But a dramatic effect was observed on chloride with a considerable increase in U/P_{Cl} = .65, UV_{Cl} = 6.59, $FE\%_{Cl}$ = 19.1. It is concluded that a portion of the rat nephron distal to the accessible proximal tubule reabsorbs actively chloride by a mechanism which is inhibited by furosemide.

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RELATIVE PERMEABILITY AND CONDUCTANCE OF Cl AND K IN RABBIT VENTRICULAR MUSCLE CELLS. Chin O. Lee* and Harry A. Fozzard, University of Chicago, Chicago, Illinois. 60637

The membrane potential changes of rabbit papillary muscle cells (muscle diameter of about 1mm) following sudden rise and restoration of external K and Cl concentrations have been studied to determine relative permeability and conductance of Cl and K. The change in membrane potential produced by a sudden rise in K concentration was faster than the change produced by a reduction in K concentration. The potential changes were compared with those analyzed for K diffusion in the muscle and the logarithmic relation between potential and K concentration. This comparison suggested that the asymmetrical potential changes between rise and reduction in K concentration must be related to other factor(s) in addition to the K diffusion and the logarithmic relation. The potential changes produced by reduction and rise in Cl concentration were smaller and faster than those produced by changes in K concentration and were symmetrical. During the potential changes, intracellular K activities measured by K^+-selective microelectrodes were not altered. The relative permeability (P_{Cl}/P_K) and conductance (g_{Cl}/g_K) were calculated from the observed potential changes and the equilibrium potential changes of K and Cl. At normal resting membrane potential, P_{Cl}/P_K and g_{Cl}/g_K are 0.11 and 0.17 respectively. (Supported by USPHS HL 11665 and USPHS HL 05673).

RELATIONSHIP OF AGE, ANESTHESIA AND HEMATOCRIT TO CENTRAL RESPIRATORY DRIVE IN PIGLETS. John C. Lee* and S. Evans Downing, Department of Pathology, Yale University School of Medicine, New Haven, Connecticut

The present study was designed to assess central respiratory drive (CRD) in piglets. All animals were initially anesthetized with pentobarbital (25 mg/kg, ip). The arterial pressure (BP), heart rate (HR) and respiratory rate (R_f) were measured. Sensitivity of CRD was tested by sequential addition of chloralose (Ch) 6 mg/kg, iv every 2 min until permanent apnea (Ap) was produced. Before Ap occurred, R_f decreased exponentially but BP and HR were unchanged. The lethal dose (LD) of Ch increased with age. The rate of reduction of R_f, and R_f immediately preceeding Ap were significantly less in older piglets (>1 month). However, CRD was much more sensitive to Ch depression in older piglets with severe anemia (Hct<10%).

Groups	Age (days)	BW (kg)	Hct (%)	LD (mg/kg)	Rf (before Ap)
A (N=13)	1-6	1.4	24	47	14.5
B (N=11)	7-10	3.8	18	74	15.9
C (N=7)	38-112	16.3	27	109	9.1
D (N=5)	42-52	7.0	9	42	11.0

The data suggest maturational changes in sensitivity of CRD in developing piglets which may be modified by severe anemia.

EFFECTS OF AEROSOLIZED PROSTAGLANDIN E_1 ON THE PULMONARY AND SYSTEMIC CIRCULATIONS OF NEWBORN GOATS. C. W. Leffler*, T. L. Tyler*, and S. Cassin. (SPON: W. N. Stainsby). Dept. of Physiology, College of Medicine, Univ. of Florida, Gainesville, Florida 32610.

The effects of aerosolized prostaglandin E_1 (PGE_1) on pulmonary vascular resistance (PVR), mean systemic arterial pressure (SAP), and heart rate (HR) of 7 newborn goats (1-7 days) were evaluated during normoxia and hypoxia. The left pulmonary artery was cannulated and the left lung pump perfused in situ with blood from the inferior vena cava (20 ml/kg·min.). Body temperature, arterial blood pH, P_{O2}, and P_{CO2} were monitored and maintained within normal limits. Indomethacin (3 mg/kg i.a.) was injected to inhibit synthesis of endogenous prostaglandins and to produce slight pulmonary hypertension. Vehicle-control (2% ethanol in saline) and PGE_1 (11 µg/kg·min. delivered to the trachea) aerosols were administered for 10 min. periods. Animals were ventilated with 5% O_2 for 45 sec. during the tenth min. of aerosolization. PGE_1 reduced PVR 8%, SAP 16%, and HR 11% compared to vehicle-control. Hypoxia increased PVR 125% during control and 83% during PGE_1 aerosols. The decreases in SAP and HR during inhalation of aerosolized PGE_1 indicate delivery of nonmetabolized PGE_1 into the systemic circulation. PGE_1 infusion (2 µg/kg·min. for 5 min.) into the pulmonary artery, however, decreases PVR and abolishes the pulmonary pressor response to hypoxia without decreasing SAP (Tyler et al., 1975, Fed. Proc. 34:274). These results suggest that aerosolized PGE_1 enters the blood downstream from the major pulmonary vascular sites of PGE_1 activity and catabolism. (Supported in part by NIH-HL10834-06, NIH-T01-HL05979-02S1, and Heart Assoc. of Palm Beach Co. and the Cooperative Funds of the Florida Heart Assoc. and its Chapters 74-AG-2).

STUDY OF LEFT VENTRICULAR (LV) BARORECEPTORS DURING VENTRICULAR FIBRILLATION (VF). J.J. Leonard, S. Einzig, D.M. Nicoloff and I.J. Fox. Dept. of Physiology, University of Minnesota, Minneapolis, MN 55455

Reflex systemic hypotension following LV distention with blood or a fluid-filled balloon, presumably due to stimulation of mechano- or stretch receptors in the wall of the LV, has been documented. In a previous study from this laboratory (Am. J. Physiol. 227:719, 1974) an LV systolic pressure of 150 mm Hg was considered to be the threshold stimulus for this reflex. An apparent inconsistency of this study was the fact that, unlike the case of the sino-aortic baroreceptor reflex, the magnitude of the hypotensive response produced by this reflex was unrelated to the rate of pressure change, LV(dp/dt) in this case. VF was felt to permit study of the LV baroreceptors under conditions comparable to those of the sino-aortic receptors. Under chloralose anesthesia (200 mg/kg), dogs on total cardiopulmonary by-pass were pneumonectomized, catheter tips placed in RV, L. atrium, thoracic aorta and a double-lumen balloon catheter (O.D. 3.5 mm) as well as a standard 6F catheter inserted into LV via an apical stab wound. Dogs were studied successively during sinus rhythm, mean aortic pressure 77 $\pm$ 1 (SEM) mm Hg and VF, mean aortic pressure 76 $\pm$ 1 mm Hg, systemic flow being held constant at 96$\pm$3 ml/kg/min. In 10 pairs of saline balloon distentions in 4 dogs, mean wt. 28 kg, the decrease in systemic arterial pressure of 27 $\pm$ 2.1% of control during VF was comparable to that of 30 $\pm$ 3% during sinus rhythm despite the much lower LV pressure in the former, 64 $\pm$ 8 mm Hg as compared to 177/7 $\pm$ 9/2 mm Hg in the beating hearts. In 8 maneuvers in 2 dogs during VF, when the rate of balloon distention was slowed from 60 ml/sec to 3 ml/sec, the systemic pressure fall was reduced from 22% $\pm$ 2 to 13 $\pm$ 2% of control pressure ($P < 0.01$) indicating that the LV stretch receptors, just as the sino-aortic, are sensitive to rate of change in the application of the stimulus.

ALTERATIONS IN RESPONSIVENESS OF PIAL ARTERIOLES AFTER PROLONGED HYPERCAPNIA OR HYPOXIA. J.E. Levasseur*, E.P. Wei*, H.A. Kontos, and J.L. Patterson, Jr., Department of Medicine, Medical College of Virginia, Richmond, Virginia 23298

The alterations in responsiveness to CO_2 of pial arterioles, which occur after either prolonged hypercapnia or prolonged hypoxia, were studied in awake rabbits chronically implanted with acrylic cranial windows. In each animal the diameter of the same pial arteriole with resting diameter about 40μ was measured in the steady state during inhalation of 0, 3, 5, 7.5, and 10% CO_2, during a control period when the animal breathed room air and following exposure to either 10% oxygen or 8% carbon dioxide in a chamber for several days. Vessel diameter was measured using a compound microscope, image splitting device and TV camera and monitor. Following prolonged hypercapnia the responsiveness to CO_2 was reduced, while following prolonged hypoxia the responsiveness to CO_2 was enhanced. Serial determinations of the responsiveness during hypercapnia showed that the alteration in responsiveness began within 24 hours following exposure to chronic hypercapnia and was fairly complete within one week. The responses to CO_2 following prolonged hypoxia or prolonged hypercapnia were restored near normal, immediately upon replacement of the cerebrospinal fluid under the cranial window with normal artificial cerebrospinal fluid. The results show that the responsiveness of cerebral arterioles to CO_2 is significantly altered by prolonged hypercapnia or prolonged hypoxia and that this alteration in responsiveness is dependent on a chemical change in the composition of the cerebrospinal fluid in the immediate vicinity of these vessels.

INTERPERSONAL AND INTERVARIABLE DIFFERENCES IN MEAL TIMING EFFECTS UPON CIRCADIAN RHYTHMS IN PULSE, BLOOD PRESSURE AND BLOOD HORMONES OF PRESUMABLY HEALTHY VOLUNTEERS. H. Levine*, D. Lakatua*, E. Haus*, E. Halberg* and F. Halberg, Dept. of Med., New Britain Gen. Hosp., New Britain, Conn., Univ. of Conn. Health Ctr., Farmington, Conn., Dept. of Lab. Med. and Pathol., Chronobiology Lab., Minneapolis, Minn., Dept. of Anatomical & Clinical Pathol., St. Paul-Ramsey Hosp., St. Paul, Minn.

Presumably healthy subjects lived on their usual daily routine consuming a limited free-choice diet at any convenient time or as a single meal - as breakfast only and as dinner only. After 3 weeks on breakfast and 3 weeks on dinner (or vice versa) following a span of ad libitum meals, a large and statistically significant difference in temporal placement along the 24-hour scale was found for some subjects but not for others and for some variables but not for others, suggesting that the extent of rhythm shifting by meal scheduling is a characteristic of the individual and the physiologic variable involved, being large for heart rate or blood pressure of some subjects and small for the same variable of others and, in most subjects being much larger for blood glucagon and insulin as compared to blood corticosteroid. The response to a change in meal timing from breakfast to dinner or vice versa (with a cross-over design) and against the double background of 1) an ad libitum intra-individual control and 2) separate concomitant control individuals (staying on ad libitum for the entire study span) demonstrates for many persons the feasibility of manipulating by meal timing the internal time relations among circadian rhythms.
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CHEMORECEPTOR INFLUENCE ON THE REDISTRIBUTION OF PULMONARY BLOOD FLOW DURING UNILATERAL ATELECTASIS. M.G. Levitzky*, J.C. Newell*, J.A. Krasney and R.E. Dutton. Dept. Physiology, Albany Medical College, Albany, New York 12208.

We have suggested that arterial hypoxemia may interfere with the mechanism attenuating blood flow to the unilaterally atelectatic lung (Fed. Proc. 33: 447,74). This study was undertaken to determine if the arterial chemoreceptors mediate this response. Mongrel dogs, anesthetized with pentobarbital (30 mg/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 on the left pulmonary artery (Q_L) and the aorta (Q_T). Following 10 min. of bilateral 100% O_2, ventilation of the left lung was interrupted, leading to its collapse. PaO_2 was maintained above 80 mmHg when the right lung was ventilated with 100% O_2. In 6 control dogs Q_L fell from 37.4±5.8% of Q_T before collapse to 26.1±5.0% of Q_T after collapse ($p<.01$). The right lung was then ventilated with room air (the left remained collapsed), causing PaO_2 to fall to 50±3 mmHg. This was accompanied by a rise in Q_L to 36.7±6.2% of Q_T. Thus, in chemoreceptor-intact dogs, blood flow to the unilaterally atelectatic lung increased to control levels during systemic hypoxemia. In 6 chronic sinoaortic denervated dogs Q_L fell from 42.8±4.8% of Q_T on bilateral 100% O_2 ventilation to 20.8±3.3% of Q_T after the left lung was collapsed, while the right lung was maintained on 100% O_2. When room air was substituted for 100% O_2 as the gas mixture inspired by the right lung during left lung collapse, PaO_2 fell to 52±3 mmHg. In contrast to the control dogs, Q_L remained at 20.4±3.3% of Q_T. Thus, the increase in flow to atelectatic lung during systemic arterial hypoxemia may be mediated by the arterial chemoreceptors. Supported by Grants HL-12564, HL-11982 and the Heart Association of Eastern N.Y.

ANS AS A PROBE OF ATP DEPENDENT H^+/K^+ TRANSPORT OF GASTRIC MEMBRANE VESICLES. M. Lewin and G. Sachs, Laboratory of Membrane Biology, University of Alabama in Birmingham, Birmingham, Alabama 35294 and INSERM, Hopital Bichat, Paris, France.

Smooth gastric vesicles (SGV) purified from hog fundus but not antrum can accumulate H^+ and extrude K^+ with the addition of MgATP. Under identical conditions (pH 6.1, 150 mM KCl) the anion, ANS (1-anilino-8-napthosulfonic acid) was shown to bind to SGV as detected by a 50-fold increase in fluorescence and a 45 nm bathochromic shift. Addition of valinomucin (5×10^{-6}M) did not change the affinity of binding sites (1.4×10^{4} M^{-1}), doubled the number of available sites (from 7.42 n moles/mg protein to 18.28 n moles/mg). Addition of ATP (5×10^{-6}M) transiently increases the fluorescence without any evident scatter change, the kinetics corresponding closely to the transient decrease of H^+ in the medium. This effect is (1) ATP specific; ITP, UTP, ADP, acetyl phosphate, PNPP being ineffective, (2) ATPase dependent since β-γ-methylene ATP is inactive, (3) valinomycin dependent, and blocked by the addition of nigericin or CCCP, (4) cation selective $K^+ > Rb^+ > Cs^+ > Li^+ > Na^+$, (5) kinetically due to an increased affinity (3×10^{4} M^{-1}) and quantum yield of bound ANS. The data may be explained on the hypothesis that ANS detects an energized charge separation in the SGV that is ATP dependent, and is related to H^+/K^+ transport in the presence of valinomycin. (NIH, NSF support).

A TRANSPORT-RELATED CONDUCTANCE PATHWAY IN FROG SKIN AND URINARY BLADDER. S.A. Lewis*, C.J. Clausen*, and J.M. Diamond, Dept. Physiology, UCLA Medical Center, Los Angeles, Calif. 90024.

Working with rabbit urinary bladder, Lewis and Diamond (Nature 253:747 (1975)) developed a new mounting technique to eliminate edge damage, and they normalized membrane parameters to capacitance as a measure of actual membrane area. By these methods they were able to demonstrate a direct relation between short-circuit current (I_{sc}) and transepithelial conductance (G_t), arising solely from a transport-related, aldosterone-stimulated, amiloride-inhibited conductance pathway in the apical membrane. We have now found that application of these methods to two more familiar "tight epithelia", frog skin and frog bladder, yields resistances considerably higher than values reported in the literature, implying significant contributions of edge-damage conductance to published values. Na-choline replacement or amiloride treatment revealed a direct relation between G_t and I_{sc} in both of these tissues. We developed a method for calculating G_j, G_a, and G_b (conductance of junctions, apical membrane, and basolateral membrane, respectively) from this experimental $G_t - I_{sc}$ relation. The resulting estimates are: frog skin, $G_j > 65{,}000\ \Omega\text{-}\mu F$, $G_b < 5{,}000\ \Omega\text{-}\mu F$; frog bladder, $G_j > 35{,}000\ \Omega\text{-}\mu F$, $G_b < 2{,}500\ \Omega\text{-}\mu F$. In both these epithelia the change of G_t with I_{sc} appears to be due solely to change in G_a. Thus, the three tight epithelia we studied possess similar transport-related conductance pathways in the apical membrane, and also share very "tight" junctions. (Supported by grants GM 14772 and AM 17328 from the NIH.)

PREDICTION OF PHYSIOLOGICAL DEAD SPACE IN CHEST CLINIC PATIENTS USING INERT GAS WASHOUT. S. M. Lewis* and C. J. Martin, Virginia Mason Research Center, 1000 Seneca, Seattle, Wa. 98104.

Anatomical dead space (VDA) is often impossible to determine in disease with single breath techniques due to the lack of a definable alveolar plateau. We used a multiple breath technique with controlled tidal volume to define anatomical dead space. The technique requires neither an alveolar plateau nor a portion of the expirate free of dead space air, is insensitive to nonuniformities in the distribution of ventilation and gives information on the emptying pattern of dead space. VDA was 176 $\pm$ 49cc in 92 normals compared with 242 $\pm$ 67 (119-427) in 80 chest clinic patients primarily with obstructive disease. VDA increased with the severity of obstruction; the correlation with FEV1/VC was 0.45. VDA explained most patient's physiological dead space (VDP) [Mean 274+87 (122-557)]; the slope of the best fit regression line was 0.85 (R = 0.65). Most of the residual was related to differences in the tidal volumes at which the tests were run. VDP was fit to VDA and the ratio of the tidal volumes at which the tests were performed giving a multiple R of 0.81. Although VDA increased with FRC, the higher dead space in patients was also the result of an increase in VDA/FRC from 0.055 $\pm$ .016 in normals to 0.067 $\pm$ .025 in the patients. Patients also expired a higher fraction of the dead space late in the breath with a mean of 18% of the flow coming from the dead space after 2 x VDA had been expired. In a third of the patients it was impossible to compute a Fowler dead space, in the others the Fowler technique predicted a mean alveolar dead space of 116cc compared with 30cc using the washout. These results indicate that the elevated physiological dead space seen in obstructive disease is primarily due to an enlarged anatomical dead space appearing throughout the breath. (Supported by NHLI SCOR Grant HL 14152).

TRANSPANCREATIC MOVEMENT OF EXOGENOUS PANCREATIC SECRETORY ENZYMES. Charles Liebow, Department of Physiology, Cornell University Medical College, New York City, N.Y. 10021.

The recently demonstrated enteropancreatic circulation of enzyme (Liebow & Rothman, Science, In Press) requires two steps involving transepithelial movement of protein; intestinal absorption and transpancreatic movement. The latter involves absorption of enzyme from blood and resecretion by the pancreas. Absorbed enzyme enters the secretory pool (Liebow & Rothman, Am. J. Physiol., 226: 1077, 1974), but the mechanism for entry and exit from the cell has not been explored. Total enzyme concentrations in secretion are higher than in blood, suggesting the need for energy input. Exogenous ^{3}H-chymotrypsinogen (Chtg) introduced into the blood via the intestine is more than twice as concentrated in secretion as in blood. Tissue incubated for one hour in Chtg accumulated 2.68 ± 0.52SEM (n=7) times as much ^{3}H if treated with 25mM iodoacetate, suggesting either interference with the release step or enhanced uptake. Studies on initial rate of enzyme uptake indicated no significant change due to iodoacetate. Tissue was loaded with exogenous enzyme and its "re-release" examined. Re-release was compared in a normal bath, with a cholinergic stimulant (methacholine chloride) and with iodoacetate. Rates were 13, 22, and 9% release per hour respectively. Re-release is therefore blocked by a metabolic inhibitor and stimulated by a secretagogue, suggesting that part of the cellular machinery for protein secretion is used in transpancreatic movement.

Charles Liebow is a Basic Science Research Fellow for the National Cystic Fibrosis Foundation.

STIMULATION OF GASTRIC AND PANCREATIC SECRETION BY THE C-TERMINAL TRIPEPTIDE OF GASTRIN IN THE DOG. T-M. Lin, G. F. Spray* and D. C. Evans, Lilly Research Laboratories, Indianapolis, Indiana 46206

Under basal conditions the C-terminal tripeptide of gastrin, Met.Asp.Phe-NH_2 or N(t).Met.Asp.Phe-NH_2 was infused for 2-hr into the leg vein of 4 dogs with gastric fistulae. In a dose range of 50-1500 µg/kg-hr the tripeptide stimulated secretion of acid. The peak response expressed as meq/hr was a linear function of the log-dose. In comparison with the peak responses induced by the C-terminal tetra- and pentapeptides of gastrin, the values for minimal (1) and half maximal doses (2) and maximal responses (3) are as follows:

	(1) µg/kg-hr	(2) µg/kg-hr	(3) meq/hr
Met.Asp.Phe-NH_2	50	500*	11*
Try.Met.Asp.Phe-NH_2	0.125	0.4	24
Gly.Try.Met.Asp.Phe-NH_2	0.125	0.4	24

*Calculated on the basis of the maximal dose, 1500 g/kg-hr, used in this study.

There was no significant difference between the activity of the N(t)-blocked and the unblocked tripeptide on gastric secretion.

Pancreatic secretion of 3 chronic dogs was stimulated by infusion of N(t).Met.Asp.Phe-NH_2 at 50-600 µg/kg-hr and by i.v. injection of 0.1-50 µg/kg under basal conditions or during background infusion of secretin. Minimal doses (0.1 µg/kg) required for stimulation were about the same for the C-tri- and C-pentapeptides. No dose response relation could be obtained for the stimulatory action of the tripeptide on the dog pancreas.

Note: The C-terminal peptides were synthesized by Dr. G. L. Southard and associates of the Lilly Research Laboratories.

RESPIRATORY EFFECTS OF EXPOSURE TO OZONE PLUS SULFUR DIOXIDE IN EASTERN CANADIANS VS. SOUTHERN CALIFORNIANS. W. S. Linn*, M. Hazucha†, D. V. Bates, K. A. Bell*, J. G. Mohler*, D. C. Law*, and J. D. Hackney. Rancho Los Amigos Hosp./U.S.C. School of Med., Downey, CA. 90242; McGill U., Montreal; U. of British Columbia, Vancouver

Adult men were exposed to a mixture of ozone and sulfur dioxide, each at 0.37 ppm, for 2 hours with intermittent exercise at 21°C and 50% relative humidity in an environmental chamber. Exposures to purified air served as controls. Respiratory function and symptoms were evaluated during exposure. Studies were conducted in Los Angeles and compared with previous studies there and in Montreal. Typical effects of exposure were reduced expiratory flow rates, less uniform ventilation distribution, cough, and substernal discomfort. Four normal Montreal residents reacted less severely on the average than in previous Montreal studies (Hazucha et. al., Fed. Proc. 33:350, 1974), although one reacted with equal or greater severity in Los Angeles. Five Los Angeles residents, previously found to be hyperreactive to ozone, reacted more severely to the mixture than to ozone alone. Their responses were less severe on the average than those of the Montreal residents. Present findings confirm enhanced acute toxicity of the gas mixture as compared to ozone alone, and suggest greater reactivity in Montreal residents as compared to Los Angeles residents. Biological adaptation of Los Angeles residents to chronic pollutant exposure may explain the latter finding. Differences in particulate concentrations in exposure chambers or in pollutant monitoring may also contribute to differences between studies. Supported by SCOR Grant No. HL 15098, National Heart and Lung Institute, and by Canadian Thoracic Society.

BARORECEPTOR AND CHEMORECEPTOR INFLUENCE ON THE CARDIOVASCULAR RESPONSES INITIATED BY STRETCH OF THE THORACIC AORTA. F. Lioy* and P.M. Szeto* (SPON: L. Kraintz). Dept. Physiology, U. of British Columbia, Vancouver, Canada, V6T 1W5

It has been shown that stretch of the thoracic aorta (STA) in vagotomized spinal (C_1) cats induces an increase of heart rate, LVdP/dt max, and arterial pressure (F. Lioy et al. Circulation Res. 34; 78-84; 1974). In 10 vagotomized cats with intact CNS, STA induced an increase in mean arterial pressure (MAP) of 29 ± 2 mm Hg. When pressure in the isolated blood perfused carotid sinus was elevated from 103 ± 3 to 212 ± 9 the effect of STA on MAP was significantly reduced (17 ± 1) but not abolished. In 11 cats constant pressure perfusion of the carotid sinus with hypoxic blood increased MAP from 117 ± 4 to 140 ± 5, and significantly reduced the STA pressor effect from 32 ± 4 to 20 ± 4. When a similar level of MAP (143 ± 10) was obtained in 5 cats by norepinephrine infusion, the STA effect was reduced from 23 ± 2 to 17 ± 2 ($P < .01$). At least part of the chemoreceptor inhibitory effect on the STA reflex could therefore be due to the higher MAP present before the stretch. The experiments show that this spinal cardiovascular reflex is at least partially under the inhibitory influence of supraspinal structures. (Supported by the British Columbia Heart Foundation).

IN VIVO STUDIES OF RHEOLOGY AND MECHANICS OF BLOOD FLOW IN MICROCIRCULATION OF CAT MESENTERY. H.H. Lipowsky* and B.W. Zweifach, Dept. AMES-Bioengineering, Univ. of Calif., San Diego, La Jolla, California 92037

Simultaneous measurements of pressure gradient and red blood cell velocity in single unbranched vessels of the intestinal mesentery were made for vessels ranging in diameter from 7 to 58μm by the techniques associated with intravital microscopy. Upstream to downstream pressure differentials from 0.1 to 5cmH_2O were measured for arterial and venous microvessels varying in length from 20 to 30 vessel diameters. Pressure gradients, apparent viscosity, vessel wall shear stress and intravascular hemodynamic resistance were determined in the successive functional segments of the mesenteric microcirculation. These dynamical parameters were found to vary spatially throughout the network and also as a function of vessel hematocrit, which ranged from 8 percent in vessels from 7 to 15μm diameter to an average systemic hematocrit of 35 percent in vessels outside the microcirculation proper. Pressure gradients averaged 0.0008cmH_2O/μm for arterial vessels from 10 to 58μm; attained a maximum of 0.026cmH_2O/μm in the "true capillaries" (7μm diameter); and averaged 0.004cmH_2O/μm in venous vessels from 10 to 58μm diameter. Apparent viscosity averaged 3.3 centipoise in these arterial vessels and increased to an average of 5.0 centipoise in venous vessels. Wall shear stresses averaged 47 dynes/cm^2 in the arterial vessels, fell to approximately 30 dynes/cm^2 in the"true capillaries," and 26 dynes/cm^2 in the venous microvessels. Wall shear stresses as high as 200 dynes/cm^2 were measured in rapidly flowing arterioles. Intravascular resistance was computed to be 0.08 x 10^3 mmHg/(mm^3/sec) in arterial vessels from 50 to 58μm in diameter, rose to a maximum of 350x10^3mmHg/(mm^3/sec) in 7μm capillaries, and decreased to 0.1x10^3 mmHg/(mm^3/sec) in venous vessels ranging from 50 to 58μm diameter.

(Supported by Training Grant USPHS HL05946.)

CONTRACTION SEQUENCES WITHIN THE CANINE LEFT VENTRICLE. D. B. Lippincott and W. C. Randall. Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

The sequence of muscle segment contraction within the canine left ventricle was studied using Walton-Brodie strain gauge arches. Strain gauge arches were sutured to the following epicardial muscle segments: anterior, lateral base, lateral apex and posterior. With the dog on cardiopulmonary bypass, strain gauges were also sutured to the following left ventricular endocardial muscle segments: septal base, septal apex, free wall apex, and free wall base. A lead II ECG was recorded and the onset of the R-wave was used as the reference point for measurement of the time intervals to the onset of electrical and contractile activity in the respective muscle segments. The anterior (37.0 msec), posterior (35.9 msec) and septal apex (36.9 msec) muscle segments were the first to contract following the R-wave. The remaining muscle test segments followed in this order: lateral base (50.0 msec), free wall base (51.0 msec), lateral apex (52.4 msec), septal base (56.0 msec) and free wall apex (57.0 msec). With the exception of the septal apex, no endocardial muscle segment began to contract before the epicardial muscle segments. Stimulation of the left stellate or right stellate ganglions decreased the time interval to the onset of contraction but did not alter the sequence, thus resulting in more synchronous activation and contraction of the total left ventricular myocardium.

(Supported by NHLI/NIH Grant HL 08682.)

INFLUENCE OF MAGNESIUM ON CALCIUM BINDING TO ARTERIAL ACTOMYOSIN. R.Z. Litten*, R.J. Solaro* and G.D. Ford*.(Spon: S.Price). Dept. Physiology, Medical College of Virginia, Richmond, Virginia 23298

The sensitivity of either glycerinated vascular smooth muscle or arterial actomyosin to trace amounts of calcium requires the presence of approximately 10 mM magnesium. We have investigated the possibility that this requirement of high magnesium reflects an influence on the binding of activator calcium to the contractile proteins. A calcium-sensitive actomyosin was prepared from bovine aorta by a modification of the method of Sparrow, et al. (Am.J.Physiol. 219:1366 (1970)). Calcium binding was measured at a constant ionic strength (0.1M) and pH (7.0) by a centrifugal method using ^{45}Ca with ^{3}H-glucose used to determine supernatant space in the pellet. There was no difference in calcium binding in the presence and absence of 3 mM MgATP at a constant free magnesium. Calcium binding in the presence of 1 mM free magnesium went from 0.14 nmoles Ca^{2+}/mg protein at 1.4 x 10^{-6}M calcium to 1.61 nmoles Ca^{2+}/mg protein at 5.4 x 10^{-4}M calcium while the actomyosin ATPase remained constant at approximately 3 μmoles Pi/mg protein,min over the same range of calcium concentrations. In the presence of 7 mM free magnesium, calcium binding went from 0.14 nmoles Ca^{2+}/mg protein at 1.4 x 10^{-6}M calcium to 0.82 nmoles Ca^{2+}/mg protein at 5.7 x 10^{-4}M calcium while the actomyosin ATPase went from 2 μmoles Pi/mg,min to 11 μmoles Pi/mg,min over the same range of calcium concentrations. From these results we conclude that there is no simple relation between the calcium binding to arterial actomyosin and the requirement for high magnesium to have calcium-sensitive ATPase activity.
(Supported by grant no. HL-15829 from NHLI to GDF and by grant no. 74865 from the American Heart Assoc. to RJS.)

EFFECT OF STAPHYLOCOCCAL ENTEROTOXIN B (SEB) ON BODY FLUID COMPARTMENTS IN CONSCIOUS RHESUS MONKEYS. C.T. Liu, M.J. Griffin* and R.T. Faulkner*. USA Med. Res. Inst. Infectious Dis., Fort Detrick, MD 21701

Various body fluid volumes were determined in control and SEB-intoxicated rhesus monkeys (1 mg/kg, iv, a lethal dose). Evans blue, thiocyanate, ^{51}Cr-labeled RBC, and $^{3}H_2O$ were used as indicators. Significant changes were observed 5 hr after injection of SEB:

Parameter (cc/kg)	Control (n=17)	5 hr post SEB (n=10)	Parameter (cc/kg)	Control (n=17)	5 hr post SEB (n=10)
Plasma volume	49.2 ±1.5	41.2 ±0.6*	Extracellular water	296 ± 9	235 ±16*
Blood volume	60.7 ±1.8	48.6 ±2.0*	Interstitial water	248 ± 9	200 ±17*
RBC volume	24.2 ±1.2	22.3 ±1.2	Intracellular water†	396 ±16	314 ±18*
Total body water†	685 ±11	545 ±21*	F cell ratio	0.91 ±0.01	0.85 ±0.02*

*Statistically significant ($P < 0.05$). †Control n=6.

Since all fluid volume compartments except RBC were decreased, a primary dehydration was demonstrated in the SEB-intoxicated monkey. The mechanisms of SEB-induced dehydration may be the result of decreased water intake, hyperventilation, vomition, diarrhea, gut fluid accumulation, and renal loss of solute-free water (Fed. Proc. 34: 364, 1975). The lowered F cell ratios support the findings that dehydration and vasoconstriction (Fed. Proc. 34: 225, 1975) were present in monkeys following iv SEB administration. Further, the reduction of plasma and blood volume may play a role in the development of shock.

OPTIMAL CONTROL EVALUATION OF LEFT VENTRICULAR EJECTION. A. Livnat*, J.A. Daubenspeck*, F. Bennett*, S. Edelman* and S.M. Yamashiro, Biomedical Engineering Laboratories, USC, Los Angeles, CA 90007

The basic question we are asking is: what is the optimal left ventricular ejection pattern which minimizes the total power required for a given level of cardiac output and how does the normal pattern compare to the optimal one? Based on a 4 element left ventricular load model (blood inertance, characteristic resistance, arterial compliance, and peripheral resistance), we have derived the theoretical aortic root flow pulse which minimizes this criterion function. The method of solution employed was the calculus of variations. Aortic root flow pulses measured in anesthetized dogs (nembutal or chloralose) under control conditions compare closely with theoretical predictions. However, theory and observation appear to diverge for conditions of load change (a-v fistulae, aortic constriction, and hypoxia). This suggests that either the anesthetized dog cannot adapt optimally to a load change or the time required for adaptation is longer than allowed in this study. (Supported by grant P3K1739-000 from NSF.)

ROLE OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN RABBITS WITH EXPERIMENTAL ASCITES. T.E. Lohmeier*, J.O. Davis, R.C. Hanson*, and G.M. WILLIAMS*. Dept. Physiology, University of Missouri, Columbia, Mo. 65201

Rabbits were studied during the formation of ascites secondary to constriction of the thoracic inferior vena cava. Following caval constriction hepatomegaly, ascites formation, and sodium retention ensued. Three days after caval constriction marked sodium retention was still present in eight animals studied and hematocrit (32±1%) was significantly less ($P<0.01$) than in control animals (39±2%). In seven of these animals arterial pressure (AP) and plasma renin activity (PRA) averaged 96±3 mmHg and 7.0±0.6 ng angiotensin/ml plasma, respectively, and these values were similar to control levels. PRA was very high (61 ng angiotensin/ml plasma) in one animal with an AP of 44 mmHg. In spite of normal levels of PRA in these seven animals, aldosterone secretion (AS) was markedly elevated in two of three rabbits analyzed thus far. Infusion of the angiotensin II antagonist 1-sar-8-ala-angiotensin II (P-113) at 6 µg/kg/min in these seven animals with normal levels of PRA had no effect on AP or AS. Nine additional rabbits were studied 10-24 days after caval constriction. At this time six of the nine animals were in sodium balance and had normal values for AP, PRA, AS, and hematocrit. In contrast to these six rabbits, three animals were still retaining sodium chronically and AS was enhanced. However, PRA was elevated (15.1 ng/angiotensin/ml plasma) only in one rabbit with a low AP (64 mmHg). P-113 infusion did not alter AP or AS in these chronic animals with normal levels of PRA. These studies give no indication of involvement of the renin-angiotensin system in this experimental syndrome unless arterial pressure is unusually low.

UPTAKE AND ELIMINATION OF CARBON MONOXIDE IN THE PREGNANT EWE AND FETUS. Lawrence D. Longo, Sylvia A. Hixson* and Tom R. Bennett*. Depts. Physiology and Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, Calif. 92354

While the relation of carboxyhemoglobin, [HbCO], to inspired CO, has been defined for adult mammals, the relation of HbCO in the fetus, [$HbCO_f$], to that of the mother, [$HbCO_m$], and inspired CO concentrations has not been described. We studied these relations in pregnant sheep with catheters chronically implanted in maternal and fetal blood vessels. Ewes were exposed to varying inspired CO concentrations. At 30 parts per million (ppm), [$HbCO_m$] increased from baseline levels of about 0.75% to about 5% over a course of 8-10 hours. [$HbCO_f$] increased more slowly from baseline of 1.5%, reaching [$HbCO_m$] by 9-10 hours, then increasing to steady state values of 6.5% by 36-48 hrs. At 50 ppm the time courses were similar with steady state [$HbCO_m$] = 7.9% and [$HbCO_f$] = 10.1%. Steady state values for 100 ppm were [$HbCO_m$] = 15.6 and [$HbCO_f$] = 19.4. Maternal HbCO levels resembled a simple exponential process with a half time of 2.5 hours. The time for fetal HbCO to reach half its final value was 7.5 hr. The decay curves for CO elimination showed similar relations, with washout in the fetus being a much slower process than that in the mother. In conclusion, fetal uptake and elimination of CO is relatively slow compared with that of the mother; and during steady state conditions in sheep [$HbCO_f$] is about 25% greater than [$HbCO_m$]. (Supported in part by USPHS Grant HD 03807).

AN EVALUATION OF CA^{++} AND MG^{++} ALTERATIONS IN ACUTE EXPERIMENTAL TRAUMATIC SHOCK. L.D. Loose. Institute of Exptl. Pathol. & Toxicol., Albany Medical College, Albany, N.Y. 12208.

Anesthetized (Nembutal, 2 mg/100 g) male Sprague Dawley rats (250-350g) exposed to Noble-Collip drum trauma manifested significant increases in serum calcium and magnesium. Serum magnesium, as determined by atomic absorption spectroscopy, had a positive correlation with the degree of drum trauma. A significant increase in serum calcium, from a control value of 10.5 mg% to an elevated level of 12 mg%, was not manifested until drum trauma mortality reached 20%. At a drum trauma mortality of 55% serum magnesium was >5 mg%, a 2-fold increase over control values of 2.5 mg%, and serum calcium levels reached 13 mg%. Rats pretreated with $MgSO_4 \cdot 7H_2O$ (16.6 mg/100g) ip 15 min prior to drum trauma demonstrated zero mortality. Serum magnesium levels in the $MgSO_4 \cdot 7H_2O$ pretreated rats exposed to drum trauma ranged from a high of 9.3 mg% to a low of 6.7 mg% whereas control animals pretreated with $MgSO_4$ but not exposed to drum trauma had serum magnesium levels of 3.8 mg%. The serum calcium in $MgSO_4$ pretreated rats exposed to drum trauma ranged from a high of 12.4 mg% to a low of 9.0 mg%, control values of 10.5 mg% were consistent with the normal physiologic calcium levels in the rat. Thyroparathyroidectomized rats exposed to drum trauma had reduced calcium levels but normal serum magnesium concentrations. It is postulated that acute hypercalcemia may act as a mediator in the release of vasoactive amines.
(Supported in part by NIH Grant No. 7Rol AI 12839-01 and 2 POl - ES0026-08).

EFFECT OF SODIUM DEFICIENCY AND CATECHOLAMINES ON RENIN RELEASE IN VITRO. Genaro A. Lopez*, Ian A. Reid and William F. Ganong, Dept. of Physiology, University of California, San Francisco, CA. 94143

The aim of this study was to investigate the effect of dietary sodium (Na) restriction on the renin response to norepinephrine (NE) in vitro. Male rats weighing 210±10 g were fed high Na (>2.2 mEq/day) or low Na (<0.02 mEq/day) diets for 1, 2.5 or 3.5 weeks. Following decapitation, paired kidney slices weighing 70±20 mg were cut and incubated for 1 hr in Robinson's medium. One of each pair was incubated with NE; the other served as a control. The rate of renin release was measured using an immunoassay for angiotensin I (AI) and expressed as ng AI/mg tissue/hr. The results are summarized below:

		1 week	2.5 weeks	3.5 weeks
High Na	Control	5.4±0.5	3.6±0.3	5.7±0.5
	NE ($2X10^{-5}M$)	5.5±0.5	3.2±0.4	5.8±0.3
	Control	5.2±0.6	4.0±0.5	8.0±0.7
	NE ($2X10^{-7}M$)	7.9±0.7*	5.0±0.6*	9.3±0.8*
Low Na	Control	7.8±0.8	10.5±2.3	13.9±1.0
	NE ($2X10^{-5}M$)	8.5±0.9*	13.7±2.3*	15.4±1.2*
	Control	8.0±0.7	13.8±3.4	16.8±1.6
	NE ($2X10^{-7}M$)	10.2±0.9*	21.1±5.9*	23.1±2.8*

*$p<0.05$ vs. control

In the low Na group, the control values and the responses to NE were greater ($p<0.05$) than in the high Na group. Thus the data show that kidneys from Na-deficient rats release more renin in vitro than do kidneys from Na-replete rats, both under basal conditions and following stimulation by NE. The lesser effectiveness of the high dose of NE in stimulating renin release suggests that this catecholamine may have an inhibitory as well as an excitatory action.

CLOSING VOLUME MANEUVERS IN SMOKING DOGS. S. M. Loscutoff and J. R. Decker*, Battelle Pacific Northwest Laboratories, P.O. Box 999, Richland, WA 99352

Detection of early pulmonary abnormalities in dogs is complicated by the extensive collateral ventilation in this species. Closing volume maneuvers using the nitrogen technique were performed on 20 anesthetized beagle dogs as a possible method for evaluating functional changes associated with 5 months exposure to cigarette smoke. Dogs were tested in the prone position and with the body elevated at 30° and 60° from horizontal. Closing volumes were approximately 20% of vital capacity in both smoking and non-smoking dogs and were not affected by the angle of the dog. Closing volumes measured at 60° showed a sharper break between Phase III and IV than tests performed in other positions. The slope of Phase III, measured during the closing volume maneuver, showed the greatest difference between smoking and non-smoking dogs. In 8 non-smokers, the slope of Phase III varied between 0.5 and 1.0% N_2/liter compared with the slopes of 1.0 to 6.5% N_2/liter in 12 smoking dogs. This difference in the slope of Phase III is the most striking functional effect we have observed in dogs smoking cigarettes for 5 months.

(Supported by NCI Contract NO1-CP-43315).

S. M. Loscutoff, previously S. M. Carlson.

PATTERN OF LH RELEASE AFTER REPEATED STIMULATION BY SYNTHETIC LRF IN FEMALE RATS DURING THE ESTROUS CYCLE. K.H. Lu*, H.T. Chen* and J. Meites. Dept. of Physiology, Michigan State University, East Lansing, Michigan 48824.

Normal cycling female rats were given 5 consecutive sc injections of synthetic LRF (100, 50, 50, 50, 50 ng/100 g body wt), each 30 min apart, and sequential blood samples were assayed for LH. The 2nd and/or 3rd injections of LRF produced much greater increases in serum LH than the 1st injection in rats on proestrus, diestrus I and II, but not on estrus. Rats on proestrus showed the greatest increases in serum LH after the 1st, 2nd and 3rd injections of LRF, but LH release declined progressively after the 4th injection. The latter is believed to be due to a decrease in releasable LH in the pituitary. Rats on diestrus II showed less LH response than on proestrus, but more than on diestrus I. Rats on estrus showed a rise in serum LH only in response to the 1st injection of LRF, but failed to respond further to subsequent injections. These results indicate (1) the initial injection of LRF increased LH in the pituitary releasable by subsequent LRF stimulation (2) in rats on the late afternoon of proestrus, the fall in LH release immediately after the proestrous surge is due primarily to depletion of releasable LH in the pituitary (3) estrous rats have only a small releasable pool of LH in the pituitary (Supported in part by NIH grants AM 04784 and CA 10771).

PROTEIN METABOLISM IN THE BLACK BEAR BEFORE AND DURING HIBERNATION. David A. Lundberg*, Ralph A. Nelson and Heinz W. Wahner*. Mayo Medical School, and Mayo Clinic and Mayo Foundation, Rochester, MN 55901

During 3 to 5 months of hibernation, the American black bear (Eursus Americanus) does not defecate, urinate, eat or drink. The bear loses 15 to 25% of its total body weight but no significant change in lean body mass occurs. In hibernation there is no net accumulation of nitrogenous end products of protein catabolism and the turnover rate of blood urea decreases considerably. This study was done to determine if protein metabolism also slows during hibernation. The disappearance rate of ^{125}I-labeled black bear serum albumin from serum was measured for two weeks before and during hibernation. Determinations of total body weight, total body water, hematocrit, serum albumin concentration, thyroxine, triiodothyronine, and thyroid binding globulin were also done before and during hibernation. It was found that a 3- to 5-fold increase in the rate of albumin disappearance occurred in hibernation when contrasted with studies done before hibernation. A 9 to 12% decrease in total body weight occurred but no significant change in lean body mass was noted. No significant change in serum albumin concentration, thyroxine, triiodothyronine, or thyroid binding globulin between the active and hibernating periods was found. Hematocrit increased slightly in hibernation. The study, therefore, did not support the hypothesis that protein metabolism decreases in hibernation as does urea metabolism. On the contrary, evidence so far indicates protein metabolism may be increased.
(Supported by Northwest Area Foundation grant 8469.)

CURRENT-VOLTAGE RELATIONSHIP OF FROG GASTRIC MUCOSA DURING CONTROL AND ANOXIC CONDITIONS. T. E. Machen* and J. G. Forte, Dept. Physiology-Anatomy, U.C., Berkeley, Ca. 94720.

The I-V relation was measured in HCO_3^- buffered solution and 95% O_2 -5% CO_2. 500 msec current pulses (0 - 285 $\mu A/cm^2$) were passed from the mucosal (m) to serosal (s) sides (I_{ms}) and in the opposite direction (I_{sm}). The resulting V was measured at each step. Histamine-stimulated mucosae gave nearly linear I-V over the entire I range. The slopes gave an average resistance (R, in $\Omega \cdot cm^2$) of 125 ±18. Anoxia caused a shift in the I-V. This relation was nearly linear when passing I_{ms} from ~ 50 to 285 $\mu A/cm^2$; R increased slowly with time to 534 ±106. When pd_0 reversed, m positive, the I-V slope I_{ms} >50 $\mu A/cm^2$ was much reduced, yielding R = 221 ±34. I-V of these mucosae thus had two essentially linear regions of different slopes with a transition between them occurring between ±50 $\mu A/cm^2$. 2-5 mM Ba^{++} to the s solution in O_2 caused an increased slope (R ≈ 289) but did not markedly alter linearity, while after N_2 Ba^{++} had only minimal effect on R; the "3-slope" I-V plot was not changed. After H^+ secretion was stopped by burimamide, I-V curves were nearly linear with R = 317 ±142. Anoxia caused pd_0 to decrease but not to invert. However, the I-V curve showed a break similar to that observed during the histamine stimulation with inverted pd_0. I_{ms} = 50 to 285 $\mu A/cm^2$ gave nearly linear I-V; R=565 ±248. I_{sm} (same range) was also linear: R=317 ±73. Thus, anoxia increased R in both histamine- and burimamide-treated mucosae, and the I-V of both exhibited similar linear regions at I>50 $\mu A/cm^2$. Increased R in N_2 is probably partially due to obliteration of the lateral intercellular spaces (J. Cell Biol. 59: 210a, 1973). After N_2, Ba^{++} has no effect on R. The apparent K^+ permeability of the s membrane has thus decreased during anoxia. (Supported by grant AM 10141 from NIH).

CHANGES IN LIVER AND MUSCLE TEMPERATURE IN THE RAT WITH INTRAVENTRICULAR ADMINISTRATION OF 2-DEOXY-D-GLUCOSE (2-DG). M. Mager*, C. Kelly and S. Robinson. U. S. Army Res. Instit. of Environ. Med., Natick, MA 01760

We have previously reported that in mice and man hypoglycemia elicits marked hypothermia; this response is probably the result of decreased heat production rather than enhanced heat loss to the environment. While central glucopenia rather than a lack of peripheral substrate effects this hypothermic response, the specific site of decreased heat production is unknown. This study was done in the rat, so that alterations in temperature could be monitored at specific organ sites. Chronic cannulae were implanted in the lateral cerebral ventricle for drug administration. For measurement of liver and shoulder muscle temperature, chronic copper-constantan thermocouples were surgically glued to appropriate sites. Subsequent experiments were carried out in unanesthetized rats. At 22°C, intraventricular (i.v.t.) doses of 4,8 and 12 mg of 2-DG produced within 1 hour nadir reductions in rectal temperature of 0.9, 1.8 and 2.3°C, respectively, with corresponding elevations of blood glucose of 20, 85 and 130 mg%. The same doses of 2-DG injected i.p. did not alter rectal temperature. In contrast to saline, 8 mg of 2-DG i.v.t. in rats with thermocouples resulted in parallel drops in rectal, liver and muscle temperatures, with no change in tail temperature. At 15°C, i.v.t. saline resulted in significant increases in liver and muscle temperatures; however, 2-DG animals (8 mg) reacted as if they were in a normothermic environment, i.e. exhibited significant decreases in the monitored tissues. This pattern of responses at 22 and 15°C after i.v.t. 2-DG indicates a disruption of normal thermoregulatory processes and a generalized decreased heat production at various sites in the body.

DIFFUSION AND CONSUMPTION OF OXYGEN IN THE RESTING FROG SARTORIUS. Michael Mahler* (SPON: E. Homsher). Dept. Physiol. UCLA,LA,CA 90024.

The validity of the one-dimensional diffusion equation for O_2 ($D(\partial^2C/\partial x^2) = (\partial C/\partial t) + Q$, where $C \equiv [O_2]$, $D \equiv$ diffusion constant for O_2, and $Q \equiv$ rate of O_2 consumption) was tested in the resting frog sartorius at 23°, 10°, and 0°C by an adaptation of the method of Takahashi et al (J. Gen. Physiol. 50:317 (1966)), in which $[O_2]$ at the muscle surface was monitored by a microelectrode. Transients in the muscle $[O_2]$ profile were induced by two methods: I. Following an equilibration period, the lower surface was sealed off by a disc in which the O_2 electrode was embedded; II. When $[O_2]$ at this surface reached steady state, a step change was made in the $[O_2]$ of the gas phase above the muscle. With either method, agreement between the measured C(0,t) and that predicted by the diffusion equation was excellent, and D and Q could thus be calculated. Methods I and II yielded statistically indistinguishable results; the pooled data had the following means (± SEM):

T(°C)	n	$Dx10^4$(cm²/min)	Q_{10}	n	Q (µl/g-min)	Q_{10}
22.8	13	8.59 (± 0.36)	>1.28	10	0.507 (± 0.045)	>2.06
10	11	6.28 (± 0.28)	>1.25	12	0.201 (± 0.022)	>4.40
0	19	5.03 (± 0.17)		14	0.046 (± 0.003)	

At each temperature (T), D was independent of muscle thickness (range, 670-1340µ). Together with established values for D in H_2O, the present data implies that $(D(muscle)/D(H_2O)) = 0.57$, independent of T; this is in excellent agreement with the relative values of 0.51-0.61 recently observed for six other diffusing species (reviewed by Caillé & Hinke, Canad. J. Physiol. Pharmacol. 52:814 (1974)). Apparently, the classical values for D in muscle are in need of revision.

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EFFECTS OF SODIUM PENTOBARBITAL ANESTHESIA ON LEFT VENTRICULAR FUNCTION AND DISTRIBUTION OF REGIONAL BLOOD FLOW. W. Thomas Manders* and Stephen F. Vatner. Dept. Med., Harvard Medical School and Peter Bent Brigham Hospital. Boston, Ma. 02115.

Sodium pentobarbital, a commonly used anesthetic for cardiovascular studies, has been evaluated extensively on individual aspects of cardiovascular function. To obtain a more comprehensive picture of the entire spectrum of cardiovascular effects induced by pentobarbital Na, 30 dogs were instrumented with electromagnetic and Doppler flow probes around the ascending aorta, coronary, mesenteric, renal and iliac arteries, arterial pressure catheters, left ventricular(LV) pressure gauges, and LV endocardial diameter transducers. Two weeks to two months after recovery from operation LV pressure, LV diameter, dP/dt/P, dD/dt, i.e., the velocity of myocardial fiber shortening, cardiac output, arterial pressure, coronary, mesenteric, renal and iliac blood flows were recorded in conscious dogs at rest and continuously for 30 minutes after induction of anesthesia with sodium pentobarbital, 30 mg/kg, i.v. After anesthesia, ventilation was controlled to maintain arterial blood gases at control levels in the conscious state. Induction of anesthesia altered every aspect of cardiovascular function substantially, but by 15 min, cardiac output, arterial pressure and coronary flow were not significantly different from control, while iliac flow rose by 32% and mesenteric and renal flows fell by 18% and 10% respectively. At this time, LV function was severely depressed, as evidenced by reductions in stroke volume 37%, dP/dt/P 41% and velocity 33%. Thus, pentobarbital Na does not affect arterial pressure and cardiac output substantially and produces a modest redistribution of blood flow from the mesenteric and renal beds to the iliac bed, while its major cardiovascular action is to depress myocardial contractility.

STUDIES OF POLYAMINE METABOLISM IN PRO/Re MUTANT MICE. C.-A. Manen*, D.H. Russell and R.L. Blake*, University of Arizona Medical Center, Department of Pharmacology, Tucson, Arizona 85724; and The Jackson Laboratory, Bar Harbor, Maine 04609.

Preliminary studies indicate that pro/re mutant mice excrete elevated levels of polyamines in their urines. Male PRO/Re mutants excrete twice as much putrescine and spermidine as their litter mate controls. Both mutant and control female mice excrete approximately equal amounts of putrescine and spermidine. Ornithine decarboxylase activity, the enzyme which forms putrescine, was significantly elevated in the kidney cortex of the male mutant. The resulting increase in putrescine synthesis in the kidney of the mutant male is probably responsible for the elevated levels of both putrescine and spermidine excreted in the urine since putrescine stimulates S-adenosyl-L-methionine decarboxylase to form spermidine. Both putrescine- and spermidine-stimulated S-adenosyl-L-methionine decarboxylase activities were slightly lower in the male mutant mice than the control mice. Analysis of the polyamine concentrations indicated the mutants have twice as much spermidine and spermine as the controls. There was no difference in the putrescine concentrations. It appears that the elevated levels of putrescine and spermidine excreted in the urine of pro/re mutant mice is due to a metabolic disorder affecting ornithine decarboxylase activity in the cortex of the kidney, and this resulting overproduction of putrescine stimulates the overproduction of spermidine, resulting in the excretion of both these polyamines.

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CALCIUM HANDLING BY THE MICROSOMAL FRACTION OF AORTA FROM THE HYPERTENSIVE RABBIT. Eric L. Mangelsen* and David F. Bohr. Dept. Physiology, Univ. of Michigan, Ann Arbor, MI 48104. (Spon: L. T. Rutledge)

The calcium sequestering ability of microsomes from vascular smooth muscles of hypertensive animals was evaluated. Male albino rabbits were made hypertensive by placing a silver block, 5 mm slit width, on the left renal artery and removal of the right kidney. Arterial systolic pressure for normotensive animals was 82 $\pm$ 1.0, that for hypertensive animals was 117 $\pm$ 3.4 (SEM) mm Hg. The thoracic aorta was homogenized and the 100,000 g microsomal fraction was obtained. This fraction was incubated for 30 min in a medium containing 100 mM KCl, 30 mM Imidazole-histidine buffer pH 6.8, 5 mM ATP, 5 mM K oxalate, 5 mM Na azide, and 20 μM $CaCl_2$ with 1 μCi/ml $^{45}CaCl_2$. A small aliquot of this calcium-loaded protein was diluted 20:1 with an identical but calcium-free medium. Efflux of Ca^{++} was followed for 40 min. Calcium uptake for the normotensive animals was 133.7 $\pm$ 4.4, for the hypertensive, 97.4 $\pm$ 9.9 (SEM) nmole calcium/mg protein (n = 4). Uptake for the hypertensive animals was 27%, $p<.025$ less than normal. Efflux was 0.0494 $\pm$ 0.0024 for the normotensive animals and 0.0540 $\pm$ 0.027 (SEM) %/min (n = 4) for the hypertensive animals. These two rates of efflux were not significantly different. The increased vascular reactivity of hypertension may be due to an increased amount of activator calcium made available to the contractile machinery by the decreased rate of sequestration of the calcium released during stimulation. Our results suggest that the defect is in the ATP-dependent sequestration of activator calcium. The slow release phase may remain unchanged.
(Supported by grant HL-03756 from NIH.)

ENERGETICS OF "CAFFEINED" ISOMETRIC TETANUS IN RAT HEART MUSCLE. J.W. Manning, Y. Matsumoto and S.J. Putnam, Dept. Physiology, Emory Univ., Atlanta, Georgia 30322

It is well known that myocardium is unique among muscles, in that, it contracts with a pulsatile force and normally it cannot be tetanized; due, among other reasons, to the nature of electro-chemical coupling. The concern of this study was to examine the isometric tetanus of the caffeine treated,rat papillary, by comparing the normal twitch to the artifically induced tetanus. Concomitantly with the isometric measurements, heat production was monitored so that an estimate of the enthalpic change could be made. These measurements were analyzed to compare the energetic cost of maintaining active tension and that expended during developed pulsatile force. A pair of papillary muscles from the left ventricle of Sprague Dawley Rat was isolated and mounted on a constructed thermopile. The preparation was immersed in modified K-H solution with Hepe as buffer at pH 7.4 and aerated in O_2. Before an experimental run, the muscles were stimulated as soon as isolation was complete at a frequency of 0.2/sec for at least 2 hrs at 25° C until steady reproducible twitches were observed. In all cases, the twitch tension with 2.5 mM caffeine showed reduction in the peak tension and a significant increase in relaxation time. During a caffeine induced tetanus (stim.freq. 1 to 3/s), the rate of heat production was greater than the "non-caffeinated" muscle stimulated at the same frequency. The ratio of twitch w.o. caffeine to tetanus w. caffeine was never less than 1. Our study suggests the muscle, developing isometric tetanic force, is expending more energy than system contracting w.o. caffeine at the same frequency of stimulation. (Sponsored in part by McCandless Fund Grant, Emory Univ.)

EXPERIMENTAL HYPERTENSION--A MODEL WITH EXPANDED FLUID VOLUMES AND HYPONATREMIA. R.D. Manning, Jr.*, T.G. Coleman, R.E. McCaa, and A.C. Guyton, Dept. Physiol. & Biophy., Univ.Miss.Sch.Med., Jackson, MS 39216

Experimental hypertension was produced in subtotally nephrectomized dogs by continuous intravenous infusion of hypotonic saline and Pitressin(ADH). The objective was to demonstrate that fluid volume loading would cause hypertension in spite of a fall in plasma sodium concentration. Also studied was the effect of chronic hyponatremia and concomitant increased fluid volumes on plasma renin activity and plasma aldosterone concentration. Four dogs previously had renal mass surgically reduced to 30% normal and were equipped with chronic catheters in the aorta and right atrium. A two week infusion of hypotonic saline(100 mEq/l) at 117 ml/kg/day and ADH at 0.067 ml/kg/day followed an 8 day baseline period. Arterial pressure was elevated during the entire infusion period and reached a final value of 138.7% baseline. Plasma sodium concentration decreased from a baseline value of 144.5 mEq/l to an average value of 126.6 mEq/l during the infusion period. Fluid volume expansion was evidenced by an increase in blood volume from 84.4 ml/kg to an average value of 104.7 ml/kg during the infusion period and an increase in sodium space from 321.9 ml/kg to an average value of 454.0 ml/kg. Both blood volume and sodium space remained elevated throughout the infusion period. Fluid loading resulted in a decrease in plasma renin activity from 0.71 ng/ml/hr to an undetectable concentration after the 2nd day of infusion, while plasma aldosterone concentration was slightly depressed from its baseline concentration during the infusion. These data show that fluid volume expansion results in hypertension even in the face of a decreased plasma sodium concentration. Plasma renin activity was apparently depressed from the expanded fluid volumes, a state which masked any effect of chronic hyponatremia on aldosterone concentration. Supported by NIH grant HL 11678.

A COMPARISON OF THE PROXIMAL TUBULAR FLUID/ULTRAFILTRATE (TF/UF) CHLORIDE CONCENTRATION IN THE RAT AND DOG. G.R. Marchand*, C.E. Ott, J.L. Cuche*, and F.G. Knox, Dept. of Physiol., Mayo Clinic, Rochester MN. 55901.

Previous studies in rats have demonstrated that the concentration of chloride in the proximal tubule fluid is greater than in plasma which has been corrected for plasma water and/or the Donnan effect. Measurements of proximal (TF/P) bicarbonate in dogs suggest that the (TF/UF) Cl may be significantly lower than in the rat, however no direct measurements of TF/UF chloride have been obtained in the dog. This study was done to simultaneously determine and compare the TF/UF chloride concentration in hydropenic rats and dogs. An ultrafiltrate of plasma was obtained by centrifugation through an Amicon membrane. The chloride concentration of TF and UF was determined by electrometric titration.

Mean ± SE

	GFR (ml/min)	SNGFR (nl/min)	TF/P_{In}	$\overline{TF}_{Cl}$ (mEq/L)	UF_{Cl} (mEq/L)	TF/UF_{Cl}	Blood pH
RAT	1.03±.13	29.8±6.7	2.40±.22	139±1.4	120±1.2	1.17±.02	7.38±.02
(N)	9	10	10	10	10	10	10
DOG	45.9±5.3	59.3±6.5	1.34±.04	143±3.3	121±1.3	1.18±.03	7.31±.03
(N)	10	8	9	10	10	10	7
p	--	--	<.001	NS	NS	NS	NS

Thus, there is no difference in the TF/UF chloride concentration between the rat and the dog. In addition, regression analysis indicates that there is no correlation between the TF/UF_{Cl} and TF/P_{In} (RAT, $TF/UF_{Cl} = 1.22 - .02\ TF/P_{In}$; DOG, $TF/UF_{Cl} = 1.20 - .02\ TF/P_{In}$) and suggests that the gradient is established early and is maintained along the accessible proximal tubule in both species.

EFFECTS OF INTERMITTENT PRESSURE LOADING ON THE DEVELOPMENT OF VENTRICULAR HYPERTROPHY. M.L. Marcus*, D.L. Eckberg, J. Braxmeier*, and F.M. Abboud. CV Center and CV Division, Dept. of Med., Univ. of Iowa College of Med. and VA Hosp., Iowa City, IA. 52242.

Although the effects of persistent pressure loading have been studied extensively, the effects of intermittent pressure loading have not been carefully examined. In docile cats, a 4 mm solid state transducer was introduced into the right ventricle (RV) and an inflatable cuff was placed around the pulmonary artery. Two weeks following recovery the cats were subjected to an intermittent pressure load. For 2-4 weeks RV systolic pressure was alternately 50±1 mmHg for 3.5 days during pressure loading (cuff inflated) and 20±3 mmHg for 3.5 days during pressure unloading (cuff deflated). At the conclusion of the study, all cats were catheterized (RV systolic and end-diastolic pressure and cardiac output were measured) and the weight of the free wall of the right ventricle was determined (gms/kg). None of the cats included in the study developed hemodynamic evidence of RV failure. The intermittent pressure loaded cats were compared with normal unoperated controls, sham operated cats, and cats with a persistent pressure load (fixed band around the pulmonary artery) for 3-4 weeks.

	Controls	Sham Operated	Fixed Obstruction	Intermittent Pressure Load
# Cats	8	7	6	7
RV Pressure (mmHg)	25±2*	27±2	69±6	59±1 and 20±3
RV Weight (gm/kg)	0.6±.1	0.6±.1	1.2±.2	1.0±.1

*mean ± S.E.

Thus, intermittent pressure loading caused significant RV hypertrophy. These data indicate that the rate of progression of RV hypertrophy exceeds the rate of regression.

SELECTIVE CONTRIBUTION OF CARDIOPULMONARY AND CAROTID BARORECEPTORS TO FOREARM AND SPLANCHNIC VASOCONSTRICTOR RESPONSES DURING VENOUS POOLING IN MAN. Allyn L. Mark, Dwain L. Eckberg, and Francois M. Abboud. CV Center and CV Division, Dept of Med, Univ of Iowa College of Med and VA Hosp, Iowa City, IA 52242.

The goal of this study was to determine the contribution of cardiopulmonary and carotid baroreceptors to circulatory adjustments during venous pooling in man. We compared a) responses to lower body suction which produces venous pooling and activates cardiopulmonary and carotid reflexes with b) responses to lower body suction plus simultaneous application of neck suction. The rationale was that simultaneous application of neck suction, which stretches carotid baroreceptors, would minimize the contribution of carotid baroreceptors to reflex adjustments during lower body suction. Central venous pressure, brachial arterial pressure, heart rate, forearm blood flow (plethysmography), and splanchnic blood flow (indocyanine green dye clearance) were measured in healthy young men. Lower body suction at 40 mmHg decreased central venous pressure and arterial pulse pressure and increased heart rate and forearm and splanchnic vascular resistances. Simultaneous application of neck suction prevented tachycardia and most of the splanchnic vasoconstriction during lower body suction, but it did not significantly attenuate the forearm vasoconstriction. The results suggest that cardiopulmonary and carotid baroreceptors contribute selectively to reflex adjustments during venous pooling in man. Carotid baroreceptors trigger the tachycardia and most of the splanchnic vasoconstriction, but have a minor role in the forearm vasoconstriction. Cardiopulmonary baroreceptors play the predominant role in the forearm vasoconstriction, but do not appear to contribute greatly to the splanchnic vasoconstriction.

INFLUENCE OF SHEARING STRESS ON REGIONAL AORTIC HISTAMINE SYNTHESIS AND TRANSMURAL ALBUMEN UPTAKE. R.A. Markle,* M.E. Katora,* and T.M. Hollis* (SPON: A. Anthony). Biology Department, The Pennsylvania State University, University Park, Pa. 16802.

The influence of shearing stress created by blood flow on thoracic aortic histamine synthesis and aortic transmural protein uptake has been examined. Male, mongrel dogs, 10-15 kg body weight, were anesthetized with methoxyflurane administered via endotracheal tube, and adequacy of ventilation was assured from measurement of blood P_{O_2} and P_{CO_2}. Different shearing stress intensities were created in the thoracic aorta through varying degrees of reduction in aortic lumenal radius; perfusion time following this procedure was from 1 to 1-1/2 hrs. Aortic regions above and below these areas of coarctation served as control segments. Shearing stress intensity in any given region was calculated from pressure drops occurring over the length of the specific aortic segment, pressures being measured via cannulas inserted from the left carotid (inflow pressure) and left femoral (outflow pressure) arteries. Typically, this graduated reduction in lumenal radius resulted in production of shearing stress intensities ranging from below 50 dynes/cm^2 to intensities in excess of 600 dynes/cm^2. Results indicate that a relationship exists between the applied shearing stress, the rate of segmental aortic histamine synthesis, and aortic transmural albumen uptake. Based on histological evaluations, a major source of this elevated histamine synthesis appears to be dependent upon an intact endothelium. These results suggest that aortic (especially aortic endothelial) histamine synthesis may be one biochemical coupling agent between an applied hemodynamic stress and the resultant aortic permeability change. (Supported by grants GB 38136 and ENG 73-03982 A01 from NSF).

ORIGIN OF ELECTRICAL PD'S IN HAMSTER THIN ASCENDING LIMBS OF HENLE'S LOOP. Donald J. Marsh and Christine M. Martin*, Dept. of Biomedical Engineering, University of Southern California, Los Angeles, CA 90007

Electrical PD's between thin ascending limbs (ALH) and ascending vasa recta (AVR) were measured differentially with sharpened 2 μ microelectrodes. The electrodes contained 3 MKCl colored with Lissamine Green, and all puncture sites were verified visually by expressing the colored electrolyte into the tubular or vascular lumen. When mineral oil covered the kidney, the PD was 1.95 ± 0.17 (SEM) mV, n = 49, lumen positive; when Ringer solution bathed the kidney, the PD was 1.92 ± 0.12 mV, n = 60, lumen positive. This result differs from previous reports that the PD was -9 to -11 mV, lumen negative, when measured with Ling Gerard electrodes used singled ended, and without visual verification. To study the origin of the PD, we used a gravity feed perfusion of ALH to modify tubular fluid electrolyte concentrations; the PD, and Na, K, and Cl concentrations were measured in collected ALH perfusates and in adjacent AVR plasma. These hamsters were all saline loaded to reduce the corticomedullary gradient. The perfusion solutions were:simulated tubular fluid, low Na tubular fluid, low Cl tubular fluid, high Cl tubular fluid, and high K tubular fluid. The transport number estimates were: Na, 0.023 ± 0.044; K, 0.018 ± 0.021; Cl, 0.45 ± 0.036. The active transport potential did not differ from zero, nor did the Na or K transport numbers. Since ALH/AVR Cl ratio is 1.07, the PD could be in part a Cl diffusion PD. The failure of the transport numbers to sum to 1.0 is unexplained, however, and other sources of the PD may exist. To test one explanation, that the PD is shunted along the axis of the tubule, we measured the length constant of ALH. The value was 92 ± 7.6 μ, and is so short in relation to the lengths of tubule perfused as to make this possibility unlikely.
(Supported by NIH Grant AM 15968)

CHANGES IN ACETYLCHOLINE SENSITIVITY OF CHICK CILIARY GANGLION CELLS AFTER POST-GANGLIONIC AXOTOMY. A.R. Martin and H.R. Brenner*, Dept. of Physiology, Univ. of Colorado Medical School, Denver, CO 80220.

Electrophysiological studies were done on cells dissociated from ciliary ganglia of 3-4 day old chicks. Cell dissociation was accomplished by incubating excised ganglia with collagenase (about 120 units/ml) for up to 45 min, followed by gentle teasing. The dissociated cells were then placed under interference-contrast optics in a chamber perfused with oxygenated saline solution. Intracellular micropipettes were placed in the cells and acetylcholine (ACh) applied by iontophoresis from an extracellular micropipette. The presence of spontaneous miniature synaptic potentials indicated that the dissociation procedure did not disrupt the integrity of the synaptic connections. Two groups of ganglia were used: one group was from normal chicks; the other was from chicks whose ciliary nerve had been sectioned at hatching. There was no significant difference between the normal and axotomized ganglion cells in resting membrane potential, input resistance or time constant. All cells had action potentials with similar thresholds and no obvious differences in amplitude or time course. However, the axotomized cells had a significantly reduced sensitivity to applied ACh. The average sensitivity was 12% of that of the normal cells. The rise-time of the ACh potentials was unchanged and there was no obvious change in reversal potential of the ACh response. The experiments suggest that a reduction in ACh sensitivity is one of the factors contributing to the failure of synaptic transmission which occurs in the ganglion after post-ganglionic axotomy.
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RESISTANCE FUNCTION OF THE CEREBRAL EXTRAPARENCHYMAL ARTERIES (CEA). J.B. Martin* and C.E. Rapela, Dept. of Physiology, Bowman Gray School of Medicine, Winston-Salem, N.C. 27103.

In previous studies we found that there was a drop in pressure across the arteries at the base of the brain (cerebral extraparenchymal arteries) during infusion of serotonin, owing to the vasoconstrictor action of this drug. The present investigation was carried out to assess the resistance function of the CEA when only normaltone is present. We use the difference (ΔP_{c-v}) between common carotid pressure and pressure measured in cannulas wedged in the two vertebral arteries as an index of resistance in the CEA. ΔP_{c-v} was determined during normocapnia and when the cerebral blood flow was increased during hypercapnia. 8 pentobarbital-anesthetized dogs were used. Common carotid pressures were measured through the thyroid arteries cannulated retrogradely. Vertebral wedge pressures were measured by threading small polyethylene cannulas up both vertebral arteries antegradely until they wedged, usually at the level of C_1 . Cerebral blood flow was measured as the outflow from the confluens sinus after occlusion of the lateral sinuses with bone wax. During normocapnia ΔP_{c-v} averaged 10.8 ± 2.1 mmHg. When hypercapnia was induced the cerebral blood flow increased to over 200% of control; no significant change in systemic pressure or common carotid flow occured. ΔP_{c-v} increased to 16.7 ± 3.9 mmHg during the increased cerebral blood flow. These data indicate that there is a finite resistance to flow through the CEA. The data are in agreement with anatomic and functional studies of others which have indicated a resistance function of the arteries leading to and comprising the circle of Willis.

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K^+ RELEASE BY SUBMAXILLARY GLAND SLICES FROM CONTROL AND RESERPINE TREATED RATS - J.R. Martinez*, D.O. Quissell*, M. Giles* (SPON: W.S. Platner). University of Missouri Medical Center, Columbia, MO 65201

Submaxillary gland slices from normal rats and from rats pretreated with seven daily doses of reserpine (0.5 mg/kg) were used to study the kinetics of K^+ release in an enriched Krebs-Ringer-bicarbonate medium maintained at 37°C and gassed with a 95% O_2-5% CO_2 mixture. Slices were preincubated for 15 minutes, washed in fresh medium and incubated in 2.5 ml of medium for 10 minutes. Secretagogues were added at 0 time and 25 µl aliquots were removed at various time intervals. K^+ release was expressed as % of the total K^+ contained in the slice homogenates. Norepinephrine (20 µM) and phenylephrine (50 µM) caused the net release of 10-15% of the total K^+ in control glands and of 25-30% in glands from treated animals. The release is rapid and reaches a new steady state level in 2 minutes. Isoproterenol did not cause K^+ release in either type of gland. Addition of ouabain (1mM) to the medium enhanced the K^+ release caused by norepinephrine to 45% in control glands and in treated glands. Phentolamine (50 µM) rapidly reversed the K^+ release induced by norepinephrine in control glands and a reuptake of K^+ into the slices occurred which was significantly smaller in glands from treated animals. K^+ release was critically dependent on the presence of Ca^{++} and of substrates (purines, glucose) in the medium. It is concluded that: 1) K^+ release is mediated by α-adrenergic receptors in rat submaxillary gland; 2) the extent of K^+ release is the resultant of a passive efflux and an active reuptake; 3) pretreatment with reserpine induces a greater net release of K^+ which is probably due to a decreased reuptake.

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RENAL CONCENTRATION AND DILUTION DURING ACUTE LITHIUM INFUSION. M. Martinez-Maldonado, San Juan V. A. Hospital and Depts. of Medicine and Physiology, University of Puerto Rico School of Medicine, San Juan, Puerto Rico

Chronic lithium (Li) administration in the rat leads to reduced renal concentration (T^cH_2O) without alterations in renal dilution (^cH_2O). To examine the acute effects of Li on T^cH_2O and ^cH_2O, unanesthetized rats were infused with a solution composed of 1% NaCl and 1% LiCl or a 0.225% LiCl solution at rates from 0.06 to 0.5 ml/min. In 8 rats, infusion of Na-Li solution resulted in marked inhibition of T^cH_2O at any level of osmolar clearance (Cosm) when compared to animals receiving 2% NaCl alone. Administration of amiloride (AM), 40 or 80 µg/kg/min throughout the experiment, to 9 rats infused with Na-Li solution resulted in marked improvement of T^cH_2O to Cosm relationship. Infusion of 0.225% LiCl to 9 rats undergoing water diuresis led to marked reductions in ^cH_2O as a function of distal delivery (V) when compared to rats receiving 0.225% NaCl alone. Infusion of AM did not improve ^cH_2O to V relationship. These studies suggest that Li interferes with Cl^- reabsorption in the loop of Henle and also reduces the permeability of the collecting duct to water. AM, probably by interfering with Li transport into collecting duct cells, corrects partially T^cH_2O defect by preventing water permeability changes. The lack of effect of AM in ^cH_2O studies may relate to the fact that collecting duct permeability is already at its lowest. It reinforces the suggestion that Li^+ retards Cl^- reabsorption in the ascending limb as infered from the T^cH_2O studies. Both Cl^- and Na^+ are required for normal loop function.

MEASUREMENT OF CENTRAL NERVOUS SYSTEM SIGNALS DURING THE ESTROUS CYCLE OF THE RAT. J.F. Masken*, R.J. Morgan*, P.J. Sheridan*, and W.W. Walker* (SPON: M.L. Hopwood). Department of Physiology and Biophysics, Colorado State University, Fort Collins, Colorado 80523.

Five adult female Sprague-Dawley rats had electrodes chronically implanted in the arcuate (ARC), pre-optic area (POA), and amygdala (AMY) regions of the brain in order to relate central nervous system electrical activity to hormonal activity during the estrous cycle. Electrical activity was recorded from these areas simultaneously from 08:00h to 16:00h on each day of the cycle. Primary analog data were recorded on FM magnetic tape, and were converted to digital data by playing back the magnetic tape to an Analog-to-Digital converter. Digital data were analyzed using crosscorrelation on a Control Data Corporation 6400 digital computer. These analyses showed relationships between the recorded areas, signal transit times, and direction of signal flow between the areas that changed during the estrous cycle. Changes were particularly evident in the AMY-ARC crosscorrelograms. On diestrus-1 the correlograms showed a signal delay of about 2 msec for signals flowing from the AMY to ARC. On diestrus-2 the AMY-ARC correlograms showed this delay for only half the samples. On proestrus the correlogram maxima were at zero time delay--there was no signal traffic between the two areas. A small number of samples showed a time delay during estrus. The possible significance of these results with respect to hormone levels is discussed.

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PULMONARY INTRA- AND EXTRAVASCULAR FLUID VOLUMES AFTER EXPERIMENTAL MYOCARDIAL INFARCTION. W.H. Massion, G. Blümel*, O. Petrowicz* and W. Erhardt*. Inst. of Exp. Surgery, Techn. Univ. of Munich, 8 Munich, Germany.

Transcapillary fluid shifts have been observed in the lung after myocardial infarction, but quantitative data are lacking. In 18 anesthetized cats the carotid artery was catheterized and connected to a flow-through radiation detection device. Blood could pass through the detector and was returned to the femoral vein. Using the "double isotope technique", a mixture of I-131 albumin (RISA) and I-125 antipyrin was injected into the right heart via the jugular vein. Simultaneous indicator dilution curves of the diffusible antipyrin and the non-diffusible RISA were obtained after transit through the lung, serving for calculation of fluid shifts. In addition, arterial bloodpressure, EKG,hematokrit,thrombocyte count and plasma volume were recorded. Two hours after myocardial infarction by ligating of the left descending coronary artery, the pulmonary intravascular volume had decreased 8.1% and the extravascular volume increased 30.5% compared to control values. Bloodpressure dropped 24.6%, hematokrit increased 35.6% and the EKG showed S-T elevation. Changes in the other parameters were not significant. 20 min after infarction, half of the animals received 50,000 KIU aprotinin (Trasylol)/kg IV , a proteolytic enzyme inhibitor. There was a significant reduction in the volume of fluid crossing into the extravascular space, but no change in the other parameters. Our results suggest that the rise in pulmonary extravascular fluid volume after myocardial infarction may in part be attributable to an increase in vascular permeability caused by proteolytic enzymes.
(Supported in part by the Alexander von Humboldt Foundation.)

FILTRATION AND REFLECTION COEFFICIENTS AND PORE SIZE IN PULMONARY CAPILLARIES OF THE NEWBORN RABBIT. Sady V. Matalon* and O. Douglas Wangensteen, Dept. Physiology, Medical School, University of Minnesota, Minneapolis, Mn. 55455

Isolated perfused lung preparations from newborn rabbits (1-3 days old) have been used to determine the reflection coefficients, σ, of the following molecules: mannitol, sucrose, raffinose, inulin and albumin. The lungs were continuously perfused at constant flow with a Krebs-Ringer solution. At a given time the solution was switched to a Krebs-Ringer solution containing one of the test molecules. The resulting weight loss (osmotic transient) was continuously monitored. The filtration coefficient (K_f) was calculated from the interstitial weight gain following an increase in arterial pressure. The average K_f value found was 8.3 ($\pm$ 4.1, SD) x 10^{-5} cm^3 sec^{-1} cmH_2O^{-1}. Knowing the initial rate of weight loss (Jv_o) for each osmotic transient the following σ values (mean $\pm$ SD) were obtained from $\sigma = Jv_o(RT\Delta C)^{-1}(K_f)^{-1}$: mannitol = 0.024 $\pm$ 0.009, sucrose = 0.032 $\pm$ 0.015, raffinose = 0.042 $\pm$ 0.020, inulin = 0.062 $\pm$ 0.024 and albumin = 0.10 $\pm$ 0.009. These results are inconsistent with a single pore model but seem to be consistent with a two pore model for the pulmonary capillaries with pore radii of 10 and 400 Å, and having one large pore for every 2 x 10^5 small pores. These results imply that pulmonary edema in the newborn could easily be caused by slight increases in pulmonary microvascular pressure and that infused albumin would be relatively ineffective in reversing the efflux of fluid from the pulmonary microvasculature.

EVOKED HIPPOCAMPAL ACTIVITY IN THE RABBIT AND CAT. J. W. B. Mates* and J. M. Horowitz. Dept. of Animal Physiology, Univ. of Calif., Davis, CA 95616.

Oscillatory averaged evoked potentials (AEPs) have been observed from the cat hippocampus following electrical stimulation of the fornix. Since the anatomical nature of the neural network from which these waveforms were interpreted as arising occurs in the rabbit as well as the cat, it was hypothesized that fornix stimulation in the rabbit would lead to similar oscillations. To compare the AEPs, cats and rabbits were anesthetized with sodium pentobarbital. Electrodes were lowered through burr holes in the skull and positioned in the fornix and across the layer of hippocampal pyramidal cells. For both animals fornix stimulation at low intensities (less than 10v, .01 msec) caused AEPs with an initial prominent peak and several subsequent peaks during the next few hundred milliseconds. In both cases, AEPs recorded across the pyramidal cell layer showed: (a) mirror image waveforms (from sites across the layer of pyramids); (b) decreased AEP oscillation and greater delay between first and second peaks for increasing depth of sodium pentobarbital anesthesia; and (c) longer intervals between first and second peaks in AEPs as stimulus amplitude increased. The multiple peaked AEPs were interpreted in terms of a network (of pyramidal cells and interneurons) with negative and positive feedback branches and an additional input of background activity exciting pyramidal cells. The records are consistent with the hypothesis that the later peaks in AEPs arise from a hippocampal network which may be functionally similar in both cats and rabbits. (Supported in part by Grant D529 from University of California and NGR-05-004-099 from NASA.)

MESH MODEL OF THE ELECTRICAL PROPERTIES OF THE TUBULAR SYSTEM OF SKELETAL MUSCLE. R.T. Mathias*, C. Clausen*, and R.S. Eisenberg. Dept. of Physiology, UCLA Medical School, Los Angeles, Calif. 90024.

The tubular system of skeletal muscle fibers has been modeled as a mesh of miniature transmission lines using difference equations at the nodes of the mesh and differential equations in the tubules between nodes. The resulting equations were solved exactly, without assumptions, for some geometries. If circular symmetry is assumed, an approximate solution is

$$Y_T^*(a,j\omega) = (S_T/V_F)\sqrt{G_W + j\omega C_W}/R \tanh\{(a/2)\sqrt{R(G_W + j\omega C_W)}\}$$

$$R = (1/2)(\delta\sigma)^2 (L_T/V_F)^2 (S_T/V_T) R_L$$

where

Y_T^* = admittance of the t-system per cm^2 of outer surface
a is the fiber radius, ω is the angular frequency, $j = \sqrt{-1}$
R_L is the resistivity of the tubular lumen
G_W, C_W are the conductance and capacitance of the tubular wall
S_T, V_T, L_T, δ = area, volume, branch length and mesh size of t-system
V_F is the fiber volume, σ is the sarcomere length.

The mesh model fits both the impedance data of Valdiosera et al. and the data of Hodgkin & Nakajima with essentially the same circuit parameters. In 5 solutions of varying resistivity, the luminal resistivity R_L approximately equals R_B, the resistivity of the bathing solution.

The network of the t-system has often been represented as a disc. The disc model, however, does not describe the properties of the networks we have solved exactly; neither does it fit our impedance data with $R_B \tilde{=} R_L$. In these respects the mesh model seems to be a better description of the electrical properties of the t-system.

ENERGY RELEASE OF THE FORCE-GENERATING PROCESS IN CHICK ALD. Y. Matsumoto & A. McPhedran, Dept. of Physiology, Emory Univ., Atlanta, GA. 30322

The anterior latissimus dorsi (ALD) of 2-week-old chicks was examined for rate of heat liberation during steady-state force development. During isometric tetani, the analysis was constrained in the region of "plateau" forces for muscle lengths ℓ_o to $1.6\ell_o$. Presumably in this region of length the degree of myofilament overlap can be changed. If the amount of overlap is known, the number of HMM crossbridges in activity can be estimated. The chick ALD muscle can be reversibly stretched from ℓ_o to $1.5\ell_o$ and back again with reproducible developed force. With experiments on frog semitendinosus, a muscle that can be stretched so that myofilament overlap is completely abolished, considerable HMM projection movement is assumed to take place (H. Huxley, 1972). The chick ALD possesses similar extensibility to the frog semitendinosus. From our results the rate of heat production in the region of muscle length $\ell_o<\ell<1.6\ell_o$ is estimated to be 0.70±0.06 mCal/g-sec/muscle force unit. The rate of heat liberation during force generation at ℓ_o is 1.02±0.08 mCal/g-sec, while the value for extrapolation to $1.6\ell_o$ is 0.32±0.04 mCal/g-sec. This stretched length of the muscle is the presumed extrapolated non-overlap configuration of the thick and thin filaments. Based on our estimate of 2.3×10^{16} crossbridges per gram of muscle, the rates of heat liberation per crossbridge are respectively 0.45×10^{-16} mCal/sec and 0.14×10^{-16} mCal/sec. Taking 10 Kcal/mole as a rough value of free energy change for ATP hydrolysis, this would amount to 1.6×10^{-16} mCal/molecule. If it can be assumed that each crossbridge cycle required the energy release equivalent of one molecule of ATP hydrolysis, our data suggest that in one second of crossbridging activity there is an equivalent energy of 2.8 molecules of ATP hydrolysis. This would amount to a crossbridge cycle period of 351 msec.

SPECIES VARIATIONS IN TOLERANCE TO BRONCHOPULMONARY LAVAGE. J.L. Mauderly and R.F. Henderson*, Inhalation Toxicology Research Institute, Lovelace Foundation, Albuquerque, New Mexico 87115

Techniques for performing repeated lung lavages via single-lumen catheters in Beagle dogs (J. Appl. Physiol. 38: 922, 1975) and Syrian hamsters (Fed. Proc. 34: 387, 1975) have been reported. When the hamster procedure was applied to Long-Evans rats, Chinese hamsters and CD-1 mice, we discovered that these species did not survive. Although they lived through the anesthetic induction, intubation, lung washing, and manual ventilation, these species could not sustain spontaneous ventilation and died. Proteinaceous fluid was recovered from the endotracheal catheter and airways terminally. We decided to use rats, guinea pigs, rabbits, and Syrian hamsters to further explore possible species differences in lavage tolerance. Six animals of each species were used. Three were anesthetized, with halothane-oxygen, intubated, maintained on the anesthetic mixture for a time equivalent to the lavage procedure, allowed to recover, and sacrificed at one hour post-recovery. The other three were anesthetized, intubated, lavaged with four washes of normal saline, and allowed to recover. Survivors were sacrificed at one hour post-lavage. Lungs were removed from all animals and both the lungs and recovered lavage fluid were analyzed for surfactant lipid (dipalmitoyl lecithin) by the cryochromatography method to determine whether the relative amount of surfactant lipid removed might relate to differences in survival. (Research performed under U.S. Energy Research and Development Administration Contract E(29-2)-1013.)

SOLUTE TRANSPORT ACROSS THE ISOLATED CORNEAL ENDOTHELIUM. David M. Maurice, Dept. Surgery, Division of Ophthalmology, Stanford University Medical Center, Stanford, California 94305.

A system has been developed for the continuous perfusion of both surfaces of the isolated rabbit cornea. Samples of perfusate can be collected from both sides so that solute fluxes can be determined under steady-state conditions. At the same time, facilities are provided for the measurement of the electrical potential and water flux across the specimen. Attention has been concentrated on measuring the simultaneous flux of two labeled solutes in the same direction across the isolated corneal endothelium. The flux ratio can be established to about 1%, and the change in ratio between the pumping and non-pumping state has been examined with the objective of identifying an actively transported ion, so far without success. Solute pairs have principally been chosen from ^{22}Na, ^{36}Cl, $S^{14}CN$, $H^{14}CO_3$ and ^{14}C-sucrose. By changing the CO_2 tension in the solution it is possible to distinguish CO_2 from HCO_3 transport. The tracer fluxes across the cellular layer are principally proportional to their free diffusion rates.

DISTRIBUTION OF SARCOMERE SPACINGS OF FROG SKELETAL MUSCLES IN THE NORMAL AND DELTA STATES. R.J. McCarter* (SPON: B.P. Yu). Dept. Physiology, Univ. of Texas Health Science Center, San Antonio, Tex. 78284

Sarcomere spacings (SS) were measured at different points along the lengths of isolated frog sartorius muscles at 20C using light diffraction techniques. At the resting length (RL, the length of the muscle in situ when the leg is held at right angles to the body) the SS was 2.22±0.04μ (mean±S.E.M., n=7) for both normal and delta state muscles measured at the muscle center. Eighty-five percent of the sarcomeres fell within this range. The non-uniformity of SS appeared within 10% of each end of the muscles. When stretched to 120% and 130% RL the degree of non-uniformity increased, such that at 130% RL only 20% of the sarcomeres were of uniform spacing. Periods of recovery (at slack lengths) between stretches greatly improved the overall uniformity of SS. SS was measured at the center and within 10% of each end of the muscle during stretch-relax cycles in the range 90%-140% RL. A linear relationship was found between muscle length and SS for proximal, center and distal readings with slopes of 1.64±0.05, 1.18±0.08, 1.58±0.07 $cm\,\mu^{-1}$ (mean±S.E.M., n=10), respectively. Values obtained for muscles in the delta state were the same for the proximal and distal sections. The slope obtained for the center readings was significantly greater ($p < 0.05$) than for normal muscles. Reproducibility of results in successive stretch-relax cycles was good for both normal and delta state muscles, in contrast with the marked hysteresis which was found in the passive tension-length relation. Since SS is a major determinant of muscular performance, the results indicate that the mechanics of contraction will be significantly influenced by the non-uniform distribution of SS at lengths greater than RL. The linear relation between SS and muscle length is different for different parts of the muscle and is changed by putting the muscle into the delta state.

EFFECT OF CORONARY HEART DISEASE ON RESPONSE TO STATIC EXERCISE AND VALSALVA STRESS. D.J. McDermott*, D.G. Kamper*, R.W. Gotshall* and J.J. Smith, Medical College of Wisconsin, Milwaukee, Wisconsin 53233

Recent evidence has indicated that patients with congestive heart failure have abnormal autonomic responses to stress. In the current study, male coronary heart disease (CHD) patients, 42 to 53 yrs of age, and control male subjects, 40 to 49 yrs of age, free of coronary or other systemic disease, underwent static exercise and valsalva tests in order to determine the response of patients not in congestive failure to these two types of stress. CHD patients had greater increments of heart rate (HR), systolic pressure and diastolic pressure than the control group, upon holding one third of maximum isometric tension for four minutes on a handgrip dynamometer. Using Elisberg's method of analyzing heart rate responses (JAMA 186:120-25, 1963) to a 15 sec valsalva maneuver while holding 40 mm Hg of intrathoracic pressure, CHD patients showed a decrease, rather than increase, in HR from Phase II to Phase III and a tendency toward a lesser slowing of HR between Phase III and Phase IV. We would conclude that the increased HR and pressor responses to static exercise and the lesser HR changes to the valsalva maneuver in the CHD group suggest that autonomic dysfunction may occur in CHD patients without failure as well as in those with congestive failure.

HEPARIN FRACTIONS REVEALED BY ELECTROFOCUSING IN POLYACRYLAMIDE GEL. N.M. McDuffie*, H.B. Nader*, and C.P. Dietrich* (SPON: J.W. Phillis). Dept. of Physiology, Univ. of Sask., Saskatoon, Sask., Canada S7N OWO, and Dept. Bioquimica & Farmacologia, Escola Paulista de Medicine, Sao Paulo, Brazil.

Isoelectric focalization of several commercial heparin preparations reveals at least 21 components. Polyacrylamide electrophoresis of the individual components indicates a family of compounds with a constant molecular weight difference. The components exhibit "properties of heparin" including meta-chromasia, degradation by enzymes of F. heparinum and anticoagulant activity. Comparative focalization of other acid mucopolysaccharides (chondroitins, heparitins) as well as polyanions, heparin degradation products and chemically modified heparins demonstrates a characteristic heparin profile. Chemical modification of heparin and the resultant change in the profile prompt interesting comparisons with the heparitins observed in disease. Some parameters of the process have been investigated, indicating that the phenomenon is related to pH, molecular weight and ampholyte availability in gel. The process is reproducible and may be carried out in gel or in batch. Moreover, it provides a rapid and reliable method of unequivocally distinguishing between mucopolysaccharides. (Work supported by grants from FAPESP,CNPq and FINEP, Brazil).

INHIBITION OF NOREPINEPHRINE RELEASE FROM SYMPATHETIC NERVE ENDINGS BY HISTAMINE. Michael A. McGrath* and John T. Shepherd, Mayo Clinic and Foundation, Rochester, Minnesota 55901.

Helical strips from dogs' saphenous veins were mounted in an organ bath (Krebs-Ringer solution, 37° C) for isometric tension recording. Contractions of the strips caused by electric stimulation (0.5 - 20 Hz) were depressed by histamine (10^{-8} - 10^{-6} g/ml) whereas contractions caused by tyramine (10^{-6} g/ml) and norepinephrine (10^{-7} g/ml) were either unchanged or augmented. Histamine (10^{-6} g/ml) also depressed contractions caused by potassium (40 mM); after alpha adrenergic blockade the contractions caused by potassium were smaller and were unaffected by histamine. Strips were incubated with [7-^{3}H] norepinephrine and mounted for superfusion and isometric tension recording. The perfusate was collected every two minutes for estimation of total radioactivity and for column chromatographic separation of norepinephrine and its metabolites. A dose of histamine (10^{-7} g/ml), which did not affect the tension or efflux of radioactive compounds from resting strips, depressed the release of ^{3}H-norepinephrine from strips contracted by electric stimulation (1 Hz). The release of radioactive compounds which accompanied contractions caused by tyramine (4×10^{-6} g/ml) was unaffected by histamine. Thus histamine causes relaxation of vascular smooth muscle by inhibiting the release of norepinephrine from the sympathetic nerve endings. This is seen both when the nerve endings are activated electrically or are depolarized by potassium ions. By contrast, histamine does not inhibit the displacement of norepinephrine by tyramine. (Supported by Bushell Travelling Fellowship, Royal Australasian College of Physicians and NIH Grant HL 5883.)

PULMONARY VASCULAR REACTIVITY IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). I.F. McMurtry, A. Tucker, J.T. Reeves, and R.F. Grover. Univ. of Colorado Medical Center, Denver, Colorado 80220

Genetic traits isolated in SHR apparently lead to an increased reactivity of the systemic vasculature to vasoconstrictive stimuli. To determine whether the low-resistance pulmonary vasculature of SHR is similarly affected, we have measured pressor responses to alveolar hypoxia (4 min of 2.5% O_2, H), 0.5 µg angiotensin II (A-II), and 10 µg prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) in blood-perfused lungs isolated from 12-week -old, male normotensive rats (NR) and SHR. Lungs were perfused at constant flow (11 ml/min) for 2-3 hours and stimulated alternately either with H and A-II, H and $PGF_{2\alpha}$, or H, A-II, and $PGF_{2\alpha}$. The mean ± SEM of 4 pressor responses (percentage increase) to each stimulus in each lung was:

H			A-II			$PGF_{2\alpha}$		
NR(16)	SHR(16)	P	NR(12)	SHR(12)	P	NR(7)	SHR(7)	P
78±3	93±4	<.01	98±5	74±2	<.001	19±1	66±7	<.001

A tendency toward lower perfusion resistance (1.27 ± 0.05 vs 1.42 ± 0.08 mmHg/ml/min) in the lungs from SHR as compared to those from NR, and the same right ventricular systolic pressure (32 ± 2 mmHg) in 6 SHR and 6 NR anesthetized with pentobarbital indicated that the pulmonary vasculature of SHR was normotensive. Mean carotid pressure was higher in 6 SHR than in 6 NR (173 ± 9 vs 128 ± 10 mmHg, $p < .05$). These data show that the normotensive pulmonary vasculature of SHR has an increased reactivity to H and $PGF_{2\alpha}$, but a decreased reactivity to A-II. It is concluded that although the pulmonary vasculature of the SHR is hyperreactive to some vasoconstrictive stimuli, such a characteristic is neither the result of, nor necessarily leads to, pulmonary hypertension. (Supported by NIH grants HL14985 and HL05973 and the Colo. Heart Assoc.)

SPONTANEOUS ALTERATIONS IN REGIONAL MYOCARDIAL FUNCTION FOLLOWING INITIAL DERANGEMENT BY ACUTE CORONARY OCCLUSION. S. Meerbaum, T.W. Lang*, J.V. Osher* and E. Corday*, Department of Cardiology, Cedars-Sinai Medical Center, Los Angeles, California 90029

Sequential regional metabolic, mechanical and electrocardiographic measurements in anesthetized dogs indicate severe segmental dysfunction within minutes of an acute coronary occlusion, but spontaneous improvement within 2-3 hours after the occlusion. In a closed chest dog series with intracoronary balloon occlusion of the proximal LAD, mean lactate extraction in the ischemic region was 48.7% in control, dropped to -4.3% (production) at 5 minutes of occlusion, and recovered partly to 19.3% at 2 hours occlusion. Corresponding values of ischemic region potassium balance were .03 mEq/L, -.45 mEq/L and -.26 mEq/L. Simultaneously recorded precordial ECG-ST segment elevations averaged .5 mV in control, 1.8 mV at 5 minutes and .7 mV two hours after occlusion. Mean coronary sinus flow (thermodilution) dropped from 121 cc/min in control to 68 cc/min shortly after occlusion, but increased to 96 cc/min at 2 hours following occlusion. Left ventricular end-diastolic pressure rose progressively during this occlusion period from a mean control level of 6.6 mmHg to 9.4 mmHg. Systemic blood pressure was maintained. In a separate series of open chest dog experiments, myocardial force gauge measurements in the ischemic segment demonstrated rapid post-occlusion development of regional dyskinesis, but indicated partial reversal of dyskinesis in the subsequent 2 hours of occlusion. Results of these studies imply spontaneous compensatory adjustments in ischemic segment coronary supply and altered mechanics of cardiac wall, which may, at least transiently, reduce the degree of ischemia and regional myocardial dysfunction experienced immediately following an acute coronary occlusion.

ALTERATIONS IN REGIONAL RIGHT VENTRICULAR CONTRACTILE PATTERNS IN THE INTACT CANINE HEART. G.D. Meier*, A.A. Bove, W.P. Santamore*, P.R. Lynch and G.H. Stewart*, Drexel University, Biomedical Engineering, and Temple University, Dept. Medicine & Physiology, Philadelphia, Pa. 19140

To evaluate regional right ventricular (RV) contractile patterns we studied four mongrel dogs with lead beads sewn transpericardially onto the RV free wall in an open chest preparation. The hearts were studied at the intrinsic cardiac rate (2.4-2.6 Hz), and several paced rates. Using a high speedcineradiographic system, the frame-by-frame bead displacement was recorded with a digitizing table connected to a computer, which yielded numerical coordinates of each bead as discrete functions of time and space. The calculated bead motion defines a geometric profile of myocardial contraction by interbead distance and velocity. Preliminary results show for a pair of beads placed on the pulmonary conus, a maximal (diastolic) distance of 24.8 mm, a minimal (systolic) distance of 20.8mm, a shortening velocity (systole) of 92 mm/sec, and a lengthening velocity (diastole) of 67 mm/sec. For a bead pair which defines a line between the apex and a point on the free wall, the maximal distance was 29. 1 mm, the minimal distance 27.2 mm, with a systolic shortening velocity of 72 mm/sec and a diastolic lengthening velocity of 54 mm/sec. These data, although preliminary in nature, indicate that the pulmonary conus region of the RV shortens more, and with greater velocity than the apical area.

RELEASE OF OXYTOCIN AND DEPLETION OF ADENOHYPOPHYSEAL (AP) PROLACTIN (PRL) IN LACTATING RATS INDUCED BY ELECTRICAL STIMULATION (ES) OF A MAMMARY NERVE. F. Mena, D. Aguayo*, P. Pacheco* and C.E. Grosvenor. Dept. Physiology, Instituto de Investigaciones Biomédicas, UNAM. México, D.F. México.

The segmental nerve of the first abdominal mammary gland of urethane-anesthetized lactating rats was stimulated electrically and its effects assessed upon intramammary-recorded pressure (IMP) and AP PRL content. A minimum 2 sec periods of ES (1 msec pulses at 50-60 per sec) provoked single IMP increments equivalent to .1-.3 mU oxytocin. High spinal section or hypophysectomy abolished ES-induced IMP responses. AP PRL was determined by disc electrophoresis. Prior to stimulation, the rats were separated from their pups for 4-8 hrs. ES was applied (15 sec on, 15 sec off during 5 min followed by 5 min rest) for either 5,15,30,90, 120 and 180 min. Sham stimulated rats were killed at 0 min and after 180 min. Results showed that ES for 5-30 min provoked an acute 50% depletion of AP PRL. In spite of continuous ES, AP PRL was restored, i.e., repleted, after 90 min and remained at a high level throughout the 180 min period. This suggests that ES provoked PRL depletion but had no effect on PRL repletion. Thus, rats stimulated only for 5 min but killed at 90 min showed repleted PRL levels. Sham stimulated rats showed high PRL levels, not different from non-suckled non-anesthetized rats. It is concluded that oxytocin is released and AP PRL is depleted in response to ES of a mammary nerve. (Supported in part by grant 70009 from the Ford Foundation).

EFFECTS OF INSULIN INJECTIONS AND OF FASTING ON PLASMA GLUCOSE, NEFA'S AND PROLACTIN IN THE NONLACTATING EWE. Mendel, V.E. and L.L. Bellinger.* Department of Animal Physiology, University of California, Davis, California 95616

The relationship between the anabolic hormones insulin and prolactin is unclear in ruminants; therefore nonlactating ewes were injected with insulin (1U/kg, i.v.) in both the fed and fasted states. Fast was continued for 3 days with insulin being injected once each day of fast. C^{14}-palmitate was injected before and after insulin to detect changes in the kinetics of fat metabolism. These experiments were repeated twice, 6 mo. apart. In the first experiment the ratios (post-injection/preinjection) of $T_{1/2}$, pool size and utilization rates were .75, .30, and .65, respectively in the fed animals and .80, .70, and .70 in the fasted animals. In the second experiment they were, 1.21, 2.97, and 2.44, respectively in the fed animals and .95, 2.44, and 2.65 in the fasted animals. NEFA first fell, on average from 200 μM/ℓ preinjection to 150 μM/ℓ 30 min post-injection then rose to 860 μM/ℓ in fed animals with the peak occurring 90 min. post-injection. In fasted animals, day two, NEFA first fell from 780 to 480 μM/ℓ then peaked at 1480 μM/ℓ 120 min. post-injection; day three the decrease was from 875 to 580 μM/ℓ and the peak at 120 min. post-injection was 1720 μM/ℓ, thus, showing a progressive increase of both the pre- and post-injection levels. Blood glucose levels were unchanged by 3 days of fasting and typically fell from 60-70 mg percent to 28-30 mg percent following insulin injection and required 300 min. to return to normal. Prolactin fell for 30 min. (40 ng/ml. to 23 ng/ml) following insulin injection then peaked at 45 min. post-injection; after 3 days of fast the peak had increased to 92.5 ng/ml. indicating that insulin may stimulate release of prolactin from the pituitary.

FORELIMB BLOOD FLOW DISTRIBUTION DURING HYPOTHALAMIC DILATOR RESPONSE. R.P. Menninger and C.H. Baker. University of South Florida, College of Medicine, Tampa, Florida 33620.

An attempt was made to determine whether hypothalamically induced forelimb vascular dilation affects primarily exchange beds or shunt circuits. In these experiments perfusion pressure was maintained at control levels during electrical stimulation of canine hypothalamic dilator areas. Slug injections of ^{131}I-albumin were used to measure the vascular volume actively circulating in the forelimb. A plethysmograph monitored changes in total vascular volume (TVV), filtration and during venous pressure elevations, the capillary filtration coeffecient (CFC). During stimulation, blood flow increased 25% and total vascular volume increased an average 1.5 ml. There was no secondary slow slope on the plethysmograph record indicating that following the initial increase in TVV an isovolumetric condition was reestablished. Active vascular volume (^{131}I-albumin) decreased 2.8 ml and CFC decreased 20%. These results can be explained on the basis of a redistribution of blood flow from exchange capillary networks to faster shunt circuits. A comparison of these results with those obtained during constant inflow perfusion indicates that although the decreased vascular resistance is of neural origin, the mechanism for blood flow redistribution may be metabolic. These results are quite different than those obtained with pharmacologic dilators and denervation. Therefore, hypothalamic dilations may be a more selective method of decreasing forelimb vascular resistance. This study supported by Northeast Florida Heart Association, a chapter, the Indian River County Division of the Florida Heart Association and NIH Grant HL-14541.

EFFECTS OF pH AND THEOPHYLLINE ON THE CORONARY RESPONSE TO ADENOSINE. G.F. Merrill*, F.J. Haddy, and J.M. Dabney, Department of Physiology, Michigan State University, East Lansing, Michigan 48824.

One objection to the adenosine hypothesis for the regulation of coronary blood flow is that reactive hyperemia is not regularly blocked by theophylline. A local increase in hydrogen ion may contribute to coronary dilation or may influence another dilator's action, e.g. adenosine. We have studied the relation of pH to adenosine dilation in an isolated, spontaneously-beating guinea pig heart with or without theophylline, a competitive inhibitor of adenosine. Reactive dilation was also studied. Adenosine ($8X10^{-7}M$) at a perfusate pH of 7.42 increased flow from a control level of 6.8 ml/min to a maximum of 12.0 ml/min. Theophylline ($10^{-4}M$) in the perfusate reduced this maximum flow to 8.2 ml/min, a 32% reduction. A perfusate with a pH of 7.20 containing adenosine ($8X10^{-7}M$) increased control flow from 7.8 ml/min to 12.2 ml/min. At this pH, theophylline reduced maximum flow to 9.8 ml/min (20% reduction). In other hearts we studied the effect of theophylline on reactive dilation. Upon release of a 30 second inflow occlusion, flow reached a maximum of 12.4 ml/min vs. control of 5.1 ml/min. With theophylline present ($5X10^{-5}M$) flow reached a peak of 12.3 ml/min following release. These data indicate that (1) adenosine ($8X10^{-7}M$) still dilates at a low pH, (2) theophylline ($10^{-4}M$) can attenuate adenosine dilation at either pH 7.42 or 7.20, and (3) theophylline does not affect reactive dilation as tested. These data allow a role for adenosine in the coronary response to lowered pH, but do not rule out adenosine's contribution to coronary reactive dilation since the concentrations of adenosine attained may be higher than can be blocked by the amount of theophylline used in this study. (Supported by a Michigan Heart Grant-In-Aid; and by NIH Grant HL10879.)

CIRCADIAN RHYTHMS OF GLYCOGEN IN SKELETAL MUSCLES. D.K. Meyer, Dept. Physiology, University of Missouri, Columbia, Missouri, 65201.

Circadian rhythms (CR) of glycogen content have been described in cardiac muscle and liver of the rat but the skeletal muscle has not been studied. Glycogen was measured in 5 different skeletal muscles, Diaphragm (D), white Vastus lateralis (V), lateral head of the Gastrocnemius (G), Cremaster (C), and Soleus (S) and in the Heart (H) of male Wistar rats at 4 h. intervals during the day. The rats (150-300g) were entrained for 2 weeks to a 12L:12D light cycle in which the lights came on at 0600 h. and went off at 1800 h. Food and water were available, ad lib. A CR was found in all skeletal muscles studied with the nadir of the cycle uniformity at 1600 h. and the peak at 0000 h. except for G where, as in the heart, the peak came at 0400 h. Liver glycogen, measured in the same animals peaked at 0800 h. The 24-hour mean glycogen values were distributed in the following order: V>C>G>D=heart>S. The greatest change in amplitude of the glycogen CR was in D (3.39 to 7.82 mg/g. wet wt) and the least in G (4.62 to 6.25 mg/g. wet wt). The consistency of the CR was demonstrated in 5 replicate studies. At nadir D has less glycogen than S, a slow red muscle and at peak more glycogen than V, a fast-twitch white muscle. The classification of skeletal muscles by glycogen content needs to take into account the 24 hour glycogen rhythm. The spontaneous and predictable CR of skeletal muscle glycogen of the light entrained, ad lib fed rat is a potential tool in the study of muscle metabolism. The glycogen rhythm should also be a factor in the design and interpretation of metabolic studies in exercising rats. (Supported by grants HL 16041 and UMC-NSF 1330).

A LINEAR NETWORK MODEL OF COUPLED SALT AND VOLUME FLOWS THROUGH EPITHELIAL MEMBRANES: DEPENDENCE OF ONSAGER RECIPROCITY ON NETWORK TOPOLOGY (LOCATION OF PUMP OR OTHER SOURCES). D.C. Mikulecky, Dept. Physiology, Medical College of Virginia, Richmond, Va. 23298.

A transcellular and a parallel shunt pathway are in series with an interstitial space and basement membrane to make up a simple epitheliar membrane between lumen and blood. A paradigim is presented for solving the series-parallel network of coupled flows by replacing the usual scalar resistances, conductances, currents and potentials by 2 x 2 resistance or conductance matrices and 2-dimensional flow or force vectors in the same computational scheme as would be used for a simple electric circuit with the same topology. A number of situations are treated which include (a) transport of isotonic fluid between isotonic blood and lumen due to active salt transport across the cells, (b) hydrostatic and osmotic differences between the blood and lumen, and (c) combinations of both. The existence or nonexistence of Onsager reciprocity between coefficients coupling the two flows in specific parts of and/or the whole network depends on the specific topology of the circuit which is in turn dependent on the location of the sources (active transport pump as a "current" source and the hydrostatic and osmotic differences as "voltage" sources). Experimentally, the tests for this reciprocity should serve as a means of locating the pump (or pumps). Other results include 1) the composition of the fluid pumped between isotonic solutions is independent of the pump rate. 2) No standing gradient is necessary in the interstitial fluid to achieve isotonic transport. The model illustrates a topology dependent Onsager reciprocity for connected elements which would always be reciprocal when isolated. This illustrates the principle that Onsager reciprocity is a topological rather than a molecular property.

CHRONOLOGICAL ADJUSTMENTS OF REGIONAL ELECTROGRAMS AND CONTRACTILITY TO TRANSIENT MYOCARDIAL ISCHEMIA AND REPERFUSION IN CONSCIOUS DOGS. Ronald W. Millard, Guy R. Heyndrickx*, Peter R. Maroko* and Stephen F. Vatner. Dept Med, Harvard Med Sch & Peter Bent Brigham Hosp. Boston, Ma 02115.

The relation between regional mechanical function and electrogram in ischemic myocardium was studied in 12 conscious dogs during a 15 minute coronary occlusion and for 24 hrs after reperfusion. Instrumentation included Doppler flow transducers and occluders on a coronary artery and pairs of ultrasonic crystals in the ischemic zone for end systolic(ES) and end diastolic(ED) segment length(SL) and velocity of SL shortening and as sites for simultaneous electrograms. Less than 1 min after coronary occlusion EDSL rose from 14.17 $\pm$ 0.83 to 14.71 $\pm$ 0.96 mm as ESSL rose from 12.87 $\pm$ 0.77 to 15.00 $\pm$ 0.98 mm, i.e., systolic velocity of shortening was 0 and paradoxical motion occurred. At this time the ST segment had not increased significantly from control (1.3 $\pm$ 0.2 mV). Holosystolic bulging reached a maximum by 90 sec after occlusion with little further rise in ST. Paradoxical motion persisted through the remaining 15 min of ischemia, as ST continued to rise reaching a maximum of 12.1 $\pm$ 1.2 mV between 5 and 15 min. With reperfusion there was immediate reactive hyperemia, ST reverted to control within 30 sec, while coronary flow returned by 15 min. In contrast, EDSL, ESSL, stroke shortening and velocity returned gradually to control over the subsequent 24 hrs. Thus, the chronological responses of mechanical and electrophysiological function differ with myocardial ischemia; maximal ST elevation occurs several minutes later than maximal depression of function in the ischemic myocardium. Conversely, on reperfusion the electrogram and coronary blood flow return rapidly to control, while recovery of mechanical function is prolonged considerably. Thus, while reperfusion repays the ischemic debt rapidly, effects of brief ischemia as reflected by depression of myocardial function, persist.

HYPEROXIA ASSOCIATED INHIBITION OF STIMULATED PAROTID TRANSPORT. *D. A. Miller* and R. G. Esquire* (SPON: K. E. Schaefer), Naval Submarine Medical Research Laboratory, Groton, CT 06340*

Acute hyperoxia has been associated recently with inhibition of transepithelial active transport in frog skin and toad bladder and histologic changes in rat parotid. These studies raise the possibility that transepithelial transport inhibition may play a role in the development of O_2 toxicity in man. Studies were performed of parotid transport before, during, and after exposure to hyperoxia (3 subjects, sour grape stimulus, twice daily parotid samples, hyperbaric air, 7 days with P_{O_2} averaging 0.61 ATA). Two subjects (O&P) had normal stimulated parotid function (J. Dent. Res. 52: 1157, 1973), while one (M) was refractory. Progressive, significant, reversible, changes were noted during hyperoxia in stimulated parotid function: pH was down 0.17, and flow rate and Na, K, Cl secretion rates were 61%, 34%, 65%, and 37% of control respectively. No inhibition was found of the unstimulated parotid transport. The above changes in stimulated parotid transport are considered to be direct parotid effects of hyperoxia because (1) no taste or neurological deficits (EEG, reaction time, problem solving ability) were found; (2) P_{O_2} was above the 0.5 ATA current recommended safe limit for chronic exposure; (3) available evidence indicates that the P_{CO_2} (0.0017 ATA) and P_{N_2} (3.0 ATA) would be without significant effect; (4) Subject O showed further parotid changes and delayed recovery following treatment for decompression sickness with 100% O_2 (P_{O_2}=1.85 ATA for 40 min); (5) other O_2 attributable changes were found: cough (O, P, M,), substernal pain (M), decreased FVC (M↓9%, P↓25% after 100% O_2). Since active Na transport plays a major role in parotid secretion, these findings are consistant with the view from in vitro studies that hyperoxia inhibits transepithelial Na transport.

MEMBRANE DIFFERENCES IN THE SOMA AND AXON OF APLYSIA GIANT NEURON. J. Miller,* R. Horn* and D. Junge. University of California, School of Dentistry, Los Angeles, California 90024.

Simultaneous intracellular recordings were obtained from the soma and axon of the giant neuron (R2) of the visceral ganglion of Aplysia californica. A fifteen minute treatment with a 1% solution of pronase, a nonspecific proteolytic enzyme, facilitated impalement through the epineurium. Axon spikes produced by intracellular somatic stimulation and recorded 2-4 cm from the soma were reversibly blocked in both sodium-free and 30μM tetrodotoxin (TTX) solutions. This indicated that the axon spike is of the "pure sodium" type at this distance from the soma. The soma spike of R2 has been previously shown to have a mixed sodium/calcium ionic dependency. In some experiments stimulation was applied several millimeters distal to the intraaxonal recording electrode with an extracellular suction electrode. The resulting depolarizations of up to 30mv failed to elicit a regenerative axonal response in both sodium-free and TTX-containing solutions. Intracellular and extracellular axonal recordings made at several distances from the soma provide evidence that the transition zone from a mixed sodium/calcium to a pure sodium spike exists within 2mm of the soma. Application of extracellular 25mM tetraethylammonium bromide (TEA) caused a 40 ms delay in the repolarization of the soma action potential. At 1.0 mm from the soma the delay was reduced while at 2 cm there was no appreciable delay of the repolarization. The graded effect of TEA along the axon may be correlated with a concommitant gradation in the calcium component of the action potential.

D-THREITOL AND SORBITOL AS CRYOPROTECTANTS IN AN ADULT INSECT: SEASONAL AND INDUCED VARIATIONS. K. Miller. Institute of Arctic Biology, University of Alaska, Fairbanks, AK 99701

The adult tenebrionid beetle Upis ceramboides tolerates temperatures as low as -55°C in its natural winter hibernaculum. Tests show that individual supercooling points remain between -5° and -9°C throughout the year, which indicates that the beetles survive freezing for extended periods. Hemolymph analysis by paper and gas chromatography shows that the polyhydric alcohols sorbitol and D-threitol accumulate with the onset of cold weather and attain winter concentrations of about 8 and 3 per cent, respectively. This is the first report of D-threitol as a naturally occurring compound. Seasonal changes in lower lethal temperatures parallel fluctuations in polyol levels, with summer lethal levels near -7°C. When artifically deacclimated in midwinter the beetles quickly lose their polyols, but they can resynthesize them when exposed to successively lower temperatures over a period of weeks.

ISOTOPE FLUX AND TENSION RESPONSES IN PHASIC AND TONIC VASCULAR SMOOTH MUSCLE IN THE RABBIT. Louis Miller* and Allan W. Jones. Dept. Physiol., U. of Mo.-Columbia, Mo. 65201

Ion turnover in phasic (portal vein) and tonic (pulmonary artery) vascular smooth muscle was compared and changes related to tension development due to vasoactive agents. Significant differences were found in ^{42}K turnover between the portal vein (0.0122 ± 0.0007 $min.^{-1}$ (n=7)) vs. the pulmonary artery (0.0038 ± 0.0002 (n=7)). ^{36}Cl turnover was also significantly faster in the phasic muscle (0.065 ± 0.004 (n=6) vs. 0.032 ± 0.002 (n=6)). Similar ED_{50}'s were noted for the effects of norepinephrine (NE) on ^{42}K turnover and tension development. Supramaximal doses of angiotensin II (AII) and 5-hydroxytryptamine (5-HT) were also studied. In the portal vein NE>5HT≥AII in increasing ^{42}K turnover; in the pulmonary artery NE=5-HT>AII. The tension responses in the portal vein paralleled the flux responses while in the pulmonary artery NE elicited a larger contractile response than did 5-HT. It is concluded that phasic vascular smooth muscle is characterized by increased membrane permeability as compared to the tonic type. Vasoactive agents which cause depolarization appear to do so by increasing membrane permeability. The close relation between permeability and tension changes indicate the primary source of activator calcium is extracellular. However, increased tension response in pulmonary artery to NE over 5-HT indicate intracellular sources as well. (Supported by grant HL 15852 and the American Heart Association.)

REVERSIBLE HYPOXEMIA IN ARTIFICIALLY VENTILATED CATS DURING ELECTRICAL STIMULATION OF THE VASOMOTOR CENTRE. Millis, R.M., Wood, D.H.; Trouth, C.O.; Tureman, J.; Nelson, S. Dept. Physiol. & Biophysics, College of Medicine, Howard University, Washington, D.C., 20059 (Spon;L.N.Cothran)

Direct stimulation of vasomotor centre in the cat medulla also produces various types of respiratory effects [1]. In order to elucidate the mechanisms subserving this interrelationship, cats were artificially ventilated with a constant volume respirator while electrically stimulating (1-4 V., 1 msec. duration, 40 Hz) the vasomotor centre. End-expiratory PO_2, PCO_2, PN_2, and blood PaO_2, $PaCO_2$, were continuously monitored (mass spectrometers). Inspiratory and expiratory tidal flows and volumes (V_t) were recorded from a pneumotachograph coupled to an integrator. Arterial blood pressure was recorded from a strain gauge. Stimulation caused an instantaneous increase in mean arterial blood pressure (MABP) as well as a marked decrease in tidal volume and flow. Mean changes in end-expired and arterial blood gases were as follows:
1. Decrease in the end-expiratory PO_2 of 35 torr; and PaO_2 of 30 torr.
2. Increase in end-expiratory PCO_2 of 20 torr; and $PaCO_2$ of 15 torr.
3. Increase in the end-expired PN_2 of 26 torr. These occurred during stimulation in the region of the nucleus parvocellularis and were not elicited 0.25-0.5 mm distant from the point described by Trouth et al 1973, returning to baseline soon after cessation of stimulation. The responses could not be elicited by increasing the MABP pharmacologically with l-norepinephine (Levophed). It is postulated that the interrelationship between the Vasomotor and Respiratory centers is reflected in changes in airway mechanics.

1. Trouth, C.O., Leoschcke, H.H., Berndt, J., Pflugers Arch. 339,185-201, 1973.
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EFFECT OF ATP AND MgATP ON PASSIVE Ca FLUXES IN FRAGMENTED SARCOPLASMIC RETICULUM. M.S. Millman* (spon: M. Bárány) Department of Physiology. University of Ill. Medical Center, Chicago, Ill., 60680.

Sarcoplasmic reticulum was isolated from homogenized rabbit white skeletal muscle and a portion suspended (10 mg protein/ml) in buffered (pH 6.8, 25°) 10 mM $^{45}CaCl_2$. This initial suspension was incubated overnight at 3°; the next day Ca efflux was initiated by dilution (37°) with enough EGTA to reduce the final external Ca concentration to 10^{-8} M, and monitored by Millipore filtration. This low external Ca concentration prevented activation of the Ca pump when the diluting medium contained ATP so that the fluxes observed were purely passive. It was found that when the diluting medium contained 5 mM ATP and 5 mM $MgCl_2$, passive efflux was significantly reduced from the control (control half time = 1.5 min). 5 mM ADP caused an initial, rapid release for about one minute, followed by a release much slower than control. 5 mM AMP, adenosine, adenine, PPi or Pi were without effect. When Mg was omitted, an initial burst of efflux occurred in the presence of ATP before the first sample could be filtered (2-4 sec in the cold), involving more than one-third of the vesicular Ca. Following this initial burst, efflux was slower than control as in the presence of Mg. The data suggest a possible mechanism of Ca release upon excitation in the physiological state as well as cellular mechanisms for the control of membrane permeability involving ATP but not its hydrolysis. (Supported by GRSG No. RR5369 and by MDAA and MDAC).

INHIBITION BY CO_2 OF RESPIRATORY RELATED, VAGAL DISCHARGE IN TURTLES. W.K. Milsom* and D.R. Jones. Dept. Zoology, University of British Columbia, Vancouver, B.C., Canada V6T 1W5.

Single fibre nerve activity was measured from vagal slips in single pithed, artificially ventilated turtles (Chrysemys picta, 600-900g) with end-tidal P_{CO_2} maintained at 0, 38 or 76 mm Hg. Only neural activity which correlated with the phases of artificial ventilation was monitored. Maximal afferent discharge occurred before end inflation and decreased throughout deflation indicating that the receptors are both rate and mean-pressure sensitive. Increasing the P_{CO_2} from atmospheric to 76 mm Hg reduced the total discharge associated with each breath (mean reduction of 51%), the discharge level at peak inflation (mean = 40%), the discharge level at end-deflation (mean = 72%), and the tonic discharge rate during maintained inflation at various volumes. This decrease in activity often began during the first inflation following a step change in the P_{CO_2} of the ventilating gas and continued to fall over several cycles of ventilation. Addition of CO_2 (P_{CO_2} = 38-76 mmHg) to the inspired air of conscious unrestrained turtles resulted in increased respiratory rate and tidal volume which also developed over the course of several breaths. Receptors which are inhibited by CO_2 have been demonstrated in the lungs of both birds and mammals and their presence in reptiles suggests that such receptors, responding to more than one modality, are phylogenetically ancient.

EFFECT OF THORACIC BLOOD VOLUME CHANGES ON CARDIAC OUTPUT. W. Mitzner, H. Goldberg* and S. Lichtenstein*. Dept. of Environmental Medicine, Johns Hopkins University, Baltimore, Maryland 21205.

Since the pulmonary compliance is small relative to that of the systemic circulation, shifts of thoracic blood volume to the periphery are thought to have only minimal effects on the magnitude of cardiac output. Increases in cardiac output which result from increased cardiac function would occur primarily by a reduction of right atrial pressure (Pra). We propose, however, that there is a significant amount of effectively unstressed volume in the heart-lung segment capable of being mobilized by changes in cardiac function or pharmacologic agents, and that the increase in cardiac output caused by such changes may occur not only by decreasing the Pra, but also by increasing the systemic stressed volume and thus the mean systemic pressure (Pms). Our experimental approach consists of an in situ canine heart-lung preparation which pumps into a mock circulation consisting of a Starling resistor, a normal venous compliance and a resistance to venous return. We measure cardiac output, Pms, Pra, aortic and left atrial pressures. Increases in aortic pressure caused reductions in cardiac output, even with no change (or a decrease) in right atrial pressure. With aortic pressure at 100 mmHg epinephrine administration (10 μg/kg) increased cardiac output 55%. About half of this increase was a result of a decreased Pra, and the other half resulted from an increased Pms due to a shift of 68 ml into the peripheral circuit. For normal 20-25 kg dogs, 68 ml is more than all the blood normally considered to be stressed in the pulmonary compliance and is approximately 1/4 the total systemic stressed volume. The transferred volume must come from the heart-lung segment and represents an important volume reservoir subject to local cardiac control.

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INVOLVEMENT OF RAPHÉ NUCLEI IN CIRCADIAN CONTROL OF RUNNING. G. P. Moberg* and L.M. Kam* (SPON: H.H. Cole). University of California, Davis, CA 95616

In order to investigate whether a serotoninergic (5-HT) system might be involved in the regulation of the circadian pattern of wheel running in rats, the effect on running of ablation of the medial and dorsal raphé nuclei was studied. Adult male rats were adapted to wheel cages in which running activity was continuously monitored. The animals were maintained under a 14:10 light-dark schedule with H_2O and food ad libitum. After the period of accommodation to the wheel, the animals were divided into three groups, sham lesioned (S), dorsal raphé lesioned (D), or medial and dorsal raphé lesioned (MD). Following surgery running activity was monitored for 21 days. The animals were then decapitated and the brain 5-HT content was measured. As compared to S animals, the level of 5-HT was reduced by 34% in the D and 56% in the MD animals. It was found that S and D lesions initially reduced total daily running, although the animals returned to preoperative running levels by the end of testing. Throughout the entire period there was no effect upon the circadian distribution of running in the S and D groups. During the first week following surgery, however, the MD lesioned animals were initially hyperactive, showing a 100% increase in running during the light period. One week following surgery and then throughout the rest of the testing period the total amount of running dropped below control levels while the circadian pattern of running returned to normal. These data suggest that although a 5-HT system projecting from the medial raphé may modulate the control of the circadian pattern of running, other neural components can compensate for the absence of this system.

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FUNCTIONAL SIGNIFICANCE OF CORONARY ALPHA RECEPTORS.

D.E. Mohrman and E.O. Feigl. Dept. Physiology & Biophysics, University of Washington, Seattle, WA 98195

Alpha receptor mediated vasoconstriction potentially opposes metabolic vasodilation of coronary vessels in circumstances of increased sympathetic activity or elevated circulating catecholamine levels. We examined this possibility using anesthetized, atropinized, closed-chest dogs. The left coronary artery was perfused at constant pressure with a cannula introduced via the right carotid. Left coronary flow and oxygen consumption ($\dot{V}O_2$) of the perfused myocardium were determined before and during intracoronary norepinephrine infusions, both prior to and following alpha-receptor blockade with Dibozane (3 mg/kg, iv). Six different rates of norepinephrine infusion produced graded increases in $\dot{V}O_2$ ranging to 197% of control. Prior to alpha-receptor blockade control myocardial oxygen extraction was 74%. Coronary blood flow increased 0.67% and myocardial O_2 extraction increased 0.33% for each one percent increase in $\dot{V}O_2$ produced by norepinephrine. Following alpha-receptor blockade control myocardial oxygen extraction was 72%. But now coronary blood flow increased 0.90% and O_2 extraction increased 0.10% for each one percent increase in $\dot{V}O_2$ induced by norepinephrine. These findings were consistent over the full range of increased $\dot{V}O_2$ studied. Similar results were obtained when cardiac sympathetic nerves were reflexly activated by carotid sinus hypotension.

We conclude that coronary alpha receptor activation significantly restricts coronary metabolic vasodilation during norepinephrine infusion or sympathetic nerve activation.

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CONTRIBUTION OF REGIONAL VASCULAR BEDS TO AUTOREGULATION OF TOTAL SYSTEMIC CIRCULATION. Leroy S. Molstad*, George E. Barnes*, Hsing I. Chen*, and Harris J. Granger. Dept. Physiology & Biophysics, University of Mississippi Medical Center, Jackson, MS 39216

To determine the extent of blood flow autoregulation in the regional vasculatures, we placed non-cannulating probes around the renal, superior mesenteric, iliac and celiac arteries of anesthetized dogs. Pressure-flow relations for each bed were obtained. Local perfusion pressure was altered by graded compression of the regional aorta. In the anesthetized dog, renal blood flow was maintained essentially constant within the pressure range of 85 to 140 mmHg. Superior mesenteric flow was also highly independent of perfusion pressure within the pressure range of 50 to 130 mmHg. The "degree of autoregulation" in the intestinal bed ranged from 50 to 100%. In contrast, the iliac and celiac beds exhibited very little, if any, tendency to maintain flow at a constant level in the face of changes in perfusion pressure. To separate iliac flow into skin and muscle components, pressure-flow relations for hindpaw and skinned hindlimb were obtained. These results indicate that under normal conditions neither muscle nor hindpaw autoregulate their blood flow to any significant extent. In conclusion, the renal and superior mesenteric vascular beds are the major loci of total systemic autoregulation in the anesthetized dog. (Supported by NIH grant HL-11678)

LOWER BODY POOLING IN MAN DURING HEAD UP TILT, L.D. Montgomery* and B.A. Williams, (SPON: R.D. Allison). NASA-Ames Research Center, Moffett Field, CA 94035

Two series of impedance plethysmographic measurements were made on 3 men to compare the effect of saddle and shoulder supports on leg and pelvic circulatory and volume changes during head up tilt. One minute tilt intervals at 20, 30, 40, 50, 60 and 70 degrees were used to monitor the onset of fluid shifts. Four minute tilt periods at 20, 40 and 60 degrees were used to determine the extent of circulatory and segmental volume changes that took place with the two types of supports. The amount of blood pooling in the leg decreased slightly at angles larger than ≈ 60° with the shoulder support. Use of the shoulder support had little effect on abdominal pooling. A large decrease in leg pooling occurred at angles greater than ≈ 50° with the saddle support. This was accompanied by a marked increase in the pelvic segment. Blood flow in the leg was found to decrease to approximately 65% of the control value within 0.2 min. of initial tilt and to remain depressed during the 4-minute tilt period. Reactive hyperemia was noted in the leg after return to the horizontal position. Leg circulation then decreased to the pre-tilt value during the 4-minute recovery period. These results suggest that both types of tilt table supports interfere with lower body fluid response to large angle tilt. The reflex abdominal tension to hold position with the shoulder support partially clears the venous pool in the leg. The saddle support appears to restrict blood pooling in the leg which results in exaggerated blood pooling in the pelvic area. Other techniques of body support for tilt table testing are currently being investigated.

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ROLE OF SPLEEN IN HYPOXIA-INDUCED HEMATOCRIT INCREASES. C.G.Morrill* and G.J.A.Cropp. Dept.Clin.Physiol., Nat.Asthma Ctr., Denver, Co. 80204

Observations in our laboratory have suggested that hematocrit (HCT) increases in dogs exposed to acute, severe hypoxia (HPX) were either small or marked. Eight anesthetized dogs were therefore studied intact and after splenectomy to assess splenic involvement. Sympathomimetics were also administered in an attempt to identify other mechanisms that could differentiate these groups. In each study, arterial PO_2 was decreased from 200 to 20 mmHg in five, 10-min steps. After a 40-min recovery period, a 2-min (I.V.) infusion of epinephrine (E), norepinephrine (NE), or isoproterenol (I) was given. The drugs were given in random order with a 40-min recovery period between drugs. Arterial blood was drawn for HCT and PO_2 measurements at the end of eac HPX period, and before and at the end of each drug infusion. On the basis of their HCT changes (Δ) during HPX, 3 dogs were responders (R) (HCTΔ>5.6%) and 5 were low-responders (LR) (HCTΔ<3.2%). The absolute Δ in HCT in response to HPX and drugs for the R and LR groups are tabulated.

	intact		post splenectomy	
	R	LR	R	LR
HPX	9.2(±1.8)	2.4(±0.3)	0.8(±0.5)	2.3(±0.2)
E	11.0(±0.4)	9.4(±1.8)	-0.9(±0.2)	-0.2(±0.1)
NE	9.6(±0.4)	9.4(±1.5)	1.2(±1.1)	0.5(±0.3)
I	4.9(±1.3)	2.8(±1.1)	-0.9(±0.4)	0.1(±0.1)

We conclude that in R, HPX- and drug-induced HCT Δ involve the spleen. In LR, only the drug-induced HCT Δ depended on the spleen while HPX-induced HCT Δ did not require the spleen and involved non-splenic mechanisms which do not appear to be adrenergically mediated.

WHEEL-CAGE RUNNING OF MERRIAM'S KANGAROO RAT (DIPODOMYS MERRIAMI) WITH REGARD TO FOOD DEPRIVATION. J. D. Morris, Jr.*, D. B. Dill, and L. F. Soholt*, Lab. of Environ. Patho-physiol., Desert Research Inst., Boulder City, Nevada 89005.

In 1927 Richter (Quar. Rev. Biol., 2:307, 1927) found activity patterns of the albino rats that were related to environmental and physiological conditions. In the present study the responses of a nocturnal desert rodent were observed. Twelve kangaroo rats trapped in the eastern Mojave Desert were maintained in cages equipped with 33 cm metered running wheels. Various periods of starvation caused significant increases in running and decreases in body weight. Upon return to the normal diet of whole oats there occurred a decrease in running lasting 2 or more days to distances well below the baseline average. The weight deficit was not regained for several days after the starvation periods, although the rats were fed their oat diet ad lib. In a similar experiment where the rats were fed carrots during the first day of recovery weight regain was more rapid. This indicates that weight loss was in part due to dehydration. The increased activity elicited by hunger caused an increased respiratory water loss which is normally regained by hydrolysis of carbohydrates. Dehydration may cause decreased appetite for oats however, delaying repayment of the water deficit. The hypothesis that some of the weight loss resulted from dehydration is further substantiated by calculations of energy cost. (Supported by NSF Grant BMS 74-04861).

LUTEINIZING HORMONE-RELEASING HORMONE (LRH) REGULATION OF NEURAL EVENTS CONTROLLING MATING BEHAVIOR. R.L. Moss, M.J. Kelly*, M.M. Foreman* and C.A. Dudley*, Dept. Physiol., U. Texas Hlth. Sci. Ctr., SW Med. Sch., Dallas, Texas 75235.

Experiments to determine the effect of LRH on lordosis behavior when infused via cannulae into either the medial preoptic area (MPOA; N=30), arcuate-ventromedial (ARC-VM; N=30) complex, lateral hypothalamic area (LHA; N=6) or cerebral cortex (CC; N=9) were conducted on estrone-primed ovariectomized (OVX) rats. Fifty nanograms (ng) of LRH infused into either the MPOA or ARC-VM complex significantly increased ($p<0.001$) the lordosis-to-mount ratio as compared to prefusion behavior, while 50 ng of LRH injected systemically or infused into the LHA or CC did not enhance lordosis behavior. To study the influence of LRH on hypothalamic neurons, experiments were conducted on urethane-anesthetized OVX rats. Iontophoretic application of LRH and extracellular recordings were made on 216 MPOA neurons of which 33 were antidromically identified (AI) by stimulation of the ARC-VM complex. The remaining 83 neurons though located in the MPOA were not antidromically identified (non-AI). The majority of MPO neurons showed little if any responsiveness to LRH (AI neurons=67%; non-AI neurons=52%). Excitation was observed in 27% and inhibition in 6% of the AI neurons while excitation was observed in 32% and inhibition in 16% of the non-AI neurons. This suggests that LRH is acting on the neural tissue of the MPOA and ARC-VM complex to initiate behavior. (Supported in part by NSF Grant #GB-43494 and by NIH-USPHS Grant #NS-10434-END.)

PULMONARY CIRCULATION IN DOGS IN DEVELOPING RADIATION PNEUMONITIS. B. A. Muggenburg and J. L. Mauderly, Lovelace Foundation, Inhalation Toxicology Research Institute, P. O. Box 5890, Albuquerque, New Mexico, 87115.

This study was conducted to determine some of the changes that occur in pulmonary circulation in developing radiation pneumonitis. Beagle dogs inhaled aerosols of either ^{144}Ce or ^{90}Y attached to fused clay particles. Particles deposited in the deep lung were tenaciously retained due to the relatively insoluble nature of the fused clay particles. The beta absorbed dose to lung from the ^{144}Ce cumulated with a half life of 180 days and the ^{90}Y with a half life of 64 hours. The dogs exposed to the ^{144}Ce developed interstitial pulmonary fibrosis over a 200-day period. No exudative stage was clinically obvious. These dogs had elevated pulmonary artery pressures, unchanged cardiac outputs and elevated pulmonary arteriolar resistance prior to death. The dogs that inhaled ^{90}Y developed severe pulmonary edema 30 to 60 days after exposure. No changes in pulmonary artery pressure or cardiac output were found. By 90 days after exposure, early interstitial pulmonary fibrosis had developed and elevated pulmonary artery pressures were found along with unchanged cardiac output. These studies indicated that pulmonary circulation is not severly impaired during the exudate phase of radiation-induced pneumonitis. During the stage of fibrosis, pulmonary hypertension developed.

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MATURATION OF RENAL SODIUM HANDLING IN THE SPONTANEOUSLY HYPERTENSIVE RAT. M.M. Mullins* and R.O. Banks* (SPON: L.I. Kleinman). Dept. of Physiology, University of Cincinnati, Cincinnati OH 45267

Renal sodium excretory response to acute saline loading was studied in anesthetized spontaneously hypertensive (Okamoto) (SHR) and Wistar (NW) rats at ages 6, 12 and 16 weeks. Glomerular filtration rate (GFR) and sodium excretion were measured in 5 animals of each group during hydropenia and at the end of 60 minutes following the initiation of a 4.5% body weight intravenous saline load. GFR during hydropenia and Na loading and Na excretion during loading were lower in SHR than in NW. At 6 weeks (prehypertensive stage) GFR during hydropenia (0.12± 0.05) and during saline loading 0.23±0.11) were lower than in NW (0.73 ±0.18 and 0.91±0.12 respectively, $p < .01$). Also SHR excreted only 14.± 3.% of the infused Na compared to 35.± 3.% for NW ($p < .01$). There was no difference in fraction of filtered Na excreted (FENa) between SHR and NW during hydropenia or saline loading. At 12 weeks GFR remained significantly lower in SHR than in NW ($p < .01$), but there was no difference between the groups in ability to excrete the saline load. At 16 weeks there was no difference in GFR between groups, but SHR excreted a higher fraction of the saline load than NW (44.± 5.% vs 30.± 5%, $p < .05$). At all ages body weight was lower and kidney weight/body weight ratio higher in SHR than in NW. These data indicate that, compared to NW, SHR have a) a slower rate of glomerular maturation, b)a diminished natriuretic response to saline loading during the prehypertensive stage due to depressed GFR and c) enhanced natriuretic response during the hypertensive stage due to enhanced tubular rejection of Na.

MECHANICAL PROPERTIES OF 100 - 250 μm ARTERIAL RESISTANCE VESSELS. M.J. Mulvany* and W. Halpern. Dept. of Physiology and Biophysics, University of Vermont, Burlington, VT 05401

The mechanical properties of intact 1.5 mm cylindrical segments of small arterial resistance vessels have been compared with those obtained from the larger vessels which have been previously reported by others. The segments were excised from the 1st and 2nd branches of mesenteric arcades in 6 month old Wistar-Kyoto (WKY) rats. These vessels had a lumen diameter (d_{100}) of 100-250 μm when relaxed at 100 mm Hg intraluminal pressure. The segments were threaded onto two parallel 32 μm tungsten wires attached respectively to a force transducer and a displacement device. After threading, the wires were tensioned reducing their mean compliance to about 1 μm/mN (≈ 0.02 d_{100}). The wall stress (σ) and diameter (d) of vessels relaxed by Ca^{++} withdrawal were related (n=10) by $\sigma = a \exp(b(d/d_{100}-1))$: a = 101±25 mN/mm^2, b = 8.8±1.2 (mean±S.D.). Vessels activated by K^+ depolarization yielded repeatable active responses (σ_o) of 153±35 mN/mm^2 (n=7) at 5mM Ca^{++}, while graded responses were obtained at lower Ca^{++} concentrations. The instantaneous elastic characteristic measured (n=5) in quick releases during active responses, could be fitted (n=5) by $\sigma = \sigma_o \exp(b\,\Delta d/d)$: b = 46±6. The transient response to small step changes was Ca^{++}-dependent and appeared to consist of two components. On the basis of these experiments and electronmicrographs of the fixed material a model of the vessel wall is proposed. Experiments using matched spontaneously hypertensive rats (SHR) suggest that for a given intraluminal pressure the wall-lumen ratio of SHR vessels is similar to that of WKY control vessels.

THE MECHANISM OF K^+-INDUCED VASODILATION IN THE CORONARY VASCULAR BED. P.A. Murray* and H.V. Sparks (SPON: A.J. Vander). Dept. of Physiology, The University of Michigan, Ann Arbor, Michigan 48104

The K^+ ion has long been considered as a possible metabolic controller of coronary vascular resistance. The purpose of this study has been: 1) to quantitatively determine the effects of initial resistance (R_i) on the magnitude of the K^+-induced vasodilation (ΔR), and 2) to further elucidate the possible mechanism of K^+-induced vasodilation. The resistance changes associated with intra-circumflex artery injections of 40 umoles KCl were observed in anesthetized, open-chest dogs. ΔR was found to vary directly with R_i over a wide range of initial resistances ($\Delta R = 0.62\ Ri - 0.69$; $r = .86$; $n = 18$ dogs). This dose of KCl produced a 28-52% decrease in CVR, depending on the initial resistance of the bed. The K^+-induced vasodilation was not accompanied by any change in HR ($p > .2$; $n = 7$), but was associated with a small (4 ± 1 mmHg), transient decrease in MAP ($p < .05$; $n = 7$). It therefore appears very unlikely that the mechanism of K^+-induced vasodilation could be secondarily related to an increase in myocardial oxygen consumption. We also investigated the possibility that the K^+-induced vasodilation might be mediated via some neuro-humoral mechanism. We thus compared the vascular response to K^+ before and after the administration of the pharmacologic blockers phentolamine, propranalol, and atropine. Taking into account both the effects of R_i and time on the magnitude of the response, we found that the administration of the various pharmacologic blockers had little if any effect on the K^+-induced vasodilation. We conclude that it is unlikely that any major portion of the K^+-induced vasodilation is mediated either by an augmented transient local release of norepinephrine(NE) or acetylcholine, or a transient diminished basal release of NE. (USPHS grant HL 16760.)

BIOCHEMICAL ALTERATIONS IN THE LUNG RESULTING FROM OZONE EXPOSURE. M.G. Mustafa* (SPON: M. Stein). Dept. of Medicine, Center for Health Sciences, University of California, Los Angeles, Calif. 90024

Metabolic response of lung tissue to O_3 was examined in rats after exposure to 0.8 ppm O_3 for 1 to 30 days. The exposure resulted in a 40-50% augmentation of O_2 utilization in lung tissue homogenate in the presence of an added substrate (e.g., 2-oxoglutarate, succinate or glycerol-1-phosphate). Activities of marker enzymes, viz., mitochondrial succinate-cyt. c redustase, microsomal NADPH-cyt. c redustase and cytosolic glucose-6-phosphate dehydrogenase, increased maximally (50-60% over control) after 3 days of exposure, and remained elevated throughout the continuous exposure for 30 days. Termination of the exposure after 3 days resulted in a decline of enzyme activities in lung tissue, the control level being attained within 7 days, in recovering rats. The enzyme activities in the lungs of recovered rats could again be stimulated to the peak level if they were re-exposed to 0.8 ppm O_3 for 3 days. After rats were exposed to a higher level of O_3 (4 ppm for 8 hours), 80% of animals died in the group previously unexposed to 0.8 ppm O_3 for 3 days, whereas no rats died if they had been exposed to 0.8 ppm O_3 for 3 days immediately preceeding the high level exposure. The results suggest that the lung cellular metabolism undergoes changes in response to O_3 exposure, and that the stimulation of enzyme activities observed may be related to an adaptive mechanism by which animals are able to withstand a continuous exposure or a lethal stress of O_3.

PLASMA RENIN ACTIVITY IN ANESTHETIZED RATS DURING THE INITIAL PHASES OF RENAL ISCHEMIA. Joseph B. Myers and Eugene West*, Dept. Biology, Atlanta University, Atlanta, GA 30314

Plasma renin activity (PRA) was measured in anesthetized male Sprague Dawley rats at specific time intervals (0-90 min) after renal ischemia was induced. One-kidney experimental rats had the right kidney removed and the renal artery to the left was constricted. The controls for this group had the right kidney removed and no constriction. The two-kidney model had both kidneys intact and the left renal artery constricted. The controls for this group had both kidneys intact with no constriction. Plasma was collected in cooled beakers containing 0.5 ml of 0.3 M EDTA at specific time intervals (0-90 min) following constriction by cutting the aorta distal and posterior to the kidneys. A summary of the results showed that there was an increase in PRA (ng/ml/hr) in experimental and controls with the peak activity at the 60 min time interval, whereas in the two-kidney systems a significant increase was also observed and the peak activity was at the 90 min time interval. When these results were compared with normotensive Sprague Dawley rats (plasma collected at 0 time) the PRA was significantly lower in the normotensive animals. These results suggest that renal mass plays an important role in elevating and sustaining PRA during the initial phases of renal artery constriction. (Supported by the NIH-MBS Project, Grant No. RR-8006-04.)

CENTRAL AND PERIPHERAL BLOOD FLOW DURING EXERCISE IN VARYING CONDITIONS
E.R. Nadel, M.F. Roberts* and E. Cafarelli*. John B. Pierce Fndn Lab. and Yale Univ. Sch. of Med., New Haven, Conn. 06519.

The distribution of the cardiac output may become an important factor which limits exercise in the heat. To study the relation between central and peripheral blood flow, four volunteer subjects underwent 20 min exercise bouts at 30, 50 and 70 per cent $\dot{V}O_2$ max in 25° and 35° environments. Each bout was performed on a separate day. Internal body temperature (T_{es}) was continuously measured from a thermocouple in the esophagus at the level of the right atrium. Eight skin surface temperatures were monitored once each minute, with mean skin temperature ($\bar{T}_{sk}$) calculated from area and sensitivity weightings. Forearm blood flow (SkBF) was measured twice each minute by venous occlusion plethysmography, using an electrocapacitance technique. Cardiac output ($\dot{Q}$) was determined four to five times during each bout, using the CO_2 rebreathing technique. SkBF was linearly related to T_{es} at a given $\bar{T}_{sk}$. The effect of increased $\bar{T}_{sk}$ was a parallel shift to the left of the SkBF/T_{es} relation, i.e. lower T_{es} threshold for increased SkBF. $\dot{Q}$ was proportional to $\dot{V}O_2$ during the early transient of exercise; however, $\dot{Q}$ tended to increase during the course of exercise, as T_{es} and SkBF became significantly elevated. This increase in $\dot{Q}$ with progressive exercise was primarily the result of an elevated stroke volume in the 25°C environment, when SkBF was not approaching very high levels (SkBF < 18 $ml \cdot min^{-1} \cdot 100\ cm^2$ forearm $skin^{-1}$. In the 35°C environment, when SkBF was significantly higher, increased $\dot{Q}$ was the result of an elevated heart rate. We conclude that cardiac filling is not affected by different levels of SkBF during conditions of low and moderate thermoregulatory demand.

INTERHEMISPHERIC RELATIONS IN SPLIT-BRAIN MONKEYS.
Richard K. Nakamura* and M. S. Gazzaniga, SUNY at Stony Brook, N.Y. 11794

Split-brain monkeys (forebrain commissures and optic chiasm sectioned) have been compared with normal controls on two visual tasks, a color discrimination reversal and a nested match to sample. The nested match to sample consists of separate color and pattern match to sample problems intermixed such that one (color) starts before and ends after the other (pattern), thus nesting the pattern problem inside the color problem. The animals were tested on these tasks with one eye or both eyes open. The one eye condition directs visual information to only one hemisphere in the split animal. Results show the splits were much worse than normals in the one eye open condition but just as good with both eyes open. Since this stimulus information does not transfer between hemispheres in the split brain monkey, it is unlikely that cortical interhemispheric facilitation can explain the performance of these animals with both eyes open. Instead it is proposed that subcortical interhemispheric interference reduces the performance of the splits in the one eye condition. Thus the single hemisphere without such interference appears equal to the normal brain in certain information processing tasks. Additional confirmation comes from one hemispherectomized monkey whose performance on the nested match equals the normals.

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HUMAN SUCCUS ENTERICUS:THE MOST VOLUMINOUS DIGESTIVE SECRETION?
E.S. Nasset, Children's Hospital Medical Center, Bruce Lyon Memorial Research Laboratory, Oakland, California 94609

Liquid meals are diluted 3-5 times in passing through the human duodenum (Borgström et al, J. Clin. Invest. 36: 1521, '57). The stomach delivers ca. 6.4 kg of chyme to the gut in 24 hr (Eve, Health Physics, 12:131, '66), which contains ca. 5 l of water. A 3-5 dilution necessitates addition of 10-20 liters of fluid in a short time. The daily volumes of bile (0.5 l) and pancreatic juice (1.5 l) are inadequate and hence the bulk of the fluid must come from the gut. Stool volumes of cholera patients may exceed 20 l/day and this represents primarily the difference between secretion and reabsorption of succus entericus. In man all essential amino acids in equimolar mixtures, < 5mM, are absorbed at the same rate (Adibi & Gray, Gastroenterology, 52:837, '67). During digestion of beef, gelatin, eggs or milk in man the post prandial concentration of individual amino acids does not exceed 3.6 mM (Olmsted, et al, J. Nutr. 90:291, '66). The average daily ingestion of Leu and Tyr e.g. is 7.9 and 3.9 g (USA). To achieve the low concentrations observed in the human gut these amounts of Leu and Tyr would be dissolved in 35 and 22 l of fluid spread over 24 hr. The rates would necessarily be higher during digestion of a meal. The data suggest that large volumes of succus entericus are required for absorption of amino acids in dilute concentrations, as actually observed during digestion. The evidence indicates that secretion of succus entericus in man may be several liters per hr. Experimental demonstration of this phenomenon is difficult because, although the 2-way flux of fluid in the gut is very great, the net flux is nearly zero. (Supported in part by NIH Grant AM 15258).

AUTOREGULATORY BEHAVIOR OF PRESSURES IN SUPERFICIAL CORTICAL STRUCTURES OF THE DOG. L. Gabriel Navar and P. D. Bell* Dept. Physiology and Biophysics. Univ. Alabama Medical Center, Birmingham, Alabama 35294

Micropuncture experiments were conducted in 16 dogs to assess the degree of association between the autoregulatory behavior of the superficial cortical nephrons and of the total nephron population. Pressures in superficial proximal tubules, distal tubules, and peritubular capillaries were measured at control and reduced renal arterial pressures. Transit times of lissamine green were also used as an index of autoregulatory ability of the superficial nephrons. Total renal blood flow (RBF) and GFR were measured to evaluate whole kidney autoregulatory behavior. At control arterial pressures (100 to 125 mm Hg), RBF and GFR averaged 3.8±1.1 (SD) and .78±.15 ml/min per g kidney weight. Proximal tubule pressure was 22.4±2.6 mm Hg; peritubular capillary pressure was 12.9±.9 mm Hg; and the pressures in the distal tubules averaged 12.2±.9 mm Hg. Renal arterial pressure was reduced by constriction of the renal artery. At arterial pressures of 80 to 95 mm Hg, proximal tubule and peritubular capillary pressures and proximal transit times were not significantly different from the control values and exhibited autoregulatory behavior in association with total kidney function. Distal tubule pressure decreased slightly to 11.1±.9 mm Hg. With further decreases in arterial pressure to the lower autoregulatory range (65 to 75 mm Hg), RBF decreased slightly (-13%). Proximal tubule and peritubular capillary pressures decreased by 18% and 23%. The results indicate that the superficial nephrons exhibit autoregulatory behavior in close association with the total nephron population when total renal blood flow is maintained. However, superficial cortical function decreases to a greater proportion than RBF when renal perfusion pressure is decreased to the lower levels of the autoregulatory range. (Supported by grants from NHLI and American Heart Association).

APPARENT DEPRESSION OF OXYGEN CONSUMPTION BY FLUOROCARBON EMULSIONS. R.M. Navari*, W.I. Rosenblum, J.E. Levasseur* and J.L. Patterson, Jr., Medical College of Virginia, Va. Commonwealth Univ., Richmond,Va. 23298

Liquid fluorocarbons (FC) carry large amounts of O_2 provided that the partial pressure of the O_2 is high. Emulsions of certain fluorocarbons, e.g., perfluorodecalin (PP-5) and perfluorotributylamine (FC-47) have been undergoing trials as blood substitutes. In the present studies, oxygen consumption (Q_{O_2}) of pulmonary bronchial rings of the rat suspended in various FC/physiologic salt solution emulsions was determined using the Cartesian Diver microrespirometer (Howard, et al. Circ. Res. 16: 187, 1965). Q_{O_2} for emulsions of PP-5 (1.63±0.15 µL/mg/hr) or of FC-47 (2.17±0.19 µL/mg/hr) was significantly ($p<0.01$) less than that of physiologic salt solution control (3.43±0.20 µL/mg/hr). Without the FC, Q_{O_2} (3.39±0.17 µL/mg/hr) of the physiologic salt solution plus the emulsifying detergent F-68 used for the emulsions was not significantly different from control Q_{O_2} (3.43±0.20 µL/mg/hr). Removal of fluoride ions liberated during emulsification, failed to eliminate the Q_{O_2} depression caused by FC-47 or PP-5 emulsions. Depression of Q_{O_2} was eliminated by using 95% O_2, 5% N_2 rather than air as the equilibrating gas for the tissue and emulsion in the microrespirometer (FC-47 emulsion, Q_{O_2} = 3.23±0.29 µL/mg/hr). It is possible that in blood substitution studies, the effect observed here may be obscured by the high O_2 concentrations mandated in the substitution studies by the shape of the FC-O_2 "dissociation curve". It seems unlikely that chemically inert FC depresses Q_{O_2}. Rather, O_2 diffusion through FC may be limited, a hypothesis compatible with the fact that emulsions of cyclic PP-5 had significantly greater effect than emulsions of linear FC-47 ($p<.01$).
(Supported by Va. Lung Association, HL-14251 and HL-16643.)

DIGITALIS INDUCED MYOCARDIAL IRRITABILITY; CRITICAL RELATIONSHIP BETWEEN SERUM CALCIUM AND POTASSIUM. N. Shokouhi Nejad, R. Verrier*, B. Lown*, Warren Arter*, and M. D. Klein*. Harvard School of Public Health, Boston, Mass. and IIT Research Institute, Chicago, Illinois.

The precise relationship between digitalis toxicity and serum electrolytes has been inadequately studied. To elucidate this relationship, a technique for quantifying the action of digitalis on the electrical properties of the heart was used. In 12 isolated canine heart-lung preparations in which serum electrolyte concentrations were controlled, a reproducible degree of myocardial irritability was determined by eliciting repetitive ventricular responses (RVR) with pulses of 5 µj delivered to the right ventricle early in diastole. All preparations were atrially paced at 180 beats/min. Acetylstrophanthidin (AS) was infused at 20 µgm/min. Serum calcium was altered by EDTA and $CaCl_2$ infusion. In five preparations, serum K^+ was kept constant by hemodialysis. Administration of AS to evoke RVR resulted in a consistent increase in serum K^+ (mean 55% above control). When serum K^+ was held constant by hemodialysis, 23% less AS (170 vs 222 µgm) was required to elicit RVR. RVR phenomenon induced by AS infusion was abolished by lowering serum calcium by 40%. When serum K^+ was not permitted to rise, it was necessary to lower serum Ca^{++} by 80% to abolish RVR. These results support the concept that there is a reciprocal relationship between Ca^{++} and K^+ in myocardial irritability to digitalis. Serum Ca^{++} level becomes critical in myocardial sensitivity to digitalis only when serum potassium has been altered significantly.

AN EFFECT OF CORTISOL ON SUPEROXIDE ANION PRODUCTION BY RAT LUNG MICROSOMES. Don H. Nelson and Ann Ruhmann-Wennhold*. Depts. of Medicine and Anatomy, University of Utah College of Medicine, Salt Lake City, Utah 84112

The harmful effects of 100% oxygen on the pulmonary endothelium, the potentiation of the damage by cortisol, and the protective effect of adrenalectomy are well known. A prime factor in producing this damage is thought to be superoxide anion. Since studies from this laboratory have demonstrated an effect of corticosteroids on the production of superoxide anion by liver microsomes, the present investigation was undertaken to determine whether production of this potent free radical by lung microsomes was influenced by cortisol. An NADPH dependent microsomal preparation of rat lungs from adrenex rats produced 198 $\pm$ 44 nmoles superoxide anion/mg protein at fifteen minutes of incubation. Administration of 5 mg of cortisol twice in 48 hours decreased superoxide to 90 $\pm$ 14 ($P < .05$). At 20 min of incubation, superoxide production was 332 $\pm$ 62 for adrenex and 167 $\pm$ 20 for adrenex cortisol treated animals ($P < .05$). Exposure of the adrenex rats to 100% O_2 for 24 hrs prior to sacrifice increased superoxide production in 15 min incubations from 216 $\pm$ 26 nmoles/mg protein at ambient conditions to 568 $\pm$ 97 ($P < .005$). Intact animals receiving the same O_2 treatment increased from 180 $\pm$ 25 to 308 $\pm$ 63 ($P > .05$). The adrenalectomized animals had significantly more superoxide anion production in the presence of 100% O_2 than the intact animals ($P < .05$). The apparent increased superoxide production by tissue from adrenex animals may be offset by differences in utilization, or production of protective enzymes such as superoxide dismutase. Further studies will be necessary to clarify the relationship between these <u>in vitro</u> effects of cortisol on superoxide production and the previously recognized <u>in vivo</u> effects.

BARBITURATE ANESTHESIA AND CO_2 SENSITIVITY IN CHICKENS. Thomas E. Nightingale* (Spon: M.R. Fedde). USDA Poultry Res Lab., Georgetown, DE

Alteration of CO_2 sensitivity resulting from 3 barbiturate anesthetics routinely used in chickens was studied. Tidal volume (V_T), respiratory frequency (f), minute ventilation ($\dot{V}_E$), and end-expiratory PCO_2 (P_ACO_2) were determined at rest and at ascending levels of CO_2 (F_ICO_2=2-8%) in three levels of O_2 (F_IO_2=100, 21, 10%). Control response curves (V_T/P_ACO_2, f/P_ACO_2, and $\dot{V}_E/P_ACO_2$) were obtained on awake, adult Leghorn males by having the birds breathe thru a tracheal cannula and pneumotach connected to the side arm of a T-tube thru which air or test gas flowed at 2 L/min. The birds were then given either pentobarbital (PENTO)(30 or 60 mg/kg,IV); phenobarbital (PHENO) (100 mg/kg,IM); or Equithesin (E)(2.5 ml/kg,IM), and the tests repeated. While awake, increasing F_ICO_2 resulted in increased V_T and $\dot{V}_E$ at all F_IO_2 levels, with f unchanged in all but F_IO_2=10% trials, when it increased. CO_2 sensitivity (S) as shown by $\dot{V}_E/P_ACO_2$ was enhanced by F_IO_2=10%, and depressed by F_IO_2=100%. After PHENO, and both dosages of PENTO, S was reduced from awake levels by 50-95%, due to greatly reduced V_T changes, as well as altered f patterns which were modified to result in negative f/P_ACO_2 relationships at all F_IO_2 levels. Administration of E caused increased S at all F_IO_2 levels, primarily due to increases in V_T, since the f/P_ACO_2 relationship was negative for F_IO_2 =21 & 100%, and reduced compared to awake F_IO_2=10%. The results indicate that in addition to modifying CO_2 sensitivity as shown by the $\dot{V}_E/P_ACO_2$ relationship, the agents studied caused extensive alteration in respiratory rate control mechanisms.

SMOOTH-MUSCLE FIBERS ASSOCIATED WITH STRIATED FIBERS IN THE CREMASTER MUSCLE OF THE GUINEA-PIG. J.G. Ninomiya*, H. Merchant* and F. Alonso-deFlorida. Instituto de Investigaciones Biomédicas and Facultad de Medicina, Univ. Nacl. Aut. Méx., México.

Certain pharmacological results have led one of us to suggest (J.G.N., in prep.) that the cremaster muscle, of the guinea-pig besides the striated fibers, contains smooth-muscle fibers (smf). Some preliminary observations made in the electron microscope, in fact, corroborate such prediction. The smf are elongated and spindle-shaped, and are about 100μ long and 5 to 15μ wide. These smf show typical arrangement of their elements. There are also cells exhibiting bundles of myofilaments that occupy only reduced zones of the cytoplasm. The smf appear either as bundles or as scattered fibers intimately associated with the dense connective tissue of the serous membrane. The smf appear to be associated by "gap junctions". Some smf are in the vicinity of the striated-muscle fibers at the surface of the striated muscle layer, but are not intermingled among the inner striated-muscle fibers, nor the smf appear at the loose connective tissue layer located at the opposite side of the striated muscle layer. Only some preparations exhibited the smf, and there are certain zones more thickly populated than others. We do not know whether these smf compose a tissue which is continous with the "internal cremaster", located at the parietal side of tunica vaginalis, in some species.

TERMINATION OF PREGNANCY BY SHEEP ANTI-LH-RH GAMMA GLOBULIN IN RATS. N. Nishi*, A. Arimura, and A.V. Schally. Tulane Univ. Sch. Med., and V.A. Hospital, New Orleans, La. 70112

Proestrous rats (Charles River, CD strain) were allowed to accept males and the vagina was examined for the presence of spermatozoa on the next morning. The day of confirmation of the presence of spermatozoa was designated as Day 1 of pregnancy. Laparotomy was performed on Day 7 or 8 and only rats showing normal number of viable sites were chosen for further experiments. Single i.v. injection of 1 ml of the sheep anti-LH-RH gamma globulin (Anti-LH-RH γG) on Day 7 did not alter the normal course of pregnancy, but in 2 out of 4 rats which received Anti-LH-RH γ G on Day 8, all the fetuses were resorbed. Similarly injection of Anti-LH-RH γ G on Day 9 and on Day 10 uniformly resulted in the termination of pregnancy. Exploratory laporatomy on Day 14 revealed that all the fetuses were under resorption. In 4 out of 5 rats which received Anti-LH-RH γG on Day 11, and in 2 out of 5 rats treated on Day 12, pregnancies were terminated. All 5 rats which received 1 ml of normal sheep gamma globulin from Days7-11 carried normal fetuses to term. Plasma progesterone levels of rats whose pregnancies were affected by Anti-LH-RHγG uniformly declined to levels lower than 20 ng/ml by Day 14. In the control rats, plasma progesterone values sharply increased by Day 14. A dose of 4 mg progesterone or 2 μg of synthetic LH-RH in 16% gelatin solution administered daily from Days 9-12 overcame the deleterious effect of Anti-LH-RH γ G injected on Day 9. The results indicate that endogenous hypothalamic LH-RH plays an important role in the maintenance of early pregnancy, probably by stimulating pituitary LH and in turn progesterone secretion. Supported in part by USPHS Grants HD 06555, AM 09094, and the Veterans Administration.

CONTROL OF THE SUPRACHIASMATIC NUCLEI OF HYPOTHALAMUS. H. Nishino*, K. Koizumi and C. M. Brooks. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203.

Recently neurons of the suprachiasmatic nuclei (SCN) have been considered to mediate optic system control of a circadian rhythm in pineal gland activity. We have shown that stimulation of both optic system and SCN inhibit tonic activity in the cervical sympathetic nerves which evoke action potentials within the pineal and augment pineal hormone production in the dark. Since the SCN have the highest concentration of serotonin-containing nerve terminals in the hypothalamus, effects of various drugs on the SCN cells were tested. In urethane or chloralose-urethane anesthetized rats 5 barrel-capillary electrodes were used for iontophoretic application of drugs and recordings from single neurons. Ach and glutamate increased the rate of firing of most cells (75-80%) and inhibited none. Norepinephrine and dopamine inhibited firing rates of 50-55% of the cells tested and augmented the activity of some (20-25%). Serotonin had a stronger and longer lasting inhibitory action than did other monoamines, inhibiting 70% of those tested, augmenting action in 15%. For a given neuron, the most common response was excitation by Ach and glutamate and inhibition by all three monoamines. On the other hand, neurons excited by one monoamine tended to be excited also by others as well as by Ach and glutamate. It is possible that in periods of darkness monoamines, particularly serotonin might play an important role in inhibiting SCN neurons, thus releasing the pineal from inhibitory influence of the cervical sympathetic nerves. (Supported by USPHS Grant #NS00814 & NSF #0IP74-19337)

FETAL HEMODYNAMIC CHANGES DURING GRADED REDUCTIONS IN UTERINE BLOOD FLOW. Miles J. Novy, Herbert Cohn,* George J. Piasecki,* and Benjamin T. Jackson,* Div. Perinatal Med., Oreg. Reg. Primate Res. Ctr. and Univ. Oreg. Health Sci. Ctr., Portland, Oreg., and Depts. Surgery, Boston Univ. Med. Ctr. and Boston V.A. Hosp., Boston, Mass. 02118.

The hemodynamic effects of graded reductions in maternal uterine blood flow were compared in acute fluothane-anesthetized in utero preparations and in chronically prepared unanesthetized fetal lambs. Umbilical blood flow (Qumb) was measured with radioactive microspheres and an electromagnetic flow transducer (EMF) implanted on the distal aorta of the fetus (Novy, M.J., et al., Prostaglandins 5:543, 1974), while continuous measurements were made of fetal heart rate (FHR), arterial and umbilical venous and amniotic fluid pressures. Graded reductions in uterine blood flow were produced by a distal aortic choker and controlled by the EMF. Control Qumb (ml/kg x min^{-1}) was 189 $\pm$ 18.1 in the chronic experiments and 143 $\pm$ 37 in the acute experiments (mean $\pm$ S.D.; $p < 0.01$). We consistently noted a fetal bradycardia, a maintenance or small increase in the umbilical perfusion pressure, and a reduction in Qumb in chronic experiments. Placental vascular resistance 5 min. after the onset of 25, 35, and 50 % reductions in uterine blood flow increased 21, 39, and 46 % respectively. Norepinephrine in doses of 2 - 6 μg/kg qualitatively reproduced the fetal hemodynamic effects of graded reductions in uterine blood flow. In contrast, animals studied under acute, anesthetized conditions showed variable changes in FHR, frequently characterized by tachycardia, an increase in umbilical perfusion pressure, a maintenance or increase in Qumb, and minimal change in umbilical vascular resistance. (Supported in part by John H. Hartford Foundation, Inc., New York, and grants from NICHD.)

CARDIAC HYPERTROPHY IN THE ENDURANCE ATHLETE. D. Nutter, C. Gilbert,* S. Heymsfield,* J. Perkins,* and R. Schlant.* Emory University School of Medicine, Atlanta, Georgia.

Cardiac structure was evaluated by echocardiography (ECHO) in 20 male, competitive, long distance runners (R) and 26 age matched sedentary controls (C). Maximal aerobic capacity (treadmill exercise) was 4.9±0.1 (±S.E.M.) L oxygen/min for R, and 3.3±0.1 for C.† The resting heart rate was 51±1.7 beats/min for R and 62±2.2 for C,† and the stroke volume index was 49.3±2.6 ml/M^2 for R and 44.6±2.0 for C.

Cardiac dimensions by ECHO	R	C	P value
Ventricular septal thickness (mm)	10.6±0.3	10.4±0.2	NS
Left Vent. posterior wall thickness (mm)	10.9±0.3	9.8 ±0.3	<.01
Left Vent. end diastolic volume index (ml/M^2)	72 ±3	62 ±3	<.05
Left Vent. mass index (g/M^2)	140 ±6	107 ±4	<.01
Right Vent. end diastolic diameter (mm)	21.5±0.8	18.4±1.1	<.05
Aortic end diastolic diameter (mm)	29.3±0.8	28.9±0.4	NS
Left Atrial end systolic diameter (mm)	35.0±1.3	33.8±0.8	NS

Resting left ventricular function assessed by ECHO (calculated variables: ejection fraction, circumferential shortening velocity, and posterior wall velocity) was comparable in R and C.

Total heart volumes calculated from chest x-rays were greater in R (480±19 ml/M^2) than in C (363±11)† and a greater left ventricular mass in the athletes was suggested by several electrocardiographic criteria (eg. R wave amplitude in leads V_4-V_6 was 2.60±.17 mv in R and 1.59±.10 in C†). The measurements of cardiac volume and mass by ECHO, x-ray, and ECG techniques in both groups correlated well with maximal aerobic capacity. The ECHO measurement of cardiac dimensions confirms right and left ventricular enlargement in the endurance athlete. †P<.01

SPLIT PULMONARY VENTILATION AND CIRCULATION BY MUTUAL BIOELECTRICAL IMPEDANCES. J. Nyboer and J.A. Sedensky*. Dept. Physiology, Wayne State University, Detroit, MI 48201.

Regional malfunctions of the lungs are definable nontraumatically by impedance spirometry and plethysmography. Our study is based only on electrical resistance as opposed to capacitance or the vector impedance to a 50 Khz constant current. The total ventilation and bloodflow are deduced from mutual leads detecting resistances between 30 cm of high back. The total $\dot{V}/\dot{Q}$ ratio is calculated from this data. These base values of ventilation and of lung pulsatile perfusion are also defined as equal to the sum of the graphic effects observed transversely in symmetrical regions derived from 2 subclavicular, 2 posterior mid-chest and 2 low-chest positions. The percentages of the total for the left and right lung deflections are derived from the respective sums of the given regions. The split function $\dot{V}/\dot{Q}$ ratio of each region is also derived. Thirteen normals and selected abnormals were studied during controlled tidal breathing and voluntary apneas for comparison with X-rays, lung scans and mechanical lung functions by others. In this study the pulse volumes are equated as $V = \rho L^2/R^2 \times \Delta R$ = ml. In an additional 16 normal subjects, the volumes of each breath are also defined by $\Delta V = 208.6 + (3474.3 \times \Delta R)$ = ml.

Supported by a Grant-in-Aid from the Michigan Heart Association.

SMALL FIBER AVIAN ATRIAL RECEPTORS EXHIBIT THREE CLASSES OF RESPONSE TO ALTERATIONS IN BLOOD VOLUME. Piers C. G. Nye*, Ray E. Burger* (SPON: Ursula K. Abbott). University of California, Davis, CA 95616.

The avian atria are exclusively innervated by a small fiber subendocardial end-net type system. The response of these receptors was monitored during infusion of Dextran and withdrawal of blood from open thorax roosters. Extracellular records of receptor activity were obtained with low impedance tungsten microelectrodes in the left nodose ganglion of the selectively denervated vagus nerve. Three responses were noted, (i) increase in firing rate as blood volume increased, (ii) increase in firing rate as blood volume decreased, and (iii) U-shaped response with a minimum close to the initial blood volume. Basal discharge was zero or had no consistent relationship to the cardiac cycle until blood volume was significantly altered. Furthermore, like other small fiber afferents, maximum discharge rate rarely exceeded 3 per cycle. The basal firing characteristics of these receptors are similar to the only published record of slowly conducting vagal fibers originating in the mammalian atria. The bird may provide data that will lead to the separation of the reflex roles of large and small fiber atrial afferent systems.

DOPAMINERGIC (DA) CONTROL OF PROLACTIN(PRL) RELEASE IN DEVELOPING RATS: ROLE OF ESTROGEN IN DETERMINING SEX DIFFERENCES. S.R. Ojeda* and H. Jameson* (SPON: J.M. Lipton). Dept. of Physiology, University of Texas Health Science Center, Southwestern Medical School, Dallas, Tx. 75235.

To study the existence of sexual differences in the tonic hypothalamic inhibitory DA control of PRL secretion, DA receptors were blocked by Pimozide (P) treatment in female and male rats and the subsequent PRL release determined by RIA. Females showed a larger release of PRL in response to P than males at all periods studied (day 15 to day 75). Testosterone propionate administered to female rats at day 0 or day 4 after birth did not change the female pattern of PRL release in response to P, even though it elevated basal plasma PRL. Similarly, the male type of response to P was not altered by orchidectomy at the day of birth or at day 21 or feminization of male fetuses with cyproterone acetate. In contrast, when males castrated at adulthood or feminized adult male rats were treated with estrogen (Eb, 5 µg, sc, 48 hr before P), the magnitude of the PRL release in response to DA blockade was much larger than that of male rats not given Eb. In androgenized or intact female rats, castrated as adults, the PRL response to P was attenuated, though it still was larger than that of normal males. However, when female rats were castrated at day 21, the PRL response to DA receptor blockade at adulthood was similar to that observed in males. Adrenalectomy did not alter the response to P. These results indicate that (a) the inhibitory hypothalamic DA control of PRL secretion is more pronounced in female than in male rats; (b) this difference is not determined by a process of neonatal or fetal hypothalamic sexual differentiation, but rather is a consequence of a modulating action of estrogen(s) at the hypothalamic-hypophyseal level during the course of sexual development. (Supported by grants from NIH [AM 10073 and HD 05151] and the Ford Foundation.)

VAGOTOMY IMPAIRS PENTAGASTRIN-INDUCED RELAXATION OF CANINE GASTRIC FUNDUS. N. Okike* and K. A. Kelly. Mayo Clinic and Mayo Foundation, Rochester, MN 55901

In five dogs, a separated, vagally innervated pouch was made from the gastric fundus. Electrodes were implanted on the pouch and on the gastric antrum, and a gastric fistula was created through which gastric juice was drained externally during the tests described below. After recovery, the fasted, conscious dogs received continuous intravenous infusions of 154 mM NaCl for 45 min (1 ml/min) while intraluminal pressure (P) from the pouch (distended to 75 ml) and fundal and antral electric activity were recorded. A dose of pentagastrin (PG), selected randomly, was then added to the infusion for 15 min, after which NaCl alone was again infused for 45 min; another dose of PG was added for 15 min, and so forth. The experiments were repeated on 5 different days on each dog. Transthoracic truncal vagotomy was then performed, and the dogs were restudied. To produce equivalent decreases in intrapouch pressure, larger doses of PG were required after vagotomy than before vagotomy; the dose-response curve was shifted to the right (Table). The D_{50} for inhibition of P was 4.2 ng/kg per min before vagotomy and 41.4 ng/kg per min after vagotomy. In contrast, vagotomy did not alter the inhibition of fundal spikes or the increase in frequency of antral pacesetter potentials brought on by PG.

PG, ng/kg per min	0.3	1	3	10	30	100	200
Mean % decrease in P±SE							
Before vagotomy	0	13±4	31±4	46±3	51±2	58±4	66±3
After vagotomy	0	0*	15±3*	23±5*	29±3*	44±8	59±6

*Differs from value above; $P<0.05$.

(Supported by USPHS, NIH grant 18,278 and Mayo Foundation.)

RELATIONSHIP OF NEURAL ACTIVITY IN THE RAPHE NUCLEI OF THE RAT TO BRAIN STIMULATION-PRODUCED ANALGESIA. T. D. Oleson* and J. C. Liebeskind, Dept. Psychology, UCLA, Los Angeles, Calif. 90024

Central gray stimulation profoundly reduces behavioral responses to painful stimuli as well as the firing rates of spinal cord interneurons thought to be involved in nociception. LSD, known to inhibit serotonergic neurons in the raphe nuclei, blocks the suppressive effect of central gray stimulation on spinal units. As there are no direct connections from central gray to the spinal cord, we sought to investigate the possible role of the raphe nuclei in mediating brain stimulation-produced analgesia. In one study, rats were implanted with stimulating electrodes in n. raphe magnus, which has descending serotonergic connections to the spinal cord. This stimulation reduced leg flexion to noxious pinch and raised tail flick latency to radiant heat in a manner similar to central gray stimulation. In another study, evoked potentials and multiple unit activity were recorded from dorsal raphe, median raphe, and raphe magnus of awake, restrained rats. Evoked potentials and multiple unit responses were elicited by either innocuous or noxious stimuli applied to any limb. Following central gray stimulation, raphe responses to noxious shock, pinch, or pin prick were greatly reduced, whereas responses to innocuous touch or air puffs were relatively unaffected. Morphine administration similarly inhibited raphe responses to noxious but not innocuous stimuli. Central gray stimulation and morphine increased spontaneous activity in the raphe nuclei, providing further evidence of their involvement in mechanisms of pain inhibition.

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EVIDENCE FOR AN "ADENOSINE RECEPTOR" ON THE CORONARY MYOCYTE SURFACE. R.A. Olsson and R.E. Patterson*, Dept. Cardiorespiratory Diseases, Walter Reed Army Institute of Research, Washington, DC 20012

An "adenosine receptor" has been invoked to explain the coronary vasoactivity of adenosine and other purine nucleosides and the antagonism of this effect by methylxanthines (Arzniemittel-Forsch. 22: 1255, 1972). Because both the agonists and antagonist can penetrate cells, it is not clear whether their effects are due to interaction with a receptor or result from nonspecific actions on cellular metabolism subsequent to uptake by the coronary myocyte. Adenosine was linked covalently via N6 and an alkyldiamine to the tetra-aldehyde produced by controlled periodate oxidation of the galactosyl moieties of stachyose. This derivative is too large to readily penetrate cell membranes (MW > 10^3 daltons), yet caused dose-dependent coronary vasodilation when infused intracoronary in 1 conscious and 6 open-chest dogs. This effect was antagonized by aminophylline. Theophylline coupled via an 8-triazenoalkylamine to stachyose competitively inhibited the coronary vasodilation produced by intracoronary adenosine. These results suggest that the coronary effects of adenosine are initiated at the surface of the coronary myocyte and that antagonism by methylxanthines is exerted at the same site. This is consistent with the existence of an "adenosine receptor" in coronary artery smooth muscle.

DOES INERT GAS EXCHANGE DATA PROVIDE ENOUGH INFORMATION TO RECOVER $\dot{V}_A/\dot{Q}$ DISTRIBUTIONS PRESENT IN THE LUNG? A. J. Olszowka, Dept. Physiol. State Univ. of New York at Buffalo, Buffalo, NY 14214

The ability to recover virtually continuous $\dot{V}/\dot{Q}$ distributions from relatively few inert gas measurements depends on the assumption that even though an infinite number of distributions are compatible with a given set of data, the reasonable appearing ones are virtually identical. However, using analytic methods for obtaining solutions to this underdetermined least squares problem, one can find equally plausible but qualitatively different $\dot{V}/\dot{Q}$ distributions which produce the same set of inert gas data. Thus the continuous $\dot{V}/\dot{Q}$ distribution recovered by a particular analysis of the inert gas data should be interpreted as an "as if" distribution for it may not always closely approximate the distribution actually present in the lungs. Supported in part by NHLI Grant 5 PO1 HL 14414-03.

ORGANIC PHOSPHATE BINDING TO HEMOGLOBIN IN INTACT RED CELLS INVESTIGATED WITH ^{31}P NMR SPECTROSCOPY. A. Omachi, W.E. Marshall*, A.J.R. Costello* and T.O. Henderson*. Departments of Physiology and Biological Chemistry, Univ. of Illinois Med. Ctr., Chicago, Ill.

We have previously described (Costello et al., Fed. Proc. 33:1450, 1974) basic relationships between changes in chemical shift ($\Delta\delta$) and organic phosphate binding in simple model systems containing hemoglobin, Mg^{++}, and either 2,3-diphosphoglycerate (DPG) or ATP, in various combinations. In the present study, we have also used phosphorus nuclear magnetic resonance spectroscopy to estimate the percent of DPG and ATP bound to hemoglobin in intact human erythrocytes. Binding was assessed by comparing the $\Delta\delta$s of DPG and ATP observed in intact cells with $\Delta\delta$s determined in model systems closely simulating intracellular conditions, in which percent binding was evaluated directly by membrane ultrafiltration. Experiments were conducted at pH 6.75 in order to maximize organic phosphate binding. The results showed that the percent of bound DPG varied with DPG concentration and with the state of oxygenation, ranging from 57% in oxygenated, high DPG cells to 100% in deoxygenated, low DPG cells. At the same DPG concentration, the changes in chemical shift revealed that a greater percentage of the total DPG was bound in erythrocytes than in the model systems. ATP was not significantly bound to hemoglobin in any of the cellular systems examined but appeared to be strongly Mg^{++}-complexed inside the erythrocyte. With this new approach, we have been able to achieve the most direct study yet attempted for the investigation of hemoglobin-ligand interactions in situ. (Supported by U.S.P.H.S. Grants AM 11702, GM 20127, HL 13567, American Heart Assn. Grant 74-1011, and Chicago-Illinois Heart Assn. Grant A74-36.

ALANINE UTILIZATION AND NH_4 RELEASE BY RAT LUNG SLICES. John J. O'Neil and Curtis Harper*, Pharmacology Branch, National Institute of Environmental Health Sciences, NIH, Research Triangle Park, N.C. 27709.

It has not been possible to account for more than 50% of the QO_2 of rat lung slices on the basis of $^{14}CO_2$ production from ^{14}C labeled glucose and palmitic acid. Although lung may have a specific requirement for glucose, other substrates such as amino acids may contribute significantly to the energy needs of the lung. We incubated 200 mg of 1 mm rat lung slices in center well flasks containing 4 ml of Krebs-Ringer bicarbonate which had been equilibrated for at least one hour with 5% CO_2 in O_2. Each 100 ml contained 5 g fatty acid free and dialyzed bovine albumin, 150 mg of glucose, 12 mg of palmitic acid, and 50 mg of amino acids (or alanine or serine alone). The $^{14}CO_2$ collected when 1-^{14}C-alanine was added to the medium amounted to 12 µmoles of alanine converted to CO_2 /(g lung [wet] x 90 min). Only 0.02 µmoles of serine were converted when 1-^{14}C-serine (U) was used. $^{14}CO_2$ production from 1-^{14}C-glucose was equivalent to 5.8 µmoles of glucose oxidized /(g lung x 90 min). $^{14}CO_2$ production from 1-^{14}C-alanine continued in a linear fashion for 5 hours, at which time 34% of the ^{14}C had appeared as $^{14}CO_2$. NH_3 was collected in 2 N H_2SO_4 in the center well after the addition of 3 ml of 2 N NAOH to the tissue. The NH_3 released by 90 min exceeded the NH_3 which might be produced from the oxidation of 12 µmoles of alanine.

VASCULAR VOLUME DISTENSIBILITY CHARACTERISTICS OF THE ISOLATED DOGFISH GUT. D.F. Opdyke and D.W. Wilde*. Dept. of Physiology, New Jersey Medical School, Newark, N.J. 07103, and Mount Desert Island Biological Laboratory, Salsbury Cove, Maine 04672.

The vascular capacitance and volume distensibility of the isolated dogfish gut and segments of dogfish arteries and veins were investigated. The volume distensibility curves for dogfish arteries and veins are very similar to comparable curves derived from arteries and veins of dogs or man. The vascular distensibility curve of the gut, however, shows a greater distensibility at higher systemic pressure than at lower pressure. Evidence is presented that significant amounts of fluid leave the vascular compartment at a lower systemic pressure than in an isolated dog hind limb preparation. This alone does not, however, explain the atypical vascular volume distensibility curve obtained from the dogfish gut. It is suggested that in the dogfish capillary filtration pore enlargement takes place at a very low capillary pressure or volume (as compared to mammals) and this complicates the construction of a volume distensibility curve because initial vascular volume is not constant. (Supported by a grant from the Bergen County Chapter, American Heart Association, New Jersey Affiliate.)

A SINGLE-BREATH METHOD FOR DETERMINING LUNG WEIGHT AND PULMONARY BLOOD FLOW FROM THE DIFFERENTIAL UPTAKE OF TWO SOLUBLE GASES. E.S. Overland* G.M. Ozanne* and J.W. Severinghaus, Cardiovascular Research Institute, University of California, San Francisco, San Francisco, CA 94143

Lung weight(W) and pulmonary blood flow(PBF) may be estimated from the uptake of inspired soluble gases by using Cander and Forster's method. We introduce a new method for calculating W and PBF. A single deep inspiration of test gas (10% He, 1% acetylene, 1% dimethylether, in air) is followed after 2 and 10 second breath-holds by rapid expirations of 30% of vital capacity. Inspired and expired gas is sampled by a Perkin-Elmer 1100 mass spectrometer. An analog-to-digital converter and a Tektronix 31 calculator permit on-line computations of W and PBF. Estimation of W using a single soluble gas requires extrapolation to a"zero time" during inspiration. If two soluble gases are used simultaneously extrapolation is unnecessary. W is uniquely determined by the differential uptake of the two soluble gases during a breath-hold:

$$W = \frac{Z\alpha_1 - X\alpha_3}{X\alpha_2\alpha_3 - Z\alpha_4\alpha_1} \times V_{alv}$$

Where X and Z are Δln concentrations of two soluble gases during the breath-hold, V_{alv} is alveolar volume during the breath-hold (STPD) and $\alpha_{1\&3}$ are blood solubilities and $\alpha_{2\&4}$ are lung solubilities of gases X and Z, respectively. By equating PBF computed from the uptake of each gas, flow and time drop out, leaving W to be calculated. This calculation also applies to the rebreathing technique. In three resting, normal subjects (n=6, each) W values were: 661 gm ± 4.4%, 700 gm ± 6.2%, and 564 gm ± 6.7% (1 sd). PBF values (L/min) were: 5.5 ± 6.3%, 6.0 ± 2%, and 6.9 ± 4.9%. W values during steady state exercise (400 kg-m/min) in the last two subjects were 797 gm ± 8.1% and 537 gm ± 7.6% with PBF of 13.4 ± 5.8% and 11.5 ± 2.5%. In three isolated, non-perfused dog lungs ventilated in a 37°C Lucite box, W values (n=6, each) were 98% ± 3.3%, 108% ± 6.7%, and 118% ± 12% of actual weight.

ALTERED GLUCOSE TOLERANCES OF RATS AND DOGS EXPOSED TO CHRONIC CENTRIFUGATION. J. Oyama and T. N. Fast*, Environmental Physiology Branch, Biomedical Research Division, NASA-Ames Research Center, Moffett Field, CA 94035, and Dept. of Biology, University of Santa Clara, Santa Clara, CA 95053.

Chronically centrifuged hyper-G adapted animals consume more food and generally have a higher metabolic rate than normal gravity controls. To study the effects of prolonged hyper-G exposures on glucose metabolism, oral tolerance tests were run on Sprague-Dawley rats and Beagle dogs. Fasted rats and dogs were given glucose by stomach tube at a dose of 3 and 4 g/kg, respectively, and blood glucose measured at 0.5 hour intervals for 3 hours. Rats centrifuged for 6-99 weeks at 3.5 - 4.7G showed an increased glucose tolerance and were more responsive to administered insulin in terms of hypoglycemia than controls. In contrast, young dogs (34-week-old) which were centrifuged for 12 weeks at 2.5G showed a decrease in glucose tolerance and a higher plasma insulin level during the test compared to controls. Mature (90-week-old) dogs centrifuged under the same conditions showed no significant differences in their glucose tolerance or plasma insulin levels compared to controls. The observed increase in glucose tolerance of chronically centrifuged rats is compatible with the increased metabolic rate found in this species when adapted to hyper-G. The unexpected decrease in glucose tolerance of young centrifuged dogs and lack of change in mature dogs indicate that hyper-G exposure may effect a decrease in metabolic rate of the immature dog but not in the mature dog. These differences may arise from differences in physical activity and degree of immobilization of the animals under the imposed G-load.

THE EFFECT OF INCREASED VENTILATION, CHOLINERGIC STIMULATION AND BLOCKADE UPON PHOSPHOLIPID CONTENT (PL) OF RABBIT LUNG LAVAGE FLUID
Manuel J. Oyarzún* and John A. Clements
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Four sets of experiments were performed using 83 New Zealand white rabbits (2.3 to 3.8 kg); PaO_2, $PaCO_2$, and pHa remained normal during the course of all experiments. In controls lung lavage yielded 1.62 (SD 0.26) mg PL/gm lung. (a) Rabbits having acetylcholine (1.9 µg/min) infused into the left pulmonary artery for 1 to 4 hrs.(causing a 25% drop in heart rate and aortic blood pressure) showed a 13% increase in PL in the lavage of the left as compared to the right (control) lung (P=0.002).(b) In rabbits having the left vagus cut and stimulated for 1 hr. (25V., 15/sec., 0.5 msec.), the PL of right and left lung washes was 27% greater than control (non-stimulated) rabbits (P=0.025). (c) Rabbits with increased minute ventilation of about 100% (using 10 ml dead space for periods of 1 and 2 hrs) had an increase of PL by 45.2% (P=0.001) and 82.4% (P=0.0001) respectively when compared to controls. However, when the period was extended to 4 hrs. the increase dropped to only 26.1% (P=0.04). (d) In the fourth group cholinergic blockade was produced for 2 hr. periods in animals with and without increased ventilation. The increase of PL in rabbits with increased ventilation was prevented by atropine and reduced by cooling the cervical vagi to 3.5°C. Since an increase in PL could be obtained with acetylcholine, vagal stimulation and increased ventilation and since PL did not increase similarly in atropinized or vagally-blocked rabbits with increased ventilation, the results suggest that surfactant release may be stimulated by a cholinergically mediated reflex.

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ISOLATION OF RAT URINARY KALLIKREIN AND PROPERTIES OF ITS ANTIBODIES. N.B. Oza, O.A. Carretero, V.A. Amin* and A.G. Scicli*. Department of Medicine, Henry Ford Hospital, Detroit, Michigan 48202.

Rat urinary kallikrein was purified by anion exchange, affinity (trasylol-sepharose) and sephadex G-100 chromatography. A purification of 695 fold was achieved with a recovery of 18% of esterolytic and 31% of kinin-forming activity. The enzyme showed a major and a minor protein band when electrophoresed in 16% polyacrylamide gel. The eluates from both the bands hydrolyzed ester and kininogen substrates. The specific activity with N-Benzoyl-L-Arginine Ethyl Ester was 124 μmoles/min/mgm and with partially purified dog kininogen it was 1795 μg bradykinin/min/mgm. The antibodies, generated against this preparation in rabbits, gave a line of identity with pure kallikrein and also with rat urine concentrate in immunodiffusion. The anti-kallikrein serum did not react with normal rat plasma and liver homogenate. Equivalent concentration of kidney cortex homogenate gave only a faint reaction. Preincubation of kallikrein with the antiserum inhibited kinin-forming activity in vitro and in vivo (hind leg of the dog). The intravenous administration of 1.0 ml of antiserum in rats did not alter the existing blood pressure. However, the depressor response of 2.0 mgm crude kallikrein or 1.1 μg pure kallikrein was completely blocked up to 1.0 hr. A partial response of exogenous kallikrein reappeared at the end of 2.0 hrs. Thus, kallikrein does not appear to play a direct role in the regulation of blood pressure in normal rats. However, its participation in the regulation of local blood flow cannot be excluded by these experiments. (Supported in part by NIH grant HL 15839-03, and the Michigan Heart Association.)

CONVERGENCE OF SKIN AND RECTAL TEMPERATURES AS A CRITERION FOR HEAT TOLERANCE. K.B. Pandolf* and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760.

Many laboratories use criteria of a rectal temperature (T_{re}) of 39.5° ± 0.5°C and/or heart rate (HR) of 180 beats/min ± 10% as tolerance limits for men working in the heat. Data from two recent studies suggest convergence of mean skin temperature ($\bar{T}_s$) and T_{re} can be a more reliable indicator of decreasing tolerance time, and a voluntary tolerance limit for individuals. Both studies (S1 and S2) involved young, fit volunteers given 5 to 7 days of heat acclimatization. In S1, involving protective clothing systems, 7 subjects were evaluated in hot-dry (46°C, 10% rh) and hot-wet (35°C, 75% rh) environments with 1.1 m/s wind and radiant load of 360 BTU/sq ft·hr. Each day, following a standard protocol, subjects did a variety of mild physical activities for 120 min. In S2, 6 different rainsuits were evaluated in a hot-dry environment (49°C, 20% rh); 6 subjects attempted a 50 min walk at 1.34 m/s on a level treadmill followed by 30 min rest. Physiological measurements included T_{re}, T_s, HR and sweat rate. In S1, wearing a completely impermeable, unventilated protective garment, convergence of $\bar{T}_s$ on T_{re} was associated, in the hot-dry phase, with early voluntary subject experimental termination (mean = 42 min) with substantial subjective distress although mean T_{re} = 38.2°C and HR = 142 beats/min were well below usual tolerance levels; in the hot-wet phase, convergence of $\bar{T}_s$ on T_{re} also led to early termination (mean = 67 min, T_{re} = 38.8°C, HR = 166 beats/min). In S2, exposures in 4 of the rainsuits were terminated (mean = 33 min) upon convergence of $\bar{T}_s$ on T_{re}, at near collapse levels despite mean T_{re} = 38.3°C and HR = 166 beats/min. Thus, convergence of $\bar{T}_s$ on T_{re} may on occasion be a more practical limit for acute heat tolerance than absolute values of T_{re} or HR, and appears to correspond more reliably with voluntary tolerance limits.

EFFECTS OF NOREPINEPHRINE, ISOPROTERENOL, HISTAMINE & ACETYLCHOLINE ON CALCIUM PUMP OF BRONCHIAL SARCOPLASMIC RETICULUM. David C. Pang* (SPON: A. J. Szumski). Department of Physiology, Medical College of Virginia, Richmond, Virginia 23298.

To study the effect of bronchodilators and bronchoconstrictors on the subcellular components of bronchial smooth muscle, sarcoplasmic reticulum was prepared from muscle of the bronchi of calf lung. After clearing aveolar tissues and pulmonary blood vessels away from the bronchial tree, the smooth muscle was homogenized in 4 volumes of 0.3 M sucrose and 10 mM imidazole, pH 7.0. The sarcoplasmic reticulum fraction was collected by differential centrifugation. After washing with 0.6 M KCl and 10 mM imidazole, pH 7.0, the sarcoplasmic reticulum was tested for calcium uptake activities. On increasing the calcium concentrations from 5 to 50 μM, the microsomal fraction accumulated maximally from 4 to 30 nmoles of calcium per mg of protein in the presence of 10 mM oxalate and 5 mM ATP. Calcium uptake was halved in the absence of oxalate. Addition of 10 mM sodium azide did not affect the accumulation of calcium. It was found that 1 mM norepinephrine or isoproterenol inhibits the calcium uptake of the sarcoplasmic reticulum by 20-30%; whereas 1 mM histamine or acetylcholine enhances the uptake by the same degree. It is concluded that the sarcoplasmic reticulum might be a target for bronchial active agents in the smooth muscle. (Supported by Young Investigator Pulmonary Research Grant HL 17099 from NHLI.)

ON THE DYNAMICS OF METABOLISM OF CORTICOSTERONE BY RAT LIVER IN VIVO: A CASE OF LINEARITY. E.Papaikonomou* (SPON: J.Vernikos-Danellis). Dept. Pharmacology, Free University of Amsterdam, The Netherlands†

With so much emphasis currently placed on non-linear properties of living systems, it may appear paradoxical that a component of an endocrine system has been shown to have linear dynamics. This study provides evidence that corticosterone metabolism by rat liver can be viewed upon as a (linear) zero-order system with gain equal to 0.92, which means that only about 8% of the corticosterone delivered to the liver portal vein does appear at the organ's venous output. The experiments were performed in anesthetized male albino rats (250-300 g). The liver portal vein was quickly cannulated towards the organ and perfusion of the liver in situ with fresh donor blood at a rate of 0.4 ml/min was started immediately, while the normal blood flow through the portal vein was directed outside the animal. Due to the inaccessibility of the venous output of the rat liver in vivo, we measured the relevant liver output signal indirectly by means of sampling of carotid artery blood as described elsewhere (Am. J. Physiol. 227, 137-143, 1974). Several corticosterone step signals in the range 0.75-6.0 μg/min, impulse signals and staircase signals were tested in different animals. A simple mathematical model was developed which describes well the measured responses. This model is consistent with the hypothesis that the metabolism of corticosterone by the liver is a linear function.

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LUNG MECHANICS FOLLOWING ANTIGEN CHALLENGE OF ASCARIS SUUM SENSITIVE MONKEYS. P. Paré* M. C. Michoud* and J. C. Hogg. Dept. of Pathology and Medicine, McGill University and Royal Victoria Hospital, Montreal.

We measured pulmonary resistance (RL) breathing air and a helium oxygen mixture, dynamic compliance (C.dyn) static compliance (C stat), respiratory frequency (F) subdivisions of lung volume and static deflation pressure volume curves before and after bronchial challenge with ascaris suum antigen in six macacca mulatta monkeys with varying skin sensitivity to this antigen. The animals were lightly anesthetized, intubated and studied in the sitting position in a volume displacement body plethysmograph; transpulmonary pressure being measured with an esophageal balloon technique. With the monkeys breathing spontaneously antigen was delivered via a De Villbus ultrasonic nebulizer and RL was determined by the method of Mead and Wittenberger.(1) Prior to challenge RL was 13 ± 3 cm H_2O/L/sec and decreased to 75% of this breathing the helium oxygen mixture. C dyn was 24 ± 8 ml/cmH_2O, C stat 36 ± 18 ml/cmH_2O, F 28 ± 6 breaths/minute, TLC 85 ± 10 ml/kg, FRC 45 ± 8 ml/kg and RV 21 ± 5 ml/kg. Following challenge 3 monkeys showed a positive response, peak RL increasing to 105 ± 70 cm H_2O/L/sec (P=.005) and a decreased response to helium suggesting combined peripheral and central airways obstruction. C dyn decreased to 4.6 ± 3 ml/cm H_2O (P= <.005) and frequency increased to 59 ± 10 breaths/min (P = <.005). No significant changes were noted in C stat, TLC, FRC or RV and no shift in the PV curves was seen. We conclude that this primate model of immediate allergic bronchoconstriction shows important similarities to and differences from human asthma.

(1) Mead, J. and Wittenberger, J. Physicial Properties of Human Lungs measured during spontaneous respiration. J. Appl. Physiol. 5: 779 1953

LITHIUM IONS INCREASE POTASSIUM CONDUCTANCE IN SNAIL NEURONS. L. Donald Partridge* and R.C. Thomas* (SPON: A.O.D. Willows). Dept. of Physiology, Univ. of Bristol, Bristol, England

Lithium has been used successfully in the treatment of manic-depressive illness but its mechanism of action has not been clearly elucidated.

Iontophoretic injection of Li ions into snail neurons causes a reversible increase in resting relative potassium conductance. A similar increase in potassium conductance is observed when the same neurons are bathed in 25 mM Li Ringer. Large injections of Na into cells in which the Na pump has been effectively blocked with ouabain produce an effect similar to that observed with Li injection. Although the role of Ca in this effect is unsubstantiated, the following mechanism is proposed. Li accumulates within neurons and substitutes for Na to decrease the effective Na gradient upon which transmembrane Na-Ca exchange operates. Increased intracellular Ca then, is known to increase potassium conductance in snail neurons.

These experiments suggest a possible mechanism for the clinical effects of Li. Increased potassium conductance resulting from the passive intracellular accumulation of Li in patients with a maintained serum level would lead to a slight increase in membrane potential and a stabilization of the cell with a resultant decrease in swings of membrane potential.

EFFECTS OF PENTOBARBITAL AND GABA ON PITUITARY HORMONE SECRETION. K.A. Pass* and J.G. Ondo, Dept. of Physiology, Medical University of South Carolina, Charleston, S.C. 29401

Most studies examining neural control of pituitary hormone secretion have been performed in anesthetized preparations, although it is well recognized that interpretation of such data may be complicated by the presence of the anesthetic. Therefore, a chronic cannulation technique was developed to provide sequential blood samples from unanesthetized animals. Plasma luteinizing hormone (LH), follicle stimulating hormone (FSH), and prolactin levels were measured by RIA. The effects of pentobarbital (PB) treatment were first examined in normal and castrated male rats. Basal LH and FSH levels in normal animals were unaffected by PB administration. In contrast, the high, fluctuating LH levels in orchidectomized rats were reduced 75% by PB; the elevated FSH levels were unaffected. Basal prolactin levels however, dramatically increased within 10 minutes following PB administration, returning to baseline within 60-120 minutes. The effects of the neurotransmitter, gamma-aminobutyric acid (GABA), were then examined by injection into the lateral ventricle of unanesthetized or PB-anesthetized male rats. Significant increases in plasma LH and prolactin were observed in PB-anesthetized animals, while increases only in prolactin levels occurred in the unanesthetized animals. This evidence indicates that PB-anesthesia significantly alters pituitary function and the mechanisms regulating LH and prolactin secretion. Supported by the NCI-CA 15574 and the American Cancer Society - DT-47.

CEPHALIC TISSUE BLOOD FLOW DETERMINED BY THE UPTAKE OF DIFFUSIBLE AND NON-DIFFUSIBLE RADIOACTIVE TRACERS. M.G. Path* and M.W. Meyer, Dept. Physiology, University of Minnesota, Minneapolis, MN 55455

The distribution of two differently sized (average diameter 15 and 8μ) and labeled (Ce-141 and Sr-85) microspheres (MS) and radioactive Rb-86 to extracranial tissues was studied in 6 young dogs anesthetized with sodium pentobarbital. Respiration was supported by a positive pressure respirator adjusted so that $PaCO_2$ averaged 31 mm Hg. After thoracotomy, a pulmonary vein was cannulated to inject MS simultaneously into the left atrium. After 10 min, Rb was injected near the right atrium via a femoral vein cannula and the heart beat stopped 50-60 sec later. Samples of salivary gland (SG), masseter muscle (MM), alveolar bone (AB), oral mucosa (OM) and dental pulp (DP) were removed, weighed and counted for radioactivity. Cardiac outputs were determined by the reference flow (MS) and the isotope fractionation (Rb) methods and averaged 123±8 (SE) and 150±7 ml/min/kg respectively. These were not significantly different. Tissue blood flow (F) could be quantitated as to MS size or label; F15, F8, and FRb. The average $\overline{F15}$ and $\overline{F8}$ for SG and MM were the same. $\overline{FRb}$ for MM was the same as the $\overline{F15}$ and $\overline{F8}$, but $\overline{FRb}$ for SG was larger (SG: $\overline{F15}$ = .16, $\overline{F8}$ = .16 and $\overline{FRb}$ = .25; MM: $\overline{F15}$ = .12, $\overline{F8}$ = .12 and $\overline{FRb}$ = .12). For AB and DP ($\overline{F15}$)'s were comparable to ($\overline{FRb}$)'s, but > ($\overline{F8}$)'s (AB: $\overline{F15}$ = .19, $\overline{F8}$ = .09 and $\overline{FRb}$ = .23; DP: $\overline{F15}$ = .48, $\overline{F8}$ = .20 and $\overline{FRb}$ = .52). For OM, FRb averaged significantly > $\overline{F8}$ and $\overline{F15}$ by paired analysis (OM: $\overline{F15}$ = .13, $\overline{F8}$ = .14 and $\overline{FRb}$ = .26). Results indicate that fractional uptake of 15 and 8μ MS and Rb varies in some tissues. Some limitations may exist in the assumptions for indirect tracer techniques to quantitate blood flow and should be taken into consideration when evaluating experimental data. (Supported by NIH grant # DE02212.)

CROSS-SECTIONAL AND LONGITUDINAL EVALUATIONS OF A MILITARY PHYSICAL TRAINING PROGRAM. J. F. Patton and J. A. Vogel, U.S. Army Rsch. Inst. of Environ. Med., Natick, MA 01760

Conclusions concerning the efficacy of physical training programs have largely been drawn from longitudinal studies. The purpose of this investigation was to compare the responses obtained from both a longitudinal and cross-sectional evaluation of a military physical training program. Two groups of 60 adult male subjects were initially tested (T_1) and then retested 6 months later (T_2). At T_1, Group I was a sample of military personnel not participating in a training program while Group II had undergone an endurance program (2-4 mile run/day) for 5 months. At T_2, Groups I and II had been participating in the program for 6 and 11 months, respectively. Testing consisted of submaximal and maximal determinations of oxygen uptake ($\dot{V}O_2$), ventilation ($\dot{V}_E$) and heart rate (HR) on each subject using an interrupted treadmill test. A partial summary of the data ($\bar{X}\pm SE$) for both groups during each testing session is as follows:

	HR submax (bpm)	HR max (bpm)	$\dot{V}_E$ max (l/min)	$\dot{V}O_2$ max (l/min)
T_1				
Group I	178±1	195±1	131±3	3.51±0.06
Group II	165±1*	190±3*	139±3*	3.86±0.06*
T_2				
Group I	157±2**	190±1**	142±2**	3.77±0.06**
Group II	157±2	189±1	144±3	3.84±0.06

(* $P < .01$, Group I vs. Group II at T_1; ** $P < .01$, Group I at T_1 vs. Group I at T_2). These results suggest that similar values indicative of an improved level of fitness can be obtained using either a cross-sectional or longitudinal design. It is concluded, therefore, that a cross-sectional study represents a valid approach to the evaluation of a physical training program.

HUMAN VENTILATORY RESPONSES TO REPEATED BICYCLE EXERCISE. D.H. Pearce* and H. T. Milhorn, Jr. (Spon. by B. H. Douglas), Univ. Ms. Med. Ctr. Jackson, MS 39216.

The objective of this study was to examine the hypothesis that the fast ventilatory components occurring at the beginning and end of an exercise period are learned responses. Breath-by-breath ventilatory responses of 3 normal males to bicycle exercise were determined on 5 successive days. These subjects were selected because of lack of fast responses in an initial set of experiments. A digital computer analyzed signals for minute ventilation and end-tidal P_{CO_2} (among other variables) recorded during each experiment on a breath-by-breath basis. Each experiment consisted of 8 min. rest followed by 8 min. of exercise at a work load of 600 (N-M)/min, and 10 min of rest. For a ventilatory response to be described as fast (F) it must have had at the onset a sharp rise in minute ventilation and a rapid decrease in end-tidal P_{CO_2}. The opposite pertained to the cessation of exercise. From the following data it is clear that a definite trend does not exist in repeated runs for subjects to develop fast responses. Hence, it must be concluded that learning does not play a role in the fast components of exercise.

		ON					OFF				
Day No.		1	2	3	4	5	1	2	3	4	5
Subject 1	$\dot{V}_E$	F	F	F	$\binom{F}{F}$	F	$\binom{F}{F}$	$\binom{F}{F}$	$\binom{F}{F}$	$\binom{F}{F}$	$\binom{F}{F}$
	P_{CO_2}	S	S	S		S					
Subject 2	$\dot{V}_E$	F	S	F	F	F	S	S	F	S	S
	P_{CO_2}	S	S	S	S	S	S	S	S	S	S
Subject 3	$\dot{V}_E$	S	S	F	$\binom{F}{F}$	S	$\binom{F}{F}$	$\binom{F}{F}$	F	$\binom{F}{F}$	F
	P_{CO_2}	S	S	S		S			S		S

Supported in part by NIH grants HL 11678 and HL 17998.

EFFECT OF OZONE ON NASAL AND PULMONARY FUNCTION IN MAN. L.D. Pengelly, J. Leon,* K. Henry,* and E.A. Rebuck*. Dep't Medicine, McMaster University, Hamilton, Ontario, Canada.

Previous studies have demonstrated a reduction in concentration as ozone transits the nasal passages, as well as a diminution of its effects on the lung when it is inhaled via the nose rather than through the mouth. There is, however, little information on the direct effects of ozone on the nose, or how these associate with pulmonary effects. We have exposed eight normal subjects seated at rest to room air (control) and to room air to which 0.5 ppm ozone was added. Forced expired volume and nasal pressure/flow characteristics were measured before, during and after the exposure period. Four subjects developed respiratory symptoms with ozone; of these, two had reduction in maximum mid-expiratory flow (10% of control); of the latter two, one had a significant reduction in maximum inspiratory nasal flow (MINF) and an increase in nasal resistance (R_n). One subject (who did not develop symptoms or spirometric changes with O_3) had a reduction in MINF and an increase in R_n. No changes were seen in the other three subjects. These studies show that changes in nasal pressure/flow characteristics may occur upon exposure to ozone, and may or may not be assoicated with symptoms or pulmonary changes.
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NEURAL CORRELATES OF AGE-DEPENDENT BEHAVIOR IN APLYSIA. B. Peretz and K. Lukowiak*, Dept. of Physiology and Biophysics, University of Kentucky Medical Center, Lexington, Kentucky 40506.

Central nervous system, i.e., parieto-visceral ganglion (PVG), control of habituation of the gill withdrawal reflex to direct gill stimulation is significantly less in young (<25g) than in older (>100g) Aplysia. L_7 is involved in the reflex to the extent that induced spiking of L_7 results in dishabituation of the reflex in both groups of animals. Coincident with habituation of the reflex is decrement of synaptic potentials in L_7. L_7 in young animals is more responsive to gill stimulation, yet its electrical properties appeared comparable to that in older animals although its size is smaller. We proposed that the reduced central control of the reflex and the greater responsiveness of L_7 in young animals results from reduced or absent inhibition in the PVG, (Peretz and Lukowiak, 1975). Implied in this conclusion is that the reflex and L_7's PSP decrement are controlled by the same source in the PVG. To test this hypothesis punctate stimuli ranging from 0.20 to 2.0 g were applied to the gill to study the effect on the rate of reflex habituation and of L_7's PSP decrement. We would expect to see a correlation between the reflex and L_7's activity with increasing stimulus intensities in older animals. This was observed; both rates paralleled each other and decreased with increasing stimulus intensities; thus, the extent of control is stimulus intensity dependent. In young Aplysia increasing stimulus intensities had no apparent effect on either the habituation rate or the rate of PSP decrement. These results show that a direct relationship exists between the control of the reflex and of evoked PSP activity in L_7. They are additional evidence that a common source in the PVG controls both the reflex and related neuronal activity in older but not in young Aplysia.
(MH 18611; Found. Fund. Psychiat. T64-205).

CARDIAC SYMPATHETIC AND VAGAL AFFERENT NERVE ACTIVITY IN THE DOG. S.R. Peters*, J.A. Armour, E.J. Zuperku*, F.O. Igler*, R.L. Coon*, and J.P. Kampine*. (SPON: E.J. Lennon). Med. Col. of Wisc., Wood, V.A. Center Milwaukee, Wisconsin 53226.

Single fiber and small multifiber afferent nerve recordings in the recurrent, innominate, dorsal and vagal cardiac nerve branches and in upper thoracic white rami communicantes were related to changes in left and right atrial, left and right ventricular and aortic pressure changes in 17 mongrel dogs. The animals were anesthetized with phencylidine hydrochloride 2 mg/kg followed by alpha chloralose 80 mg/kg. Changes in intracardiac and aortic pressures were produced by volume infusions, caval constriction, descending aorta constriction, and infusions of epinephrine or isoproterenol. Spike activity was analyzed for discharge characteristics during small intervals of the cardiac cycle (5-10 msec) and presented as nerve frequency histograms related to pressures in the cardiac chamber where receptor location was established by probing. Sixteen or more cardiac cycles were used for each histogram analysis. Through the use of computer techniques the nature of receptor responses to altered cardiac dynamics was studied over a large number of cardiac cycles for atrial, ventricular, and aortic receptors.

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HEMODYNAMIC RESPONSES TO CORONARY OCCLUSION IN EXERCISING DOGS. D. Fred Peterson, Lawrence D. Horwitz and Vernon S. Bishop. Depts. Pharmacology & Medicine, U. Tex. Hlth. Sci. Ctr. & VA Hosp., San Antonio, Tex. 78284

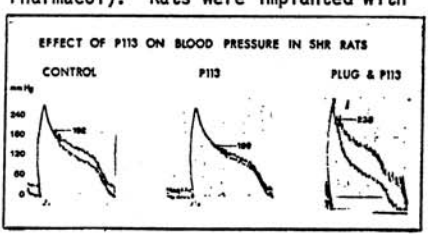
Exercise (EX) induces increased left ventricular function whereas coronary occlusion depresses the heart. Their combined stress effects on cardiac dynamics are unknown. Seven mongrel dogs were trained to run on a level treadmill and then surgically instrumented to record left ventricular pressure, thereby permitting evaluation of systolic (LVSP) and end diastolic (LVEDP) pressures, the maximum derivative (dP/dt) and heart rate (HR). Aortic flow probes were implanted to yield stroke volume (SV) and cardiac output (CO). Cuff occluders were placed around the left circumflex coronary artery. After full recovery, responses to coronary occlusion (Occ) at rest and during EX, 6-8 mph, were compared. Measurements were taken approximately 3 minutes after onset of EX and 50 seconds after onset of Occ. During EX, all control values were elevated above resting controls: i.e., HR (96-196 b/min); SV (32.8-33.9 ml/b); CO (3.39-7.03 l/min); dP/dt (3171-4751 mmHg/s); LVSP (123-161 mmHg); LVEDP (3.6-6.8 mmHg). Occ caused further increases in HR and LVEDP at rest and during EX but produced decreases in all other parameters measured. Changes due to Occ were parallel in all cases except HR and CO when rest and EX were compared. Tachycardia due to resting Occ was significantly greater than that observed due to Occ during EX (29 vs 9 b/min). The fall in CO during EX occlusion was significantly greater than the small fall in CO due to resting occlusion (1.32 vs 0.13 l/min). It is apparent that the effects of Occ on myocardial function at rest and during moderate EX are similar, however, CO is compromised by ischemia during EX since increases in heart rate no longer compensate for the fall in stroke volume. (Supported by NIH grant #HL12415-07, AFOSR 71-2075 and NIH #HL16656-03).

POWER SPECTRUM ANALYSIS OF EMG DURING STATIC EXERCISE.
J.S. Petrofsky, T.E. Dahms* and A.R. Lind. St. Louis Univ. Med. Sch., St. Louis, MO 63104

Surface EMG affords a simple, non-invasive technique to measure the activity of muscle during fatiguing and non-fatiguing exercise. However, because of the aperiodic nature and uncertain origin of the waveform, analysis of events in the muscle becomes uncertain by simple analysis. Various methods to analyze these complex waveforms such as slewing and absolute integration or zero crossing frequency distribution plots have all failed to produce a concise picture of the electrical activity in the individual muscle fiber during work. In the past few years, frequency analysis of the surface EMG by Fast Fourier Transform (FFT) has been attempted to unravel this dilemma. Although results are encouraging, to date no study has systematically examined the power spectral density by FFT during activity in man. In the present investigation, we have examined the power spectral density of surface EMG of the forearm in man during fatiguing isometric contractions at 25, 40, 55 and 70% of the subjects own maximal strength in 3 female and 3 male subjects. Results indicate a marked decrease in the center frequency of surface EMG during fatiguing static effort. (Partially supported by Air Force contract AFSOR-72-2362.)

REDUCTION OF BLOOD PRESSURE BY INTRACRANIAL INJECTION OF ANGIOTENSIN BLOCKER (P113) IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). M. Ian Phillips, J. Phipps*, W. Hoffman* and M. Leavitt*. Dept. Physiology, University of Iowa, Iowa City, Iowa 52242

Angiotensin II injected into the brain ventricles of chronic rats elevates blood pressure. When the rats are nephrectomized we find that this pressor effect is prolonged, suggest that kidney function shortens the pressor action of central AII injections. The pressor response to IVT AII injections is decreased at 12-17 and 24 hours post nephrectomy. This is possibly due to the increased brain renin-AII which has been found following nephrectomy. This data would mean that certain hypertensive states may be due to increased brain renin-angiotensin levels, (as Ganten has proposed). To test this hypothesis we used SHRs (n=7) and the appropriate controls (n=5) with the specific AII blocker P113 (Norwich Pharmacol). Rats were implanted with lateral ventricular cannulae and stable BP was measured chronically by a tail cuff method. Injection of P113 in doses of 0.1 µg, 5 µg, and 10 µg/µl significantly lowered BP ($p<0.05$-0.001). BPs were lowered by up to 50 mmHg. They produced no change in normotensive controls. Plugging of the anterior third ventricle abolished the effect of P113 on SHR. (Supported by NIMH RSDA and NSF GB2.)



ROLE OF THE VAGUS NERVES IN VENTILATORY LOAD COMPENSATION IN AWAKE AND SLEEPING DOGS. E.A. Phillipson, L.F. Kozar* and E. Murphy*. Dept. of Medicine, Univ. of Toronto, Toronto, Ontario M5S 1A8.

The ventilatory response to external elastic loads is thought to be mediated in large part by vagal reflexes that stabilize the respiratory system by increasing its "effective" elastance (EE). However, this concept has arisen from studies on anesthetized animals. Accordingly we have examined the role of the vagus nerves in ventilatory load compensation in unanesthetized dogs, while awake and during physiological, slow-wave ("quiet") sleep. Studies were performed on three trained dogs with exteriorized cervical vagal loops that were cooled with encircling radiators. The stage of sleep was determined by EEG recording. Elastic loads were applied at end-expiration for 1 to 6 successive breaths by having the dogs breathe from rigid containers of varying size. EE of the respiratory system was calculated from the airway pressure-tidal volume relationships of the loaded and unloaded breaths. EE ranged from 50 to 63 cm H_2O/l in the 3 dogs, both awake and asleep. Complete vagal blockade (VB) produced marked slowing and deepening of respiration, but no change in EE whether the dogs were awake or asleep. Furthermore, the progressive increase in tidal volume and respiratory frequency that occurred when the load was applied for more than one breath was unaffected by VB whether the dogs were awake or asleep. The results indicate that afferent vagal impulses are not involved in the immediate or progressive ventilatory response to external elastic loads. Results obtained in the dogs while awake cannot be attributed to conscious, voluntary reactions to loading since identical findings were noted during sleep. (Supported by MRC of Canada, Grant MA-4606).

A RAT MODEL FOR BODY COMPOSITION IN CHRONIC ALCOHOLISM, STARVATION, AND RECOVERY. R.N. PIERSON,Jr.; P. DUBNER;* and J.WANG* St. Luke's Hospital Center Columbia University, N.Y.C. 10025

Separation of the toxic effects of alcohol from those of protein-calorie malnutrition is tenuous in man, has been accomplished in primates, and is now addressed in rats, a species in which hepatic histologic changes after alcohol fail to model human cirrhosis.

32 male Sprague-Dawley 5-week rats took rat chow and 20% ethanol as only water source for 22 weeks. Pair-fed rats took tap water and chow reduced in calories to match the ethanol cohort. Normal controls, ethanol, and starvation groups were followed by sacrifice of random members at 2,5,9,14, and 20 weeks, and after 10 weeks of ad lib dietary recovery. In whole body, liver, and muscle, assays for water, fat, Na^+, K^+, extracellular fluid, (ECF) Cl^-, DNA, and protein were measured by standard methods.

Both alcoholic and semi-starved rats showed K^+ depletion and Na^+ excess in liver, carcass, and muscle. The ethanol defect was 17% greater than in pair-fed starvation, (75 cal/rat/day, 70% of normal control rats.) Full recovery in body composition parameters occurred in ethanolic but not in starvation rats. Body K^+ returned to normal from an average 34% deficit in alcoholic rats, but starvation pairs remained K^+ depleted after initiation of the ad lib diet.

Na^+ and Cl^- excess, larger ECF, and reduced K^+ concentration in the rat model are in common with human cirrhosis, matching in degree as well as direction the changes seen in this study. The 10-week recovery period resulted in very substantial restitution of body composition. The rat model appears satisfactory to follow serial body composition parameters of chronic alcohol toxicity.

SOLUBILITY AND DIFFUSIVITY OF INERT AND RESPIRATORY GASES IN RAT SKELETAL MUSCLE. J. Piiper*, T. Kawashiro* and P. Scheid*. (SPON: H. Rahn). Dept. Physiology, Max Planck Institute for Experimental Medicine, Göttingen, Federal Republic of Germany

All measurements were performed in freshly excised rat abdominal muscle forming a thin sheet of uniform thickness, at 37°C. For inert gases, the solubility coefficient, α, was determined by measurement of the amount of gas extracted from an equilibrated muscle sample, and Krogh's diffusion constant, K, was obtained from gas transfer rate at steady state. K for O_2 and CO_2 was determined from the kinetics of equilibration of these gases in a small closed gas chamber separated by the muscle from another chamber with constant gas composition; the method allowed determination of K in tissue consuming O_2 and producing CO_2. The following mean values were obtained:

α (in μmol/(l·torr)): H_2, 1.13; He, 0.608; CH_4, 2.42; C_2H_2, 55.5; N_2O, 27.7; $CHClF_2$, 56.0; SF_6, 0.559.

K (in 10^{-9} mmol/(cm·min·torr)): H_2, 1.67; He, 1.42;, CH_4, 1.27; C_2H_2, 41.2; N_2O, 20.0; $CHClF_2$, 18.8; SF_6, 0.081; O_2, 1.31; CO_2, 28.9.

Values for the diffusion coefficient, D, calculated as K/α, were found to be about half the D values in water at 37°C for gases with moderate lipid/water partition coefficient, λ. Model calculations show that D for gases with high λ is underestimated by this method in tissues containing lipid. Graham's law (inverse proportionality between D and square root of molecular mass) was found to represent a useful approximation for the gases studied, but the correlation between D and the molecular diameter was still better.

CREEP IN CARDIAC MUSCLE. J.G. Pinto* and P.J. Patitucci*, (SPON:Y.C.Fung) Dept. AMES Bioengineering, University of California, San Diego, La Jolla, California 92037

Development, rate of development and reversal of dimensional changes of the chronically overloaded (pressure or volume) intact heart are of clinical significance. The visoelastic creep phenomenon has been suggested as possible mechanism responsible for ventricular cavitary enlargement. In view of this, the basic features of creep and creep recovery are studied using isolated cat and rabbit heart muscles. Modified creep testing procedure was adopted under controlled conditions of temperature, pH and chemical enviroment. The specimen were in the passive state in that they were not stimulated electrically. Spontaneous contractions were, however, observed during the study in cat muscles particularly at higher temperatures. From the short duration creep and creep recovery experiments, the following observations have been made: 1) Cardiac muscle (papillary, trabeculae, right ventricular strips) under maintained stress, creeps 3 to 4% of its original length in 100 sec.; 2) this creep is recovered almost entirely in the same time period (100 sec.) when the stress is removed, and 3) when the spontaneous contractile activity is abolished by chelating the internal calcium stores by 2 molar EGTA solution, amount of creep in cardiac muscle was found to be less than without the drug in the same time interval of 100 sec. Whether the creep and creep recovery features observed in isolated muscle can account for the reported increase and decrease of cavitary volume in the intact ventricle, remains to be investigated. (Supported by San Diego County Heart Association Fellowship, PHS Fellowship 1 F22 HL00903-01 and grants NSF GK-32972x and USPHS HL 12494.)

CORTISOL MEDIATES RESTITUTION OF BLOOD VOLUME AFTER HEMORRHAGE. J. C. Pirkle, Jr.* and D. S. Gann. Dept. of Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

Experiments conducted on splenectomized dogs showed that 30-60% of blood volume (BV) was restored within 2 hr after hemorrhage (10% of BV/3 min), but full restitution required 12-24 hr and was accompanied by restitution of plasma protein. Plasma cortisol, osmolality, and glucose increased for 2-3 hr after hemorrhage, but glucose accounted for only 8% of the osmolality increase. Adrenalectomized-splenectomized dogs infused with cortisol at basal rate (2 μg/min) restored 30-60% BV within 2 hr, but added no additional volume or protein during the next 22 hr. Plasma osmolality fell or did not rise. Adrenalectomized dogs infused with cortisol at typical post-hemorrhage rates (17 μg/min) showed full restitution of BV and protein, and hyperosmolality equivalent to intact dogs. Adrenalectomized dogs infused with 2 μg/min of cortisol and 7.5 ml/kg of 5% dextrose in 0.9% NaCl also showed full restitution of BV. Adrenalectomized dogs subjected to an increase of cortisol infusion rate from 2 μg/min to 17 μg/min, but no hemorrhage, showed no change in plasma osmolality. These results suggest that full restitution of blood volume depends upon the following sequence: 1) Hemorrhage and the subsequent increase in cortisol lead to extracellular hyperosmolality. 2) Intracellular fluid shifts to the interstitium down the osmotic gradient. 3) The increased extracellular fluid increases interstitial pressure, leading to 4) return of interstitial protein and concommitant intravascular movement and retention of fluid. (Supported in part by NIH grant AM14952 and by RCDA HL00068 to J.C.P, Jr.)

EFFECTS OF ALTERED CARBON DIOXIDE TENSION ON INTRAVASCULAR HEMOGLOBIN OXYGENATION. R.N. Pittman and B.R. Duling, Dept. Physiology, Medical College of Virginia, Richmond, Virginia 23298, and Dept. Physiology, University of Virginia, Charlottesville, Virginia 22901.

Carbon dioxide (CO_2) exerts a dual effect on microvascular oxygen delivery to tissue. Increased blood carbon dioxide tension (PCO_2) shifts the oxyhemoglobin (HbO_2) dissociation curve to the right and produces arteriolar vasodilation. The vasomotor effect of CO_2 was eliminated in these experiments by inducing maximal vasodilation with 10^{-4} M adenosine, which by itself did not appear to influence the HbO_2 dissociation curve. Thus, the blood component of oxygen delivery could be studied by itself. Simultaneous determinations of intravascular percentage HbO_2 and PO_2 were made in large and small arterioles of the suffused hamster cheek pouch. A video densitometric technique was employed to measure % HbO_2 and PO_2 was determined with oxygen microcathodes. The PCO_2 of the suffusion solution was altered from 32 to 10 mmHg or from 32 to 75 mmHg and the resulting % HbO_2 and PO_2 data pairs were analyzed in terms of Hill's equation for the HbO_2 dissociation curve. The P_{50}'s were found to be 25±3, 30±3, and 41±4 mmHg for PCO_2's of 10, 32, and 75 mmHg, respectively. These in vivo values are in general agreement with predictions from published HbO_2 dissociation curves, although the predicted P_{50} for suffusion with the low CO_2 solution was somewhat higher than expected. A pronounced decrease in PO_2 with an accompanying fall in % HbO_2 was observed in the arterioles. This longitudinal gradient in arteriolar oxygen content confirms and extends the previous reports of a progressive decline in precapillary PO_2.

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CALCIUM ACCUMULATION IN INTACT HUMAN ERYTHROCYTES. Gordon A. Plishker* and Hillel J. Gitelman*, (SPON: A.L. Finn). Dept. of Medicine, University of North Carolina School of Medicine, Chapel Hill, N.C. 27514

Intact human erythrocytes can be readily loaded with calcium by incubation in hyperosmotic media at alkaline pH. Erythrocyte calcium content increases from 15-20 to 120-150 nanomoles per gm hemoglobin after incubation for 2 hrs at 20° C in a 400 mOsmol, pH 7.8 solution containing 100 mM Na, 90 mM tetramethylammonium (TMA), 1 mM K and 10 mM Ca. This process of calcium accumulation is associated with modest metabolic depletion (the ATP content remains at 70% of normal), occurs without alteration in cellular Na and K and cannot be solely explained by hyperpolarization of the membrane, as determined by chloride ratios. Calcium accumulation is influenced by the cationic composition of the external media. The response to K is diphasic. With increasing K concentrations the net accumulation of Ca initially increases becoming maximal at 1 mM K, then diminishes, falling below basal levels at concentrations above 3 mM K. Ouabain inhibits the stimulatory effect of low concentrations of K. The inhibitory effects of higher concentrations of K are shared by other cations, K > Na > Li > TMA. Ca efflux from loaded erythrocytes is not significantly altered by changes in osmolality, medium ion composition or ouabain.

We conclude 1) hypertonicity increases calcium accumulation by an increased calcium influx, 2) a portion of this calcium influx is mediated by a carrier mechanism which is part of the Na-K transport system.

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KINETICS OF TRANSCAPILLARY MOVEMENT OF AMINO ACIDS IN BRAIN. M. Pollay, Division of Neurosurgery, University of New Mexico School of Medicine, Albuquerque, New Mexico. 87131

In anesthetized rats the single pass brain uptake of an ^{113m}In-chelate and ^{14}C-phenylalanine was measured at various concentration levels following carotid injection. The extraction of each solute was in reference to a tritiated water standard included in the injection mixture. Regional cerebral blood flow (rCBF) was determined from the distribution of ^{131}I-iodoantipyrine in brain post i.v. infusion. The flux of phenylalanine in six brain regions was computed from the extraction data, injection conc, and rCBF. It was shown that the single pass uptake of phenylalanine by brain was saturable and competitively inhibited by L-dopa and L-leucine. The magnitude of brain uptake was affected by low sodium conc in the injectate. The presence of ouabain in the injection mixture (0.1 and 1.0 mM) did not influence the extraction of this amino acid from cerebral blood although 2,4-dinitrophenol (.05 mM) did result in a significant reduction in the extraction of phenylalanine from the cerebral capillaries. The kinetics of phenylalanine transport in six different brain regions were virtually identical. The calculated V_{max} was 0.25 $\mu m\ min^{-1}g^{-1}$ with a Km of 1.38 mM. The results suggest that the transcapillary movement of amino acids into brain occurs by a carrier mediated process which is similar in all areas of the rat brain.

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THE RELATIONSHIP OF OXYGEN DEFICIENCY AND MESENTERIC REACTIVE HYPEREMIA. George P. Pollock. Department of Physiology, Loyola University of Chicago, Stritch Sch. of Medicine, Maywood, Il. 60153.

Recently the myogenic mechanism was determined to be the most suitable explanation for the reactive hyperemia responses observed in cat mesentery capillaries. Alternatively, other investigators have suggested that reactive hyperemia results from the oxygen deficiency incurred during arterial occlusion. The validity of this latter theory was evaluated in this study using the following experimental procedure. Isolated and autoperfused cat mesentery preparations were housed in a gas chamber whose atmosphere could be altered. The red cell velocity of 15-30 μ arterioles was measured with the dual slit method while periarteriolar P_{O_2} was measured with oxygen microelectrodes. Reactive hyperemia was induced by 30 sec arterial occlusions during control (normoxic) and test (hyperoxic) trials. The chamber atmospheres were 95% N_2 - 5% CO_2 and 5% O_2 - 90% N_2 - 5% CO_2 during control and test conditions, respectively. The perivascular P_{O_2} decreased from 28 ± 4 to 8 ± 3 mm Hg during control occlusions but was maintained at 33 ± 4 mm Hg during test trials. No significant differences were determined in the peak flow to control flow ratio, the response duration, the excess flow, or the time to peak flow of the control and test hyperemia responses. These results suggest that reactive hyperemia induced by short duration occlusions is independent of oxygen deficiency or the accumulation of an oxygen dependent metabolite. It is proposed that this response occurs via a pressure related myogenic mechanism.

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WORKING CAPACITY, CARDIORESPIRATORY, AND BODY COMPOSITION CHARACTERISTICS OF WORLD CLASS MIDDLE AND LONG DISTANCE RUNNERS. M.L. Pollock*, J. Ayres*, A. Ward*, J. Sass*, and S. White*. (SPON: P. Raven). Institute for Aerobics Research, Dallas, Texas 75230.

Nineteen outstanding runners, 8 long distance (LD), and 11 middle distance (MD) were evaluated. All runners had distinguished themselves in national or international competition. Working capacity and cardiorespiratory function were determined by submaximal and maximal treadmill tests. The submaximal test included an 11 min run (7 min, 10 mph plus 4 min, 12 mph) at 0% grade, while the maximal test was run at 11 mph with the grade increasing 2.5% every 2 min until exhaustion. Body density was determined by the hydrostatic technique. The basic characteristics found for MD and LD runners respectively were: age, 25.4 vs 27.4 yr; height, 176 vs 176.8 cm; weight 63.1 vs 62.1 kg; percent fat, 5.0 vs 4.3%; heart rate (HR) at rest, 48 vs 45 beats/min; heart volume (HV), 1087 vs 938 cc ($P < .10$); $\dot{V}O_2$ max, 78.8 vs 74.4 ml/kg·min ($P < .05$); $\dot{V}_E$ max, 169 vs 163 L/min-BTPS; max HR, 199 vs 196 beats/min; and maximal treadmill time, 7.6 vs 7.2 min ($P < .10$). Lactic acid concentrations were similar for MD and LD runners under both exercise conditions. Although percent of $\dot{V}O_2$ max was not different between groups during submaximal work, the actual $\dot{V}O_2$ requirement was significantly lower for the LD group. The data showed only slight differences between outstanding MD and LD runners, but suggested that MD runners tended to have a higher $\dot{V}O_2$ max, HV, and ability to run uphill. This difference found between groups in treadmill performance suggests the importance of leg strength and endurance in MD running. The lower $\dot{V}O_2$ required at a given running speed found in the LD runners would be advantageous for LD events.

THE PROTECTIVE EFFECT OF GLUCOSE IN EXPERIMENTAL SEPSIS. John Postel* and Paul R. Schloerb. University of Kansas Medical Center, Kansas City Kansas 66103.

The present study was undertaken to evaluate the effect of I.V. glucose on hemodynamic and metabolic events and survival in dogs subjected to a lethal 5-hr infusion of Pseudomonas aeruginosa at a dose of 10^8/ml/min. Blood glucose and insulin, body temperature, hemodynamic parameters and WBC were measured before and at 1-hr intervals during controlled bacterial infusions. Induced bacteremia in the upper 10^4 range per ml of blood was accompanied by a decline of mean arterial blood pressure from 130 ± 6 mm Hg to 84 ± 12 mm Hg at 4 hrs, fall in temperature, leukopenia (70%), and hypoglycemia. Dogs dying within 24 hrs following the 5-hr bacterial infusion consistently developed hypoinsulinemia at 5 hrs. In survivors insulin remained unchanged or increased. In another group of dogs hypoglycemia during bacteremia was corrected by administration of a 50% glucose infusion (1 ± 0.2 g/kg). Mean arterial blood pressure fell from 136 ± 5 mm Hg only to 117 ± 12 mm Hg at 4 hrs, accompanied by a febrile response, leukopenia, and lower bacteremia levels at the end of the 5-hr infusion period. Nearly all animals survived with glucose infusion and developed hyperinsulinemia. It is concluded that in lethal bacteremia correction of hypoglycemia by administration of glucose improved survival, characterized, in survivors, by increased insulin secretion in response to the glucose infusion.

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LOCALIZATION OF (Na^+-K^+)-ACTIVATED ATPase IN "FORWARD" AND "BACKWARD" EPITHELIA IN SALIVARY GLANDS. J.H. Poulsen* M. Bundgaard* and M. Møller* (SPON: J.A. Williams). Institutes of Medical Physiology A and Medical Anatomy A, University of Copenhagen, Denmark.

Isolated cat submandibular glands were perfused with Locke's solution containing ^{3}H-ouabain (10^{-6}M). Light microscopic autoradiography combined with conventional electron microscopy revealed that: 1. ^{3}H-ouabain was predominantly found in the contraluminal half of the epithelial cells of the striated ducts. This localization corresponds to the extensive infoldings of the plasma membrane. These findings support the view that a "forward" type active reabsorption of sodium takes place in the striated ducts and that the process is mediated by a (Na^+-K^+)-activated ATPase. 2. At the acinar level ^{3}H-ouabain was bound almost exclusively to the "demilunar" cells. The intercellular space between these cells was found to be long and tortious with a junctional complex located between the intercellular space and the secretory canaliculus. These observations suggest that the isotonic primary saliva is formed by the "demilunar" cells. The localization of the junctional complex close to the lumen indicates that the secretory "demilunar" epithelium belongs to the "backward" type of transporting epithelia. It is unclear whether the (Na^+-K^+)-activated ATPase of the "demilunar" cells plays a direct role in the secretory processes or the enzyme is solely responsible for maintaining normal intracellular concentrations of sodium and potassium in the resting state.

IN VIVO BUBBLE GROWTH FOLLOWING DECOMPRESSION. M. R. Powell* (SPON: M. P. Spencer) Inst. Appl. Physiol. and Medicine, 1700 E. Cherry St., Seattle, WA 98122

An investigation was made on the locus of bubble formation in animals following decompression. This was made at the microscopic levels and differs from earlier efforts by others in that histologically preparative techniques were not employed thus reducing gas loss by diffusion. Rats and rabbits were used as subjects and were killed at pressure or at a later post-decompression period. The following general observations and conclusions were made: (1) Gas loss from tissue sections was rapid; (2) bubbles were not found to originate in capillaries but grew into capillaries from venules; (3) when a gas phase was observed in the microvasculature, cylindrical rather than spherical bubbles were found; (4) few extravascular bubbles were ever seen, even in adipose tissue; (5) the gas phase caused a great distention of the capillary; (6) formation of a gas phase did not require an actively functioning circulatory system; (7) as expected from classical studies, more bubbles were found in adipose than muscle tissue; (8) when the gas phase was seen to resolve, capillaries lost gas first and then venules; (9) even when the gas phase was very extensive, extravascular bubbles were seldom seen; (10) sections of saphenous nerve axons were examined for a gas phase and bubbles were not seen; (11) ends of the gas phase were hemispheres such that endothelial lining must be hydrophilic.

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DIFFERENTIAL SENSITIVITY OF CARDIAC EFFECTORS TO ACETYL CHOLINE AND TO VAGAL STIMULATION. Donald V. Priola, Dept. Physiol., Univ. New Mexico Sch. Med., Albuquerque, N.M. 87131.

Recently, we observed that significant decreases in cardiac contractility are produced by intracoronary injections of as little as 0.05 mcg of acetyl choline (ACh). At these dose levels, however, very little effect on heart rate was noted. The present work was performed to test the differences in inotropic, dromotropic and chronotropic sensitivity to ACh and to compare these effects with those obtained using graded stimulation of the cervical vagus. Dogs were prepared on cardiopulmonary bypass so that ventricular isovolumic pressure, His bundle activity and heart rate could be simultaneously recorded. Dose-response curves were constructed for these parameters vs. ACh dose and the intensity of vagal stimulation (constant duration and frequency). It was found that negative inotropic responses could be produced by as little as 20 ng (.02 mcg) of ACh injected intracoronary while at least 1000 times this amount (2.0 mcg) was necessary to produce significant decreases in A-V nodal conduction or HR. This degree of differential sensitivity was not observed with vagal stimulation. It is concluded that differential sensitivity of cardiac effectors to ACh is probably the result of accessibility to the effector cell and not of differences in muscarinic receptor types.

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ACTIVE AMMONIUM TRANSPORT. R.D. Prusch, Division of Biological and Medical Sciences, Brown University, Providence, R.I. 02912

The isolated hindgut of larval Sarcophaga bullata is capable of secreting K^+, Na^+, NH_4^+, and Cl^- into the gut lumen under the appropriate conditions. The hindgut of Sarcophaga also maintains a transepithelial potential (TEP) difference such that the lumen of the gut is normally negative in respect to the hemolymph. On the basis of net ion fluxes and TEP measurements in the isolated hindgut of S. bullata, it was suggested that K^+, NH_4^+ and Cl^- were actively secreted. Addition of small amounts of NH_4^+ to the external medium resulted in a large decrease in K^+ secretion and a concomittant large increase in NH_4^+ secretion. In both cases, i.e., in the presence and absence of external NH_4^+, Cl^- secretion was maintained. These results were used to develop a model of the hindgut system in which Cl^- was constantly, and independently of cation movements, being secreted into the hindgut lumen. In addition, a cation pump was thought to be present in the hindgut epithelium in which K^+ and NH_4^+ competed for the same transport site. In order to determine if this is the case, unidirectional ion fluxes across the larval, isolated hindgut were measured with the appropriate radioisotopes. The results of this study have shown that Na^+ is distributed passively in this system while K^+ and Cl^- are actively secreted into the hindgut lumen. In addition, NH_4^+ is secreted independently of K^+ into the gut lumen. Because NH_4^+ is transported independently of other cations and because of the relatively simple structure of the gut, the isolated hindgut of S. bullata represents an ideal model system in which to investigate the active transport of the NH_4^+ ion.

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Intracellular recording in sensory neurons of the retina of Strombus. F.N. Quandt* and H.L. Gillary (sponsored by G.C. Whittow), Dept. of Physiology and Laboratory of Sensory Sciences, Univ. of Hawaii, Hono. HI 96822

Intracellular recordings have been obtained from cells in the isolated retina of a marine gastropod: Strombus luhuanus. Conventional methods for recording and current passing through a single microelectrode were used. Three types of cells were identified on the basis of their responses to illumination and electrical properties. Membrane potentials (in the dark) were -20 to -25 mV. for type I cells and -80 mV. for type II cells. Both of these types responded to tungsten light flashes with slow, graded, two wave depolarizations reaching a maximum amplitude of 30 mV. Additionally, cell type I exhibited a steady state depolarization to a long duration stimulus with a rapid return to dark potential upon termination of the light stimulus. In contrast, cell type II showed no steady state response with a slow return to dark potential. A third type of cell, only rarely encountered, hyperpolarized in response to light inhibiting spontaneous action potentials. Input resistance and time constant, respectively, were 40 MΩ and 20 msec. for type I cells and 20 MΩ and 0.4 msec. for type II cells. In both cases, input resistance decreased with illumination and the two waves of the light evoked response appeared to have different reversal potentials. These observations indicate that this retina is capable of complex processing of sensory input. (Supported in part by N.S.F. grant GB-32091).

TRANSPORT PROPERTIES OF MICROBIOLOGICALLY ACTIVE 7-ARYLGLYCYLAMIDO-CEPHEM DERIVATIVES IN ISOLATED RAT INTESTINE. J. F. Quay, Lilly Res. Labs., Indianapolis, IN. 46206

In pieces of rat jejunum incubated at pH 6 and 37° C in a bathing solution containing the efficiently absorbed antibiotic cephalexin the uptake of the drug into intravillus water proceeds via an active transport process. The apparent maximum rate of uptake of cephalexin under these conditions is 3.3 mM/L.min. and the apparent K_T is 19 mM/L. The concentrative uptake is abolished when tris(hydroxymethyl) aminomethane is used to replace sodium in the bathing solution. In the presence of sodium the uptake is competitively inhibited by the dipeptide L-phenylalanylglycine. Alteration of the chemical structure of the antibiotic by substitution of 3-chloro, 3-methoxy, or 3-methoxymethyl moieties in place of the 3-methyl group of cephalexin reduces the uptake slightly. However, substitution of 3-(methylthiadiazole)thiomethyl or 3-(methyltetrazole)thiomethyl moieties at the same position reduces uptake drastically. For all compounds tested with a given substituent in the 3 position the addition of a p-hydroxyl group to the phenylglycyl side chain stimulates uptake. The 7-arylglycylamidocephem antibiotics appear to be transported in rat intestine by a pathway shared with dietary peptides and the study of their uptake provides some unique insights into the specificity of this process.

EFFECT OF LUNG INFLATION AND ALVEOLAR HYPOXIA ON ARTERIAL BLOOD VOLUME (V_a) IN ISOLATED CAT LUNGS. E.J. Quebbeman* and C.A. Dawson. Med. Col. of Wisconsin and Wood VA Ctr., Milwaukee, Wis. 53193.

In isolated cat lungs perfused at constant flow, pulmonary artery pressure (P_a) increased from 15.4 cm H_2O to 18.6 cm H_2O as the lung was inflated by decreasing pleural pressure (P_{pl}) from 3 to 16 cm H_2O during control conditions (P_AO_2 100 torr). Hypoxia (P_AO_2 24 torr) increased P_a. However, as pleural pressure decreased from 3 to 16 cm H_2O, P_a decreased from 29.0 to 26.5 cm H_2O. To determine if these differences in response to lung inflation could be accounted for by the effects of interdependence between pulmonary arteries and the level of lung inflation, pulmonary arterial volumes (V_a) were determined using the ether bolus method. During control conditions V_a increased with lung inflation (0.111 ml/cm H_2O P_{pl}). Hypoxia decreased arterial volume, and the increase in volume due to lung inflation was less ($p < 0.01$) than that during control (0.074 ml/cm H_2O P_{pl}). Changes in effective perivascular pressure (P_{ex}) which occurred during lung inflation were calculated from V_a/P_{pa} curves obtained at various P_{pl}. Assuming that when a given V_a was achieved at two different P_{pa}'s, a change in P_{ex} equal to the difference in P_{pa} must have occurred. The decrease in P_{ex} was 1.4 times the decrease in P_{pl} during control conditions and was not significantly different from this value during hypoxia (1.35). Thus, the effect of lung inflation on arterial P_{ex} was not altered by hypoxic vasoconstriction. (Supported in part by USPHS Grants HL00115-01 and HL17112-01.)

EFFECT OF PINEALECTOMY AND MELATONIN ON EEG ACTIVITY IN CHICKENS. C.L. Ralph, S.F. Pang* and J.A. Petrozza*. Department of Zoology and Entomology, Colorado State University, Fort Collins, CO 80523, Department of Psychology, University of Iowa, Iowa City, IA 52242, and Department of Biology, University of Pittsburgh, Pittsburgh, PA 15260.

Pinealectomy was performed on 3-7-day old White Leghorn male chickens (Gallus domesticus). When they were 10-12 weeks old, four stainless steel screws were inserted into the skull, in a rectangular pattern, about 3 and 8 mm rostral to the parietal-occipital suture and 5.5 mm lateral to the midline, with the tips of the screws touching the dura overlying the cerebrum. Electroencephalographs of restrained, awake birds were recorded from the four screw electrodes using a polygraph (Grass, Model III D). Pinealectomized chickens had significantly lower cycle frequencies of amplitudes greater than 50 μV, but tended to have higher overall frequencies (not significant) than intact ones. When 1-2 mg of melatonin was injected intravenously into intact 10-16 week-old White Leghorn chickens the EEG changed, within 2 min, from a cycle frequency of 6-8 Hz with an amplitude of 30-100 μV to a frequency of 3-6 Hz and an amplitude of 100-200 μV. The changes persisted throughout the 30-min recording period. These findings suggest that pinealectomy diminishes brain wave synchronization and that melatonin administration enhances it. Pineal melatonin may have an important influence on brain function in birds. (Supported by grant NS-08554 from NIH.)

TRANSMURAL GRADIENTS OF HIGH ENERGY PHOSPHATE METABOLITES IN THE TRANSIENTLY ISCHEMIC CANINE MYOCARDIUM. Craig A. Ramey* and James W. Holsinger, Jr., (Spon: R. I. Sha'afi). The U.S.Veterans Administration Hospital, Newington, Ct. 06111

The subendocardial region of the left ventricle may be the first layer of the heart to suffer from inadequate tissue perfusion. In the ischemic area there is shift from aerobic to the less efficient anaerobic metabolism. Yet, the ischemic injury is reversible if coronary blood flow is restored within 20 minutes. Since ATP, ADP and phosphocreative (PCr) are sensitive indicators of hypoxia in the heart, these metabolites were examined to test the hypothesis that transient ischemia may affect their transmural gradients. After a midline sternotomy, a portion of the left circumflex artery (LCA) was isolated and either ligated in experimental animals or left patent in controls. Following 20 minutes of ligation and a similar period of blood reflow, transmural tissue samples were obtained from the center of the ischemic zone and placed in liquid N_2. The frozen sample was divided into epicardial (EPI), midmyocardial (MID) and endocardial (ENDO) portions. Metabolite levels were determined by standardized assay techniques with values expressed as μmol/g dry wt. for each layer: EPI, MID, ENDO. Control values ATP: 28.5±5.6, 35.5±2.0, 35.9±5.0; ADP: 3.5±0.5, 4.2±0.4, 4.2±4.6; and PCr: 29.2±6.0, 34.5±4.3, 32.9±2.9. In experimentals, ATP and ADP levels were not significantly different (P=.25 and P=.86) from controls with no significant overall transmural difference (P=.67 and P=.47) although ATP ↓ 27% ENDO. PCr levels ↑ significantly (P<.001): EPI ↑ 33% (43.5±5.8), MID ↑39% (56.8±8.0) and ENDO ↑ 40% (55.0±7.4). This data supports the restoration of aerobic metabolisms. Also, ATP changes suggest that the subendocardium is more vulnerable to ischemic changes produced by LCA ligation.

EFFECT OF STEROIDS ON RED CELL PHYSICAL PROPERTIES. P.W. Rand and E. Lacombe*, Research Dept., Maine Medical Center, Portland, Me 04102.

In vitro experiments were performed to investigate our observation of increased red cell deformability in cardiac surgical patients receiving large doses of methylprednisolone sodium succinate (MP). This drug was added in concentrations of 0.7 and 1.4 mM to aliquots of hct 47 defibrinated blood before or after 24 hrs incubation (no added glucose) at 37° C; or, alternatively, was added before or after exposure of red cells to an echinocytogenic concentration (0.15 mg/ml) of lysolecithin. Similar experiments were performed with hydrocortisone sodium succinate (HC). Vehicle only was added to control samples. Measurements included red cell membrane deformability (pipette method), blood viscosity, osmotic fragility, microscopic observation, red cell cholesterol, and certain glycolytic metabolites. Incubation transformed discs to echinocytes, sharply increased membrane rigidity, increased blood viscosity and osmotic fragility. MP and HC markedly inhibited membrane stiffening and moderately inhibited the increase in blood viscosity and osmotic fragility. The drugs were minimally effective in reversing these responses to metabolic depletion, once established. Lysolecithin only slightly increased normal membrane rigidity and failed to alter fragility, but produced a marked increase in blood viscosity. Viscosity was significantly reduced by the addition of MP or HC before or after exposure of red cells to lysolecithin. Steroid effectiveness against either stress was associated with an increase among the echinocytes of smooth, flat cells which retained the ability to form small rouleaux. While these effects may result from preservation of membrane surface area by steroid inclusion into the phospholipid bylayer, the possibility that MP and HC effect energy-dependent membrane changes has not been ruled out.

CARDIOVASCULAR DYNAMICS DURING EMOTIONAL CONDITIONING BEFORE AND AFTER EXPERIMENTAL MYOCARDIAL INFARCTION IN THE MONKEY. David C. Randall, Joseph V. Brady* & David M. Hasson*. Division of Behavioral Biology, Johns Hopkins University School of Medicine, Baltimore, Md. 21205.

Changes in left ventricular pressure (LVP), its first derivative (d(LVP)/dt), left ventricular end-diastolic pressure (LVEDP) and heart rate (HR) evoked by Pavlovian (ie, "emotional") conditioning were studied in unanesthetized, chair-restrained rhesus monkeys before and after experimental myocardial infarction (EMI). The experiment quantitatively defined the effect of infarction upon cardiovascular responses during stress in the non-human primate. Emotional conditioning was accomplished by following a 1-minute tone with an unavoidable electric shock. The tone (or "conditional stimulus") evoked a tachycardia, pressor response and an increase in d(LVP)/dt in the monkeys prior to EMI. The left anterior descending coronary artery was then occluded by tightening a snare previously implanted about 1 to 2 cm from its origin, resulting in a well defined transmural infarct on the anteriolateral and septal portions of the left ventricle. During the 2 weeks following EMI the LVP observed while the monkeys were resting quietly was reduced by approximately 15 mmHg ($P < 0.01$) relative to pre-infarction controls. HR was elevated by 20 or more bpm ($P<0.01$). LVEDP was also increased. There was little or no change in the maximal (positive) d(LVP)/dt observed during rest, but the conditional increase during presentation of the tone was attenuated relative to pre-EMI trials. Arrhythmias of ventricular origin were often evoked by emotional stress after EMI. (Supported by NHLI Grants HL 06945 and HL 17680)

CARDIAC PACEMAKER LOCATION DURING EXERCISE FOLLOWING DESTRUCTION OF THE SA NODE. W. C. Randall, J. Talano,* M. P. Kaye, D. Euler† and G. Brynjolfsson* Loyola University of Chicago, Stritch School of Medicine, Department of Physiology, Maywood, Illinois 60153.

Contrary to conventional impressions, the cardiac pacemaker does not invariably succeed to the AV node or junctional region following SA nodal destruction (confirmed histologically) but rather, may remain in supraventricular locations. To study the functional responses of subsidiary pacemakers, 12 dogs were trained to run on a treadmill, and the SA node surgically excised (6 dogs) or crushed and infiltrated with formalin (6 dogs). Bipolar electrograms from Bachman's Bundle, inferior right atrium, and left atrium, together with surface ECGs were recorded in the awake animal during severe exercise. Atropine and/or propranolol were administered intravenously either immediately prior to or during exercise testing. Four control, unoperated dogs were exercised in parallel experiments. Resting heart rate declined from an average of 120±6 beats/min in controls to 85±9 ($p=0.001$) and attained 220±8 during maximum exercise as compared with 260±20 ($p=0.05$) in controls. Maximum heart rate response following propranolol was 148 ±12 in operated animals but 230±17 in controls. Earliest atrial activity in resting operated animals occurred at the lower right atrial electrode in 5, upper right atrial in 2, left atrium in 1, and AV junctional region in 4 animals. During exercise, earliest activity shifted to the upper right atrium in 10 and to lower right atrium or left atrium in 2 animals. All of the animals showed periodic bradydysrhythmia at rest and this became exaggerated during exercise. All such arrhythmias were abolished by atropine. These data indicate active parasympathetic regulation of non-nodal, latent supraventricular pacemakers at rest and during exercise. (Supported by NHLI/NIH HL 08682.)

EFFECT OF PROSTAGLANDIN E_2 ON THE UTERO-PLACENTAL BLOOD FLOW. J.H.G. Rankin and T. Phernetton*, Dept. of Physiology & Gyn-Ob, University of Wisconsin Medical School, Madison, WI 53706.

The presence of relatively large quantities of prostaglandin E_2 (PGE_2) in the uterine venous outflow and the action of prostaglandin synthetase inhibitors in decreasing the blood flow to the near-term uterus have caused several investigators to postulate that PGE_2 is responsible in part for the relatively low resistance of this vascular bed. A series of experiments was performed using chronically catheterized near-term sheep at 127 days of gestation in an attempt to obtain direct evidence for the vasodilating action of PGE_2 on the uterine vascular bed. In 8 sheep, 1.5 minutes after 20 µg/kg intra-arterial PGE_2 we observed no significant change in blood pressure or brain or non-cotyledonary uterine blood flow. The renal blood flow increased from 693 ml/min to 892 ml/min and the cotyledonary blood flow decreased from 673 ml/min to 317 ml/min. Both of these changes were significant at the 1% level. These injections were accompanied by an increase in intrauterine pressure and the changes in cotyledonary flow were probably an artifact of the occluding effects of the uterine contraction. PGE_2 was administered via the fetal compartment in an effort to bypass the myometrium. In 11 cases the administration of PGE_2 to the fetal compartment caused no change in maternal blood pressure or brain or non-cotyledonary blood flow. There was an increase in both the renal blood flow from 592 to 669 ml/min and the cotyledonary blood flow from 762 to 853 ml/min. Both of these changes were significant at the 2% level. Maternal arterial pressure remained unchanged. These data support the conclusions that: 1) PGE_2 crosses the placenta quite readily and 2) PGE_2 causes a decrease in the resistance of the uterine vascular bed. Supported by grant no. HD-06736.

PALYTOXIN: EFFECTS ON MEMBRANE POTENTIAL AND CONTRACTILITY IN TOAD SKELETAL MUSCLE. M.D. Rayner, R. Wong* and T.I. Kosaki*. Dept. of Physiology, Univ. of Hawaii School of Medicine, Honolulu, HI 96822.

Suppression of phasic contraction and initiation of tonic contracture, associated with a La^{3+}-sensitive increase in Ca^{2+} uptake, have previously been noted in mammalian cardiac muscle exposed to 10^{-9} M palytoxin (PTX). Similar results have now been obtained in toad skeletal muscle where these changes in contractility are accompanied by membrane depolarization. A maximum of about 38 mV depolarization is reached at 10^{-9} M PTX and half-maximal depolarization occurs at 8×10^{-11} M PTX. This depolarization was prevented in Na^{+}-free Tris-substituted saline and reduced but not eliminated by 10^{-6} M Tetrodotoxin (TTX) or 2 mM La^{3+}. Contracture was prevented by exposure to the Na^{+}-free medium or by 2 mM La^{3+} but was not markedly affected by 10^{-6} M TTX. It is concluded that the observed effects of PTX on contractility may be secondary to a Na^{+}-mediated depolarization which can be separated into two components: a) a TTX and La^{3+} insensitive component, and b) a component sensitive to these agents which only becomes apparent at PTX concentrations greater than about 5×10^{-11} M. It appears that the TTX insensitive component is capable of initiating contracture when Ca^{2+} uptake is not blocked by the presence of La^{3+} ions. (Supported in part by NOAA Office of Sea Grant, Grant number 04-5-158-17).

RATE INDEPENDENT CODING OF TEMPERATURE BY PREOPTIC NEURONS. Troy Albert Reaves* and James Edward Heath. Dept. of Physiol. & Biophys. Univ. of Illinois, Urbana, Illinois 61801.

Since the inputs can be controlled and the outputs easily monitored, the thermoregulatory system provides an excellent model for studying neural coding and integration in the central nervous system (CNS). Earlier studies of thermoregulatory neurons have been limited to describing the characteristics of rate sensitive neurons that respond to thermal stimuli with a significant change in firing rate. Data from the present study indicate that rate insensitive (RI) neurons also code information in the CNS. Single unit activity was recorded extracellularly from preoptic (PO) area neurons in New Zealand white rabbits chronically implanted with a movable recording electrode array, thermode, and temperature sleevings. The rabbits were not restrained or anesthetized during recording sessions. Examination of interspike interval (ISI) histograms from RI neurons in the PO revealed significant changes ($P < 0.01$) in the temporal distribution of intervals during central or peripheral thermal stimulation. Control ISI histograms typically displayed unimodal, exponential or non-modal type distribution. During central or peripheral thermal stimulation the distribution shifted to a bimodal type. Removal of the thermal stimulus resulted in an ISI distribution that did not differ significantly ($P > 0.05$) from the control distribution. It is suggested that this form of interval coding represents a useful example of the interval variation or temporal microstructure code as described earlier by Bullock (PNAS 60: 1058, 1968). (Supported by NSF Grants GB 13797 and GB 43994).

OXYGEN DISTRIBUTION IN THE CAT GRACILIS MUSCLE. D.L.Reisdorf*,J.F.Gross, and P.C.Johnson, Departments of Chemical Engineering and Physiology, University of Arizona, Tucson, Arizona 85721.

Oxygen concentration in the extravascular tissue plays an important role in the homeostatic regulation of blood flow in the microcirculation. Recent data [*Whelan et al,Am.J.of Physiol, 224:763,1975*] has demonstrated that the concentration profiles as represented by oxygen tension distributions in the cat gracilis muscle change with the flow rate of the blood in the microcirculatory bed. Analytical equations for the oxygen concentration in the capillary and for oxygen diffusion in the pericapillary tissue were used to obtain the oxygen concentration mapping in the tissue as a function of (1) flow in the capillary, (2) capillary morphology, (3) distance to the nearest capillary and number of adjacent capillaries, and (4) the entering oxygen concentration of the blood. The system was based on the Krogh Model. Physical and transport properties such as solubility of oxygen in the blood and its diffusion coefficient appear to have little influence. On the other hand, capillary dimensions, blood velocity and oxygen consumption rate play an important role in establishing the oxygen tension mapping. Whelan's data in the cat gracilis muscle was obtained by measuring oxygen tensions at different stations in the tissue and noting the percentage distribution in several oxygen tension ranges. In this way, it was determined that 66% of the tissue has a tension below 5 mm Hg, 22% between 5-10 mm Hg, 13% between 10-15 mm Hg, and 4% between 15-18 mm Hg. The model predicted a distribution 65/24/10/0. The cat gracilis model was based on a capillary radius of 2.65 microns, a tissue radius of 65.7 microns, a capillary length of 1000 microns and a consumption rate of $5.2 \cdot 10^{-5}$cc O_2/cc tissue-sec. The distribution of tensions for flow rate 0-2, 2-3, and 3-8 ml/100 gm-min were calculated and agreed well with Whelan's data. (Supported by Grant HL17421-01 from NHLI)

Effects of elevated plasma FFA on glycogen breakdown during exercise in rats. M.J. Rennie*, W.W. Winder* and J.O. Holloszy, Dept. of Preventive Medicine, Washington University Medical School, St. Louis, Mo. 63110

Increased levels of free fatty acids (FFA) result in a decreased utilization of carbohydrate in the contracting heart. This appears to be partly due to inhibition of phosphofructokinase as a result of citrate accumulation. No such effect has been demonstrable in resting skeletal muscle. We have studied the effects of high plasma FFA levels (HFFA) on glycogen breakdown in muscle and liver of exercising rats. Plasma FFA levels were increased by corn oil feeding followed by heparin injection. Controls were fed placebo. Rats from each group were killed at rest or after a 30 min-long treadmill exercise test. The exercise caused considerable glycogen depletion in soleus (81%) and the deep, red portion of the vastus lateralis muscle (74%), and in liver (84%) of controls. HFFA rats had less glycogen depletion in soleus (40%) deep vastus (50%) and liver (22%). Lactate levels were lower (2.65 vs. 3.29 μ moles/g) and citrate levels higher (0.31 vs 0.24 μ moles/g) in deep vastus muscle of HFFA rats. There were no differences for white muscle. Thus, HFFA causes muscle glycogen sparing during exercise only in the red types of muscles. After exercise, HFFA rats had higher blood glucose (3.45 vs 3.20 mM) and lower lactate (3.50 vs. 4.50 mM) than controls. Plasma insulin was higher (16.7 vs. 5.2 ng/ml) and glucagon lower (335 vs. 505 pg/ml) in the HFFA rats. Liver glycogen may be spared by HFFA due to its stimulation of insulin and suppression of glucagon release. The higher blood glucose and liver glycogen levels in the HFFA rats suggests that glucose transport into working muscle was also depressed. Supported by NIH Research Grant HD 01613, NIH Training Grant AM 05341 and a grant from the Muscular Dystrophy Associations of America. MJR is a United Kingdom Medical Research Council Travelling Fellow.

DIFFERENCES IN THE AUTORADIOGRAPHIC LOCALIZATION OF ^{3}H-DEXAMETHASONE AND ^{3}H-CORTICOSTERONE IN THE RAT BRAIN AND PITUITARY. R.W. Rhees*, B.I. Grosser*, and W. Stevens. Dept. Zoology, Brigham Young University, Provo, Ut. 84601, and Depts. Psychiatry and Anatomy, University of Utah Medical Center, Salt Lake City, Ut. 84112

Localization of ^{3}H-corticosterone by neurons in limbic structures of the brain and over the anterior pituitary was recently demonstrated in this laboratory using thaw-mount autoradiography. The concentration of ^{3}H-corticosterone was significantly greater in the brain and pituitaries from adrenalectomized rats when compared to the same regions from intact animals (Brain Res. 83:293, 1975). In charactizing the properties of the receptor protein(s), it was found that dexamethasone, a potent synthetic glucocorticoid, lacked significant ability to compete with ^{3}H-corticosterone for its specific receptor sites in the brain. Therefore, in the present study autoradiography was used to determine whether the regional and cellular distribution of ^{3}H-dexamethasone in the rat brain and pituitary was different from that of ^{3}H-corticosterone. ^{3}H-Dexamethasone was found in high concentrations adjacent to the choroid plexus in the lateral ventricles and in the walls of many small blood vessels of the brain. Large numbers of silver grains also were present over the anterior pituitary. Few silver grains were concentrated over neurons of limbic structures. Differential grain counts made in the various brain regions showed no difference in localization between adrenalectomized and non-adrenalectomized animals. These results provide further evidence for the possibility that dexamethasone and corticosterone may exert their actions at different sites in the brain, but may have similar actions at the site of the anterior pituitary. (Supported by NIH MH-25926, NS-07761, Res. Sci. Award 5KO2-MH-10270, GM-0958, and ERDA AT(11-1)-119).

INFLUENCE OF HYPOCAPNIA AND HYPERCAPNIA ON METABOLISM IN THE PERFUSED RAT LUNG. R.A. Rhoades and S. Wali*, The Pennsylvania State University, University Park, PA 16802

Influence of altered CO_2 tension on metabolism was investigated in an isolated perfused lung preparation. For hypocapnia, lungs from normal rats were removed, perfused and ventilated with 21% O_2 - 3% CO_2 (balance N_2) for 1.5h. For hypercapnia, lungs from normal rats and rats exposed to 24h hypercapnia (12% CO_2) were removed, perfused and ventilated with 21% O_2 - 10% CO_2 for 1.5h. Control lungs for all groups were ventilated with 21% O_2 - 5% CO_2. The perfusion medium consisted of washed bovine RBC diluted (15% Hct) in Krebs Henseleit bicarbonate buffer containing 5g% bovine serum albumin with 6mM glucose and 0.5mM palmitate. Exposure of normal rat lungs to 1.5h in vitro hypocapnia (PCO_2 = 22.8mmHg ± 0.3SE) significantly ($P < 0.05$) increased lactate (42%) and pyruvate (20%) levels, with no effect on U - ^{14}C glucose incorporation into lung lipids or oxidation to $^{14}CO_2$. Normal rat lungs removed and made hypercapnic in vitro (PCO_2 = 65mmHg ± 1.6SE) did not alter U - ^{14}C glucose incorporation into lung lipids, glucose oxidation to $^{14}CO_2$, or lactate production, but did result in a significant 26% decrease in pyruvate levels. In contrast to normal lungs, prior exposure to hypercapnia (12% CO_2) for 24h and subsequent perfusion under hypercapnic conditions significantly depressed glucose uptake (47%), lactate production (34%), pyruvate levels (48%), glucose incorporation into phospholipids (29%) and glucose oxidation to $^{14}CO_2$ (39%). (Supported by AFSOR Grant 2767).

PROGRESSIVE ALTERATIONS IN RESPIRATORY RESPONSES OF THE POSTNATAL PIGLET. C. RICHARDSON* and A.J. Miller. Dept. Physiol., Univ. Illinois, Chicago 60680, and Dept. Physiol. and Sect. Orofacial Anomalies, Univ. California, San Francisco, 94143.

Previous investigations using acute preparations have shown that the ventilatory responses of early postnatal animals to hyperoxia (100% O_2),hypoxia (10% O_2), and hypercapnia (6% CO_2) are different from the ventilatory responses of mature animals. The goal of this research was to follow the individual animal and its ventilatory responses as a function of age and the transitional period over which changes occurred.

Eight piglets from two litters were stressed with three different gas mixtures under ketamine anesthesia (50mg/kg) with a low dose of pentobarbital (7mg/kg). The gases were administered sequentially in 5 minute trials separated by 5 minute recovery periods. Piglets were tested from the age of 5 to 70 days. Intraesophageal pressure was recorded as a measure of respiration and the signal was differentiated, clipped, and integrated to estimate minute ventilation. All 8 piglets hyperventilated on 100% O_2 with a maximum increase in minute ventilation (30-65%) occurring between 16-22 days of age. The minute ventilation with 10% O_2 suggested 3 stages of response with a sustained hyperventilation at the earliest age of 5 days and after 22 days, and a transient hyperventilation between the ages of 8-22 days depending on the piglet. Administration of 6% CO_2caused the largest hyperventilatory response of all three gases. This response was found in all ages studied of the eight piglets. Respiratory patterns varied from occasional deep sighs to short apneic pauses (appr. 15 seconds). The smallest piglet of a litter of five demonstrated severe hypoventilation on 10% O_2 at age 22 days with recovery occurring after administration of room air.

OXYGEN CONSUMPTION BY SMALL BATS DURING 24-HR INTERVALS AT 5 TO 35 C. M. L. Riedesel[1] and B. A. Williams. Department of Biology, University of New Mexico, Albuquerque, NM 87131; and NASA-Ames Research Center, Moffett Field, CA 94035.

Oxygen consumption measurements of small insectivorous bats, Myotis velifer, were made for 24-hr intervals at 5, 10, 20, 30, and 35 C. Previous investigators have described a wide range of metabolic rates for bats at any given temperature. The studies described here confirm variability in oxygen consumption; and describe the time intervals animals spend at minimal, resting, and high metabolic rates.

Mean Oxygen Consumption (ml $g^{-1}hr^{-1}$)

Temp, C	5	10	20	30	35
Minimal	0.07	0.16	0.19	0.65	1.35
Resting	0.25	0.25	0.35	1.00	1.55

Bursts in oxygen consumption occurred when lights were turned off. Additional bursts in oxygen consumption occurred at apparently random times during the 24-hr periods at all temperatures. The caloric requirements of isolated captive bats at 5 and 10 C agree favorably with weight-loss data collected on bats hibernating in their natural habitat.

1 Research conducted during tenure of National Research Council Associateship and supported in part by NASA Grant NCAR-510-402.

PROTEIN DEPRIVATION OF PRIMATES: VII. EARLY INFANT BEHAVIOR. A.J. Riopelle, P.A. Hale*, and C.W. Hill*. Dept. of Psychology, Louisiana State University, Baton Rouge, LA 70803 and Univ. New Orleans, New Orleans, LA 70122

Pregnant rhesus monkeys were fed semisynthetic diets containing 3.4, 6.7, or 13.4% protein as casein and affording 1, 2, or 4 grams protein per kilogram body weight per day beginning on the 30th day of pregnancy and continuing until delivery. Forty-five infants born of these mothers, all of which were fed adequate diets, were tested on a series of 13 behavioral measures during the first 40 days of life. Tests were designed to assess simple reflexes such as rooting and startle, sensory capacity such as visual following and response to gravity, motor coordination and locomotion. Tests were given during two age blocks, early and late in the age period. Later performances were generally superior to earlier. Despite the 4:1 difference in dietary protein intake, there were no effects of maternal diet on test performances. It is likely that the primate mother since she has but one infant per pregnancy and thus, in contrast to animals bearing litters, monitors the development of the fetus and makes metabolic and gestational adjustments during pregnancy to prevent or at least to minimize deficiencies in the infant despite being fed a diet that obviously would be inadequate for her if she were not pregnant.
(Supported by grant HD 07479 from NICHD).

HEAT ACCLIMATION IN THE DEER MOUSE. J.C. Roberts and R.R.J. Chaffee. Dept. Biology, Creighton Univ., Omaha, NB 68178 and Dept. Ergonomics, Univ. Calif., Santa Barbara, CA 93106.

Adult deer mice (Peromyscus maniculatus sonoriensis), from a sea level colony, were acclimated to 24+1 and 35+1 C for 2 months. Metabolic rate (MR) of heat-acclimated (HA) deer mice was 9-27% below that of control mice when measured at ambient temperatures (T_A) between 20-37 C. Body temperatures (T_B) of HA mice, taken at the end of MR measurements, were significantly below those of controls at T_A = 20-30 C. At 37 C the T_B of both groups increased significantly. HA deer mice weighed significantly less than controls. Organ/body weight ratios for kidney, liver, heart and brown fat decreased significantly in the heat. Absolute adrenal wt., but not adrenal/body wt. ratio, also decreased in the heat. Heat acclimation produced significant decreases in kidney β-hydroxybutyrate (BOH) oxidase activity and liver serine and threonine dehydrase activities; a significant increase in liver mitochondrial P/O ratio with BOH as substrate; and no significant changes in either liver or kidney succinoxidase activity. Brown fat mass, protein content and qO_2, with BOH as substrate, all decreased in the heat. In general, enzyme changes seen in HA deer mice are the reverse of those previously reported in cold acclimated Peromyscus (Roberts et al. Fed. Proc. 25:1275, 1966). The combined metabolic, biochemical and organ weight changes seen in HA deer mice provide further evidence of decreased total heat production in a hot environment and support the hypothesis that chemical thermosuppression occurs during HA.

INTERACTION OF SKIN TEMPERATURE AND POSTURE IN THE CONTROL OF SKIN BLOOD FLOW. M.F. Roberts* and C.B. Wenger*. (Spon: A.P. Gagge). John B Pierce Fndn. Lab and Yale Univ. Sch. Med., New Haven, Conn. 06519

Skin blood flow (SkBF) appears to be controlled by thermoregulatory as well as postural reflexes. High mean skin temperature ($\bar{T}_{sk}$) leads to peripheral pooling of blood, thus possibly reducing cardiac filling pressure, especially when combined with upright posture. We thus designed these experiments to determine whether the level of $\bar{T}_{sk}$ has an effect on the SkBF/ internal temperature relation obtained during exercise under two different postural conditions: upright and semi-recumbent. Three subjects exercised at 50% $\dot{V}O_2$ max at ambients of 15° and 35°C, and on upright and semi-recumbent bicycle ergometers. Forearm blood flow (ABF) was measured with Whitney strain gauges and electrocapacitance plethysmographs. Internal temperature (T_{es}) was measured with an esophageal thermocouple, and $\bar{T}_{sk}$ was computed from a weighted mean of 8 local skin temperatures. At 15°C ($\bar{T}_{sk}$ = 30°C) there was no differences between the ABF/T_{es} relations in upright and semi-recumbent exercise. However, at 35°C ($\bar{T}_{sk}$ = 35°C), the ABF/T_{es} relation obtained in upright exercise was shifted toward higher T_{es} compared with semi-recumbent exercise. These data suggest that at high $\bar{T}_{sk}$, with considerable peripheral pooling of blood, upright exercise elicits a reflex vasoconstriction not seen at lower $\bar{T}_{sk}$.

DISTRIBUTION OF BLOOD FLOW TO THE RESPIRATORY MUSCLES WITH INCREASED WORK OF BREATHING. C.H. Robertson, G. Foster & R.L. Johnson, Jr. The Univ. of Texas Southwestern Medical School, Dallas, Texas 75235

Using a radioactive microsphere technique the distribution of blood flow to respiratory muscles was measured in dogs on a ventilator, at graded levels of minute ventilation (CO_2 rebreathing), and at graded inspiratory resistances. Pressure-volume work (W) was measured by computer integration of change in thoracic gas volume and esophageal pressure. Total respiratory muscle O_2 consumption (VO_2) was calculated as the sum of individual blood flows X the arterovenous O_2 content difference across the diaphragm. Efficiency =W(in O_2 equivalents/min)/ VO_2. During CO_2 rebreathing diaphragmatic (Q_D) and external intracostals blood flows increased linearly with W, whereas internal intracostals and transverse abdominals came into play at medium and high loads only. Inspiratory resistance resulted in an exponential increase in Q_D while other muscles were used only at high work loads.

Of the total respiratory muscle blood flow (Q_{RS}), the fraction distributed to the diaphragm did not change significantly during rebreathing (mean 0.27) but with inspiratory resistance rose progressively to 0.53. VO_2 increased linearly with rebreathing work and efficiency was unchanged (mean 15.2%), but with resistance VO_2 increased exponentially and efficiency fell progressively to 4.5%.

	CO_2 Rebreathing				Inspiration Resistance			
	Vent	Rest	Med	High	None	A	B	C
W(Cal/min)	0	.54	2.40	4.65	.68	2.19	3.94	9.74
Q_D(ml/min)	4.20	11.17	20.45	32.96	7.74	18.21	41.16	209.54
Q_{RS}(ml/min)	19.48	34.21	75.90	117.48	36.52	56.46	109.67	486.63
Q_D/Q_{RS}	.22	.33	.27	.28	.22	.38	.44	.53
VO_2	.78	1.40	4.59	7.04	2.65	5.34	13.14	55.32

RENAL IMPULSE RESPONSE FUNCTION FROM ^{131}I-HIPPURAN RENOGRAM. J.S. Robertson, Diagnostic Nuclear Medicine, Mayo Clinic, Rochester, MN. 55901

The renogram is widely used clinically as a simple test of renal function. It is particularly useful in assessing unilateral kidney disease including renal hypertension, renal arterial stenosis, acute and chronic obstruction, tubular disease and pyelonephritis. The clinical applications have usually involved semi-quantitative approaches relying heavily on pattern recognition. More recently, it has been recognized that some physiological data such as effective plasma flow rates in human beings can be extracted from the renogram by deconvolution analysis (Reeve and Crawley, Clin Sci and Mol Med 47, 317-330, 1974; Fleming and Goddard, Phys Med Biol 19, 546-549, 1974). The studies to be presented involve the use of a CDC-3600 Computer and the method of deconvolution analysis described by Britton and Brown (Clinical Renography, Year Book Publishers, Chicago, 1972) for obtaining the spectrum of renal transit times for ^{131}I ortho iodo hippuran. Theoretically, this spectrum is the equivalent of the impulse response that would be obtained if it were possible to deliver a spike type bolus of the radiopharmaceutical to the kidney. This offers the possibility of distinguishing those disorders that affect only portions of the nephron population. In normal subjects, the spectrum is approximately Gaussian. Various renal diseases distort the spectrum.

MODULATION OF CALCIUM EFFECTS ON THE ACTION POTENTIAL PLATEAU IN GUINEA PIG ATRIUM. R.B. Robinson* and W.W. Sleator, Dept. of Physiology & Biophysics, Univ. of Ill., Urbana, Ill. 61801

The activation process in mammalian heart muscle was studied by means of simultaneous microelectrode and tension recording of isolated electrically driven guinea pig atria. Specifically, conditions which alter the action potential plateau were explored to determine the role played by calcium in controlling its configuration. Reducing external calcium from 2.5 to 1.25 mM prolonged the plateau, but further reduction shortened it. On the other hand, progressively increasing doses of D600 (up to 1.4 μM) monotonically decreased plateau duration. Addition of isoproterenol or epinephrine restored plateau duration in either a calcium free or D600 containing bathing solution; the isoproterenol effect, but not that of epinephrine, could be eliminated by the specific β-antagonist propranolol. When EDTA was added to the calcium free solution bathing an atrium, epinephrine was found to have at least as great an effect on plateau duration as in a calcium free solution alone. Moreover, combination of EGTA and epinephrine in a calcium free solution extended the plateau duration to more than three times normal. An hypothesis has been developed which explains these unexpected results in terms of two opposing effects of a change in calcium concentration on plateau formation, one action being through the slow inward current and the second through a shift in the voltage dependence of the potassium conductance system.
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AGE-RELATED CHANGES IN CARDIAC ACTOMYOSIN ATPASE ACTIVITY IN THE MALE FISCHER RAT. Morris Rockstein and Jeffrey Chesky. Department of Physiology & Biophysics, University of Miami, School of Medicine, Miami, Fl. 33152.

A reduction in cardiac actomyosin ATPase activity has been reported for older rats on the basis of a limited number of determinations. This study was designed to determine the time-related rate and ultimate extent of loss of contractile protein ATPase activity during the total post-maturation period. Actomyosin was extracted from total heart homogenates for over 100 male rats from a long-inbred (by brother-sister matings) Fischer rat colony, maintained under controlled conditions of temperature, humidity, and light. The contractile proteins were isolated by modifications of standardized procedures of utilizing differential ionic strength solubility properties of these proteins. The calcium-activated ATPase activity was estimated by measuring the liberation of phosphate from ATP at 25° C in the presence of 1 mM Ca^{++} and 60 mM KCl at pH 7.2. ATPase activity increased from the time of weaning to a maximum in the two-month old individuals, with an average value of 258 nmoles of phosphorus formed/minute/mg protein. This was followed by a progressive loss throughout the first year of life, so that the enzyme activity was 15% lower at eight months of age and 28% lower at 1 year of age. However, this loss in cardiac actomyosin ATPase activity is independent of body weight, beginning at three months of age.

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THE INHIBITION OF THEOPHYLLINE DIURESIS BY BARBITURATE ANESTHESIA. L. L. Rolf, Jr., Dept. Pharmacology, U. Fla., Gainesville, Fla., 32610 and Dept. Physiol. Sci., College Veterinary Medicine, Oklahoma State University, Stillwater, Oklahoma 74074

This study confirmed the work of Nechay (J.P.E.T., 1964) which demonstrated a synergistic action on the urinary output of HCO_3^- and Cl^- ions when a carbonic anhydrase inhibitor (Acetazolamide (A), 25 mg/kg, i.v.) was combined with theophylline (T) (25 mg/kg, i.v.) in water loaded (20 ml/kg) unanesthetized dogs. If however, this same combination of drugs at the same doses was administered within one hr of induction of anesthesia with pentobarbital (35 mg/kg, i.v.) the mean Cl^- output for 2 hr was not significantly different than control values while the HCO_3^- output achieved was that demonstrated with A (25 mg/kg, i.v.) alone in the same unanesthetized animals. When the diuretics were administered within 2 hr of anesthesia, 2 hr mean Cl^- output was significantly increased above control values, but significantly below that achieved by T (25 mg/kg, i.v.) alone in the same unanesthetized animals. Bicarbonate output, in this situation was similar to that attained with the 1 hr anesthesia interval. Repetition of these experiments under alpha-chloralose and methoxyflurane anesthesia produced results similar to those in the unanesthetized animals. Since all experiments exhibited comparable urinary flows and glomerular filtration rates, it was concluded that the effects of the pentobarbital was not due to hemodynamic factors. Rather, it appears that a chemical antagonism exists, perhaps because of structural similarities, between the barbiturate and T, both of which can bind to the same as yet unspecified receptor responsible for the saluresis exhibited with T. (Supported by NIH grant GM 16934-06 and Department of Physiological Sciences, College of Vet. Med., Oklahoma State University)

THE ROLE OF THE ISCHEMIC KIDNEY IN THE CHRONIC MAINTENANCE OF TWO KIDNEY GOLDBLATT HYPERTENSION (2KGH) IN RABBITS. J.C. Romero, C.E. Ott, J. Jones*, J.A. Diaz-Buxo* and C.G. Strong, Div. of Neph. & Dept. of Physiol., Mayo Medical School, Rochester, Minnesota 55901.

The removal of the ischemic kidney in rats with 2KGH results in a significant reduction in mean blood pressure (MBP) when performed in the early (1-2 month) but not in the chronic (7 month) stages of hypertension. This study examined the effect of the removal of the ischemic kidney on blood pressure (Grant-Rothschild capsule) and on plasma renin activity (PRA, radioimmunoassay) in 6 rabbits with 2KGH for 18 months and determined the effect of high salt intake (70 ± S.E. 5 mEq of sodium/day) on MBP and on PRA 30 days after the ischemic kidney was removed. An equal number of rabbits submitted to a similar protocol but undergoing sham-clipping and left nephrectomy (18 months later) were used as a control. In the hypertensive group the removal of the clipped kidney was followed in 24 hours by a significant decrement in MBP from 121 ± 6 to 91 ± 8 mm Hg and in PRA from 13 ± 3 to 2 ± 5 ng/ml/hr. Thirty days later PRA had recovered to levels similar to those before nephrectomy but MBP remained normal (91 ± 3 mm Hg). In the control group, the excision of the sham-clipped kidney did not affect MBP (from 80 ± 1.4 to 94 ± 8 mm Hg) or PRA (from 10 ± 3 to 12 ± 1 ng/ml/hr). High salt intake for 21 days significantly reduced PRA in both groups (to 2.0 ± 1.0 and 2.0 ± 2.0 ng/ml/hr) and did not change blood pressure. The kidneys removed in both groups were histopathologically normal. It is concluded that the presence of the ischemic kidney is necessary for the maintenance of chronic 2KGH in rabbits. After the removal of the ischemic kidney, MBP was not affected by high salt intake.

EFFECTS OF NEONATAL CORTICOSTERONE TREATMENT ON PUBERTY IN FEMALE RATS. Oline K. Rønnekleiv*, Berrilyn J. Branch* and Anna N. Taylor. Dept. of Anatomy and Brain Research Institute, UCLA, Los Angeles, CA 90024.

The effects of early exposure to corticosterone on the onset of puberty, hormone levels in the peripubertal period and alterations in steroid feedback sensitivity were studied in Sprague-Dawley rats implanted s.c. at 4 days of age with corticosterone (30 mg/100 g body wt) imbedded in silastic polymer. At 28 and 32 days of age, on the day of vaginal opening (v.o.) and 3-4 days later, blood samples were obtained at 7 AM and 5 PM by jugular vein puncture under ether anesthesia and by decapitation. Significantly delayed v.o. was observed in corticosterone-treated animals (day 40±0.8) as compared to sham-implanted (day 37±0.5) and intact controls (day 33±0.2). The animals showed high AM- and low PM-levels of TSH irrespective of treatment, the patterns being more regular prior to the onset of puberty. AM and PM serum prolactin levels were elevated on the day of v.o. in all rats. In addition, a more pronounced prolactin response to ether stress was observed on the day of and after v.o. Early corticosterone-treatment delayed development of this stress response. FSH was elevated on the day of v.o. in some of the animals. All rats showed a gradual increase in PM-corticosterone levels with highest values after v.o. Early corticosterone-treated animals showed delayed but normal development of the adult circadian corticosterone rhythm and a normal response to dexamethasone inhibition of corticosterone release at 40-45 days of age. Dexamethasone (100 µg/kg) suppression of TSH and prolactin levels was greater in corticosterone- than in sham-implanted rats. These data indicate that neonatal treatment with corticosterone delays the maturation of neuroendocrine processes. Further experimentation is necessary to determine whether these alterations are permanent. (Supported by NIH grant NS-9122 and NSF grant GB-33474.)

DIAPHRAGMATIC FATIGUE IN MAN. C. Roussos and P.T. Macklem
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We measured the time required to produce diaphragmatic fatigue (t_{lim}) in two normal subjects breathing against a variety of high resistive loads. In a given run the subjects generated a transdiaphragmatic pressure (Pdi) for each breath that was a predetermined fraction of their maximum Pdi at FRC (Pdi_{max}), and continued breathing until they were unable to generate this Pdi. Pdi/Pdi_{max} ranged between 0.4 and 0.9. The relationship between Pdi/Pdi_{max} and t_{lim} was quasi-hyperbolic. Pdi/Pdi_{max} that could be generated indefinitely (Pdi_{crit}) was ca. 0.4 representing a diaphragmatic power of ca. 6.6 Kg.M/min and an inspiratory breathing power ($\dot{W}_{crit}$) of ca. 3.6 Kg.M/min . Pdi_{crit} was uninfluenced by breathing 13% O_2. Nor was t_{lim} at Pdi/Pdi_{max} of 0.9. At intermediate values of Pdi/Pdi_{max}, t_{lim} was much shorter during hypoxia. Although the respiratory system can tolerate remarkably high loads indefinitely, fatigue should develop when $\dot{W}_{crit}$ is exceeded and may lead to respiratory failure in diseases with high resistance and/or low compliance. Hypoxia does not decrease the critical load but markedly shortens the time to fatigue once that load is exceeded. (Supported by the MRC of Canada)

EFFECT OF VAGAL COOLING ON ESOPHAGEAL PERISTALSIS AND SPHINCTER RELAXATION. James Ryan, William Snape, Jr.* and Sidney Cohen. Hosp. of the Univ. of PA., Philadelphia, PA. 19104

The purpose of this study was to examine the effect of unilateral and bilateral vagal cooling on a) lower esophageal sphincter (LES) pressure, b) esophageal peristalsis, and c) LES relaxation with swallowing. All studies were performed on adult opossums. Swallowing was elicited by pharyngeal stimulation. A 2 cm section of each cervical vagus was exposed and enclosed in a metal casing containing dry ice and alcohol. Pressure was measured using a pressure transducer attached to a continuously perfused catheter. The mean control LES pressure recorded was 34.2 $\pm$ 2.0 mm Hg; this was unaffected by either unilateral vagal cooling (40.0 $\pm$ 3.9 mm Hg, Rt. Vagus; 39.6 $\pm$ 1.1 mm Hg, Lt. Vagus) or bilateral vagal cooling (40.0 $\pm$ 2.6 mm Hg). The velocity of peristalsis prior to vagal cooling was 3.0 $\pm$ 0.4 cm/sec. Neither right vagal cooling (2.8 $\pm$ 0.4 cm/sec), left vagal cooling (3.5 $\pm$ 0.4 cm/sec) nor bilateral vagal cooling (3.6 $\pm$ 0.3 cm/sec) produced statistically significant changes in the velocity of peristalsis. Similarly, neither right vagal cooling (94.5 $\pm$ 2.1%) nor left vagal cooling (97.9 $\pm$ 0.8%) affected the degree of LES relaxation upon swallowing when compared with control (98.0 $\pm$ 0.7%). However, bilateral vagal cooling significantly decreased LES relaxation following pharyngeal stimulation (37.3 $\pm$ 4.8%; $p<.001$). In some instances, LES relaxation was completely abolished although peristalsis remained. The percentage of time esophageal peristalsis could be elicited following bilateral vagal cooling (63.3%) was considerably less than for the control period (99.3%). These findings suggest that esophageal peristalsis and LES relaxation may be mediated by different nerve fiber populations, with differing sensitivities to cold blockade.

HUMORAL PARAMETERS OF RETICULOENDOTHELIAL FAILURE FOLLOWING TRAUMATIC SHOCK. T.M. Saba, W.A. Scovill*, J. Kaplan*, S. Powers,Jr.*, and H. Bernard*, Dept. Physiology & Surgery, Albany Medical Col., Albany,N.Y.

Humoral control (opsonin) of reticuloendothelial (R.E.) host defense was evaluated in rats and humans following traumatic shock. Additionally, the effect of immunologic supression (anti-opsonic protein antibody) of the R.E.S. on mortality following shock was investigated. Pentobarbital anesthetized (2mg/100g) rats subjected to Noble-Collip drum (NCD) shock were evaluated over a 24 hr. period. Humans sustaining whole-body trauma were investigated over an approximate 1-28 day interval. In rats, hepatic R.E. phagocytosis and opsonic activity following sublethal shock (300 rev) were decreased ($p<.001$) over the 0.5-6 hr post-trauma period. Recovery of opsonin levels was associated with R.E. recovery, while lethal shock was correlated with severe R.E. failure and a maximum 86.4% decline in opsonin levels. Administration (IV) of antibody to rat opsonic protein induced hypo-opsonemia and an associated decreased ($p<.05$) survival time to LD_{50} shock and increased (100%) mortality. In trauma patients (n=12) an acute 34-53% depletion ($p<.05$) in the plasma opsonin level occurred over the 1-2 day post-trauma interval. The patients studied suggested 3 groups (A,B,C) of responses. These were: (A) a rapid restoration in opsonin activity by 5-8 days and early recovery; (B) prolonged hypo-opsonemia, periodic bacteremia or liver dysfunction with delayed restoration in opsonin levels; (C) non-survivors with severe and maintained hypo-opsonemia. Patients which recovered manifested hyper-opsonemia ($p<.05$) prior to discharge. These studies suggest an important role for opsonin activity and R.E.S. function in survival to shock. Furthermore, they document hypo-opsonemia in humans following trauma. (GM-21447 and GM-15426).

PRESENCE OF NOREPINEPHRINE IN THE BOVINE MYOMETRIAL AND OVARIAN TISSUES. A.J. Sadiku* and O.P. Verma, Laboratory for Reproductive Physiology, School of Veterinary Medicine, Tuskegee Institute, Alabama 36088.

The presence of Norepinephrine (NE) in myometrial and ovarian tissues was determined by using fluorometric technique. Pregnant and non-pregnant bovine tissues obtained from the local slaughter house were cleared of all loose connective tissue and frozen immediately. The tissues were homogenized with chilled, acidified butanol to extract NE as described by Chang (Int. J. Neuropharmacol. 1964, 3: 643-649). The released catecholamines were adsorbed on acid-washed alumina and the eluate was converted to a fluorescent compound by EDTA. The fluorescence intensity of NE was read by Turner Fluorimeter (Model III).

The results indicated that the NE concentration of the ovarian tissue was significantly higher than that of the myometrial tissue of both pregnant and non-pregnant groups. The pregnant uterine tissues had a lower concentration of NE than the non-pregnant ones; however, the concentration in the ovarian tissues of the two groups did not differ significantly. The follicular size (diameter <5 and 5-10 mm) of non-pregnant group did not change the NE concentration of the uteri as well as the ovaries.

It is concluded that the presence of NE in the myometrial tissue is influenced by the hormones of pregnancy. The significance of this change needs further investigation. (Supported by grant #316-15-134 from CSRS, USDA.)

INTEGRATION OF CHEMORECEPTOR STIMULI BY PONTILE AND MEDULLARY RETICULAR FORMATION SITES, W. M. St. John and S. C. Wang, Dept. Pharmacology, Columbia Univ., College of Physicians & Surgeons, New York, N. Y.10032. The purpose of this study was to define anatomically and examine functionally sites within the brain stem having a role in the generation of respiratory tidal volume. To fulfill this aim, the respiratory responses of decerebrate cats to hypercapnia and hypoxia were examined under three sequential experimental conditions: 1) after the midcollicular decerebration, 2) following removal of the pneumotaxic center by midpontile transection or punctate lesion placements, 3) after caudal pontile transection or placement of lesions in various pontile and/or medullary sites. Upon exposure to hypercapnia or hypoxia following pneumotaxic center ablation, tidal volume responses were either unchanged or elevated whereas frequency responses were diminished. Transection at the caudal pontile level markedly shifted tidal volume and frequency responses to both hypercapnia and hypoxia such that tidal volume responses were diminished and frequency responses were elevated. A qualitatively similar shift in tidal volume and frequency responses was obtained subsequent to the placement of punctate lesions in the pontile and/or medullary reticular formation. The magnitude of this shift was dependent both on the size and location of the lesions. Proceeding from rostral pons to mid-medulla, successively smaller midline lesions produced equivalent or greater diminutions of tidal volume responses and elevations of frequency responses. These data demonstrate that a locus of tidal volume generation for both peripheral and central chemoreceptor afferent stimuli may be ascribed to the pontile and medullary reticular formation. These data further imply that efferent activity from these reticular formation sites involved in tidal volume generation converges upon midline structures of the medulla. (Supported by NIH Grants HL 18009 and NS 05173.)

EFFECT OF NEONATAL HYPERTHYROIDISM ON CORTICAL RESPONSIVENESS TO SENSORY STIMULI. M. Salas, S. Díaz* and L. Cintra*. Dept. Physiology, Instituto de Investigaciones Biomédicas, UNAM. México 20, D.F. México.

Using cortical evoked responses and number of dendritic spines as indicators of neocortical maturation, the effects of neonatal hyperthyroidism were studied in rats at different ages. When administered before day 20 thyroxine shortened mean peak latencies, advanced the organization and the configuration of potentials, caused higher amplitude of the evoked activity and shortened the duration of the evoked repetitive secondary discharges to sensory stimuli. However, from the 20th postnatal day a subsequent retardation of the development occurred, as indicated by a prolonged mean peak latency of primary responses, prolonged duration of the repetitive secondary discharges to sensory cues and persistance of increased amplitude of the waves. The electrophysiological effects were correlated with similar maturational variations in the number of dendritic spines of the large cortical pyramidal cells. Since at later ages thyroxine appeared to affect more markedly the repetitive secondary discharges than primary potentials, the present results suggest that thyroxine permanently interferes more with the cortical integration than with the reception of sensory impulses.

DOPAMINE MEDIATION OF NEURALLY-EVOKED INHIBITION OF CAROTID BODY CHEMORECEPTORS IN CATS. S.R. Sampson, M.J. Aminoff*, R.A. Jaffe*, and E.H. Vidruk* (SPON: Allan H. Mines), Univ. of California, San Francisco CA. 94143.

Electrical stimulation of the peripheral cut end of the carotid sinus nerve (CSN) inhibits carotid body chemoreceptors in cats, as does dopamine administered intra-arterially close to the carotid body. Dopamine is contained in Type 1 cells of the carotid body. The possibility that the former effect is mediated by release of endogenous dopamine was, therefore, investigated by examining the effects of dopamine blockers on the inhibition of chemoreceptor activity evoked individually by both means. Experiments were performed on cats anesthetized with sodium pentobarbital, paralyzed with gallamine triethiodide and artificially ventilated. Recordings were made from single or few fiber preparations of chemoreceptor afferents dissected off the peripheral end of the cut CSN, the remainder of this end of CSN being laid across a pair of stimulating electrodes. Two dopamine blockers were used; dihydroergotamine (DHE, 250-400 μg/kg) was given I.V., and droperidol (drop., 25-50 μg) was injected intra-arterially close to the carotid body as was dopamine (5 μg). DHE and drop. both increased spontaneous chemoreceptor activity. In addition, each reduced or abolished the inhibitory effects of both dopamine and nerve stimulation. These results are consistent with the previous proposal that CSN activity releases dopamine, which inhibits the discharge of chemoreceptors. (Supported in part by NIH grants HL14201, GM00927 and HL00448).

POSTEXTRASYSTOLIC POTENTIATION AND ITS RELATIONSHIP TO E-C COUPLING IN MAMMALIAN MYOCARDIUM. Warren G. Sanborn* (Spon: G.A. Langer). UCLA School of Medicine, Los Angeles, California 90024

Excitation-contraction coupling in mammalian myocardium (dog, cat, and rabbit papillary and trabecular muscles) was examined by making use of postextrasystolic potentiation, quiescence and restimulation, changes from lower to higher Ca concentration, and Mn. The ideas (1) that intracellular stores of contraction-related Ca (i.e., terminal cisternæ) are augmented by Ca derived from the extra stimulus and (2) that these intracellular stores exchange with the interstitial space slowly during quiescence ($t_{\frac{1}{2}}$ > 100 sec) but rapidly during rhythmic contraction ($t_{\frac{1}{2}}$ = few beats) are not supported by these experiments. For example: a) An extra stimulus given in low-Ca medium followed by quiescence and a return to control-Ca medium yields, upon restimulation, a contraction displaying marked potentiation. b) An extra stimulus given in control-Ca medium followed by quiescence and the inclusion of Mn for as brief a period as 20 sec, yields, upon restimulation, a contraction devoid of potentiation. c) An extra stimulus given in a Mn-containing control-Ca medium (98% reduction of contractile force) followed by quiescence and the removal of Mn yields, upon restimulation, a contraction displaying marked potentiation. These data suggest that the location of the releasing sites is indistinguishable from the interstitial space and that, in the absence of a blocking agent like Mn, the extra stimulus conditions them to deliver an increment of Ca determined primarily by the Ca concentration in the interstitial space.

REGULATION OF GASTROINTESTINAL MUCOSAL AND LIVER HEXOSAMINE SYNTHESIS. L.D. Sander and L.R. Johnson, Dept. Physiology, University of Texas Medical School, Houston, Texas 77025.

The specific activity of L-glutamine:D-fructose-6-phosphate aminotransferase (EC 2.6.1.16, glucosamine synthetase) was measured in the oxyntic gland, antral, and duodenal mucosae and liver of male, albino rats of varying weights after feeding, fasting and acid stimulation. Variations in fed body weight (50 g, 125 g, 275 g) had no effect on enzyme specific activity in any tissue. Fasting for 48 hrs tended to decrease enzyme specific activity in the antral and duodenal mucosae and liver. These decreases were significant only in the 275 g rats. Fasting had no effect on oxyntic gland mucosal specific activity. Pentagastrin (250 μg/kg) or histamine (20 mg/kg), administered every 8 hrs for 2 days to fasted 275 g rats significantly increased enzyme specific activity in the oxyntic gland mucosa and liver. These increases could be blocked by metiamide (1.8 mg/kg). Single injections of pentagastrin or histamine were without effect. Urecholine (10 mg/kg), also administered every 8 hours for 2 days to fasted 275 g rats, increased oxyntic gland and antral mucosal specific activities. This increase could not be blocked by metiamide. These findings suggest that acid or the process of secreting acid may be responsible for the regulation of hexosamine synthesis in the GI tract. This may be important not only in the control of mucus secretion but in the synthesis of cell membrane glycoproteins. (Supported by NIH Grant AM 00411 and AM 16505.)

EFFECTS OF THIOCYANATE ON TRANSMUCOSAL ELECTRICAL RESISTANCE AND H^+ RATE OF FROG GASTRIC MUCOSA IN PRESENCE OF Ba^{++}. S. S. Sanders, R. L. Shoemaker and W. S. Rehm. Department of Physiology and Biophysics, University of Alabama Medical Center, Birmingham, Alabama 35294

Under standard conditions, addition of thiocyanate (SCN) (15 mM - SCN^- replacing Cl^-) to secretory side of the in vitro frog gastric mucosa increases resistance (R) and potential difference (PD) and decreases H^+ rate to zero. With Ba^{++} (1 mM) on nutrient side (which markedly increases R without much change in PD or H^+ rate) addition of SCN^- to secretory side abolishes H^+ rate but R gradually decreases and PD, after initially rising, also decreases. R levels off about 30% below previous Ba^{++} level in about 20 min. Removal of SCN^- results in a) return of H^+ rate b) initial decrease in R and c) a slow return of R to previous high Ba^{++} level. PD concurrently dips with the initial decrease in R and then returns to control level. Detailed examination of relationship between ΔH^+ rate and ΔR with Ba^{++} and SCN^- shows that following addition of SCN^- about half of the total R drop occurs after the H^+ rate has reached zero: in some experiments almost all the decrease in R occurs after the H^+ rate is zero. When SCN^- is removed, R decreases as H^+ rate is reestablished. Most of the slow R increase occurs after H^+ rate reaches control level. On basis of a 79 mM K^+ pulse method (K^+ in nutrient fluid increased from 4 to 79 mM) the resistance of secretory membrane in absence of secretion (i.e., Ba^{++} + SCN^-) is higher regardless of total R than with Ba^{++} alone. Assumption with pulse method is that with 79 mM K^+ the nutrient membrane resistance is minimal, i.e., invariant. These results and those of Rangachari (AJP 228:511, 1975) on the relationship between R and H^+ rate will be discussed in the light of our separate site theory. (NIH and NSF support)

A COMPARISON OF CARDIOVASCULAR HEMODYNAMICS OF UNTRAINED DOGS AND SWINE DURING SIMILAR EXERCISE STRESS. T.M. Sanders, F.C. White*and C.M. Bloor Department of Pathology, School of Medicine, University of California, San Diego, La Jolla, California 92037.

To evaluate two species for use in cardiovascular studies during exercise stress, we compared cardiovascular responses from instrumented dogs (12) and miniature swine (14). The responses were determined during steady state (SS) and exhaustive (EE) exercise on a treadmill. We measured heart rate (HR), cardiac output per kg (CO), stroke volume (SV), mean aortic pressure (MAP), acceleration of aortic flow (DF/DT), left atrial pressure (LAP), cardiac work (CW), diastolic to systolic time ratios (D/S), heart wt. to body wt. ratios (H/B) and blood flow (BF) to the myocardium, kidneys and abdominal viscera. Dogs had greater ($P<0.05$) H/B ratios. At EE dogs had a greater ($P<0.05$) CO due to higher ($P<0.05$) HR and SV. Pig SV did not change. In the pigs at all conditions DF/DT was greater ($P<0.05$). Dog CW was greater ($P<0.05$) at the same relative workloads. Changes in D/S ratio indicate the pig diastolic flow period may be more sharply decreased than that of the dog. In the pigs myocardial blood flow was greater, suggesting greater O_2 usage for less CW. At EE dogs did not exhibit redistribution of abdominal BF; pigs redistributed splanchnic BF inversely to the level of stress, as reported in humans. No significant differences were noted in MAP and LAP between species. Both species are suitable for acute exercise stress studies; however, dogs appear to have a greater cardiovascular reserve than pigs and exercise more efficiently. Based on these cardiovascular responses, BF studies and subjective evaluation of performance during exercise, we conclude that pigs respond to exercise stress in a manner more similar to responses reported in humans than do dogs.

CHARACTERIZATION OF ESTROGEN AND ANDROGEN-CONCENTRATING CELLS IN THE MALE AND FEMALE RAT PITUITARY USING A COMBINED AUTORADIOGRAPHIC AND IMMUNOHISTOCHEMICAL TECHNIQUE. Madhabananda Sar, Peter Petrusz* and Walter E. Stumpf*, Laboratories for Reproductive Biology, and Departments of Anatomy and Pharmacology, U.N.C. Chapel Hill, N. C. 27514

We earlier demonstrated that in rat anterior pituitary, estradiol concentrates in all cell types whereas androgen concentrates only in gonadotropes (Stumpf, Z. Zellforsch. 92:23, 1968; Sar & Stumpf, Science 179:389, 1973). In order to better characterize estrogen and androgen concentrating cells in pituitary, the dry-mount autoradiography was combined with the immunohistochemical staining technique using rabbit antisera to human chorionic gonadotropin, ovine luteinizing hormone (G.D. Niswender), rat thyrotropin and prolactin (NIAMDD), and bovine growth hormone. Four male and four female rats, 2 mo old, castrated for 4 wk were used. Two male and 2 female rats were each injected intravenously with either 2,4,6,7 ^{3}H estradiol, spec. act. 110 Ci/mM, or 1,2,6,7 ^{3}H testosterone, spec. act. 95 Ci/mM, at a dose of 0.5 µg/100 g body weight. The animals were killed at 1 h. Pituitaries were removed, frozen and cut at 4 µm section thickness. Sections were freeze-dried and exposed for autoradiography. After exposure, the slides were fixed in Bouin's fluid followed by 70% alcohol, developed, fixed, rinsed with water and stained immunohistochemically by a modified immunoperoxidase bridge technique. The results demonstrate that in both male and female rat anterior pituitary estrogen is concentrated in gonadotropin, prolactin and growth hormone secreting cells while androgen concentrates only in gonadotropic cells. Thyrotropic cells concentrate little or no radioactivity.

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THE PERFORMANCE OF HYPERTROPHIED LEFT VENTRICLE IN CONSCIOUS DOGS. S. Sasayama*, D. Franklin, D. McKown*, S. Kemper* and J. Ross, Jr. Univ. of Calif., San Diego and Scripps Clinic, La Jolla, Calif. 92037

Twelve dogs were instrumented with left ventricular (LV) micromanometer, pairs of ultrasonic crystals for measurement of LV wall thickness (WTh) and internal diameter (ID) and a cuff around the ascending aorta. On cuff inflation (INF) LV systolic pressure (SP) and peak wall stress (WSt) were increased by 59 and 55% above control values (C) of 140 $\pm$ 6 mmHg and 112 $\pm$ 12 x 10^3 dynes/cm^2 ($p<0.001$). End-diastolic (ED) diameter (D) increased by 3% from C of 31.0 $\pm$ 2.1 mm ($p<0.01$), mean shortening velocity (V_{CF}) was decreased to 61% of C of 1.80 $\pm$ 0.18 circ/sec. ($p<0.001$). During 2.5 weeks of aortic constriction ED WTh increased by 11% from C of 10.6 $\pm$ 0.9 mm ($p<0.0001$). The cross sectional area of the LV wall (calculated from ED WTh and EDD) was increased by 15 $\pm$ 3% ($p<0.001$) and although LVSP had been sustained at more than 210 mmHg, WSt fell to 22% above C and EDD had returned to normal and V_{CF} returned to 93% of C (NS). Immediately after cuff release (R) WSt fell to -8% of C and V_{CF} increased to 10% above C and was not significantly different from control at matched heart rates 24 hrs later. Instantaneous WSt was plotted against velocity (V) and ID in differently afterloaded beats produced during the course of INF and R. WSt-V relations at peak WSt and WSt-length relations (SLR) at end ejection during R were not different from control. The diastolic SLR was shifted to the left with a steeper slope after hypertrophy. These data indicate that moderate hypertrophy per se does not depress contractility although the LV became less compliant. (Supported by grants HL-12373 and HL-17682 from NHLI)

PERICRUCIATE CEREBRAL NEURONS IN THE DOMESTIC CAT ACTIVATED BY VENTRAL MEDULLARY STIMULATION. W. R. Satterthwaite* and A. L. Towe. Dept. of Physiol. & Biophysics, Univ. of Wash. Sch. of Med., Seattle, WA 98195

Extracellular recordings were made of single neurons in the forepaw region both anterior and posterior to the lateral edge of the cruciate sulcus in chloralose-anesthetized, paralyzed cats. Neurons identified with a ventral medulla (VM) hunting stimulus were tested for responses to electrical stimulation of each of the four paws and to natural skin and deep stimulation. In a sample of 977 neurons, 852 were adequately tested for classification according to their responses to the four paw stimuli. Only two-thirds of the neurons would have been identified by a contralateral forepaw (CF) hunting stimulus, for one-third would not respond to that input. The relative proportions of the different sets of neurons (sa, sb, m and others) that would respond to CF stimulation were comparable to those obtained in other studies using CF input as a hunting stimulus. Two-thirds of the neurons not sensitive to CF input would not respond to electrical stimulation of any paw; one-quarter of these responded to natural stimulation. One-eighth of the neurons not sensitive to CF input responded only to ipsilateral input, and a tenth responded only to hindlimb input. Many s neurons showed a decrease in excitability to CF input following stimulation of either hindlimb; the time course of the effect was consistent with a presynaptic inhibitory mechanism. A few s neurons showed facilitation after the conditioning stimulation, and thus may have been incorrectly classified. Pyramidal tract neurons were seen much more frequently than in previous studies. The increase was due to the addition of neurons to the sample that did not respond to CF input; these neurons preferentially sent their axons into the medullary pyramid. Natural fields were often smaller in size than the electrical fields. (Supported by USPHS grants NS 396 & 5136)

CHANGES IN PULMONARY COMPLIANCE AND TOTAL LUNG CAPACITY DURING ACUTE NORMOCAPNIC HYPOXIA. N.A. Saunders*, M.F. Betts* and A.S. Rebuck, Dept. Medicine, McMaster University Medical Centre, Hamilton, Ontario.

Transient changes in pulmonary compliance and lung volume have been noted in man during exposure to high altitude, and in hypoxic experimental animals. These observations led us to study the effects of acute isocapnic hypoxia on pulmonary mechanics in 4 healthy subjects. Hypoxia was induced over a 6 minute period using a rebreathing technique, with the subject seated in a volume displacement body plethysmograph. Steady state hypoxia (P_AO_2 40-50 mmHg) was then maintained for 20 minutes, with the end-tidal PCO_2 held constant at the eucapnic level. Measurements of lung volume, static pulmonary compliance and airway resistance were made using standard techniques. In all subjects, static lung compliance increased during hypoxia (mean and SD: 0.63 $\pm$ 0.16 liters/cmH_2O; control, 0.31 $\pm$ 0.05 liters/cmH_2O). Maximal changes occurred after 20 minutes at a P_AO_2 below 50 mmHg. In 3 of the 4 subjects studied, pressure volume characteristics of the lung returned to normal within 3 minutes of reoxygenation. In all subjects there was an increase in total lung capacity of 0.63 $\pm$ 0.34 liters, residual volume, 0.71 $\pm$ 0.23 liters and FRC, 0.32 $\pm$ 0.2 liters, accompanied by negligible changes in airway resistance. We conclude that acute exposure to hypoxia induces a transient, reversible increase in pulmonary compliance and total lung capacity in healthy subjects.

ATP REGENERATION BY LIVER SLICES IN HEMORRHAGIC SHOCK. M.M. Sayeed, G.I. Perry*, R.A. Romano*, I.H. Chaudry and A.E. Baue., Dept. of Surgery, Washington Univ. Sch. Med. and The Jewish Hospital of St. Louis, St. Louis, MO. 63110

We have quantitated directly the capability of liver slices from animals in hemorrhagic shock to regenerate ATP in vitro. Rats were bled to a mean arterial pressure of 40 mm Hg and maintained at this pressure until 30% of the shed blood was returned (1½ hrs. of shock). Animals were sacrificed with or without reinfusion of the remaining shed blood and liver slices prepared. Tissue ATP content was measured prior to and after chilling (0.5 C for 90 min) of liver slices in a Krebs-Ringer phosphate (KRB) medium. The slices were then rewarmed (37 C 60 min) in KRB and their ATP content determined. ATP content of chilled and rewarmed liver slices from unbled control animals were measured with and without 1.0 mM dinitrophenol (DNP) in KRB medium. The net changes in liver slice ATP (mean $\pm$ SE μmoles/g protein) were:

	Control		Shock	
	-DNP	+DNP	Before reinfusion	After reinfusion
Preincubation	11.9 ± .6	*	3.1 ± .8	4.2 ± .7
Chilled	6.5 ± .4	4.8 ± .3	1.9 ± .4	3.3 ± .5
Rewarmed	11.2 ± .6	3.1 ± .4	4.0 ± .6	5.7 ± .8

*No DNP present before incubation

These data show that liver slices from both shock and control groups were able to regenerate ATP on rewarming. However the net increase in tissue ATP in shock was about 50% of control. This approach now provides a method for further assessment of tissue energy turnover.
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DISTRIBUTION AND METABOLISM OF ^{125}I SALMON CALCITONIN IN YOUNG AND OLD RATS. P. J. Scarpace and W. F. Neuman*, Dept. of Radiation Biology and Biophysics, University of Rochester, Rochester, N. Y. 14642

Synthetic salmon calcitonin was labeled electrolytically with ^{125}I and following IV injection (3 mU/gm live weight) the *in vivo* distribution and metabolism of the hormone was determined in 22-day- and 8-month-old Holtzman rats. In the young rat the hormone localized in kidney (18.9 % of dose), liver (13.6 %) and bone (7.2 %) at 10 min while in the older rats much less was found in bone (2.8 %), more in the kidney (35.2 %), and similar amounts in the liver (12 %). 97 % of the hormone was cleared from the serum by the first time point (10 min). The hormone was extracted from target organs and the extent of metabolism determined by column chromatography. No apparent specific metabolites were found though the half-life per intact hormone was greater than 60 min in both kidney and bone. Of the intact calcitonin present in the kidney at 10 min, 73 % was still unmetabolized by 30 min and 57 % by 60 min. In bone there was no significant metabolism between 10 and 30 min and 77 % remained unmetabolized by 60 min. In contrast, 80 % of the intact calcitonin present in the liver at 10 min was metabolized by 30 min and 94 % by 60 min. The hypocalcemic response to calcitonin is reduced or absent in the older animal and it is widely accepted that the resistance is due to reduced bone turnover in the older animal. The serum calcium response to 3 mU/gm of calcitonin in these 8-month-old rats was found to be from + 0.1 mg % to - 0.7 mg %. The reduced accumulation of intact calcitonin by the older animals could account for the lack of the hypocalcemic response.

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BALANCE OF SODIUM AND WATER IN FROGS: A SYSTEMS ANALYSIS. B. T. Scheer and M. W. Mumbach*, Dept. Biology, Univ. of Oregon, Eugene, OR 97403

Measurements of ^{22}Na efflux from intact frogs (Rana esculenta, R. pipiens) acclimated to continuous immersion in NaCl solutions from 0.1 to 150 mM-L^{-1} are used, with data on rates of urine elimination and drinking, and on body weight, Na^+ dilution space, and concentrations of Na^+ in plasma and urine, to formulate a systems representation of control mechanisms. Analysis of the system and the experimental results predicts changes in blood levels of aldosterone and arg vasotocin as accounting for changes in active Na transport and osmotic fluxes, and oscillatory phenomena which may account for much of the variance. The changes in aldosterone and the oscillatory phenomena have been confirmed.

(Supported by grant AM 03539 from N.I.H.)

CYCLIC NUCLEOTIDE METABOLISM IN COMPENSATORY RENAL HYPERTROPHY. D. Schlondorff,* H. Weber* and W. Trizna* (SPON: J.J. Bourgoignie). Department of Medicine, Albert Einstein College of Medicine, Bronx, New York 10461

The cyclic nucleotides, cAMP and cGMP have been implicated as being significant in the initiation and modulation of growth and proliferation in cell culture studies. Studies were carried out to see whether they are also important in organ growth in-vivo. Compensatory renal hypertrophy was induced in adult rats by unilateral nephrectomy and the growing kidneys were analyzed at timed intervals after surgery. Renal cortical cAMP and cGMP levels were measured and cGMP phosphodiesterase activity in the 10^3 x g supernatant and guanylate cyclase activity in the 10^6 x g supernatant were determined. cAMP levels fell 30% for 2-8 hrs and returned to baseline at 24 hrs. In contrast cGMP levels changed markedly: at 15 min they fell to <50% of baseline, increased to 150% at 1 hr, 300% at 2-24 hrs and stabilized at 200% at 72 hrs. cGMP phosphodiesterase remained unchanged. Guanylate cyclase fell to 65% of control 15 min after nephrectomy and rose to 195% at 2 hrs. At 4, 8 and 72 hrs guanylate cyclase activity was 122%, 124% and 117% respectively (not different from control.) These findings indicate that the metabolic events which occur in the first few hours after unilateral nephrectomy and lead to renal hypertrophy, are associated with marked changes in guanylate cyclase activity resulting in parallel changes in cGMP tissue levels. Factor(s) governing in-vivo inhibition and/or stimulation of guanylate cyclase activity may play a determinant role in the modulation of renal growth.

EVIDENCE FOR ABNORMAL VITAMIN D METABOLISM IN THE DIABETIC RAT. L.E. Schneider*, J. Omdahl*, and H.P. Schedl, Univ. of Ia. Med. School, Iowa City, Ia. 52242, and Univ. of New Mexico Med. School, Albuquerque, N.M.

Effects of diabetes (Dia) on duodenal (Du) calcium (Ca) absorption (abs) in the rat are similar to those of vitamin D depletion. To determine whether Du of Dia has the capacity to respond to vitamin D or its metabolites, we studied 5 day streptozotocin Dia rats and matched controls (Con). Dietary vitamin D was 30 IU/day for both groups. At the appropriate time following IV injection of 10 IU of either vitamin D_3 (Vit D; 24 hr), 25-hydroxycholecalciferol (25-OHD; 12 hr), 1,25-dihydroxycholecalciferol (1,25-$(OH)_2$D; 7 hr), or 1α-hydroxycholecalciferol (1α-OHD; 12 hr) into half of each Dia and Con group, Ca transport was evaluated using everted Du sacs with 0.4 mM ^{40}Ca and tracer ^{45}Ca on both mucosal and serosal surfaces. Con responded to all agents by increasing Ca abs (Table). Dia responded only to 1,25-$(OH)_2$D, the metabolite that acts directly on Du, and to its synthetic analog, 1α-OHD. 1α-OHD is activated by 25-hydroxylation to 1,25-$(OH)_2$D; 25-OHD must be 1α-hydroxylated to be active. Since Du responded to 1α-OHD but not 25-OHD, a defect in 1α-hydroxylation appears to be in part responsible for depressed Ca abs in Dia. Even 1,25-$(OH)_2$D did not increase Ca abs in Dia to the level of the treated Con. Hence, an additional factor may be lacking in Dia. However, based on increases above untreated states, the Dia response to 1,25-$(OH)_2$D was virtually normal.

^{45}Ca Appearance in Serosa/g Dry Wt Mucosa X 10^{-5}

Rx	None	Vit D	25-OHD	1α-OHD	1,25-$(OH)_2$D
Con	45	64†	63†	58†	89†
Dia	9	15	7	40††	46††

†Differs from untreated Con, $p < 0.01$; ††Differs from untreated Dia, $p < 0.01$.

TETANIC HYPERPOLARIZATION OF SINGLE MEDULLATED NERVE FIBERS.
G. M. Schoepfle. Department of Physiology and Biophysics, University of Alabama Medical Center, Birmingham, Ala. 35294.

On repetetive stimulation of an isolated Xenopus single fiber with very brief shocks at a rate of 200/sec. it is possible, in favorable preparations, to obtain a steady state level of tetanic hyperpolarization at the end of each interspike interval which is very nearly that of the maximum voltage obtained during the posttetanic period. This is, of course, consistent with the idea that both tetanic and posttetanic changes in membrane potential are proportional to the rate of electrogenic sodium pumping which of itself would attain a maximum during the period of prolonged tetanization. However, it should be realized that repetetive stimulation induces a passive non-specific depolarization which underlies all other voltage changes, including those dependent upon ionic conductance variations as well as those associated with active pumping. Since membrane potential returns to its previous resting level after repetetive stimulation, even in the presence of cyanide, it is concluded that no time dependent changes in sodium or potassium equilibrium potentials can account for tetanic hyperpolarization under normal circumstances. This is at once obvious, since accumulation of intracellular sodium should lead to a hyperpolarization which would not be offset by subsequent pumping in the poisoned fiber. Similar considerations apply to potassium ions. Prolonged exposure to lithium Ringer may result in the eventual reappearance of a tetanic hyperpolarization suggestive of lithium pumping.

(Medical Center Faculty Research Support Grant.)

AUTOREGULATION OF CORONARY FLOW AND DISTRIBUTION OF MYOCARDIAL O_2 TENSION.
Roy W. Schubert*, W.J. Whalen and P. Nair*, Research Dept., St. Vincent Charity Hospital, Cleveland, Ohio 44115. (Spon: M. Levy)

In an isolated, paced, isovolumic cat heart perfused with modified Krebs-Henseleit solution, we measured the response of flow (F), A-V O_2 difference (E), O_2 consumption ($\dot{V}o_2$), peak left ventricular pressure (P_V), and its time derivative (C) to changes in perfusion pressure (P). In addition, the myocardium was sampled with our micro O_2 electrode at "high" and "low" P. An analysis of variance and Scheffe contrasts separated the results into normals (N) that displayed good flow autoregulation and deviates (D) that had no, or poor, flow autoregulation. Histograms of myocardial O_2 distribution for the N group showed little change with changes in P except for a small but significant increase in the number of "hypoxic" (Po_2 < 6 mmHg) locations (H) at low P. D group histograms were extremely variable. The slope of the linear regression line, with respect to changes in P, for the variables, normalized to their initial values ($_o$), are summarized in the Table. All slopes are significantly different from 0 and the N and D groups are significantly different from each other at the 95% confidence level.

Response of the heart to a unit change in P/P_o

Class	Animals	F/F_o	E/E_o	$\dot{V}o_2/\dot{V}o_{2o}$	P_V/P_{Vo}	C/C_o	H/H_o
N	20	.24	-.08	.16	.19	.15	-.63
D	11	.85	-.29	.56	.53	.31	-2.22

An hypothesis we offer to explain some of this data is that coronary flow (F) and extraction (E) are under intrinsic control, with the feedback signal arising from small local "hypoxic" areas of myocardium.
(Supported by grants HL 11906 and HL 52718 from USPHS)

ALDOSTERONE-INDUCED PROTEINS IN MUCOSAL CELLS OF THE TOADS URINARY BLADDER. Walter N. Scott & Victor S. Sapirstein, Dept. of Physiology, Mount Sinai School of Medicine, New York, N. Y. 10029.

We are studying the mechanisms by which aldosterone (Aldo) stimulates sodium transport in the urinary bladder of the toad. Using a double-isotope technique, we isolated an Aldo-induced protein from the "soluble" fraction of the MR cell (PNAS, in press). We have now examined the effects of Aldo upon the synthesis of membrane proteolipids. Paired tissues were incubated in ^{3}H- or ^{35}S-labeled methionine; one set was treated with aldosterone ($5 \times 10^{-8}M$). The intact mucosal cells were separated by density gradient centrifugation and the MR cells from each set of bladders were mixed, sonicated and the membranes sedimented. The separated G cells were treated similarly. The proteolipid fraction of the membranes was extracted with organic solvents and chromatographed on Sephadex LH-20. The MR cell preparation yielded three proteolipid fractions. The ratio $^{3}H/^{35}S$ was increased 15-fold in one MR cell proteolipid, indicating this protein was induced by Aldo. The G cell preparation yielded only two peaks; none of the proteins of G cell preparation had an elevated $^{3}H/^{35}S$ ratio. Similar experiments were carried out using kidney slices prepared from adrenalectomized rats. Aldo induced the synthesis of a proteolipid fraction in microsomes prepared from this tissue. A possible role for this proteolipid in Na^{+} transport is being examined. We find the MR cell proteolipid displaceably binds ^{14}C-amiloride. Our data indicate Aldo induces the synthesis of membrane proteolipids in the MR cell and kidney, and that these proteins may be involved in sodium transport. (Supported by the American Heart Association).

GLUCOSE HOMEOSTASIS: THE MECHANISM OF ACTION OF DICHLORACETATE G.L. Searle, J.M. Felts, R. Shakelford*, and W.F. Ganong, Veterans Administration Hospital and Department of Physiology, University of California, San Francisco, California 94121

Pancreatectomized dogs were studied to determine the effectiveness and mechanism of action of the oral hypoglycemic agent Sodium Dichloracetate (DCA). Each animal was fed a horse meat and chow diet with added pancreatic enzymes. Insulin therapy was discontinued 24 hours prior to study. At 16 hours postprandial 25 uCi of ^{14}C-6 labeled glucose was injected intravenously. Four blood samples were collected at 20 minute intervals for baseline glucose kinetics. DCA (180 mg/kg in normal saline) was then injected intravenously over a period of 10 minutes and blood was again collected at 20 minute intervals through the end of the experiment. Each blood sample was immeadiately deproteinized and glucose was separated from lactic acid and other ionized metabolites by ion exchange chromatography. Glucose concentrations were determined enzymatically. Glucose specific activities were determined from derivative fractions of the molecule after periodic acid oxidation; carbon 6 as formaldimedone and carbons 1-5 as $BaCO_3$. The specific activity of lactic acid was determined from an acetyldimedone derivative of lactate. Kinetic analysis of the specific activity and concentration data obtained in one experiment computed to date indicate that DCA caused a transient complete inhibition of gluconeogenesis (lasting from 80 to 100 minutes) followed by a partial (approx 50%) inhibition of gluconeogenesis that persisted throughout the experimental period. Glucose utilization was also reduced and as a result the hypoglycemic effect of the drug was limited. We conclude that the effectiveness of this drug lies in its ability to limit the delivery of glucose to the body glucose pool. (Supported by The Veterans Administration, The American Diabetes Association, and The Kroc Foundation)

ACTIVE PHOSPHATE TRANSPORT BY TOAD BLADDER. B.B.Sellers, Jr.*, Julia Hall* and Stanley A. Mendoza, Dept. Pediatrics, University of California, San Diego, School of Medicine, La Jolla, Ca. 92037

The urinary bladder of the toad Bufo marinus transports inorganic phosphate from the mucosal to the serosal bathing solution in the absence of an electrochemical gradient. Net flux was calculated as the difference between the mucosal to serosal flux across one bladder area and the serosal to mucosal flux across a contiguous area of the same bladder. This net transport is stable for at least three hours and does not result from a discrepancy between the potential differences or short-circuit currents (S.C.C.) of the two areas. Net phosphate flux was essentially proportional to the concentration of phosphate over a range of 0.5 to 10 mM. At higher phosphate concentrations, both SCC and net phosphate flux were inhibited. The net transport of phosphate is totally inhibited by metabolic inhibitors such as fluoroacetate, iodoacetate or anaerobiasis. The addition of 25munits/ml of parathyroid hormone (PTH) to the serosal bathing media caused an 85% decrease in net phosphate flux ($p < .025$). The addition of 2mM N^6-2'-0 dibutyryl cyclic AMP (dbC-AMP) abolished net phosphate transport ($p < .01$). PTH did not change SCC while dbC-AMP stimulated SCC. It seems likely that the toad bladder will be a useful in vitro model for the study of the regulation of phosphate excretion.

CONCENTRATION OF NOREPINEPHRINE AND DOPAMINE IN THE MEDIAN EMINENCE DURING THE ESTROUS CYCLE. M.K. Selmanoff*, M.J. Pramik* and R.I. Weiner, Dept. of Obstetrics and Gynecology, U.C. San Francisco, San Francisco, CA 94143

Four day cycling female Sprague-Dawley rats were sacrificed at 1000 hours on diestrus I, diestrus II or proestrus. The median eminences were microdissected using the Palkovits technique. In separate animals the validity of this technique was histologically verified. The concentrations of dopamine and norepinephrine in individual median eminences were determined by a microadaptation of the radioisotopic-enzymatic catechol-O-methyl-transferase assay. Protein content of the samples was measured using the semi-micro Lowry method and values are expressed as ng of catecholamine per mg protein. The concentration of dopamine in the median eminence of rats on diestrus I, diestrus II and proestrus did not differ: the means ± SE were respectively 131.8 ± 11.5, n=8, 129.8 ± 11.7, n=9 and 136.8 ± 11.3, n=11. However, the median eminence concentration of norepinephrine on diestrus I (11.7 ± 1.2, n=8) was significantly lower than the level on diestrus II (16.5 ± 1.5, n=9, $p < .03$) and proestrus (19.3 ± 1.5, n=11, $p < .01$). These changes in norepinephrine concentration in the median eminence provide additional evidence for an involvement of norepinephrine containing neurons in the control of the ovulatory surge of gonadotropins.

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THE HYPEROSMOTIC STOMACH: EFFECTS OF INSTILLING CONCENTRATED SALT SOLUTIONS. Thomas J. Sernka and Anne F. Jackson*. Department of Physiology and Biophysics, LSU Medical Center, School of Medicine in Shreveport, Shreveport, Louisiana 71130.

In the course of normal digestion, the lumen of the stomach can become hyperosmotic to plasma by a factor of three. We sought to characterize ion movements across the gastric mucosa at this high but normal concentration in the secreting stomach of the anesthetized rat. Isosmotic and then hyperosmotic salt solutions were instilled into the stomach through a pyloric cannula. Collected instillates were analyzed for concentrations of H^+, Cl^-, Na^+ and K^+. The electrical potential difference was measured across the stomach wall. Hyperosmotic NaCl caused a transitory rise in potential followed by a prolonged decline. The fall in potential was immediate and more pronounced in equally hyperosmotic KCl. H^+ concentration fell uniformly in hyperosmotic NaCl or KCl. Cl^- concentration change and net Cl^- flux reversed from secretory to absorptive direction upon replacing isosmotic with hyperosmotic NaCl or KCl. Na^+ concentration change and average net Na^+ flux increased in the absorptive direction for hyperosmotic NaCl. K^+ concentration was constant in isosmotic and hyperosmotic NaCl instillates. These results indicate that active as well as passive transport of H^+, Cl^- and Na^+ across the gastric mucosa assume altered values when certain ingesta produce a hyperosmotic stomach lumen. Many of these altered transport characteristics appear after ingestion of ethanol solutions, that almost invariably make the stomach lumen hyperosmotic.

ADH AND IMMUNOREACTIVE ^{131}I-ADH CLEARANCE BEFORE AND AFTER NEPHRECTOMY. R. E. Shade and L. Share. University of Tennessee Center for the Health Sciences, Memphis, Tn. 38163.

Seventeen acutely hypophysectomized, anesthetized dogs were given a constant infusion of arginine vasopressin and ^{131}I labelled arginine vasopressin. After 90 min, 3 blood samples were collected at 15 min intervals for determination of total body clearance of AVP (CAVP) and immunoreactive ^{131}I-AVP (CIRI^{131}-AVP). Eight dogs were then nephrectomized. 90 min later, a second set of 3 blood samples was collected for clearance measurements in these and the 9 control dogs. CAVP and CIRI^{131}-AVP did not change significantly during the 90-120 min of infusion in either the time control or prenephrectomy dogs. These data indicate that plasma levels of AVP and IRI^{131}-AVP had achieved a steady-state within the 90 min infusion period. Prenephrectomy CAVP averaged 6.6 $\pm$ 1.1 ml/min·kg (M $\pm$ SE), and the 210-240 min postnephrectomy CAVP was 6.0 $\pm$ 0.9 ml/min·kg. This 10% reduction in CAVP was not statistically significant, nor was it significantly lower than the average CAVP of 8.6 $\pm$ 1.1 ml/kg·min during the 210-240 min infusion period in the time control dogs. CIRI^{131}-AVP before nephrectomy was 3.3 $\pm$ 0.6 ml/min·kg and 2.9 $\pm$ 0.6 ml/min·kg after nephrectomy. This was a significant 10% reduction ($p < .01$). CIRI^{131}-AVP after nephrectomy was also lower than the average CIRI^{131}-AVP of 3.9 $\pm$ 1.0 ml/min·kg for the 210-240 min infusion period in the time control dogs ($p < .05$). CIRI^{131} before nephrectomy was 64 $\pm$ 10% of CAVP ($p < .005$) and after nephrectomy was 62 $\pm$ 13% of CAVP ($p < .05$). Thus, CIRI^{131}-AVP may qualitatively indicate changes in CAVP, but it is not a quantitative measure of CAVP. Supported by USPHS research grants HL-12990 and HL-14242 (Specialized Center of Research in Hypertension) from the National Heart and Lung Institute.

EFFECTS OF THORACIC DORSAL RHIZOTOMIES ON THE RESPIRATORY PATTERN IN ANESTHETIZED CATS. Roger Shannon, Dept. of Physiology, University of South Florida, College of Medicine, Tampa, Florida 33620.

Afferents from intercostal muscles have been shown to alter the rhythm of breathing via bulbopontine pathways (Remmers et al, Physiologist 16:432, 1973). Experiments were conducted to determine if chest wall proprioceptor afferents are involved in the modulation of central respiratory activity during eupnea. The effects of thoracic dorsal rhizotomies (T_1-T_{12}) on tidal volume, frequency, inspiratory time, expiratory time and blood gases were studied in 11 vagotomized, anesthetized (Dial) cats. EMG's were monitored to test intercostal activity prior to the rhizotomies (DR^-); only animals with EMG activity were used in these experiments. Rhizotomies resulted in a decreased V_T, t_i and t_e and an increased f in 8 animals (table); there was no significant change in these parameters in 3 animals.

Mean Values for 8 Animals

	$\bar{V}_T$(ml)	$\bar{f}$(Br/min)	$\bar{t}_i$(sec)	$\bar{t}_e$(sec)
Vagotomized	46	17	1.90	1.64
Vag. + DR^-	38	21	1.39	1.46
% Δ	16	26	26	11

Negligible changes in blood gas values with DR^- indicate that the alteration in respiratory pattern is not totally due to decreased alveolar ventilation. Alterations in blood pressure with DR^- were also ruled out as responsible for the respiratory changes. The results suggest that chest wall afferents do reflexly influence central respiratory activity during eupnea.

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THE EFFECT OF GASTRIN ON THE ISOLATED BLOOD-PERFUSED STOMACH OF THE DOG. J. E. Shaw, L. S. Adair*, F. P. Brooks and J. Urquhart, ALZA Research, Palo Alto, CA 94304 and Dept. of Physiol., University of Pennsylvania, Philadelphia, PA 19174

We have previously reported that gastrin may play a permissive role in vagal stimulation of acid secretion. In the isolated blood-perfused stomach of the dog, (J. Physiol. 226: 107 P, 1972), injection of antibodies to synthetic human gastrin, (SHG:2-17), inhibited vagally induced acid secretion, but had no effect on the acid secretory response to infused histamine (Fed Proc 33:596, 1974). Further evidence for a permissive role of gastrin in the response to vagal stimulation was obtained by excluding the pyloric antrum from the isolated stomach and removing the entire stomach from the large donor dog, to prevent the release of antral gastrin. In such preparations the maximal acid response to vagal stimulation (7 v, 5 msec, 2 Hz) was 0.24 mEq/hr, while with i.a. infusion of SHG:2-17 (4ng/min), no acid secretory response was obtained. However, when the gastrin infusion and vagal stimulation were combined, a maximum acid output of 6.02 mEq/hr was obtained. (Physiologist 17:169, 1974). In the isolated perfused stomach preparation gastrin also interacted with vagal stimulation in a synergistic manner. Thus, combination of an i.a. infusion of gastrin with vagal stimulation produced an acid output of 3 mEq/hr, while neither stimulus alone produced any increase in acid secretion. Finally, at higher concentrations, gastrin alone, in the absence of vagal stimulation, can elicit an acid secretory response.

CONCLUSION: In the isolated perfused canine stomach we have obtained evidence which indicates that when following the acid secretory response, gastrin exerts not only a permissive, but also a synergistic effect with vagal stimulation. In addition, when using higher concentrations, gastrin alone can stimulate acid secretion.

LACTATE METABOLISM IN THE PERFUSED RAT LUNG. M.E. Shaw*, M.L. Eskew*, and R.A. Rhoades, The Pennsylvania State University, University Park, PA. 16802

Lactate utilization and production were investigated in perfused lungs under aerobic conditions. Rat lungs were ventilated with 21% O_2 - 5% CO_2 for 1.5h and perfused with a medium consisting of washed bovine RBC resuspended to a 10% Hct with Krebs-Henseleit bicarbonate buffer - 5g% Pentex bovine serum albumin. Substrates added to the medium included 6mM glucose and 0.5mM palmitate. Twenty μCi of U-^{14}C lactate were added as a single pulse to the medium. Blood gases and pH remained stable throughout the perfusion period. The perfused lung incorporated labelled lactate with 44% of the total tissue radioactivity appearing in the TCA-soluble fraction, 16% in lipids and 15% in lung protein, and 24% oxidized to $^{14}CO_2$. Hydrolysis of phospholipids (PL) resulted in over 84% of PL radioactivity appearing in phospholipid fatty acids (PLFA) with the remainder distributed equally in the non-saponifiable and phospholipid glycerol fractions. Lactate utilization showed a 15 fold increase when circulating levels of lactate were raised from 0.35 to 11mM. In a separate experiment, glucose incorporation into lung lipids, nucleic acids and proteins as well as oxidation to CO_2 were significantly ($P<0.05$) depressed with elevated levels of circulating lactate (6mM). Lipogenesis from glucose was proportionally more depressed in PL than neutral lipids with a 64% decrease in incorporation of glucose into PLFA. Rate of lactate production in the perfused lung was not altered when circulating levels of lactate were raised from 0.35mM to 6mM. These data indicate that the lung can produce and utilize lactate simultaneously and that lactate serves as a potential substrate for the lung (Supported by NIH grant HL16528).

FRACTIONATION OF FIVE FORMS OF CHICK OVIDUCT PROGESTERONE RECEPTORS. M.R.Sherman* and L.K. Miller* (SPON: C.R. Martin). Memorial-Sloan Kettering Cancer Center, New York, N.Y. 10021

Discrimination among the multiple forms of individual steroid receptors is essential to the elucidation of their role in steroid action. Five distinct forms (I-V) of progesterone receptors from cytoplasmic extracts of chick oviduct have been separated and characterized by adsorption to DEAE-coated filters or precipitation with protamine sulfate and extraction with salt-containing buffers, polyacrylamide gel electrophoresis (PAGE) in gels of systematically varied concentration with a Tris-glycine-HCl buffer system, Agarose gel filtration in buffers of pH 10.2 and low ionic strength or pH 7.4 and high K^+, and centrifugation in glycerol gradients. The bound steroid associated with I in low salt media is converted to III by high K^+. II and III, the major complexes in K^+-treated cytosol, correspond respectively to components B and A of Schrader and O'Malley (J. Biol. Chem. 247, 51, 1972). K^+ and Ca^{2+} extracts of protamine-precipitated cytosol contain III and V as the major components, respectively; IV is a minor constituent of both. The properties of I-V are summarized below.

	I	II	III	IV	V
Stokes radius, A.	>80	54	44	28	20
$s_{20,w}$, S.	>8	4.2	3.8	3.5	2.6
$[K^+]$ for release from DEAE filters		0.35	0.15		
PAGE mobility at pH 10.2	low	high	low		

Forms I and IV may be artifactual; II and III apparently represent physiologically active forms, and V, the smallest unit containing all the determinants of steroid binding, may be a sub-component of II and III. (Supported by grants CA-16814 and CA-08748 from NCI and the Paul Garrett Fund.)

REVERSAL OF THIOCYANATE INHIBITION OF GASTRIC SECRETION, IN VITRO, BY USE OF DBcAMP. R. L. Shoemaker, E. B. Buckner* and W. S. Rehm. Department of Physiology and Biophysics, University of Alabama in Birmingham, Birmingham, Alabama 35294

The stimulatory pathway for gastric acid secretion, in vitro, using the pH stat method was investigated and the interaction of pentagastrin (P.G.), thiocyanate (SCN^-), and $N^6,02'$ Dibutyryl Adenosine 3',5' Cyclic Monophosphate (DBcAmp) will be reported. SCN^- ($10^{-2}M$) inhibited either spontaneous or P.G. ($10^{-6}M$) stimulated acid secretion; with the reduction of the acid rate there was a significant increase in the transmucosal potential (P.D.); and the effects on the H^+ rate and P.D. was reversed by removing the SCN^- from the nutrient (serosal) bathing solution. As the concentration of P.G. was increased the concentration of SCN^- necessary to inhibit the acid rate had to be increased. Starting with a low concentration and increasing these in a stepwise manner it was possible to stimulate the H^+ rate with DBcAmp, inhibit the H^+ rate with SCN^-, then re-establish the rate with a higher concentration of DBcAmp, etc. By using a concentration of SCN^- two to ten times greater than DBcAmp, the H^+ rate could be inhibited. The inhibition by use of [SCN^-] of 40 mM or greater could not be reversed by DBcAmp. DBcAmp would not re-establish an acid rate inhibited by amytal or Dinitrophenol. Theophylline produced effects similar to DBcAmp but the time sequence was longer. CAmp was not effective in reversing SCN^- inhibition. (NIH support.)

DCR SENSITIVITY RELATED TO ENDOGENOUS CONCENTRATIONS OF PROGESTERONE (P) AND 5α-PREGNANDIONE (5AP) IN THE RAT. Laurence S. Shore*, (SPON: C.A. Snipes), Depts. of Obstetrics-Gynecology and Physiology, Temple University Medical School, Phila., Pa.

These studies were performed to relate the endogenous progesterone concentration in uterine tissues to its physiological effects. The conversion of P to 5AP by uterine tissue as its major metabolite prompted the investigation of its concentration especially as 5AP is a more potent inducer of endometrial glycogenolysis than P. An obligatory role for P has been established in both the inductive and proliferative phases of the decidual cell reaction (DCR) in the rat. Determination of the endogenous concentrations of P and 5AP in the inductive and proliferative phases was therfore sought by radioimmunoassay. The radioimmunoassay for 5AP was new and highly specific. Studies were performed in mature rats made pseudopregnant by cervical stimulation. On the 4th day of pseudopregnancy the uterine concentration was 281±28 ng/g for P and 266±41 ng/g for 5AP. Horns were traumatized on the 4th day of pseudopregnancy. On the 4th day following trauma the endometrial concentration of P was 100±7 ng/g and for 5AP was 104±10 ng/g. Plasma concentrations were 35.5±4.1 ng/ml for P and 16.1±4.9 ng/ml for 5AP. When one horn was removed and the contralateral horn was traumatized, there was a direct correlation between the endogenous concentrations of P and 5AP in the previously removed untraumatized horn and the amount of decidual tissue in the contralateral horn 4 days following trauma (r^2=.8949). These experiments indicate that the endometrial response to progesterone is a complex process determined in part by local metabolism and the ability of the uterus to concentrate P. Supported by NIH research grant AM-9125.

FEEDING BEHAVIOR OF WEANLING RATS IN RESPONSE TO REGULATORY CHALLENGES. G. C. Sieck*, J. A. Ramaley, A. N. Taylor, R. A. Gorski and D. M. Nance*. Dept. Physiol. Biophys., U. Nebraska, Omaha, Ne. 68105 and Dept. Anat. and Brain Res. Inst., UCLA, Los Angeles, Ca. 90024.

Experiments were designed to test long-term regulation of feeding behavior in weanling female rats. In the first experiment animals were presented a high fat chow diet ad lib for 7 days, after which feeding was limited to 2 hours during the light period (12-12 light-dark cycle). The amount of food consumed by both the weanlings and adult female rats during this 2-hour limited access period increased across days. This increase indicates an ability for both groups to compensate for the depletion of energy stores resulting from the limited access to food. In a second experiment animals were allowed a high fat chow diet ad lib and after 7 days were presented two solutions of glucose (10% and 50%) in addition to the high fat chow. The weanlings displayed a greater preference for the 10% solution than did adults across a 5-day period. During the glucose challenge, consumption of high fat chow decreased for both groups such that daily caloric intakes were comparable to baseline levels. These findings indicate that the weanling rat, like the adult female, is capable of long-term regulation of feeding behavior. Since these regulatory challenges can differentiate between normal and ventromedial hypothalamic lesioned adult rats, our findings suggest that the VMH is not functionally inactive in the weanling female rat as is generally accepted. (Supported by NIH grants HD-080703, NS-09122, and HD-01182.)

RESTRAINT-INDUCED CORTICOSTERONE RELEASE IN RATS PRETREATED WITH INTRAVENTRICULARLY AND INTRACEREBRALLY ADMINISTERED 6-HYDROXY-DOPAMINE. E.B. Sigg and K.L. Keim*. Dept. of Pharmacology, Hoffmann-La Roche Inc. Nutley, N.J. 07110

The possible role of an adrenergic control of stress-induced corticosterone (CS) release was investigated in male Sprague-Dawley rats after intraventricular or intracerebral injection of 6-hydroxy-dopamine (6-OHDA) administered 2 weeks prior to restraint. Restraint of sham-injected rats for 30 minutes diminished central norepinephrine (NE) and increased CS. In rats pretreated with a single dose of 250 g of 6-OHDA intraventricularly, endogenous hypothalamic, forebrain and brainstem NE was diminished by 43, 75 and 45% respectively while basal plasma CS was similar to sham-injected controls. Restraint in 6-OHDA treated rats did not deplete central NE stores further and the CS response to stress remained the same as in sham-injected controls. Reduction of hypothalamic NE (by 33%) and forebrain NE (by 54%) after bilateral injection of 4 g 6-OHDA into the anterior hypothalamus did not alter basal CS titers. The CS response to restraint was not different from controls, and no further diminution of brain NE was observed. In rats with 6-OHDA lesions in the medial forebrain bundle in which forebrain and hypothalamic NE was diminished by 64 and 32% respectively, the CS rise in response to restraint was the same as in the appropriate controls although the basal CS concentration was slightly higher in the lesioned rat. Neither intraventricular nor intracerebral injections of 6-OHDA altered peripheral (heart) NE. It is concluded that the 6-OHDA induced reduction of brain NE does not impair the restraint-induced release of CS.

ABSTRACT WITHDRAWN

INDUCTION OF GRANULATION TISSUE AND EPIDERMIS BY BOVINE EMBRYO SKIN(BES)
Anthony N. Silvetti* (SPON: A.A. Hakim). Burn Unit, Cook County Hospital, Chicago, Illinois.

Previous observations indicate that the healing of wounds such as split-thickness skin grafts, 2nd and 3rd degree burns and trophic ulcer is accelerated by application of bovine embryo skin (BES) either as a "biological dressing" or as a fitted skin graft. In the present studies report on acceleration of growth and wound healing in the rabbit and rat, DES was obtained from bovine embryos, 3-4 months of age under surgical aseptic conditions from intact uteri of freshly slaughtered cows. BES was washed in normal saline and cut in small pieces, 2x4 cm, and preserved in Normosol-M with 10% amniotic fluid at 4°C. After shaving and epilating the dorsal skin of 2 to 2.5 kg New Zealand rabbits, two identical suprapenicular skin defects were produced. The dermal tissue of the proximal skin was resected with sharp iris scissors. These skins were exchanged and grafted to the opposite rabbit and sutured in place. Similar distal defects were recovered with BES, placed with the dermis down and sutured in place as a fitted graft with 5-0 Dermalon. Vaseline and pressure dressings were applied. On the 3rd, 7th, 14th and 20th days the animals were sacrificed and biopsied. Macroscopic examination of 7-day grafts showed that the homograft was firmly attached to its bed, drying up with some areas of necrosis. BES grafts were still present with areas of erosions and highly vascularized granulation tissue. Microscopic examination revealed the following: Under BES grafts the advancing epithelium was fully across the grafted site. (With homograft, partial.) A layer of basal cells with an abundance of mitotic figures and several layers of keratinizing cells were also observed. The granulation tissue was more vascularized; mitotic activity, the development of hair follicles and parafollicular glands were more pronounced than under the homograft.

MEASUREMENT OF ALLOXAN PULMONARY EDEMA IN DOGS BY TRANSTHORACIC GAMMA RAY ABSORPTION. D.S. Simon*, N.C. Staub and J.F. Murray. Cardiovascular Research Institute and Depts. Physiology and Medicine, University of California, San Francisco CA 94143.

Using a collimated 1.2 mCi 57-Co source, we measured the γ-ray attenuation (GRA) in 16 frozen, isolated lung lobes. The GRA was linearly proportional to the total water content (5-17 g) of each specimen ($r=+.96$, $P<.01$). In anesthetized, supine dogs, we measured the GRA through the thorax, with the beam coursed laterally through the midportion of the lower lung lobes. Terminally, we compared GRA to the blood-free lung water/dry lung weight (Qwl/dQl). GRA varied considerably among 5 control dogs, but was very constant in each dog up to 2 hr (C.V. $\pm$ 1.9%) and Qwl/dQl was 4.2 $\pm$ .3 (mean $\pm$ SD). We gave alloxan (90 mg/kg body weight i.v.) to 11 dogs. An increase in GRA began within 14 minutes. The GRA rose linearly for at least 10 min, reaching a maximum at 30-45 min. There was considerable variation among the dogs for GRA during the control period and for the magnitude of GRA increase after alloxan. All dogs developed severe pulmonary edema with Qwl/dQl = 8.1 $\pm$ .8. Since pulmonary vascular congestion is not a component of alloxan pulmonary edema, we infer from these results that the GRA increase was due to a linear accumulation rate of edema fluid. This simple method has promise as being non-invasive, safe, and sensitive for measuring the time course and quantity of pulmonary edema. [Supported in part by HL14201 (Pulmonary SCOR).]

DOSE-RESPONSE ANALYSIS OF ANGIOTENSIN-INDUCED DRINKING AT SUBFORNICAL ORGAN (SFO) AND THIRD VENTRICLE. John B. Simpson*, Alan N. Epstein and Joseph S. Camardo*. Institute of Neurological Sciences, University of Pennsylvania, Philadelphia 19174

Intracranial angiotensin II is dipsogenic. The dipsogenic receptors for AII appear to be in the SFO, in part because 0.1 ng or more of Val^5-AII applied there reliably provoked drinking (Simpson & Routtenberg, Sci., 181, 1973). The dose-response characteristics of AII-induced drinking were reinvestigated using the Ile^5 analog of AII, which is endogenous in the rat, and a remote injection procedure. Unrestrained animals bearing a cannula terminating in the body of the SFO (n=9) or in the dorsal third ventricle (n=13) received 1 µl intracranial injections of 0.1 pg - 1 ng of AII, in doses of order-of-magnitude increments. A regular dose-response relationship was observed in SFO placements. The threshold dose, defined as that at which 50% of injected animals drank, was between 0.1 - 1 pg at the SFO. Average intake in 20 min to 1 pg was 1.6 ml and to 1 ng was 5.2 ml. Latency from injection until onset of drinking varied inversely with dose of AII, being 48 sec at 1 ng and 99 sec at 1 pg. The threshold for drinking following third ventricular injection was higher, between 0.1 - 1 ng. The SFO threshold of 10^{-16} - 10^{-15} moles (10^{-10}-10^{-9} M) of AII is well within the dose range for other physiological effects of the hormone. Thus, application of physiological quantities of AII to the SFO, but not to the adjacent ventricle, elicits drinking. The elicitation of thirst is one of the physiological actions of AII, and the hypothesis that the SFO contains the dipsogenic receptors for AII is supported. (Supported by MH 26151 and NDS 03469)

DIURETIC RESPONSE TO NOREPINEPHRINE FOLLOWING PHENOXYBENZAMINE AND/OR INDOMETHACIN TREATMENT. R. J. Sinclair,* E. Teegarden* and W. Cheng* (SPON: M. J. Keyl) Dept. of Anesthesiology, Univ. of Oklahoma Health Sciences Ctr., Oklahoma City, Okla. 73190.

This study was undertaken to determine if the diuretic response to exogenous norepinephrine (NE) occurred following blockade of prostaglandin (PG) synthesis by indomethacin (I) and/or alpha-adrenergic blockade by phenoxybenzamine (P). Renal blood flow (RBF), renal venous pressure (RVP), arterial pressure (AP) and urine flow were continuously monitored in the anesthetized dog before, during and after IV NE (0.25 ug/kg/min). In five dogs P (2 mg/kg) was administered prior to a second NE infusion while I (2 mg/kg) was administered to three other dogs before NE. AP and renal resistance increased with NE but fell in the P treated group even during a second NE infusion. RBF and RVP did not significantly change following NE, recovery, or P. Urine flow increased 200-400% during NE but dropped 86% in the P treated group during the second NE infusion. In the dogs pretreated with I, urine flow increased 278-1750% during the initial NE infusion but fell during the second NE infusion, after P. RBF was elevated in two dogs during NE infusion, before and after P. IV NE produced a diuresis as AP increased but P reversed the diuresis when, presumably, PG synthetic function was still intact. Following the administration of I, NE still increased urine flow, but not after P. NE increases urine flow whether or not PG synthesis is blocked while lowering AP by P decreased urine flow even in the face of unchanging RBF. These data suggest that intrarenal PG synthesis does not play an important role in the diuretic response to increased renal perfusion pressure while blocking the response to alpha-adrenergic drugs abolishes the phenomenon.

PANCREATIC ACINAR CELLS: STUDY OF "STIMULUS-SECRETION" COUPLING WITH IONOPHORE A-23187 AND CYCLIC NUCLEOTIDES. Manjit Singh*. V.A. Hospital and Medical College of Georgia, Augusta, Georgia 30904 (P.D. Webster)

Secretion of digestive enzymes by the exocrine pancreas conforms in many ways to the "stimulus-secretion" coupling model in which calcium acts as an intracellular mediator. The role of cyclic nucleotides has been debated. Ionophore A-23187 is known to transport Ca^{++} and other divalent cations across biological membranes. Studies were conducted to determine the effect of this ionophore on amylase secretion from the rat pancreas in vitro to obtain an insight into the mechanism of "stimulus-secretion" coupling. Pancreatic slices were incubated under the effects of various agents for a period of 60 minutes and secretion of amylase estimated. Ionophore caused a dose dependent increase in amylase secretion up to a concentration of 5 µg/ml. Ionophore induced secretion was dependent on extracellular Ca^{++} concentration. Cholecystokinin-Pancreozymin stimulation had an additive effect on ionophore induced secretion. CCK-PZ stimulated amylase secretion even with total lack of extracellular Ca^{++}. La^{+++} blocked ionophore induced secretion at 2 mM and CCK-PZ stimulated secretion at 10 mM. Mg^{++}, Ba^{++} and Sr^{++} inhibited ionophore induced secretion. Caffeine, Theophylline and Dibutyryl-c-AMP had an additive effect. Cyclic-AMP had an additive effect at 1 mM and 10 mM and cyclic-GMP at only 1 mM. These studies point out that Ca^{++} is important in "stimulus-secretion" coupling as evidence by ionophore induced amylase secretion. Other divalent cations i.e. Mg^{++}, Ba^{++} and Sr^{++} competed with Ca^{++} for transport and inhibited amylase secretion. Additive effect of CCK-PZ was due either to mobilization of intracellular Ca^{++} or formation of cyclic nucleotides. The latter is supported by the additive effect of caffeine, Theophylline, Dibutyryl-c-AMP, cyclic-AMP and cyclic-GMP on ionophore induced secretion.

MYOCARDIAL BLOOD FLOW DISTRIBUTION DURING CARDIOPULMONARY BYPASS (CPB).
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(Spon: Howard M. Klitgaard)

Myocardial blood flow distribution was obtained as a time constant of the thermal washout curve when a measured bolus of cold blood of known temperature was injected into the aortic root during CPB. Y.S.I. thermister probes (24 gauge) with 0.1 second time response were placed in the subendocardium and the subepicardium furthest away from major coronary vessels. The basal temperature was measured by a separate probe and maintained constant by a heat exchanger. The effects of varying aortic root pressures on the subendocardial and the subepicardial flow ratio were studied in the empty beating and the empty fibrillating heart. A coefficient of correlation of 0.998 was obtained between the reciprocal of the time constant and measured flows into an isolated aortic segment. A study correlating 1/time constant and microspheric measurement of subendocardial flow using Ce^{141} Cr^{51} Sr^{85} (14 ± 2) at known coronary blood flows (CBF) was performed. At all pressures and CBF studied the endo/epi ratio was significantly higher for the empty beating than the empty fibrillating heart ($p<.001$). The highest flows to the subendocardium occurred in the beating heart at aortic root pressures above 60 mmHg. The dynamics of subendocardial flow as measured by thermal washout may explain ischaemic necrosis of the subendocardium during CPB. The method proved sensitive to changes in regional myocardial blood flow during CPB.

ADRENOCORTICAL RESPONSE TO ACUTE STRESSES IN RATS PRETREATED WITH AMINERGIC AGENTS. N. Sithichoke*, S.F. Marotta and J.P. Marbarger,
Dept. Physiology and Research Resources Laboratory, University of Illinois at the Medical Center, Chicago, IL. 60680

Pharmacological agents, which are known to alter brain serotonin and catecholamine content and/or turnover rate, were employed to study monoaminergic influences on plasma corticosterone levels during hypoxic and hypercapnic stresses in male rats. The agents were injected ip and the animals (10-15/grp., on a 12L:12D schedule) were subjected to either ambient air, 10% O_2 or 10% CO_2 for one hour prior to decapitation at 1000 to 1130 hr. Trunk blood was collected for plasma corticosterone analysis. The following data were obtained:

Agent	Dose (mg/Kg)	Duration (hr)	Pl. Cort. (μg/100 ml) air	10% O_2	10% CO_2
Saline	-	4	4.3	33.6	33.1
Reserpine	2.5	24	9.3	37.5	37.4
α Methyl Tyrosine	100	4	6.5	25.5	30.9
L-Dopa	100	4	5.2	23.3	23.0
FLA-63	25	4	29.1	37.1	29.1
p-Chlorophenlyalanine	300	48	27.7	33.3	29.5
Pargyline	100	24	17.6	17.8	23.9
Phentolamine	4	2	6.3	40.8	27.6

These results indicate that serotonergic, as well as catecholaminergic systems are inhibitory to the hypothalamus-pituitary-adrenal axis of control rats, and that the adrenocortical response to hypoxia or hypercapnia, although modified, is not greatly affected by agents which impair the aminergic system.
(Supported by the Office of Naval Research Contract NR 201-020.)

THE EFFECT OF AEROSOLIZED PULMONARY LAVAGE FLUID ON ALVEOLAR MACROPHAGE FUNCTION IN BURNED RATS. William A. Skornik*, Donald P. Dressler* and Paul Nathan. Harvard Med. School, Boston, Mass. and Shriners Burns Institute, and Univer. of Cinti, Cinti, 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. However, a severe defect in the clearing mechanism has been demonstrated following burn injuries. With P. aeruginosa a 50% mortality due to bacterial pneumonitis occurs following aerosol challenge of rats one day post burn. In vitro studies confirmed that phagocytosis and intracellular killing by alveolar macrophages were decreased. At a bacteria/macrophage ratio of 10:1, alveolar macrophages from normal, unburned rats incubated in control media alone (pooled normal rat serum) phagocytosed 1.7×10^3 P. aeruginosa organisms. Of this number phagocytosed, 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 rats one day post burn were incubated in their own lavage fluid, phagocytosis (0.16×10^3) and intracellular killing (20%) were markedly reduced. Macrophages washed from the lungs of rats 5 days later had excellent phagocytosis (123×10^3) and intracellular killing (33%), and no mortality resulted from rats challenged by bacterial aerosol. Protection from bacterial aerosol challenge was observed when test rats were treated with aerosolized normal lavage fluid 1 hour prior to bacterial challenge. Sixteen of 24 treated rats survived compared to 12 of 24 in control experiments. These studies indicate that a humoral alveolar macrophage enhancement factor, present in the lungs of normal rats, may be used to activate alveolar macrophage function in susceptible, burned rats.

EFFECTS OF PGA_1, PGE_2 AND DIAZOXIDE ON MYOCARDIAL CONTRACTILE FORCE. Lawrence M. Slotkoff, John C. Rose and Peter A. Kot. Dept. of Physiology and Biophysics, Georgetown University Medical Center, Washington, D.C. 20007

Experiments were conducted in eight sodium pentobarbital-anesthetized dogs comparing the effects of PGA_1 (5 ug/kg), PGE_2 (5 ug/kg) and diazoxide (5 mg/kg) on systemic arterial pressure and myocardial contractile force (MC). The three agents were given in successive bolus injections intravenously and MC was measured by means of a Walton-Brodie strain-gage arch attached to the right ventricle. Drugs were administered before and during combined ganglionic (hexamethonium) and beta-adrenergic (practolol) blockade. Adequacy of blockade was tested by carotid occlusion and isoproterenol injection respectively. In these doses, all three agents produced a decrease in systemic arterial pressure of the same magnitude. Both PGA_1 and PGE_2 caused a marked rise in MC, 24% S.E.M. $\pm$ 5.0 and 20% $\pm$ 6.3 respectively before blockade and 10% $\pm$ 4.6 and 11% $\pm$ 3.5 during blockade. Diazoxide caused only a minimal rise (0.9% $\pm$ 7.1) before blockade and a marked fall (27% $\pm$ 4.9) during blockade. These studies indicate that PGA_1 and PGE_2 have a direct positive inotropic action on the heart. The cardiac receptor sites for PGA_1 and PGE_2 appear to differ from beta-adrenergic receptor sites. The minimal increase in MC following diazoxide before blockade represents a reflex response mediated by the baroreceptor reflexes. With the reflexes blocked, diazoxide had a negative inotropic effect.

FEEDBACK MECHANISMS AND MALE PUBERTY IN THE RAT. E.R. Smith, D. A. Damassa* and J. M. Davidson, Department of Physiology, Stanford Univ., Stanford, California 94305

A rising threshold of testosterone(T) negative feedback on luteinizing hormone(LH) secretion has been frequently implicated in mechanisms controlling the onset of male puberty. However, possible age-related changes in distribution and/or clearance of T might explain the results of experiments purportedly demonstrating greater gonadotropin suppressibility in prepuberal subjects. In the present experiment, effects on LH secretion of comparable plasma titers(not doses) of T were compared before, during and after puberty. Prepuberal(26 day old), puberal(55 day old) and adult(115 day old) male Long Evans rats were castrated and immediately implanted subcutaneously with T-filled polydimethylsiloxane capsules of various sizes. Five days later, blood samples for plasma LH and T were taken via cardiac puncture and the animals autopsied. Higher circulating levels of T were needed to suppress LH in the two older groups. Total inihibition of the castration-induced LH rise resulted from T levels lower than those of intact rats of corresponding ages, particularly in the puberal group. This and other data on accessory sexual glands suggested that the T treatments were more effective for LH suppression and did not entirely duplicate androgenic effects of the testes. In the puberal, and to a lesser extent the adult group, low plasma T concentrations resulted in LH levels above those of castrate controls. A similar effect has not yet been found in prepuberal rats under the present experimental conditions. These results support the differential feedback sensitivity hypothesis of the onset of puberty and also suggest a possible role for "positive feedback" of T.

(Supported by grant HD-00778 from NIH)

MYOCARDIAL CYCLIC 3',5' ADENOSINE MONOPHOSPHATE LEVELS: The Effect of In-Vivo Phosphodiesterase Inhibition and Glucagon Stimulation. Louis L. Smith*, Richard D. Catalano* and Weldon B. Jolley. Loma Linda School of Medicine, Surgical Research Laboratory, Loma Linda, California 92354.

The effect of a potent new phosphodiesterase inhibitor (3-bromo-5, 7-dimethylpyrazolo [1,5a] pyrimidine)* on cardiac levels of cyclic 3',5' adenosine monophosphate (c-AMP) was studied in intact rats with and without a simultaneous glucagon administration. A cannula was inserted into the inferior vena cava and infusions of test solutions performed. Upon completion of the infusions, the chest cavity was opened and the heart quickly removed and immediately immersed in liquid nitrogen. A protein binding assay was used to determine the levels of myocardial c-AMP. A significant 48% ($P < 0.005$) increase in myocardial c-AMP levels was observed following simultaneous infusions of the phosphodiesterase inhibitor (PDI) and glucagon when compared to control animals receiving saline. PDI alone gave 15% increase in c-AMP but was not statistically significant ($P > .08$). Glucagon gave a similar non-statistically ($P > 0.4$) significant 15% increase in myocardial c-AMP. These findings indicate that PDI in intact rats is followed by the accumulation of c-AMP in the myocardium. The simultaneous administration of PDI plus glucagon gave significantly higher levels of c-AMP than either saline, glucagon, or PDI alone.

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*Drug ICN #3009, ICN Pharmaceuticals, Inc., 2727 Campus Drive, Irvine, alifornia 92664.

HYPOTHALAMIC THERMOSENSITIVITY IN CALIFORNIA QUAIL (LOPHORTYX CALIFORNICUS). B.D. Snapp*, S.M. Gospe, Jr.*, and H.C. Heller, Dept. of Biological Sciences, Stanford University, Stanford, CA, 94305

Examination of pre-optic anterior hypothalamic (POH) thermosensitivity in California quail indicates that metabolic rate is unaffected by changes in POH temperature. Water perfused through thermodes chronically implanted around the POH produced deviations in POH temperature of 0.5 to 3.0 C above and below unmanipulated values. These deviations induced no significant changes in oxygen consumption from control values at ambient temperatures (T_a) of 10, 20, or 30°C. Changes in body temperature (T_b), measured subcutaneously in the mid-dorsal region, occurred occasionally with deviations in POH temperature, but these were on the order of 0.2°C, and if larger, were probably due to proximity of T_b thermocouple and water perfusant hoses. The quail did respond to variations in T_a. Control oxygen consumption values were highest at 10°C (0.191 ± .014 cal/g min), and lower at 20°C (0.138 ± .022) and 30°C (0.095 ± .008). Vasomotor responses (leg temperature) to changes in POH temperature were unpredictable. Two birds responded appropriately on occasion at 30°C, but consistent responses were absent in other birds and at other T_a. Evaporative water loss changed very little during the experiments, and changes that did occur were correlated with movement and not variation in POH temperature. (Supported by grant 2 RO1 NS 10367 from NIH to H.C. Heller)

LUNG WATER IN EXTRACELLULAR FLUID VOLUME EXPANSION IN DOGS. (Spon: J. H. Comroe) P.D. Snashall*, W.J. Weidner*, and N.C. Staub, Cardiovasc. Res. Institute, University of California, San Francisco, CA 94143

Guyton and Lindsey (Circ. Res. 7:649, 1959) demonstrated a critical microvascular pressure below which lungs are protected from developing edema. Are the lungs also protected from water accumulation in response to extracellular fluid volume expansion? We anesthetized 11 dogs and ventilated them with IPP. We tied off the kidneys and infused Krebs-Henseleit buffer to volumes equal to 10, 20, 30 and 40% body weight (bw) at 2 ml/(kg x min). After the infusion, we waited until pulmonary and systemic vascular pressures were stable, then injected ^{14}C-sucrose and ^{125}I-albumin at 10 and 5 min, respectively, before death to measure lung interstitial (Qiw) and plasma volumes. Terminally, we opened the chest, rapidly removed and froze the lungs and measured the extravascular lung water/dry weight ratio (Qwl/dQl). In 3 control dogs Qwl/dQl = 3.78 ± .23 (SD) and Qiw = .30 ± .01 of blood-free lung. After 10% bw infusions, Qwl/dQl rose to 4.15 ± .14 (n=3) and at 20% bw to 4.98 ± .93 (n=3); the ratios predicted from control Qiw were 4.50 and 5.22, respectively. Infusions of 30 and 40% bw increased Qwl/dQl distinctly above predicted. We conclude there may be some slight protection of the lung against water accumulation at low infusion volumes. The disproportionate increases in lung water at higher infusion volumes were probably due to alveolar flooding.

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CHARACTERIZATION OF THE NONINVASIVE OXYGEN PROBE PYRENEBUTYRIC ACID IN HEART MITOCHONDRIA. T. Russell Snow* and Frans F. Jöbsis (SPON: L.J. Mandel); Department of Physiology & Pharmacology; Duke University; Durham, N.C. 27710

Before utilizing pyrenebutyric acid (PBA) to monitor intracellular oxygen tension, it is first necessary to determine the metabolic effects and the functional relation between PBA fluorescence and the oxygen tension. To determine the metabolic effects, the steady state (States 1 2,4 and 5) redox levels of cyt a-a_3, b and c with and without PBA were determined using the splitbeam spectrophotometer. In addition, the effect of PBA on State 4-3-4 transitions of NADH, cyt b and cyt c were determined. The results indicate that PBA does not affect the metabolic integrity of the mitochondria. To determine the approximate affinity of PBA for mitochondrial membrane, the amount of PBA taken up by mitochondria was determined. The results (37.4±8.1 pM PBA/mg M_w/nM PBA added) are consistent with previous results on whole cells where the partition coefficient was found to be 200. The observation that the peak absorption of the PBA-mitochondrial suspension remains at 342 nm indicates that PBA is adsorbed on or near the surface of the mitochondrial membrane rather than buried within it. The functional relation between PBA fluorescence and O_2 tension was determined by comparing pO_2 values obtained with a platinum electrode to the observed intensity of the PBA fluorescence. The relation was found to obey the Stern-Vollmer relation ie. $F_o/F = 1 + k[O_2]$ with no higher orders of $[O_2]$ necessary. The quenching coefficient, k, was found to be 0.0019 ± 0.00023 torr^{-1}. Thus PBA has been found to be a noninvasive oxygen probe which permits accurate determination of intracellular oxygen tension without affecting either the cell function or the oxygen tension.
(Supported in part by grants HF-136-74, HL17391-01 and HL16828-01.)

EFFECT OF ETHANOL ON GLUCONEOGENESIS IN PERFUSED LIVER OF NORMAL AND THYROXINE-TREATED RATS. Ann K. Snyder* and Sant P. Singh, VA Hospital and Dept. of Medicine, Chicago Medical School, Downey, Ill. 60064.

Several hormones and other factors influence gluconeogenesis. In the present study inter-relationship between effects of thyroid hormones and ethanol on gluconeogenesis was investigated in perfused rat liver. Livers isolated from 24 hr fasted normal and hyperthyroid rats weighing 150-170 gm were perfused with medium to which alanine, a gluconeogenic precursor, was added at initial concentration of 10 mM and continuously infused at a rate of 5 umoles/min. At 60 min of perfusion, the medium was made 20, 40 or 80 mM of ethanol. The rates of hepatic glucose production (expressed as umoles/hr/100 gm body weight) before and after 40 mM ethanol were as shown in the table.

Animal	Before Ethanol (30-60 min) **	After Ethanol (60-90 min)**	P
Normal (8)	77.1 ± 6.0	132 ± 11	0.005
Hyperthyroid (8)	163 ± 12	166 ± 9	NS

( ) Number of Animals; **Time of Perfusion; Results shown as Mean ± SEM

Perfusate lactate pyruvate ratio, an index of cytoplasmic NAD system, was increased significantly after ethanol addition in normal rat liver experiments, but the results were inconsistent in hyperthyroid rat liver experiments. Experiments with 20 mM or 80 mM ethanol showed essentially similar results to those with 40 mM ethanol. The data suggest that under the given metabolic conditions of our experiments ethanol increased alanine conversion into glucose in liver of normal rat but not of hyperthyroid animal.

OVARIAN LDH ACTIVITY IN RELATION TO OVULATION IN THE RAT. K.F.A. Soliman and C.A. Walker*, School of Pharmacy, Florida A & M University Tallahassee, Florida 32307.

Lactate dehydrogenase (LDH) activity was studied in the ovaries of immature rats treated with pregnant mare serum gonadotropin (PMS). In 24-day-old rats a single injection of PMS causes follicular development, ovulation and luteinization. Animals were sacrificed at 6-hour intervals and LDH activity was measured in the ovaries on the basis of its oxidation to NADH. LDH activity increased sharply in the period between 30 and 42 hours after PMS injection, with increase of the enzyme activity at 36 hours, about 10-fold its activity before PMS injection or after ovulation. The enzyme specific activity of blood reaches a peak at 36 hours after PMS injection. Cellulose acetate paper electrophoresis of ovarian homogenate at pH 7.8 revealed three electrophoretically distinct bands. The three bands which were comparable to M_4, HM_3 and H_2M_2 were not equally intense; the least cathotal band M_4 was by far the most intense and the intermediate bands were sometimes difficult to distinguish. The high concentration of M_4 isozyme might indicate the ovarian capability of supporting anearobic glycolysis. The significance of this finding is that LDH activity may be related to LH release from the anterior pituitary which induce LDH enzyme.

ISOLATED CANINE GASTRIC MUCOSAL CELLS: STIMULATION OF OXYGEN UPTAKE BY PENTAGASTRIN AND ACETYLCHOLINE. Andrew H. Soll* (SPON: M. I. Grossman). V. A. Wadsworth Hospital Center, Los Angeles, California 90073.

Viable cells were isolated from canine gastric mucosa by enzyme digestion using a technique adapted from the studies of Amsterdam and Jamieson (J. Cell Biol. 63:1037, 1974), and oxygen uptake by these cells was studied in response to various secretagogues. Normal dog gastric mucosa was separated from submucosa by blunt dissection, lightly scraped with a glass slide, and sequentially placed in Earles balanced salt solution (EBSS) with 0.1 mM Ca^{++}, EBSS with 2 mM EDTA, and EBSS with 1.2 mM Ca^{++}. Crude collagenase I (Worthington), 0.5mg/ml, was added to the first and third incubations. Viability was greater than 90% by dye exclusion, and cell morphology was normal by electron microscopy. Oxygen uptake was determined using a Clark type electrode. The combination of pentagastrin (PG), 10^{-6}M, acetylcholine (Ach), 10^{-4}M, and eserine (E), 10^{-4}M, produced a 20 to 50% stimulation in basal O_2 uptake. Ach plus E alone produced from 50 to 100% of this maximal response. PG alone produced from 20 to 60% of the maximal stimulation. Additive interactions between Ach and PG were present at submaximal concentrations. These data indicate that isolated cells can be prepared from mammalian gastric mucosa which in vitro respond directly to both pentagastrin and acetylcholine.

WHY IS THE PLASMA RENIN ACTIVITY (PRA) OF NEWBORN RATS HIGH?

S. Solomon, A. Iaina* and H.E. Eliahou*, Dept. of Nephrology, Sheba Medical Center, Tel Hashomer, Israel.

PRA of neonatal rats has been measured on blood obtained from infant rats. From birth until three weeks of age PRA is high. Mean values range from 62.1 (n=2) at 1 day to 76.1 ± 7.8 (n=7) at 2 weeks. One week and three week means are 72.2 ± 14.2 (n=7) and 66.9 ± 12.9 (n=8) ng. angiotensin I generated/hr/ml. Between three and four weeks of age PRA decreases to adult levels (13.2 ± 1.2, n=8). Mothers of infant rats have a high PRA for the first week post partum, but the PRA is not as high as in infants (29.2 ± 3, 3 ng/hr/ml, n=5). By two weeks after delivery PRA of mothers has returned to control levels. Since the higher PRA of postnatal life would result from either hypersecretion or a reduced rate of destruction, we measured the disappearance of renin in nephrectomized rats. PRA decrease is best described by a semilogarithmic relationship. Mean half times (T 1/2) of disappearance is longer (24.6 ± 2.35 min, n=7) in rats 2 weeks old or less than for any other group (17.6 ± 2.25, n=7) for 4-6 weeks old rats, 16.0 ± 1.64 (n=6) for mothers up to two weeks post partum and 17.7 ± 2.55 (n=4) for control females. One can conclude that part of the cause of the high postnatal PRA is reduced destruction of renin. Of the known triggers for suppression of PRA, we found no effect of feeding pregnant dams 1% saline for as much as 2 weeks before delivery. Neither did propranolol (10 mg/kg/hr administered subcutaneously) have any effect on PRA two hours after injection in two weeks old infants.

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EFFECT OF ADRENALECTOMY ON MEDULLARY COLLECTING-DUCT TRANSPORT.

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The in vivo microcatheterization technique was used to study medullary collecting-duct transport in adrenalectomized rats before and during iso-oncotic blood volume expansion. During antidiuresis significant inhibition of sodium reabsorption from outer medullary duct was evident in adrenalectomized animals, compared to sham-operated controls. Continued Na transport in the inner medulla, however, coupled with reduced filtration rate (GFR adr.=0.71±.06 SE, sham=0.95±.07 ml/min·g kidney wt) resulted in sodium excretion not significantly different from control ($U_{Na}V$ adr.=237±51, sham=143±15 nEq/min·gKW). Following intravascular volume expansion with donor blood, both groups exhibited diuresis and natriuresis, associated with inhibition of fluid and sodium reabsorption from the collecting duct in both outer and inner medulla. The smaller natriuretic response of the adrenalectomized group ($U_{Na}V$ adr.=4151±638, sham=14900±3623 nEq/min·gKW) was associated with relative reduction in filtration rate (GFR adr.=1.08±.07, sham=1.40±.11 ml/min·gKW). It is concluded that a) lack of aldosterone results in reduction of sodium reabsorption from collecting duct fluid in outer but not in inner medulla, and b) the inhibition of medullary collecting-duct transport normally seen after blood volume expansion does not depend on reduction of plasma aldosterone levels. (Supported by MRC Grant No. MT 4043).

RETINAL CIRCULATORY CHANGES MONITORED BY ELECTRORETINOGRAPHY.
G. Soria,* W. Crandall* and P. Bach-y-Rita. Smith-Kettlewell Institute of Visual Sciences, Pacific Medical Center, San Francisco, California 94115.

Changes in the B wave of the electroretinogram have been studied in cats and dogs under hypoxia or breathing 100% O_2. These have been correlated with circulatory changes in the retina. A diminished B wave is observed in severe hypoxia as well as with 100% O_2 during 30 minutes of exposure. An increased B wave is observed associated with moderate hypoxia or 100% O_2 for short periods of time. The autoregulatory changes observed in the blood vessels of the retina to changes in PaO_2 or systemic blood pressure (in order to maintain a constant and appropriate supply of O_2 to the retina) are insufficient when the stress stimulus is sufficiently intense and sustained. In such cases, the metabolism of the retinal cells is altered, manifested by the decrement in response to the light stimulus. Our preliminary results with cats and dogs suggest the possibility of developing a practical means of using ERG changes as an indication of metabolic activity of the retina and possibly of the brain during by-pass cardiac surgery.
(Supported by grants EY00299 and EY01186 from NIH, and the Smith-Kettlewell Eye Research Foundation.)

ENERGY LEVELS AND VOLUNTARY HARD WORK OUTPUT, R.G. Soule, M. Bonney*, K.B. Pandolf*, and R.F. Goldman. US Army Research Institute of Environmental Medicine, Natick, MA 01760 and Exercise Physiol. Lab., Boston University, Boston, MA 02215.

Prediction of mobility (distance/time) as a function of total weight (body plus load) and terrain has been demonstrated for a homogeneous, reasonably fit male group ($\dot{V}O_2$ max in the 40-50 ml/kg·min range), based on the concept that, for such a group, self-paced "hard work" corresponds to 425 kcal/hr, i.e., 45 ± 10% of this $\dot{V}O_2$ max. To explore the more general concept that self-pacing may be set, and mobility predicted, as a percentage of $\dot{V}O_2$ max, 5 very fit (>50 ml/kg·min) and 5 less fit (<45 ml/kg·min) men and six women (42.5 ml/kg·min; range 33.8 to 51.6) walked with 10 and 20 kg loads (and 30 kg for 9 men) at self-paced "hard work" on our 6.1 km course (4 terrains: 1.6 km blacktop, 1.8 km gravel road, 1.4 km lt. brush, 1.3 km heavy brush); order of terrain and load were randomized. $\dot{V}O_2$ max, $\dot{V}O_2$ at a 4.8 km/hr fixed pace on blacktop, and HR, time and perceived exertion for each terrain segment, and overall time were measured. Overall time was clearly a function of load, and also of terrain, but did not correlate significantly with $\dot{V}O_2$ max (n=16; for 10 kg, r=0.27; 20 kg, r=0.09; n=9 for 30 kg, r=0.15); other factors, e.g., load as % weight, perceived exertion level, etc., may be involved. However, sex per se does not seem to be a determinant of self-paced work level. Calculated energy cost for the 6 women (as a function of body weight, load and terrain) was approx. 400 kcal/hr at the speeds adopted, which was, on average, 50% of their measured $\dot{V}O_2$ max. Thus, the general hypothesis that mobility can be estimated as that self-paced speed at which the weight and terrain requires 425 kcal/hr ± 10% still seems tenable, but the relationship of this work level with individual $\dot{V}O_2$ max is still unclear.

CONSTANT FLOW AND VASCULAR DYNAMICS WITH EXERCISE. H.V. Sparks and J.A. Faulkner. Dept. of Physiology, Univ. of Michigan, Ann Arbor, Mi.

We have compared the dynamics of vascular conductance changes of dog skeletal muscle during 2 minute periods of twitch and tetanus exercise during free flow (FF) and constant flow (CF). Twitch exercise at 2 and 4 twitches/sec produced steady state FF of 43 ± 8 and 54 ± 11 ml·100g^{-1} min^{-1} and oxygen consumptions ($\dot{V}O2$) of 5.9 ± 1.7 and 8.0 ± 2.2 ml·100g^{-1}.min^{-1}, respectively. Tetanic exercise (30 impulses/sec for 1 sec every 15 sec) produced an average FF of 43 ± 4 ml·100g^{-1}.min^{-1} and a $\dot{V}O2$ of 4.3 ± 1.0 ml·100g^{-1}.min-1. At CF of 43 ± 4 ml·100g^{-1}.min^{-1}, VO2 was 3.8 ± 1.0 (2/sec), 5.9 ± 1.2 (4/sec), and 3.2 ± 0.8 (tetanus) ml·100g^{-1}.min^{-1}. Times (sec) to reach 10, 50, and 90% of the steady state resting vascular conductance following cessation of exercise were:

	2/sec		4/sec		tetanus	
	FF	CF	FF	CF	FF	CF
t_{10}	7.9	6.2	11.1	13.2	10.1	9.3
t_{50}	17.5	16.5	21.9	25.3	14.3	23.8
t_{90}	47.0	46.8	60.0	57.7	43.6	43.6

If flow washout were important in determining the concentration of the metabolic vasodilator(s), holding flow constant should alter the dynamics of vascular conductance by altering the washout of the vasodilator(s). Since no significant change occurred in the dynamics of vascular conductance in these experiments, we conclude that vascular conductance was not increased by vasodilator(s) which are subject to substantial flow washout. (Supported by USPHS grant HL 14516.)

HYPOTHALAMIC LESIONS: EFFECTS ON IMMUNOLOGICAL RESPONSES. N.H. Spector, L.T. Cannon*, C.L. Diggs*, J.E. Morrison*, and G.F. Koob*. Depts of Neurophysiology and Immunology, Walter Reed Army Institute of Research, WRAMC, Washington, D.C. 20012.

In our previous work, hypothalamic lesions failed to produce significant changes in circulating antibody (Ab) titers or parasitemia levels induced by malaria when the lesion groups were compared to sham-penetrated animals (e.g. Spector et al, Proc. XXVI Int. Cong. Physiol. Sci. 1974). Therefore, an attempt was made to repeat an experiment, reported by others, where Ab titers were shown to be lower in immunized lesioned animals. Following procedures similar to those of Tyrey and Nalbandov (Am. J. Physiol. 222:179, 1972) we innoculated, i.p., adult male rats with ovalbumin and pertusis vaccine. Rats were divided into 6 groups; those with (a) large bilateral anterior hypothalamus and preoptic (AH-PO) lesions, (b) medium-sized bilateral AH-PO lesions, (c) small bilateral AH-PO lesions, (d) sham operations, including bilateral penetration of electrodes to AH-PO region, (e) sham operations without rupture of the meninges, and (f) no operation. Taken as a whole, mean Ab titer (modification: hemagglutination method of Bing et al, P.S.E.B.M. 124:1166, 1967) for all lesioned animals was slightly lower (~1 $\log_2$ unit) than that of the two (e,f) control groups. However, no consistent relationship was observed between size of lesion and consequent Ab level. Penetration alone (no lesions) resulted in an average titer 4 $\log_2$ units lower than that of unoperated controls, and also lower than the means of 2 of the lesioned groups. We conclude that all such results must be viewed with caution, that several types of controls are essential in such experiments, and that much more experimental work is needed before we can begin to understand the complex relationships between hypothalamus, "limbic system", endocrines, and immune responses.

CERTAIN ASPECTS OF FLUORIDE METABOLISM IN MAN. Herta Spencer, Dace Osis*, Emilie Wiatrowski*, and Clemontain Norris* Metabolic Research Section, Veterans Administration Hospital, Hines, Illinois 60141.

The intake of fluoride which is due to the fluoride content of the diet and of the drinking water, the excretions of fluoride in urine and stool, the retention of fluoride, and the plasma levels of fluoride were determined in man under strictly controlled conditions. The dietary fluoride intake ranged from 1.4 to 2 mg per day, and, depending on the intake of the fluoridated drinking water the total fluoride intake ranged from 4.0 to 4.5 mg per day. The urinary fluoride represented about 50% of the fluoride intake, the fecal fluoride was very low and the retention of fluoride determined by balances averaged +1.5 mg per day. Increasing the fluoride intake about 10-fold increased the urinary fluoride promptly, representing 50-60% of the intake, the fecal fluoride represented 11%, and the fluoride balance became markedly positive. The net absorption of fluoride was high and ranged from 88% to 94%. The total plasma fluoride level averaged 0.17 mg/liter and changed little with time. Following a single dose of 10, 15, or 20 mg fluoride, the plasma levels reached a peak within 1/2-1 hour, decreased with time thereafter, and returned to control values in 24 hours. The daily intake of 10 or 20 mg fluoride as sodium fluoride for 1 or 3 months, respectively, did not increase the fasting plasma fluoride levels. However, when 45 mg fluoride was given daily as treatment for osteoporosis the plasma fluoride levels increased promptly to about twice the control level and remained elevated throughout the high fluoride intake. Following discontinuation of all doses of fluoride the plasma fluoride levels and fluoride excretions decreased promptly and only a small percentage of the retained fluoride was excreted. (Supported by USPHS grant DE-02486.)

APPLICATIONS OF TISSUE DISPLACEMENT ASSAY (TDA) WHEN USING RADIOPHARMACEUTICALS. Richard P. Spencer. Dept. Nuclear Medicine, Univ. Connecticut Health Center, Farmington, Conn. 06032

Conventional studies with radiopharmaceuticals utilize carrier-free or high specific activity materials. When carrier is added, or analogues or inhibitors are utilized, the resulting kinetic curves are displaced, or the activity in a particular locale is altered. Hence, the designation of TDA. One application involves the use of gamma ray emitting radiopharmaceuticals, which can be detected externally. 1. The site and rate of displacement has potential use in distinguishing normal from disordered tissue. 2. Displacement of a radiopharmaceutical may yield data as to in vivo tissue binding affinities (for example, the displacement of ^{131}I-aminopterin by methotrexate). 3. Inhibitors can be employed to test whether metabolic pathways are intact. An example is the use of perchlorate to block iodide transport by the thyroid, to determine if trapped iodide has been organified or is free to leave the gland. 4. If a particular medication is effective only when tissue bound, then its displacement from tissue terminates its action (and may promote excretion by the urinary system). Thus TDA has applications as a physiological tool and in clinical practice. The principles are illustrated by use of radiolabeled folate analogues and their displacement by more avidly bound inhibitors of the enzyme dihydrofolate reductase. (Supported by USPHS CA 17802 and by American Cancer Society DT-34E).

DIFFERENT PATHWAYS FOR NICOTINE AND GASTRIN STIMULATION OF H^+ SECRETION IN BULLFROG GASTRIC MUCOSA. J. G. Spenney. University of Alabama in Birmingham and Birmingham V.A. Hospital.

A neurogenic pathway for stimulation of H^+ secretion by gastrin should be sensitive to tetrodotoxin (TTX). Thus gastrin-stimulated H^+ secretion like gastrin stimulated motor activity would be blocked by TTX.

Bullfrog gastric fundus stripped of its outer muscle layer was mounted in a plexiglas chamber. After measuring basal J_{H+}, acid secretion was inhibited by 5×10^{-4}M Burimamide. After removal of Burimamide and repeated washout, the following data were obtained upon addition of 5×10^{-5}M nicotine (NIC) or 3.3×10^{-6}M pentagastrin (PG) in the presence or absence of 3×10^{-6}M TTX.

J_{H+} Basal μMoles/cm^2-hr	J_{H+} Burimamide μMoles/cm^2-hr	Additions μMoles/cm^2-hr	J_{H+} μMoles/cm^2-hr
1.92	0	TTX, PG	2.61
2.46	0	TTX, NIC	0
2.46	0	TTX, NIC, PG	2.51
2.44	0	NIC	2.93

Thus, it would appear that stimulation of J_{H+} by nicotine involves a neurogenic (TTX sensitive) component while J_{H+} stimulated by gastrin is independent of this pathway.

NITROGEN BALANCE AND PROTEIN REQUIREMENT IN THE PIG-TAILED MONKEY *(MACACA NEMESTRINA)*. G.A. Spiller*, N. Pace, and D.F. Rahlmann*. White Mountain Research Station, University of California, Berkeley, CA 94720.

Adult, male pig-tailed monkeys were fed isocaloric liquid homogenates of natural foods, supplemented with vitamins and minerals to meet the nutrient requirements of this monkey except for protein. Mean weight of the monkeys was approximately 10 kg. Whole eggs were added in graded amounts to determine nitrogen (N) balance at levels of intake ranging from 0.15 to 2.7 g N/day/monkey. Animals were individually housed in metabolic cages, and urine and feces were collected daily and analysed for N. Each diet, for a total of 16 diets, was fed for a 10-day period and the mean values for the last 4 days were used in all calculations. In addition, the integumental losses were determined separately. The mean integumental N for a 2-week period was 0.2 g N/day/monkey. The mean endogenous level of N in the urine was 0.42 g/day and in the feces 0.22 g/day. Nitrogen balance was achieved at approximately 1.0 - 1.2 g dietary N/day; definite positive balances were achieved at 1.5 g N/day. Analysis of the data suggests that the recommended daily allowance for dietary N for adult, male *M. nemestrina* is between 0.18 and 0.22 g N/day/kg body weight when the protein is of high biological value. Because positive N balances without change in body weight were observed in all diets containing over 1.5 g N/day, it may be hypothesized that there are N losses other than urine, feces and integumental. A possible excretion of dietary N as N_2 has been suggested, and could account for the apparent positive nitrogen balances frequently observed during high-protein intakes.

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HYPERINSULINISM FOLLOWING HYPERGLYCEMIA IN ENDOTOXIN SHOCK DOGS. J.J. Spitzer, F.C. Nance*, W.G. Blackard*, J.H. Anderson*, J.R. Lee*, and J.T. Bechtel*, Depts. Physiology, Surgery, and Medicine, Louisiana State University Medical Center, New Orleans, La. 70112

We previously reported that dogs given an approximate LD_{70} dose of E. coli endotoxin exhibited marked hyperinsulinism (immunoreactive insulin (IRI) values of 500-1500 μU/ml) when made hyperglycemic by the infusion of 50% glucose. The present experiments were performed to further investigate the genesis of this phenomenon. Impaired insulin degradation, pancreatitis, intestinal insulin releasing polypeptide(s), or pancreatic ischemia were postulated as possible mechanisms responsible for the marked hyperinsulinism. When labeled insulin was administered to endotoxin-treated and control dogs, the rate of disappearance of the hormone was the same. Thus, insulin degradation did not appear to be altered by endotoxin treatment. Pancreatitis was also eliminated as a cause for hyperinsulinism under these conditions. The marked hyperinsulinism following glucose in endotoxin shock was also present after resection of the small bowel and colon distal to the pancreatic duct or after resection of the alimentary tract from esophagus to anus. These findings rule out an intestinal insulin releasing factor as the cause of the observed hyperinsulinism. When experimentally induced pancreatic ischemia preceded the infusion of 50% glucose (without endotoxin administration), marked hyperinsulinism also occurred, despite stable hemodynamic parameters. Thus, it is postulated that alterations of pancreatic blood flow may sensitize the β cells to respond with an exaggerated glucose-induced IRI release. (Supported by NIH grant HL 16850.)

MAXIMAL OXYGEN CONSUMPTION IN COLOMBIAN AND U.S. LABORERS. G.B. Spurr, M.G. Maksud and M. Barac-Nieto*. Med. Coll. of Wisconsin, Univ. of Wisconsin-Milwaukee and Wood VA Ctr, Milwaukee, Wis., and Univ. del Valle, Cali, Colombia.

The purpose of this study was to compare maximal aerobic power in several populations of manual laborers in the U.S. and in Colombia, South America. Four Colombian populations (sugar cane cutters (N = 55) and loaders (N = 27), farm laborers (N = 18) and sedentary students (N = 20)) and two U.S. populations (migrant farm workers (N = 15) and civil service laborers (N = 20)) were studied. Per cent body fat was calculated from skinfolds. Maximal heart rates (f_H max), ventilation ($\dot{V}_E$ max) and oxygen uptake ($\dot{V}_{O_2}$ max) were determined by the Balke Treadmill Test. Fat percentage was highest in the group of U.S. civil service laborers (15.2%) and lowest in sugar cane loaders (9.9%). f_H max's were significantly lower in the cane cutters (182 beats/min.) and loaders (181 beats/min.) than in the other populations studied (190-198 beats/min.). $\dot{V}_E$ max's were generally similar (106-119 L/min.) in all groups. $\dot{V}_{O_2}$ max's were significantly higher in the Colombian populations of laborers (44-49 ml/kg·min^{-1}) than in the U.S. workers (39-41 ml/kg·min^{-1}) and Colombian students (38 ml/kg·min^{-1}). The lower f_H max of the sugar cane workers may reflect poor nutritional backgrounds. The higher $\dot{V}_{O_2}$ max values may reflect higher fitness levels demanded by the occupations and/or a selection process resulting from the strenuous labor requirements of sugar cane cutting and loading. (Supported in part by AID/CSD-2943.)

CORRELATION OF ACETYLCHOLINE CONCENTRATION WITH THE PERIOD OF THE HEART CYCLE. STAVINOHA, W.B.*, S.T. WEINTRAUB*, A.T. MODAK*, A.P. DEAM* AND L.J. O'BRIEN. The University of Texas Health Science Center at San Antonio and Medical Arts Clinic, Lubbock, Texas.
Acetylcholine is important in the regulation of the heart beat and is implicated in the automaticity of the heart. Proper study of the role of acetylcholine in the cardiac cycle demands rapid inactivation of heart enzymes at specific points in the cycle. The isolated turtle heart was used because of its facultative anaerobic nature and slow heart rate. This has now been achieved through the design, construction and use of a microwave irradiation instrument coupled with an EKG. Using this device, heart enzymes are inactivated within 200 msec at specific points in the cardiac cycle. After inactivation of the enzymes, acetylcholine concentrations were measured by pyrolysis-gas chromatography in the right and left auricles, ventricular base and apex at 28 points within the beat cycle. The acetylcholine levels in the ventricular base were remarkably consistent throughout the cardiac cycle (9.6±2.6nM/Gm). The right auricle showed the greatest variation in acetylcholine content during the beat cycle as seen from the range of acetylcholine content (11-43nM/Gm) followed by right auricle (7-27nM/Gm) and the ventricular apex (8-23nM/Gm). The acetylcholine concentration in the left auricle and the ventricle did not correlate with the heart rate. The concentration of endogenous acetylcholine in the right auricle correlated with the rate of the isolated spontaneously beating turtle heart. The lower the endogenous acetylcholine concentration in the right auricle the faster the rate of the heart.
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ONTOGENY OF SWINE ADIPOSE TISSUE LIPASES. D. G. Steffen* and H. J. Mersmann* (SPON: H. D. Johnson). Shell Development Company, Biological Sciences Research Center, Modesto, California 95352

Lipoprotein lipase (LPL) activity was assayed in a 10,000 x g infranate of fresh swine adipose tissue at pH 8.5 using radiolabeled triolein in the presence of albumin and gum arabic. Activity of LPL, expressed on a tissue basis, was low in newborn animals and increased 3-4 times during the next 14 days. A marked decline in LPL activity was evident at day 25 followed by recovery to previously elevated levels by day 45 and gradually diminishing activity in the older animals. Extrapolation of the data to a cell basis suggested significantly less LPL activity per cell at day 25 compared to younger and postweaning animals. Kinetic changes (Vmax) could partially explain the fluctuations in LPL activity of adipose tissue. Assay of adipose hormone-sensitive lipase (HSL) activity in a 1,200 x g infranate at pH 6.8 indicated low activity at birth which doubled at 2 days of age and then decreased at 14 days to the activity levels measured in newborn pigs. HSL activity again doubled and remained elevated at intermediate ages followed by a decline in activity at the oldest ages (150 days). A similar developmental pattern emerged when HSL activity was expressed on a cell basis.

EFFECTS OF PROPYLTHIOURACIL INDUCED HYPOTHYROIDISM ON CIRCADIAN RHYTHM OF THYROID ACTIVITY, P. Stein* Dept. of Physiology, SUNY College at New Paltz, New Paltz, N.Y., 12561 (SPON: S. Kraus, Brooklyn College of Pharmacy, Brooklyn, N.Y.)

The purpose of this research was to observe the effect of propylthiouracil induced hypothroidism on a circadian rhythm of locomotor activity and actual metabolic rate in male albino rats. Carworth CFE strain rats, allowed to consume food and water ad liberatum were subjected to a 12:12 L:D cycle and at 0900, 1400, and 1900 hrs. during the 0645:1845 hrs. L:D cycle, the metabolic rate was measured by means of a water-monameter type respirometer and the oxygen consumption recorded as liters of oxygen consumed per square centimeter of rat per hour. The activity was recorded by the use of an activity board and expressed as the number of times both hind feet crossed a line per 5 minute time interval. These conditions were maintained and measurements taken 6 weeks prior to the initiation of the experimental period to allow the rats to entrain their rhythmic functions to the environmental conditions. This procedure was followed for three weeks after the initiation of the experiment, at which time the experimental group received a propylthiouracil supplemented diet with the drug mixed in the food at a concentration of 0.2% of propylthiouracil per gram weight of food. After the initiation of the drug the experiment continued for three more weeks. The activity rate of the experimental group remained rhythmic, however, analysis of variance showed a significant difference at the 0.05 level existing between the 1900 hrs. control and experimental group activity rates. It would appear that the thyroid, acting through a neuroendocrine mechanism sensitive to environmental fluctuations, is responsible for the observed animal activity rhythm and metabolic rate rhythm.

TURBULENT BLOOD FLOW IN THE ASCENDING AORTA OF PATIENTS WITH NORMAL AND DISEASED AORTIC VALVES. Paul D. Stein and Hani N. Sabbah*, Univ. Oklahoma Med. College and V. A. Hosp., Okla. City, Okla. 73104

Turbulent blood flow may contribute to a variety of pathophysiological effects, including platelet deposition, intimal damage, augmented sickling, and cardiac murmurs. Because of its postulated importance, this study was undertaken to determine if turbulent flow does in fact occur in the human body. In 15 patients (7 normal, 7 aortic valvular disease, 1 prosthetic aortic valve), point velocity was measured in the ascending aorta with a hot-film anemometer probe (frequency response 200 kHz). In one normal patient with a high cardiac output, definite turbulence occurred above the aortic valve during peak flow which corresponded to a peak Reynolds number of 10,000. In the other six normal subjects (peak Reynolds numbers of 5,700 to 8,900), flow was highly disturbed during peak flow. Each of the patients with aortic valvular disease and the patient with a prosthetic aortic valve showed definite turbulent flow during nearly the entire period of ejection with Fourier components of frequency of significant magnitude to 320 Hz (the maximum frequency component we could evaluate with the equipment available). The turbulence energy density was higher in patients with abnormal valves (3.2 to 14.6 ergs/cm^3), than in normal subjects (.6 to 2.9 ergs/cm^3). In patients with aortic stenosis, turbulence was observed throughout the ascending aorta and in the innominate artery. In others, the turbulence dissipated more proximally. These results indicate that turbulent flow can occur in the ascending aorta of patients with normal cardiac function; and it occurs routinely in the ascending aorta of patients with abnormal aortic valves.

PEPTIDE REGULATION OF A DECAPOD AUXILLIARY HEART.
A. Steinacker*(SPON: S. M. Highstein), Department of Neuroscience, Albert Einstein College of Medicine, Bronx, New York 10461.

Many decapod crustaceans have an auxilliary heart which functions to maintain the blood pressure of the cerebral nervous system. Application of pericardial peptides to the system produces an increase in the output frequency of the four motor neurons which control the heart. In addition the peptides appear to have a direct effect on the muscle or neuromuscular junction when these are isolated from the ganglion. When the nerves are stimulated electrically with a bursting pattern which will produce contractile beating of the heart and the pericardial peptides applied the overall level of tension increases and the Δ t or tension swing of each individual beat is increased. This results in a much more effective heart function as reflected in an increased pulse pressure. This peptide action is of long duration and does not appear to significantly affect the excitatory junction potentials, rather the action appears to be a direct one in the muscle membrane. Input resistances and specific ionic conductances are currently under investigation.

RELEASE AND REACCUMULATION OF CA-45 IN SKINNED MUSCLE FIBERS.
E.W. Stephenson. NIAMDD, Bethesda, Md. 20014

In skinned fibers from frog skeletal muscle, sudden exposure to high chloride (Cl) can cause large force transients, attributed to net Ca release from the sarcoplasmic reticulum (SR) to the myofilament space (MFS). The response varies with the (Mg^{++}) and the Cl gradient between MFS and internal membrane system (Stephenson and Podolsky, Fed. Proc. (1974) 33:1260). In the present experiments, Cl-induced Ca release was measured directly with Ca-45 and analyzed further. Segments of skinned fibers from semitendinosus muscles dissected in normal Ringer solution were mounted isometrically at 19-20°C and loaded with Ca-45 in a buffered solution containing 5mM ATP and 1 mM Mg. Subsequent Ca-45 release into various wash solutions could be expressed as a fraction of total Ca-45 in the segment initially. Exposure to Cl solution (1 mM Mg) caused rapid force development and net loss of 0.27 initial Ca-45, if released tracer was trapped quickly by 1 mM EGTA. When the Cl force transient was allowed to go to completion before trapping MFS Ca-45, net loss was only 0.17; thus Ca-45 was reaccumulated even in 1 mM Mg. When Mg was increased from 1 to 3 mM just after release, subsequent Ca-45 diffusion into the bath decreased significantly; thus Mg stimulated reaccumulation of released Ca-45, in accord with indirect evidence that Mg acts on net release mainly by promoting SR Ca uptake. When EGTA was present during exposure to Cl, Ca-45 release was blocked; therefore, Cl-induced Ca release is Ca-dependent under these experimental conditions (small Cl gradient, low Mg). The Ca requirement under other conditions remains to be determined.

BEHAVIORAL MODULATION OF THE BAROREFLEX. R.B. Stephenson*, O.A. Smith and A.M. Scher. Dept. Physiology & Biophysics, Regional Primate Res. Center, Univ. of Washington, Seattle, Washington 98195

The heart rate response to sinusoidal changes in arterial blood pressure was studied in baboons during four behaviors: sleep, lever pressing for food reinforcement, eating, and mild dynamic leg exercise reinforced by shock avoidance. An indwelling hydraulic cuff on the descending aorta was cyclically inflated to drive systolic blood pressure sinusoidally at frequencies between 0.032 Hz and 0.18 Hz with peak amplitudes of 6-18 mm Hg. An aortic arch cannula allowed measurement of blood pressure and heart rate. At all frequencies the change in heart interval per unit change in systolic blood pressure was distinctly greater during sleep than exercise. Lever pressing and eating were characterized by intermediate reflex sensitivity values. The use of heart rate rather than heart interval in calculating sensitivity changed the observed relations only in that sleep matched lever pressing more closely. Blood pressure and heart rate were markedly elevated during exercise, but diminished reflex sensitivity during exercise persisted in two baboons when systolic blood pressure was lowered to non-exercising levels by tightening a cuff around the inferior vena cava. For all behaviors, heart interval changes lagged sinusoidal pressure changes by a phase angle which increased with frequency. When this phase relation was expressed as a time lag, exercise was characterized by a long lag compared to the other behaviors, suggesting a relative dominance of sympathetic (slow compared to vagal) control of heart rate in exercise. These data support the hypothesis of a functional, behavioral modulation of the baroreflex.

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CARDIOVASCULAR RESPONSES OF THE RHESUS MONKEY TO PROGRESSIVE HYPERTHERMIA. A. Sternberg*, R. West*, and E.T. Angelakos (SPON: E.A. Reed) Dept. of Physiology & Biophysics, Hahnemann Medical College, Philadelphia, PA 19102

Anesthetized male monkeys (M. Mulatta) were heated progressively from 37° to 44° C which was the mean terminal temperature. Rectal temperature (TR), systolic and diastolic arterial pressure (AP), left ventricular pressure (LVP), dP/dt, heart rate (HR), ECG, respiration rate (RR), central venous pressure (CVP), arterial pO_2, pCO_2, pH and hematocrit (Hct) were determined every 0.5° C. Plasma catecholamines (CAs) were determined at 37° C and 42.5 C. Between 37 to 41° C, there was an increase in HR (30%), RR (76%), LVP (12%) and dP/dt (57%); AP averaged 153/80 mmHg; arterial pO_2 and pCO_2 both declined by 20% while pH became more alkalotic (7.41 to 7.49); CVP and Hct did not change significantly. In the critical period (41 to 44° C), there were pronounced respiratory difficulties (Chayne-Stoke's breathing) combined with a progressive decline in RR, HR, LVP, dP/dt and AP. Arterial pO_2 and pCO_2 declined further at 44° C to 61 and 21 mmHg respectively. Animals became progressively hypotensive (50/23 mmHg) and died in respiratory arrest or in ventricular fibrillation secondary to respiratory difficulties. Plasma CAs rose significantly (0.32 µg/l to 1.36 µg/l) but not to levels indicating expected sympathico-adrenomedullary response to hypotension. It is concluded that effects on the CNS respiratory center play a dominant role in death due to progressive hyperthermia. (Supported by ONR contract N00014-72-A-0317-0002).

THE RESPONSES OF THE PASSIVE AND ACTIVE TRANSPORT PATHWAYS IN THE FROG BLADDER TO STRETCH. D.F. Stiffler, K.L. Thornburg and R.E. Swanson. Dept. Physiol, UOHSC School of Medicine, Portland, OR. 97201

Frog urinary hemi-bladders, mounted as flat sheets (3 cm^2) on vertical chambers, were gently stretched by a pressure difference of +1 cm H_2O applied to the mucosal fluid (physiological stretch—PS) or serosal fluid (nonphysiological stretch—NPS). Steady state changes (stretch - control) in potential difference—PD, resistance—R, urea permeability—P_u, net volume flux—J_v, and short circuit current—SSC, are tabulated below. Prestretch control values (in PS and NPS series, respectively) were: PD, 34 mV and 38 mV; R, 572 Ω (1700 Ω-cm^2) and 604 Ω (1740 Ω-cm^2). After PS, PD and R returned to the prestretch control values, in contrast to post-NPS in which PD and R failed to return to the prestretch values. PS caused a 10% increase in SCC (winter animals only); P_u and J_v were unaffected. NPS caused a 20% decrease in SCC, and striking increases in P_u and J_v. Electronmicrographs revealed that the intercellular spaces were widely dilated in bladders fixed during NPS, but were nearly normal in bladders fixed during PS. Tight junctions appeared normal in both PS and NPS preparations. Also, NPS caused the submucosal elements to separate from the epithelial layer. We postulate that smooth muscle and/or connective tissue helps to maintain the structural and functional integrity of the intact bladder when distended by urine.

	ΔPD mV	ΔR Ω	ΔP_u %	ΔJ_v %	ΔSCC %
PS	+ 2.5	0	0	0	+10
NPS	-25	-404	+3000	+2500	-20

Supported by grants from the Medical Research Foundation of Oregon and NIH Training Grant 5 T01 GM00538.

EFFECTS OF HIPPOCAMPAL STIMULATION ON RETENTION OF ^{3}H-HYDROCORTISONE IN THE HYPOTHALAMUS. Rex D. Stith and R.J. Person*. Dept. Physiology and Biophysics, Univ. Okla. Health Sciences Center, Oklahoma City, OK 73104.

The dorsal hippocampus of adrenalectomized, anesthetized cats(groupI) was stimulated for 10 sec. by rectangular constant current pulses(0.1 msec. duration, 100 Hz, and 250 μA) followed by a 50 sec. period of no stimulation, beginning 30 min. prior to and ending 30 min. after adminis tration of 100 uCi(.0068 mg/mCi) of ^{3}H-hydrocortisone into a lateral ventricle. Sixty min after administration of radioactivity, the hypothalamus was excised, homogenized, and cytosol(C) and nuclear extract(NE) analyzed for radioactivity and protein content. Control animals(groupII) were identically treated, but sham stimulated. The cpm/mg protein appea ring in C of group II(49,842±6,015) was considerably less than that from group I(76,401±9,953). The bound fraction of radioactivity in hypothala mic C of group I was greater than that of group II, 6,750±1,762 cpm/mg vs. 3,620±737, respectively. The same is also true of the protein bound fraction in NE of group I, 2,029±490 cpm/mg, and group II, 1,215±112. Whereas hippocampal stimulation had no effect on the ratio of C cpm/mg to total homogenate(H) cpm/mg, the ratio of NE/H was significantly depre ssed in the stimulated group, .415±.045, compared to controls, 1.238±.27. Also, the percent of cpm/mg protein in C appearing in NE was also signi ficantly less in group I, 12.5±2.0, than in group II,24.6±4.2. There was no detectable difference between the two groups in the ratio of bound to free radioactivity of C. The most significant difference was in the ratio of bound to free in NE, .223±.048(group I) vs. .082±.011 (group II). Hippocampal stimulation appeared to increase the proportion of bound ^{3}H-hydrocortisone in hypothalamic nuclei by a mechanism other than increased uptake into H or C.

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THE ROLE OF SKIN AND HYPOTHALAMIC TEMPERATURES IN THE REGULATION OF RESPIRATORY EVAPORATIVE HEAT LOSS IN THE RABBIT. John T. Stitt, J. B. Pierce Foundation Lab., Yale Univ. Sch. of Med., New Haven, Ct. 06519.

We have previously described a multiplicative interaction between skin temperature (T_{sk}) and hypothalamic temperature (T_{hy}) in the regulation of heat production in the rabbit. We have now examined the role of these temperatures in the control of respiratory evaporative heat loss (E_{res}). Four male New Zealand rabbits, previously implanted with hypothalamic thermodes, were exposed to ambient temperatures (T_a) of 20°, 29° and 39°C. At T_a=39°C, the animals were kept in thermal balance by a water perfused heat sink enclosing one ear. E_{res} was determined by wet and dry bulb hygrometry in an open-draw mask system. At each T_a, T_{hy} thermosensitivity (determined as the change in E_{res}/°C change in T_{hy}) was measured by observing changes in E_{res} during step displacements in T_{hy}. Each displacement lasted 15 min. and the changes in E_{res} were determined as the average of 10 readings taken one min. apart during the final 10 min. of the T_{hy} clamp. E_{res} was found to have a maximum value of 1.1 W/kg. and a minimum value of 0.3 W/kg. At T_a=20°C, the T_{hy} threshold for panting (TP) was 40.1°C and T_{hy} thermosensitivity (m) was 0.31 W/kg.°C, at T_a=29°C TP was lowered to 37°C and m was reduced to 0.14 W/kg.°C and at T_a=39°C TP was lowered to 21°C and m to 0.04 W/kg.°C The control of E_{res} by T_{hy} and T_{sk} can be described by the equation:

$$E_{res} = 1.1 - 0.12(T_{sk} - 39.7)(T_{hy} - 43.0) \geq 0.3 \text{ W/kg.°C.}$$

This equation is qualitatively similar to that describing thermogenesis in the rabbit, in that increases in T_{sk} reduce T_{hy} thermosensitivity. These results raise the possibility that regulation of both heat production and heat loss is a continuum originating from a single CNS controller whose major inputs are T_{sk} and T_{hy}.

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ION TRANSPORT ACROSS THE RAT COLON. David P. Stoebel* and Andrew M. Goldner. Dept. of Human Physiol., Univ. of Calif. Med. Sch., Davis, Calif. 95616

The unidirectional fluxes of sodium and chloride were measured across the in vitro rat descending colon under short circuited conditions. The fluxes from mucosa to serosa ($J_{m\to s}$) and serosa to mucosa ($J_{s\to m}$) as well as the net fluxes (Jnet) and short circuit current (Jscc) are as follows.

$\mu Eq/hr/cm^2$

Buffer	$J^{Na}_{m\to s}$	$J^{Na}_{s\to m}$	J^{Na}_{net}	$J^{Cl}_{m\to s}$	$J^{Cl}_{s\to m}$	J^{Cl}_{net}	Jscc
Ringers	10.0±0.7	6.3±0.3	3.6±0.5	16.1±0.4	12.6±0.5	3.6±0.6	0.7±0.1
Cl^- Free	6.9±0.3	6.3±0.3	0.7±0.3	-	-	-	1.1±0.1
Na^+ Free	-	-	-	10.6±0.5	9.2±0.3	1.4±0.4	0.1±0.1
HCO_3^- Free	9.2±0.6	5.8±1.0	3.6±0.9	13.9±1.4	13.8±1.2	0.1±0.2	0.9±0.1
K^+ Free	11.7±0.8	8.9±0.5	2.8±0.8	14.8±0.8	10.7±0.5	4.1±1.0	0.8±0.1

The following conclusions can be drawn from these results. 1) Net sodium and chloride fluxes are at least partially coupled. 2) Sodium is required for the maintenance of a short circuit current. 3) Under none of the conditions tested do the sum of the unidirectional fluxes of sodium and chloride equal the short circuit current. 4) Approximately 80% of the net sodium flux is coupled to chloride flux. 5) The net chloride flux seems to be dependent on the presence of bicarbonate. 6) Removal of potassium has little or no effect on the net transport of either sodium, chloride or short circuit current. With the exception of the bicarbonate free data, these results are qualitatively similar to those obtain by Binder and Rawlins (Am. J. Physiol. 1973. 225:1232).

ABSORPTION & PROTEOLYSIS OF CHOLERAGEN IN JEJUNUM. Donald R. Strombeck, Dept. of Med., Sch. Vet. Med., U. of Calif., Davis, CA.95616.
The fate of Vibrio cholerae enterotoxin is unknown after it binds to the mucosal surface and stimulates secretion. The toxin is resistant to proteolysis by pancreatic enzymes. The purpose of this study was to label choleragen with ^{14}C and investigate its fate in loops of rat jejunum. ^{14}C choleragen (40 µg in a 12 cm loop) stimulated the secretion of 4.87 g fluid/g intestine/6 h in conventional and 4.96 g fluid/g intestine/6 h in germfree rats. The addition of protamine (P), aprotinin (A) or soybean trypsin inhibitor (SBTI) did not alter this rate of secretion. ^{14}C choleragen (40 µg) mixed with one mg mixed bovine brain gangliosides (G) or one mg gangliosides with 9 mg cerebrosides (GC) resulted in no fluid production. Heat inactivated ^{14}C choleragen (HIC) resulted in 0.61 g fluid/g intestine/6 h. At the end of 6 h the amount of ^{14}C recovered from the loops (tissue and fluid) was for choleragen, 70% in conventional and 68% in germfree; choleragen +A, 88%; choleragen + SBTI, 72%; choleragen + protamine, 84%; choleragen + G, 85%; choleragen + GC, 89%; heated choleragen (HIC), 39%; HIC + A, 62% and HIC + G, 53%. Incubation of mucosal cell homogenates and lysosomal preparations with ^{14}C choleragen at pH 7 for 4 hr resulted in a release of 2.6% of the label as TCA-soluble. At pH 4.5, 25% of the label was present as TCA-soluble. Proteolysis was not inhibited by P, A or SBTI but inhibited 50% by G. When HIC was incubated in either pH 4.5 or 7 buffer with cell proteases 25% of the label was TCA-soluble. Conclusions are ^{14}C choleragen is absorbed into mucosal cells, a process in which: (1) other small basic molecules (P and A) compete and (2) ganglioside binding to choleragen interferes. ^{14}C choleragen is degraded by acid proteases only, while subunits of choleragen can be degraded by neutral proteases.

β-BUNGAROTOXIN IS A POTENT PHOSPHOLIPASE A_2

By Peter N. Strong*, Regis B. Kelly* and Jon Goerke
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β-Bungarotoxin was purified according to our own published procedures, followed by CM-Sephadex and CM-cellulose ion exchange chromatography. The cellulose column yielded 2 peaks, the first of which (89% of total protein) was neuro-toxic to mice at 0.1 µg/g mouse and exhibited a phospholipase A_2 (PLA_2) activity which closely followed the A_{280} elution profile. The minor peak was toxic at 0.4 µg/g but possessed no phospholipase activity. We studied enzymatic activity in a pH-stat over a range in which rate was proportional to toxin concentration, using soya phosphatidylcholine (soya PC) as substrate with a two-fold molar excess of deoxycholate, 0.1 M NaCl and 0.01M $CaCl_2$ at pH 8.0.

Ca was required for activity, and hydrolysis of PC was inhibited at pH 4 or by the addition of EDTA, Ba^{2+} or Sr^{2+}. We used egg PC specifically tritiated in the 2-position fatty acid as a substrate and thin layer chromatography to establish that the products of hydrolysis were 2-lysophosphatidylcholine and fatty acid, thus confirming PLA_2 action. Enzymatic activity (µEequiv fatty acid liberated/min/mg protein) was twice that of a heat treated preparation of Crotalus adamanteus venom.

The implications of PLA_2 activity for the neurotoxic mechanism of β-bungarotoxin will be discussed.

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HEPARIN & SULFATED MUCOPOLYSACCHARIDES - A MICROSYSTEM FOR QUANTITATIVE DIFFERENTIATION. T.K. Sue*, N. McDuffie* and L.B. Jaques, Dept. of Physiology, University of Saskatchewan, Saskatoon, Canada S7N OWO.

Tissues are digested with pronase and precipitated with organic solvents to give a crude polysaccharide fraction. This is subjected to electrophoresis on agarose gel, fixed with Cetavlon (hexadecyltrimethylammonium bromide), stained with Toluidine Blue. Optical density of the spots produced is measured and expressed in equivalent units of heparin to give quantitative values for total sulfated mucopolysaccharide (SMPS). Differentiation is accomplished by color and migration in agarose with different buffers (barbital, pH 8.6, ethylenediamine, pH 8.5, acetic acid-Li, pH 3.0), treatment of aliquots with enzymes, (heparinase, heparitinase, chondroitinases), critical electrolyte concentration (molarity of NaCl in fixation with cetylpyridinium chloride). Optical density of electrophoretic spots is determined on each treatment. The resulting values for each fraction in units are converted to µgs. with factors 6.5 for heparin, 13.0 for chondroitin, dermatan, heparitin sulfates to obtain % (weight) composition of SMPS and concentration in the tissue sample for each SMPS. Molecular weights for chondroitin, dermatan, heparitin sulfates are determined on acrylamide gel electrophoresis and molecular weight distribution pattern for heparins demonstrated by isoelectric focusing. A portion of the fresh tissue sample is subjected to histological examination for mast cells and another portion to immediate extraction with 2.0 M potassium acetate to determine "free" heparin by electrophoresis. Examples are shown of examination of SMPS for rabbit white blood cells, dog mastocytoma, rat endothelium on heparin administration. The procedure is sensitive, reproducible, flexible, adaptable to rapid tissue examination, giving significant new information.
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NONLINEAR COUPLING OF WAVE AND PULSE ACTIVITY IN A NEURAL MASS. Dan Sunday and Walter J. Freeman. Dept. of Physiol.-Anat., Univ. California, Berkeley 94720.

The gross EEG and extracellular unit pulse activity of neurons, granule and mitral-tufted cells resp., in the olfactory bulbs of rabbits were measured simultaneously with a tungsten microelectrode. Data were amplified, clipped and digitalized in 1 msec. time bins. 10 to 100 sequential 1 sec. samples were read onto magnetic tape for further processing.

A table for the normalized pulse probability conditional on the occurrence of EEG amplitude value (-3_σ to 3_σ) at a variable lag time (-25 to +25 msec) was constructed. This table displays oscillatory pulse density waves at the frequency of burst activity in the EEG (40 Hz), occurring with a phase lead of 1/4 cycle. This had been predicted on the basis of previous linear analysis of olfactory dynamics. From this, it was inferred that sections of the table obtained by fixing the time variable at extremums of the probability wave provide data curves representing the nonlinear lumped wave-pulse conversions of the neural mass.

Previous analysis has shown this nonlinearity to be a sigmoid bilateral saturation curve asymetric about the mean EEG, and with an upper asymptote at 3 times the mean background activity. A more detailed analysis of the numerical derivatives has demonstrated multimodality, a positively offset dominant operating point at 1/2 to 1_σ, and functional dependence of the curve's parameters on the level of background activity. Theoretical reconstructions and implications for the dynamics of the resulting nonlinear system are to be discussed. NINCDS# F32 NS 05029-01, and MH 06686.

POSSIBLE SPINAL CORD INVOLVEMENT IN CHICKEN MUSCULAR DYSTROPHY A. K. Susheela*, M. W. Seraydarian and B. C. Abbott, Dept. Biological Sci., University So. California, L. A., CA 90007 and School of Nursing, U. C. L. A., L. A., CA 90024.

In an attempt to understand the pathogenesis of muscular dystrophy, this laboratory has been engaged in the study of the two major flight muscles: Anterior latissimus dorsi (ALD) and Posterior latissimus dorsi (PLD) of chicken. Both muscles receive their innervation from the same segment of the spinal cord, however, only the PLD is involved in the disease process. The present report deals specifically with the possible involvement of the spinal cord in the chicken model. The brachial segment of the spinal cord which innervates the musculature of the trunk and upper extremity was studied. Normal and dystrophic chicken, line 200 and 307 respectively, Davis, Calif., were perfused with Karnovsky's fixative, sections of the spinal cord, 5 μm thick were stained with Thionin for Nissl substance. Motor neurons of the lateral and medial columns of the anterior horn were counted and diameter measurements were made. The results obtained indicate a significant increase in the neuron population of the dystrophic animal compared to normal. Differences between the normal and dystrophic animals do not seem to be age dependent. In order to evaluate the functional integrity of the motor neuron, choline acetyltransferase activity is used as a marker. It is impossible at present to state whether the structural changes observed in the spinal cord are primary or compensatory in nature.
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EFFECTS OF INSPIRED CO_2 ON CO_2 REGULATION IN MAN. G. D. Swanson and J. W. Bellville*, Depts. of Anesthesiology and System Science, University of California, Los Angeles, CA 90024.

Inspired CO_2 may degrade CO_2 regulation in man. To assess this, the lung CO_2 clearance slope defined by $\Delta P_{ET}CO_2/\Delta \dot{V}_E$ was determined using a voluntary hyperventilation maneuver. The subject was given visual and audio cues so that he could voluntarily hyperventilate his inspired tidal volume to follow a 2 cpm sinusoidal pattern ($\dot{V}_E \cong 24 + 3 \sin 2\pi 2t$ ℓ/min). Constant inspired CO_2 or constant cycle-ergometer exercise was added so that $P_{ET}CO_2$ remained at the resting value. $\Delta P_{ET}CO_2/\dot{V}_E$ was diminished during inspired CO_2 loading as compared to tissue loading via exercise. Further studies in spontaneously breathing subjects exercising with a work rate varying sinusoidally at .2 cpm and constant pedaling frequency indicate that the addition of constant inspired CO_2 degrades the normal regulation of arterial CO_2 during moderate work rates. We conclude that inspired CO_2 reduces the lung CO_2 clearance slope and that during moderate exercise and inspired CO_2 load, ventilation does not compensate sufficiently to maintain CO_2 regulation. These results are consistent with a feed forward/feedback regulation structure for exercise where the feed forward component cannot sense a change in lung CO_2 clearance. Alternatively, these results are consistent with a feedback regulation structure where the effectiveness of the arterial CO_2 sensors is degraded by the addition of inspired CO_2.
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RELATIONSHIPS BETWEEN DEPLETION AND RELEASE OF IMMUNOREACTIVE (IR) RAT PROLACTIN (PRL). Karen C. Swearingen*, C.S. Nicoll and F. Mena*, Biology Dept., Mills College, Oakland, Cal., Dept. of Physiol-Anat., Univ. of Calif., Berkeley and Inst. Invest. Biomed., Nat'l. Univ., D. F. Mexico.

Changes in serum and pituitary (AP) PRL were measured by RIA in lactating rats after different suckling periods. Assuming that depletion of IR-PRL from AP represents secretion, expected serum levels of PRL can be calculated using AP depletion data, serum $t_{\frac{1}{2}}$ and volume of distribution. A "standardized" rat with 10 mg AP and 10 ml volume of PRL distribution was used for these calculations. In two experiments, AP level of IR-PRL decreased by 50% in 10 min. Serum levels of IR-PRL observed (OL) were much lower than expected levels (EL) in both experiments using $t_{\frac{1}{2}}$ values of 1-5 min. The amount of IR-PRL secreted during 0-10 min., estimated from OL, ranged from 8.5% ($t_{\frac{1}{2}}$ = 5 min.) to 26% ($t_{\frac{1}{2}}$ = 1 min.) of amount depleted. Thus, all of the IR-PRL that depleted between 0 and 10 min. was not released as RIA-detectable hormone. In both exp'ts. AP level of IR-PRL increased between 10 & 15 min. then declined slowly. Comparison of EL with OL by 30 min. (ignoring initial rapid depletion between 0-10 min.) and calculation of amount secreted based on serum levels showed that slow depletion corresponded to OL with $t_{\frac{1}{2}}$ of 5 min. in one exp't., and with $t_{\frac{1}{2}}$ of 2 min. in 2nd exp't. These results indicate that the detectability of AP-PRL by the RIA may change. This change may be conformational. (Supported by NIH grant AM-13605.)

SYSTEMIC ARTERIAL MECHANICS DURING HYPOXIC HYPOXIA (HH) AND CARBON MONOXIDE HYPOXIA (COH). J.T. Sylvester*, R.D. Gilbert* and R.J. Traystman* (SPON: S. Permutt), Dept. of Environmental Medicine, Johns Hopkins University, Baltimore, Maryland 21205.

When cardiac output ($\dot{Q}$) was suddenly reduced to zero by means of a cardiac by-pass preparation in 9 dogs exposed to HH and 10 dogs exposed to COH, mean arterial pressure (Pa) fell as a single exponential function of time to a "closing pressure (Pc)." In our analysis, we assume that Pc equals the surrounding pressure of vessels acting as Starling resistors at a site downstream from a constant compliance discharging across constant parallel resistances. The resistance of the vasculature upstream from this site, Ra, therefore equals $(Pa-Pc)/\dot{Q}$. During normoxia (CaO_2 = 16 vol%), Pa = 98 mm Hg, Pc = 25 mm Hg and Ra = 49 mm Hg·min·L^{-1}. The arterial time constant, Ta, was 2.52 sec, and compliance, Ca, Ta/Ra was 0.93 ml/mm Hg. During hypoxia (CaO_2 = 6 vol%), Pa and Pc increased in the HH group (14 and 5 mm Hg) and decreased in the COH group (-22 and -5 mm Hg). HH and COH caused equal decreases in Ra (-15 mm Hg·min·L^{-1}) and Ta (-1.03 sec). Ca did not change in either group. The changes in Pc indicate that vasomotor tone at the Starling resistor was increased by HH and decreased by COH. Since HH and COH caused equal decreases in arterial resistance upstream from this point while arterial compliances were constant, the change in vasomotor tone at the Starling resistor constitutes the major difference in the effects of the two types of hypoxia on the systemic arterial bed. We attribute this difference to activation of the sympathetic nervous system by carotid chemoreceptor stimulation that occurred with HH, but not with COH. (Supported by PHS Grants HL-10342, HL-05453.)

REDUCTION OF EXERCISE DILATION BY THEOPHYLLINE. H. Tabaie, J. Scott, and F. Haddy, Dept. of Physiology, Michigan State University, E. Lansing, MI 48824

Biochemical and bioassay studies suggest that adenosine and/or one or more of the adenine nucleotides participate in exercise hyperemia. To further test this hypothesis we have examined the effect of theophylline (Theo), a competative inhibitor of the dilation produced by these compounds, on exercise dilation in the denervated collateral-free gracilis muscle of the anesthetized dog perfused at constant flow (N=11). Blood flow to the gracilis was set such that perfusion pressure approximated arterial pressure. Initially, gracilis vascular responses to local injections of adenosine (.25,.5,1,5 and 10γ all in 0.1 ml) and acetylcholine (0.5 and 1γ in 0.1 ml) were determined. The vascular responses to 2 levels of exercise were then obtained by stimulating the gracilis nerve at 6v, 1.6 msec, 1 psec for 30 sec and at 6v, 1.6 msec, 6 psec for 30 sec. Theo was then infused into the gracilis arterial supply at a rate that produced a Theo blood level of ∿ 10^{-3}M. This lowered resistance. Norepinephrine was therefore infused I.A. at a rate that returned resistance to the control level. At this time, the response to 10γ adenosine was blocked but the response to Ach was still present. The 2 levels of nerve stimulation were then repeated and the responses compared to control values (pre-Theo infusion).

Nerve stimulation	S, mm Hg/sec		M, mm Hg		D, sec		A, cm^2	
	Control	Theo	Control	Theo	Control	Theo	Control	Theo
6v, 1.6 msec, 1 psec	3.0	2.6	45	23*	260	108*	2.3	0.9*
6v, 1.6 msec, 6 psec	6.5	3.9*	74	51*	835	274*	14.9	3.2*

S=slope of initial fall in pressure; M=max. fall in pressure; D=duration of response; A=area of response; *$p<0.005$ compared to control value. Thus exercise dilation at constant flow seems to be partly mediated by adenosine and/or the adenine nucleotides.

THE ROLE OF HYPOTHALAMIC RECEPTORS IN THE CONTROL OF FREE FATTY ACID AND INSULIN RELEASE. Gerald J. Taborsky, Jr.* and Richard N. Bergman. Dept. of Biomedical Engineering, University of Southern California, Los Angeles, CA 90007

This study was performed to test the hypotheses that 1) glucose receptors in the region of the third cerebral ventricle can trigger a decrease in plasma free fatty acids (FFA), and that 2) insulin sensitive receptors in the same area can stimulate pancreatic insulin secretion. The role of medial hypothalamic receptors in triggering changes of plasma FFA and insulin was studied in unanesthetized dogs using third cerebral ventricular infusions. Dogs receiving the maximum tolerable rate of intraventricular (IVT) glucose infusion (0.18-0.20 mg/kg/min) showed no significant change in plasma FFA, insulin or glucose. However, dogs receiving IVT insulin (6.9-7.7 mU/kg/min) showed a drop in FFA (Δ-147 μEq/L, $p < 0.05$, N=4) always correlated with a rise in insulin (Δ+23 μU/ml, $p < 0.025$, N=4) with no change in plasma glucose. In each experiment, at least one spike in plasma insulin occurred during the first 30 minutes of the infusion (peak mean = 114 μU/ml; peak range = 45-149 μU/ml). These rapid transients in plasma insulin suggest a neurally mediated stimulation of pancreatic insulin secretion rather than a leakage of the infusate from the cerebrospinal fluid into the systemic circulation.

CONCLUSION: Brain tissue in the region of the third ventricle does not contain glucose receptors that trigger a decrease in plasma FFA, however it does contain insulin sensitive receptors capable of stimulating pancreatic insulin secretion which in turn suppresses lipolysis.

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CANINE TISSUE THROMBOPLASTINS. Y. Takeda and H. Gonmori*, Dept. Medicine, Univ. Colo. Med. Ctr., Denver, Colo. 80220

Electrophoretically pure protein moieties of canine tissue thromboplastins(TTPs) from brain(BTTP), lung(LTTP), arteries(ATTP) and veins (VTTP) were prepared and their properties were determined. The maximum specific activity was 1395 units per mg BTTP, 1130 units per mg LTTP, 630 units per mg VTTP and 435 units per mg ATTP. The amino acid contents of the protein moieties of LTTP, ATTP and VTTP were closely similar but that of BTTP was significantly different. The Ouchterlony analysis showed that BTTP did not react at all with the antibody against VTTP, but that 3 other TTPs did and showed the reaction of complete identity. Then, the reactivity of I-125-TTPs with the anti-VTTP antibody was studied. The results showed that 0.8 % of I-125-BTTP, 10.2 % of I-125-LTTP, 19.4 % of I-125-VTTP and 5.9 % of I-125-ATTP added were bound to the antibody in two hrs. Next, the molecular weight of each TTP was determined by Sephadex G-200 filtration, which was 80,000 for BTTP, 113,000 for LTTP, 62,000 for ATTP and 47,000 for VTTP. Finally, the in vivo behavior of each I-125-TTP was studied. The plasma half-life averaged 8.1 hrs for I-125-BTTP, 14.6 hrs for I-125-LTTP, 7.4 hrs for I-125-ATTP and 24.3 hrs for I-125-VTTP. These results indicate that the protein moieties of canine TTPs from brain, lung, arteries and veins are closely similar in some aspects but dissimilar in others and that they are definitely not identical.

(Supported by grant HL-11686.)

PREDICTION OF NORMAL DOG POSTURAL RESPONSE FROM RESPONSES DUE TO OPTOKINETIC STIMULI AND TO ELIMINATION OF VISUAL FEEDBACK. Richard E. Talbott. Univ. Oregon Health Sciences Ctr., Portland, OR 97201.

A model of the postural control system of the dog was tested by using the model to predict the normal frequency response of a dog responding to perturbations of the support platform on which the dog stood. The model is in the form of a simple feedback system in which vision is explicitely represented as a major component of the feedback pathway. Hence the equation of the postural control system is:

$$H(\text{normal dog}) = \frac{H(\text{blindfolded dog})}{1 + H(\text{optokinetically driven dog})} \cdot$$

All of the terms in the equation were independently measured. The normal and blindfolded dog responses were obtained by placing the quietly standing dog upon a platform which could be moved in the forward-rearward direction. The position of the dog along that axis was used as the system response variable. The optokinetically driven response was obtained by placing the dog upon a stationary platform and moving a large array of vertically oriented stripes past the dog. All inputs were single sinusoids, and a Fourier analysis of the input and output data provided the means of establishing the system frequency response to the various conditions. The frequency response data were fitted by appropriate transfer functions, and these transfer functions were then used to check the validity of the model equation. The predicted fit was remarkably good considering the fact that many of the postural control system variables (1) are nonlinear functions of the sinusoidal input, and (2) are best described by non-minimum phase characteristics. (supported by NSF Grant GB-35416, NIH Grant NS-04744, NIH Grant 5-KO-4-NS-70021).

MODE OF STIMULATION BY ALDOSTERONE OF SODIUM EFFLUX IN BARNACLE MUSCLE FIBERS. Robert B. Tallitsch* & E. Edward Bittar (intr. by S.S. Chen). Dept. of Physiology, Univ. of Wisconsin, Madison, WI 53706.

Single muscle fibers from the barnacle Balanus nubilus are found to be sensitive to aldosterone following exposure of the barnacle in vivo to a large dose of the steroid. The response of the radiosodium efflux is always biphasic. First, aldosterone promptly releases sequestered or bound Na, an effect which is blocked by prior microinjection of spironolactone SC-14266. Evidence supporting the concept of 'release' is provided by experiments in which fibers injected with inactive saline (graded concentrations) show kinetic changes similar to those observed with aldosterone. Second, aldosterone following an average lag period of 68 mins (with a range of 25-110 mins) causes a transitory rise in the Na efflux in the order of 62.6±19.9% (n=7) (10^{-5}M-aldosterone). This membrane response is augmented by preinjecting these fibers with $[ATPMg]^{-2}$ e.g. a 0.5M-solution (i.e. an extra myoplasmic ATP concentration of 5×10^{-3}M) followed by external aldosterone (10^{-5}M) causes 220.1±15.7% stimulation (n=5). The magnitude of the response in ATP-enriched fibers is also dependent on external K & H, but not on Na, Ca or Mg. The response is completely abolished by prior microinjection of actinomycin D or spironolactone, and by prior application of ouabain followed by ethacrynic acid or by application of diphenylhydantoin. The delayed response in unenriched fibers is completely abolished by atractyloside, bongkrekic acid or oxythiamine. It is concluded that (i) the delayed response is due to increased activity of both membrane Na^+-K^+ ATPase and adenyl cyclase, and that the involved ATP comes from mitochondria, and (ii) these changes are attributable to RNA induction. (Supported by a grant from NSF).

MUCOSAL ARCHITECTURE OF THE CANINE EXTRAHEPATIC BILIARY TREE. M.F. Tansy, L.M. Salkin*, F.M. Kendall, D.L. Innes, and J.S. Martin*, Dept. of Physiol. and Biophys., Temple Univ. Hlth. Sci. Ctr., Philadelphia, Pennsylvania 19140

Low power scanning electron microscope (SEM) studies have revealed that the topography of the mucosa of the canine extrahepatic biliary tree is morphologically distinct depending upon the particular segment that is examined. The mucosal surface of the intramural common bile duct is characterized by prominent folds. The mucosa of the extramural portion is relatively smooth with numerous pit-like cavities. The mucosal surface of the hepatic duct contains numerous parallel grooves running along the long axis. In contrast the mucosal folds of the cystic duct tend to present an interlacement with the weave running at right angles to the long axis of the duct. High power SEM observations indicate that the surfaces of all of the mucosal cells of the extrahepatic ducts are covered with microvilli, but these structures appear to possess subtle variations in morphology according to the location of the cells within the tree. Furthermore ordinary light microscopic studies of cross-sections of these segments reveal a high density of surrounding smooth musculature in those regions where the mucosa tends to lay in folds. These morphological observations indicate that the mucosa of discrete portions of the extrahepatic biliary tree have a structure consistent with valvular function. Also the presence of microvilli on the epithelial cells of the entire extrahepatic biliary tree suggests that this mucosa may play a role in determining the ultimate composition of bile.

EFFECTS OF BARIUM ON ISOLATED MESENTERIC ARTERIAL RINGS AND THEIR RESPONSES TO NOREPINEPHRINE. Marshall Taxer* and Gordon Ross, UCLA School of Medicine, Los Angeles, Ca. 90024.

The effects of barium (Ba^{++}) on the responsiveness of isolated cat mesenteric arterial segments to norepinephrine (NE) were studied at 37°C and pH 7.4 in an oxygenated physiological salt solution containing: Trizma base, 5mM; NaCl, 130mM; KCl, 5mM; $MgCl_2$, 1.25mM; $CaCl_2$, 2.5mM; EDTA, 0.03mM; ascorbic acid, 0.012mM; and dextrose, 5.5mM. Ba^{++} produced dose dependent contractures. The threshold dose was 0.5mM, and the maximum effect was reached at 10.0mM. Maximum Ba^{++} contracture was approximately equal to the maximum NE effect, but whereas the NE response faded considerably over a five minute period, the Ba^{++} contracture was sustained for about forty-five minutes after which oscillations of tension with a periodicity of twenty minutes frequently developed. Subthreshold concentrations of Ba^{++} potentiated the NE response and delayed the onset and degree of fade. These effects were dose dependent over the range of 0.05 to 0.5mM Ba^{++}. Both Ba^{++} and NE produced contractions in vessels depolarized by a solution containing: Trizma base, 5mM; NaCl, 85mM; KCl, 50mM; $MgCl_2$, 1.25mM; $CaCl_2$, 2.5mM; EDTA, 0.03mM; ascorbic acid, 0.012mM; and dextrose, 5.5mM, but Ba^{++} failed to potentiate the NE response. These observations suggest that Ba^{++} potentiates the NE response mainly by an effect on the electrical component of activation.

(Supported by PHS, grant HL 18199.)

FRACTIONAL DISTRIBUTION OF CARDIAC OUTPUT TO THE BRAIN AND FLUID AND ELECTROLYTE CONTENT OF THE BRAIN OF THE HYPOTHERMIC HAMSTER. George E. Tempel* and X. J. Musacchia. Dept. of Physiol., and Dalton Research Center, Univ. of Missouri, Columbia, MO 65201.

Percent of cardiac output (CO) to the brain and brain swelling were examined, because of suggestions of eventual death due to failure of respiratory centers, and to cerebral edema. Hypothermia, rectal temperature (T_{re}) 7 and 11°C, was induced by a helium-cold method. Percent of CO to the brain was determined using I-131 antipyrine via a jugular cannula. Animals were sacrificed 30 sec after injection; activity of whole brain (B), cerebrum (C), cerebellum (CB), and brain stem (S) was measured. Swelling was examined as percent tissue water, and electrolytes by flame photometry. B received 1.39±0.33 % CO/g tissue in controls (T_{re} 37°C). Hamsters T_{re} 7 and 11°C for 18 hrs, were not different ($P>.05$) from controls; values were 1.38±0.33 and 1.11±0.14 % CO/g, respectively. C, CB and S likewise failed to show any change in percent of CO in hypothermia. After 24 and 48 hrs, at T_{re} 7°C, brain water content was 77.2±2.6 and 78.8±0.6%, respectively, and did not differ significantly ($P>.05$) from a control value of 77.7±0.5%. Neither Na^+ nor K^+ demonstrated a change from control values after periods of 0, 24 and 48 hrs of hypothermia ($P>.05$). Brain Na^+ concentration was 255.3±5.2 in T_{re} 37°C animals, 250.5±6.3 immediately upon reaching T_{re} 7°C, 262.2±20.1 after 24 hrs, and 257.4±3.6 μ eq/g dry wt after 48 hrs of hypothermia. K^+ content was 515.3±9.7, 527.3±7.5, 522.2±5.8, and 533.2±9.5 μ eq/g dry wt in control, 0 hrs, 24 hrs, and 48 hrs hypothermic animals, respectively. The data suggest: distribution of CO in hypothermic hamsters is unchanged, although CO is decreased, and cerebral edema does not limit survival. Supported by NASA NGL 26-004-021 S10 and Dalton Res. Ctr.)

EFFECTS OF EXERCISE TRAINING ON CORONARY BLOOD FLOW IN RATS. Ronald L. Terjung and Kim L. Spear.* Dept. of Physiology & Biophysics. University of Illinois, Urbana, 61801.

Coronary blood flow (CBF) was measured using labeled microspheres (15μ dia.) in sedentary and endurance trained rats during hypoxemic conditions designed to develop coronary dilatation (PaO_2 45-50 mmHg). Rats that were trained for 12-weeks (1 mph, 15% grade, 1 hr/d) had significantly greater CBF (4.59 ± .70 ml/min) than sedentary animals (2.59 ± .43). To evaluate whether the coronary circuit was maximally dilated, myocardial oxygen demands were increased during hypoxemia by elevating aortic pressure approximately 2-fold by methoxamine infusion. CBF was increased proportional to the increase in coronary perfusion (diastolic) pressure with the trained CBF again greater than the sedentary. Thus, coronary conductance was unchanged with methoxamine infusion and averaged 54% greater in the trained animals. It was, therefore, probable that hypoxemia itself was sufficient to cause maximal coronary dilatation. Although cardiac hypertrophy (17%) was apparent in the trained animals, this increase in perfused mass accounted for only 1/3 of the increase in total CBF. Thus, there was a greater CBF per unit mass of the myocardium in the trained rats. This increase in CBF probably reflects functional anatomic differences since the time for diastole was the same for the sedentary and trained groups. These data of CBF measured In Situ are consistent with previous studies suggesting that training increases the size of the coronary tree and myocardial vascularization.

(Supported by the Illinois Heart Association.)

DOCA HYPERTENSION IN YOUNG, UNINEPHRECTOMIZED MALE SWINE. J.M. Terris*, B. Gewertz*, J.W. Crudup*, P.J. Moore*, C.D. White*, E.L. Cohen*, J.C. Stanley*, and D.F. Bohr. Dept. Physiology, Univ. of Michigan, Ann Arbor, MI 48104.

Attempts to produce mineralocorticoid hypertension in experimental animals have been largely unsuccessful except in the rat. We have recently demonstrated that the uninephrectomized pig, following implantation of DOCA impregnated silicone rubber strips, will very rapidly develop hypertension on a diet of conventional pig chow (Purina) and tap water. Chester White and Yorkshire White boars, 8 to 12 weeks of age, are uninephrectomized, instrumented with an electromagnetic flowprobe on the ascending aorta for cardiac output measurements and indwelling catheters in the aorta and thoracic vena cava for measurement of pressures. After recovery from surgery, silicone rubber (Dow Corning) strips, containing a total of 100 mg/Kg of DOCA, are implanted intraperitoneally and subcutaneously under local anesthesia. Within 4 to 6 days arterial pressure rises, accompanied by a fall in plasma renin activity and plasma aldosterone concentration, marked polyuria and polydipsia, and hypokalemia. The hypertension has persisted for over 60 days following a single implantation. Work is currently being done to evaluate the participation of salt and water balance, cardiac output, and body fluid volumes (plasma volume, extracellular fluid volume, and total body water) in the initiation and maintenance of this type of hypertension. This work demonstrates that the pig may serve as a new model for the study of mineralocorticoid hypertension. (Supported by grant HL-03756 from NIH.)

STUDIES ON PURIFICATION OF HUMAN ANGIOTENSINOGEN. D.A. Tewksbury*, M.L. Dumas*, and M.R. Premeau* (SPON: E.D. Plotka). Marshfield Medical Foundation, Inc., Marshfield, Wisconsin 54449.

Angiotensinogen (A'n) is a plasma protein upon which the enzyme renin acts to release angiotensin I (AI). The results of a four step method for the purification of this protein from outdated blood bank plasma are given below. The first step is removal of albumin by affinity chromatography on blue dextran conjugated to sepharose followed by chromatography on DEAE-Sephadex at pH 8.0. The second through fourth steps are chromatography on hydroxylapatite at pH 6.8, chromatography on DE-52 at pH 6.5, and gel filtration on Sephadex G-100, respectively.

Step	Protein mg	A'n Total μg AI	A'n ng AI/mg protein	Purification Factor
plasma	10,000	300	30	1
1	276	246	890	30
2	37	221	5,900	197
3	11	37	3,400	113
4	7	18	2,600	87

The final product exhibits two closely spaced bands on polyacrylamide electrophoresis and on isoelectric focusing. This may represent polymorphism similar to that exhibited by other glycoproteins. From the second step on A'n readily loses its ability to yield AI upon reaction with renin. Although the cause of this is not known it could be due to a conformational change in the protein so as to make the bond that renin attacks unavailable or to a cleavage of the molecule with loss of the portion containing AI or to inhibition of renin.
(Supported by a grant from the Wisconsin Heart Association.)

PRODUCTION OF HYPERTENSION BY LOW-LEVEL CADMIUM FEEDING IN THE RAT Gurdarshan S. Thind and Mary H. Misuraca*, Cochran VA Hospital & Dept. of Medicine, Washington University, St. Louis, Missouri 63125

Three colonies of weanling Long-Evans female rats were housed in an environmentally controlled room with minimal airborne contamination. A low-cadmium (Cd) diet and deionized drinking water fortified with essential metals was fed to all rats ad libitum. The Cd-fed rats had 5 ppm cadmium added to the drinking water. Total body weights and indirect systolic blood pressures (BP) were determined every 3 months in 1, 2 or all rat colonies. There was no mortality or significant difference in the body weights of the control and Cd-fed rats. The BP was significantly higher in Cd-fed rats at 6 months, but did not show a progressive increase with continued Cd feeding.

Rats	Systolic BP (mm Hg), MEAN ± SEM				
	3 months	6 months	9 months	12 months	15 months
Control	90.3	94.3	81.3	99.3	94.0
	±2.3	±1.5	±3.9	±1.8	±1.9
	(42)	(124)	(41)	(85)	(71)
Cd-fed	91.5	102.3*	101.1*	105.0†	101.6**
	±2.7	±1.5	±3.9	±1.8	±2.1
	(36)	(132)	(47)	(91)	(82)

( ) = Number of rats; † P < .025; * P < .001; ** P < .01

It is concluded that low-level Cd exposure, not unlike that of an average American, results in mild but significant hypertension in the rat without other obvious ill-effects. This confirms the original observations of Schroeder & Vinton (Am J Physiol 202:515-518, 1962) and more recently, of Perry and Erlanger (J Lab Clin Med 83:541-547, 1974), that ingestion of trace amounts of cadmium produces hypertension in the rat.

IONIC SELECTIVITY OF THE SODIUM CHANNEL IN RABBIT TRABECULAE CARNEAE CORDIS. Stephen M. Thompson* and F.P.J. Diecke (SPON: J.D. Thomson). Dept. Physiol. and Biophys., Univ. of Iowa, Iowa City, IA and Dept. Physiol., New Jersey Medical School, Newark, NJ 07103

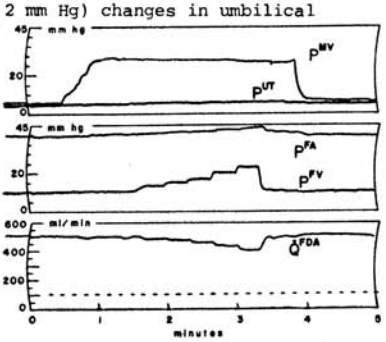
Current-voltage relations were investigated in small trabeculae carneae (dia.<80μ,length~2mm) from rabbit hearts using a double sucrose gap voltage clamp technique. Membrane currents were corrected for leakage and capacitative currents by the addition of alternate depolarizing and hyperpolarizing pulses. During the inward current the membrane acts as a pure Na-electrode with respect to external Na concentration. The inward current disappears when all external Na is replaced with an impermeant cation, but is not completely blocked by tetrodotoxin (2×10^{-5}M). The TTX insensitivity of this Na channel led to determination of its relative permeability to other cations. Changes in reversal potential resulting from isosmotic substitution of test cations for Na were used to compute permeability ratios using the GHK equation. Permeability ratios are significantly larger than those obtained for the node of Ranvier and frog skeletal muscle (Hille, 1971, 1972; Campbell, 1975), but the basic selectivity sequence is unchanged with the exceptions of hydroxylamine>Na; aminoguanidine>K.

P_{ion}/P_{Na}	Ion
1.26	Hydroxylamine
1	Na
.96	Li
.84	Hydrazine
.33	Ammonium
.32	Guanidine
.18	Aminoguanidine
.13	Potassium
	Rubidium
	Cesium
	Choline
	TMA
<.06	Methylamine
	Methylguanidine
	Methylhydroxylamine
	Methylhydrazine

(Supported by NIH Grant HL 14388.)

EFFECTS OF UTERINE AND UMBILICAL VENOUS PRESSURES ON UMBILICAL BLOOD FLOW IN CHRONICALLY PREPARED FETAL LAMBS. K.L. Thornburg, J.M. Bissonnette and J.J. Faber. Dept. Physiol. & Obstet. & Gynec., Medical School, Univ. of Oregon Health Sciences Center, Portland, OR 97201

In 11 chronically prepared fetal lambs, we measured pressures in the amniotic space, fetal umbilical artery and vein and maternal carotid artery and uterine vein. Fetal distal aortic blood flow was measured by an electromagnetic flow sensor and its placental fraction determined by use of labeled microspheres. Umbilical and uterine venous pressures were elevated by inflatable occluders around the umbilical cord and vagina. Control values 3 days post surgery (mean ± SEM) were: fetal umbilical artery pH 7.37 ± 0.01, umbilical blood flow 186 ± 14 $ml \cdot min^{-1} \cdot kg^{-1}$ fetus; fetal arterial and umbilical venous pressures were 39 ± 3 and 7.4 ± 1.0 mm Hg above intrauterine pressure. Umbilical blood flows were affected by the first small (± 2 mm Hg) changes in umbilical venous pressure over a range of 2 to 40 mm Hg. Increased uterine venous pressures ranging from 2 to 30 mm Hg did not affect umbilical blood flow. Umbilical blood flow was equally sensitive to alterations in umbilical venous pressure at elevated uterine venous pressures. There was no evidence of a placental surrounding pressure even during anesthesia, supine position of the ewe, and/or ganglionic blockade of the fetal ANS.



(Supported by HL 13444)

AEROBIC CHARACTERISTICS OF ISOLATED LIGAMENTS AND TENDONS.
C.M. Tipton, A.C. Vailas*, M.H. Laughlin*, and J.M. Diana. Exercise and Cardiovascular Physiology Laboratories, University of Iowa, Iowa City, Iowa 52242

Published and unpublished results from experimental animals have shown that ligaments or ligament-bone junctions are functionally responsive to increased or decreased physical demands. To better understand these findings, we reinvestigated the metabolic characteristics of isolated ligaments and tendons. Respirometry techniques to measure oxygen consumption were modified for tissue homogenates using a Krebs-albumin medium, collagenase, elastase and centrifugation. Oxygen utilization [$\mu l O_2$/gram wet weight/min: $\bar{X}$, SE, (N)] from selected tissues of adult male rats were: patellar ligament 3.5±.32 (10); Achilles tendon 4.0±.37(9) and liver 44.1±1.9(10). When cytochrome oxidase activity was measured in other males, the following results were secured ($\mu l O_2$/gram wet weight/min); lateral collateral ligament 189±13(10), medial collateral ligament 186±12(9), gastrocnemius muscle 530±34(19). Microspheres (^{85}Sr, ^{46}Sc) were injected into resting anesthetized dogs and the flow values for the gastrocnemius, soleus, and tibialis anterior muscles were 1.13, 1.40, and 2.03 times greater respectively than the mean for the medial collateral ligament [2.11±.31(11), ml/min x 100 grams]. When compared to other tissues, the aerobic capacities of tendons and ligaments were markedly lower; however, these findings do not support the concept that isolated ligaments or tendons are "metabolically inert" tissues. (Supported in part by AM-08893-10 and HL 16997 and HL 14388.)

EFFECTS OF THYROXINE UPON ATPase ACTIVITIES OF SEVERAL SUBCELLULAR FRACTIONS OF LIVER.
R.B. Tobin and R. Serpan*, V.A. Hosp. and Univ. of Nebraska College of Medicine, Omaha, NE 68105.

Study of thyroxine (T_4) effects upon ATPase activity of rat liver subcellular fractions (Fed. Proc. 33:249, March 74) showed that physiological doses of T_4 did not stimulate Na-K activated ATPase of cell membranes, microsomes, or mitochondria. Large doses of T_4 did stimulate Mg ATPase of plasma membranes (PM) and microsomes. A systematic study was performed of the effects of T_4 and of Na, K, Mg, and Ca ions upon the ATPase activity of rat liver PM, mitochondria, microsomes, and nuclear membranes (NM). Rats were injected with 15 µg L-T_4/100g body weight daily for 7 days. Control animals received diluent. Subcellular fractions were isolated by standard published methods. T_4 stimulated mitochondrial Mg and Ca-Mg ATPase but not Na-K-Mg ATPase. Microsomal Mg and Ca-Mg ATPase were stimulated by T_4. Nuclear membranes isolated by the method of Kay et al. (Europ. J. Biochem. 30:145, 72) showed no effect of T_4 upon ATPase activity. A dose response study with up to 150 µg T_4/100g body weight was without effect upon ATPase activity of NM. Guinea pig liver (GPL) preparations were treated similarly. GPL PM showed essentially no stimulation of ATPase activity by T_4. GPL NM showed modest increase in Mg, Na-K-Mg, and Ca-Mg ATPase activity in animals receiving 15 µg L-T_4/100g body weight, a dose producing maximal stimulation of mitochondrial respiration. Microsomal ATPase activity appears to be the most sensitive of the liver subcellular preparations to T_4. T_4 did not stimulate Na-K ATPase of any subcellular preparation. Mg and Ca-Mg ATPase of mitochondria and microsomes were increased by T_4. GPL NM appeared to differ from rat liver NM in the response of ATPase activity to T_4.

THE EFFECT OF HEMORRHAGIC SHOCK ON THE PULMONARY CAPILLARY MEMBRANE. T.R.J. Todd‡ E.M. Baile‡ J.C. Hogg (SPON: M.R. Becklake). Depts. of Pathology and Medicine, McGill University, Montreal.

We estimated the pulmonary capillary filtration coefficient (K_F), equivalent pore radii (r) and pore number (Pn) in dogs before and after induction of hemorrhagic shock (mean BP≈40 mmHg for approximately 3 hours). K_F was estimated in dogs where right duct lymphatic flow (RDL_F) was $\leq$ 0.1 of LDL_F and was not contaminated by chyle. Under these conditions we assumed that RDL_F was 1/3 of the net fluid movement (FM) across the pulmonary capillaries. K_F was calculated by dividing FM by the change in pressure across the capillary wall. Capillary hydrostatic pressure was calculated by measuring pulmonary artery (Pa), pulmonary wedge (Paw) and left ventricular end diastolic pressures (Plv edp). Oncotic pressure in blood and lymph were estimated from measurements of blood and lymph protein and interstitial hydrostatic pressure was assumed to be -10 mmHg. Peroxidase (HRP) was injected at the beginning of the experiment and a constant blood level was maintained by subsequent small injections (total dose 100 mg/Kg). Peroxidase flux ṅ/100 g lung was FM x RDL [HRP]. The contribution of HRP to the oncotic pressure of blood and RDL was estimated from the van't Hoff equation. These parameters allowed us to calculate Pn and r using the equations of Landis and Pappenheimer (Am. Physiol. Soc. 1963). We found that the K_F was increased by hemorrhagic shock ($P \leq .05$), n=4. That pore number increased while the equivalent pore radius tended to decrease slightly. We conclude that hemorrhagic shock results in increased capillary permeability by increasing pore number rather than the radius of pores in the pulmonary capillary membrane.
Supported by MRC of Canada.

THE EFFECT OF CONCANAVALIN A ON SODIUM EFFLUX IN SINGLE BARNACLE MUSCLE FIBERS. E.Y. Tong* and D.A. Coyle* (SPON: L.D. Davis). Dept. Biology, Wheaton College, Norton, MA 02766

Externally applied Convanavalin A (Con.A) at 5μg/ml, 50μg/ml, and 100μg/ml did not alter the typical single exponential decline of the efflux of microinjected radioactive sodium from single barnacle muscle fibers. At 200μg/ml, Con.A caused a slight increase in the sodium efflux. However, when Con.A was externally applied to fibers bathed in a ouabain containing solution ($5x10^{-5}M$), the increase of the sodium efflux was greatly enhanced. In an ouabain-treated fiber, Con.A at 50μg/ml induced a significant stimulation of the sodium efflux (47%), and at 100μg/ml maximum stimulation was obtained (217%). The effect was dependent on the presence of external calcium ions. Thus, when the fiber was bathed in a calcium-free Ringer's solution, the Con.A-induced stimulation of the ouabain-inhibited sodium efflux did not occur. The results suggest that the binding of Con.A on the cell membrane does not take place in the absence of calcium ions, and when binding does occur in the presence of calcium ions, there is an alteration in the sodium transport mechanisms. Apparently, the rise in the sodium efflux cannot be attributed to a stimulation of the sodium pump; a change in permeability or other transport mechanisms may be involved. The Con.A-induced stimulation of the ouabain-inhibited sodium efflux cannot be blocked by α-methyl-D-mannopyranoside (α-MDM) at $6.4x10^{-7}M$. However, a stimulation of the ouabain-inhibited sodium efflux also can be produced by α-MDM alone. Hence, even if α-MDM would be able to inhibit the effect of Con.A on sodium transport, the blocking action would have been masked by the stimulating action of α-MDM itself.

EFFECTS OF STRESS ON CATECHOLAMINE CONTENTS OF HYPOTHALAMI OF NEWBORN AND GROWING ANIMALS. Clara Torda. 101 West 12 Street, New York,N.Y.,11.

The effects of prolonged recurrent stress on catecholamine (CA) release and metabolism have been observed by a series of independent studies: 1) First the release of catecholamines and norepinephrine (NE) into the perfusion fluid was ascertained during stimulation of various areas of the hypothalamus, or changes of the physicochemical composition of the perfusion fluid comparable to hunger. Both the CA and NE release of hypothalamus increased in a manner comparable to adult animals. 2) The NE, dopamine (DA) and epinephrine (EP) contents of the hypothalami of newborn and growing animals were ascertained. Electrical stimulation of various areas of the hypothalamus, or witholding feeding were used as recurrent stressful events. At birth NE, DA, EP did already occur in the hypothalamus. In absence of stressful stimuli all three substances reached adult values during the second postnatal month, even though the slopes of the growth-curves differed. Exposure to repeated postnatal stresses resulted in an increase of norepinephrine content of the hypothalamus. Adult values were reached sooner. Persistence of stressful situations resulted in higher than normal values in the adult rat. The increase of DA and EP during stressful situations also increased,but the amount of the increase seemed to depend on various aspects of the norepinephrine metabolism, and thus on the manner the growing animal became conditioned to handle stresses. These results offer some insight into the nature of subcellular mechanisms of generation of future compulsive aggressive or anxious behavior(Torda,C.,Federation Proceedings 34, # 1001 (1975).

METABOLISM OF ENDOGENOUS LIPID BY ISOLATED PERFUSED RAT KIDNEY. M.E. Trimble and R.H. Bowman, VA Hospital, Syracuse, N.Y. 13210

Kidneys were prelabeled in vivo by i.v. injection of [U-^{14}C]palmitate. After 20 min, the right kidney was removed and perfused in a closed preoxygenated system. The left kidney, removed at the same time, served to provide zero time values. $^{14}CO_2$ production was measured during the course of perfusion and kidneys were assayed terminally for radioactivity and fatty acid (FA) content in phospholipid (PL), neutral lipid (NL) and free fatty acids (FFA). In non-perfused kidneys prelabeled for 20 min, the s.a. (cpm/μmol FA) was PL=1406 ± 146; NL=5755 ± 633; FFA=1503 ± 281 (N=9). Following perfusion for 1 hr with no exogenous substrate, net loss of lipid could not be detected. Significant loss of ^{14}C was not observed from PL or FFA but ^{14}C in NL declined linearly with time (40% in 1 hr). Loss of NL ^{14}C could be accounted for by $^{14}CO_2$ production. The 40% loss of ^{14}C from NL was unaffected by the presence of a mixture of exogenous substrates (glucose, lactate, pyruvate, glutamine), although $^{14}CO_2$ production was reduced; under such circumstances, most of the ^{14}C lost from NL appeared in the perfusate as unidentified metabolites. Perfusion with clofibrate, insulin or protamine did not prevent the loss of ^{14}C from NL. Anerobic perfusion did not inhibit the loss of ^{14}C from NL but did greatly reduce $^{14}CO_2$ production. Under this condition, the amount of ^{14}C appearing in both tissue and perfusate FFA was increased. It is concluded that: a) at least a portion of the NL pool turns over rapidly; b) some FA in the PL fraction may be exchangeable with at least a portion of FA in the NL fraction; c) certain exogenous substrates effectively compete with FA of NL as a source of CO_2; d) exogenous FA may potentially mix with several pools of endogenous fatty acid prior to oxidation. (Supported by USPHS grant AM-14401)

FINER LOCALIZATION OF THE VASOMOTOR CENTRE IN THE MEDULLA OBLONGATA OF THE CAT. Trouth, C.O., Millis, R.M., Harrison, N., Holloway, J.A., Moolenaar, G.M. Dept. Physiol. & Biophysics, College of Medicine, Howard University, Washington, D.C., 20059

The medulla oblongata of cats anaesthetized with Cholralose-urethane was electrically stimulated (Rectangular impulses, 40/sec, 1m sec,1-4V) from the lower Pons to C_1-C_2. Fifty points in a millimeter grating on the ventral surface were each stimulated in ventrodorsal direction at intervals of 0.1-0.2mm for the first millimeter, thereafter at millimeter intervals, with fine Tungsten electrodes (Tip diameter 3-5µm) mounted on a stereotaxic co-ordinate system. Blood pressure was measured via a catheter in the right femoral artery connected to statham strain gauge. Vascular resistance in the left hind limb was measured during perfusion at constant flow via a strain gauge. A spot was located 3 mm below the ventral surface which consistently yielded a strong vasopressor response in 7 cats stimulated at this point. This vasopressor response could be elicited irrespective of the respiratory response to stimulation. Stimulation at 0.2 mm intervals in all directions revealed that the vasoactive zone was confined to a region less than 1 mm in all directions. It is located in the nucleus reticularis parvocellularis, ventrolateral to the Tractus solitarius between the nucleus of the spinal tract of the Trigeminal nerve and the facial nerve nucleus, (Nomenclature: Reinoso-Suarez, 1961, and Snider and Niemer, 1964). It corresponds well with the most rostral tip of the vasomotor centre described for the rabbit [1]. Bilateral electrocoagulation resulted in an irreversible fall in blood pressure. 1. Fallert, M., Bucher, V.M.: Lokalisation eines blutdruckaktiven Substrats in der Medulla oblongata des Kaninchens. Helv. Physiol. Acta 24, 139-163,1966. (Supported by NIGMS Training Grant 1 TO 2 GM 05010-01 MARC).

PROSTAGLANDIN INHIBITORS AND ANTIHISTAMINES REDUCE PULMONARY VASOCONSTRICTION FOLLOWING EMBOLIZATION. A. Tucker, E.K. Weir*, J.T. Reeves and R.F. Grover, Univ. Colo. Med. Ctr., Denver, Co. 80220

Prostaglandins and histamine have been shown to be released into the venous effluent of embolized lungs. In order to determine the role of these vasoactive agents, pulmonary vascular responses to microembolization (200 µ glass beads, 0.15 ml/kg) were determined in 8 untreated anesthetized dogs and compared to responses obtained in prostaglandin (PG) synthetase blocked (meclofenamate, 2 mg/kg; n = 8), PG receptor (PG-R) blocked (polyphloretin phosphate, 50 mg/kg; n = 4), histamine (H) blocked (metiamide, 5 mg/kg/min for 35 min and chlorpheniramine, 1 mg/kg; n = 8), and combined PG and H blocked (n = 6) dogs. In the table are shown the changes from control, 5 min post embolization, in pulmonary arterial pressure (PAP), pulmonary vascular resistance (PVR), and arterial oxygen (PO_2) and carbon dioxide (PCO_2) tensions.

	Untreated	PG	PG-R	H	PG+H
ΔPAP (mmHg)	22.5	15.9	8.2	16.8	11.2
ΔPVR (units)	9.7	5.8	3.8	6.6	4.8
ΔPO_2 (mmHg)	-17	-6	-2	-20	-4
ΔPCO_2 (mmHg)	5	0	1	5	2

The increases in PAP and PVR were attenuated with both PG inhibitors and antihistamines at 5 min and were still attenuated 30 min post embolization. The alveolar hypoventilation was attenuated only with PG inhibitors. Cardiac outputs and systemic arterial pressures were unchanged from control by embolization in all groups of dogs. The results suggest that pulmonary embolization in intact dogs causes vasoconstriction mediated partially by prostaglandin and histamine action, and alveolar hypoventilation (perhaps due to bronchoconstriction) mediated by prostaglandin, but not histamine, action.

AVIAN PANCREATIC GLUCAGON HETEROGENEITY: RADIOIMMUNOLOGIC AND RADIORECEPTOR CHARACTERIZATION. A.K. Tung*, S.A. Rosenzweig* and P.P. Foà. Dept. of Research, Sinai Hosp. of Detroit, MI 48235.

Recent studies of glucagon biosynthesis suggested the existence of precursor molecules. We attempted to characterize these precursors using receptor binding and radioimmunoassays. Pigeon islets (collagenase) were homogenized in 15% TCA and extracted with acid-ethanol. Lyophilized extracts were dissolved in 1 M acetic acid (HAc), applied to Sephadex (S) G-50 columns and eluted with 1 M HAc. Three components with glucagon immunoreactivity were evident. ~90% of the activity was found in fractions corresponding to Peak II (9,000Δ) and to pancreatic glucagon (PG, 3,500Δ). <10% was in the void volume (Peak I). When Peak II was rechromatographed on S G-50, ~50% of the immunoreactivity initially associated with it emerged in the PG region; this change was prevented by inhibitors of proteolysis. When eluted with NaCl from a DEAE-cellulose column, 3 M urea, Peak II behaved as a single immunoreactive peak. Gel filtration analysis of ^{125}I-Peak II so purified showed a single component of 9,000Δ, which appeared to consist of 76 amino acids, including all those of turkey glucagon. Rechromatography of Peak I, on S G-100 revealed a discrete immunoreactive peak of 69,000Δ, showing PG displacement curves when assayed with an anti-glucagon serum for PG and one for total glucagon. When gel filtration fractions of acid-ethanol extractable proteins were assayed by means of a rat liver membrane receptor system (Neville, Step 11), ~90% of the activity was associated with PG, <10% with Peak II, and none with Peak I. Avian PG competed effectively with ^{125}I-labeled porcine glucagon for binding to rat liver membranes. Thus, two large "glucagon" species, previously implicated in the biosynthesis of glucagon by avian islets, appear to exist. (Aided by NIH Grants AM18358 & AM06034)

DISTURBANCES IN SERUM GLUCOSE REGULATION FOLLOWING EXPERIMENTAL BURN INJURY. J. Turinsky and T.M. Saba. Dept. Physiology, Albany Medical College, Albany, New York 12208

Long-term metabolic and endocrine alterations were studied in rats from 4 hr to 21 days after burn injury (20% surface burn under ether anesthesia). Body weight declined from 203±1 g to 188±2 g by 2 days after injury, returning to pre-burn weight by one week, with subsequent growth at a rate slower than in controls. At 20 days burned rats weighed 258±4 g, while control animals weighed 338±5 g. The delayed and slower growth of burned rats was associated with a decreased food consumption following injury. The consumption during the first three days was respectively 3.3±0.5, 5.9±0.4, and 11.9±0.8 g/rat/day returning to control rates (20-22 g/rat/day) by 10 to 13 days. Glucose tolerance and insulin secretory response to 1 g glucose/kg i.v. were studied at 4 hrs, 3 days, and 21 days post-burn in overnight fasted rats. Hyperglycemia and decreased tolerance to glucose was apparent at 4 hrs post-burn and related, in part, to decreased insulin secretory response. Three days after burn, glucose tolerance was normal and associated with hyperinsulinemia suggesting the development of insulin resistance and an adequate compensatory increase in insulin production. At 21 days post-burn, glucose tolerance and insulin secretory response approximated normal. Diaphragms excised from control and burned rats (4 hr, 3 days, and 21 days post-injury) showed the same increase in glucose uptake in response to insulin (0.1 units/ml) suggesting that insulin resistance in vivo at 3 days was not mediated by a decrease in the capacity of muscle to bind insulin. The importance of the observed insulin resistance and gluco-regulatory alterations to survival from thermal injury remains to be determined (GM-21447).

TRYPSIN INHIBITORY CAPACITY OF CANINE PULMONARY LAVAGE PROTEIN FOLLOWING INHALATION OF ^{90}YTTRIUM. Waneta C. Tuttle and Carol T. Schnizlein*, Pathobiology Department, Inhalation Toxicology Research Institute, Lovelace Foundation, Albuquerque, New Mexico 87115

The effect of pulmonary irradiation on the concentration of trypsin inhibitor associated with pulmonary surfactant was determined. Bronchopulmonary lavage was performed on anesthetized Beagle dogs on days 10, 24, 38, 52 and 66 following inhalation of ^{90}Y in fused clay. The initial lung burden (800 μCi/kg) produced radiation pneumonitis in previous studies within 196 days after exposure. Total protein and trypsin inhibitory capacity (TIC) were determined for the whole pulmonary washings and for the surface active material isolated from the lavage fluid. Average TIC/mg protein was progressively increased over control values in the whole lavage fluid from exposed animals at each sampling day after exposure. The TIC/mg protein of the surface active fraction, however, was unchanged or reduced following irradiation. There was no substantial change in TIC/mg protein in lavage fluid or isolated surface active material from controls at any time during the study. The results indicated that the concentration of trypsin inhibitor in pulmonary lavage fluid increased during the development of radiation-induced pulmonary injury while the quantity of trypsin inhibitor associated with the surface active phospholipid remained unchanged or decreased. These alterations in functional trypsin inhibitor concentration may play a significant role in changing enzyme - enzyme inhibitor relationships that are key factors in the development of radiation pneumonitis and fibrosis. (Research performed under U.S. Energy Research and Development Administration Contract E(29-2)-1013.)

MODULATION OF PULMONARY VASCULAR RESISTANCE OF PERINATAL GOATS WITH PROSTAGLANDINS E_1 AND E_2. T. Tyler*, C. Leffler*, R. Wallis*, and S. Cassin. Dept. of Physiology, Univ. of FL., Gainesville, Fl. 32610.

Prostaglandins (PGs) of the E-series may be involved in the local regulation of pulmonary blood flow. Atypical transition of fetal to neonatal circulation at birth may result in pulmonary hypertension with or without hypoxia. Effects of exogenous PGE_1 and PGE_2 on left pulmonary arterial pressure at constant flow, left atrial pressure, systemic arterial pressure (SAP), and heart rate (HR) were measured in unventilated fetal (n=26) and ventilated neonatal goats (n=9). Dose-response characteristics of pulmonary and systemic circulations to intrapulmonary PGE_1 and PGE_2 were evaluated. Effects of PGE_1 and PGE_2 were compared in neonates breathing either air or 5% oxygen for 1 min. A 60-70% decrease in pulmonary vascular resistance (PVR) of the fetus was maintained with PGE_1 (1.47 μg/Kg·min) for up to 35 mins without changing SAP or HR. PGE_2 was far less effective than PGE_1 as a pulmonary vasodilator. Increased rates of infusion of PGE_1 or PGE_2 (>2.3 μg/Kg·min) decreased HR and SAP. Effect of PGE_1 was not different following partial cord occlusion which increased PCO_2 and decreased PO_2 and pH. PVR was reduced by PGE_1 and PGE_2 in neonates 21% and 14%, respectively during normoxia. During PGE_1 infusion hypoxia did not increase PVR, although SAP was increased. During PGE_2 infusion hypoxia increased PVR 43% (hypoxia alone increased PVR 54%). Indomethacin (2 mg/Kg) did not alter effects of exogenous PGs. These results demonstrate that intrapulmonary PGE_1 infusion in perinatal goats may decrease PVR without systemic effects. Pulmonary vasodilator activity of exogenous PGE_1 which is quantitatively greater than PGE_2 was not influenced by hypoxia, hypercapnia, pH or indomethacin. (Supported by NIH-HL10834-06, NIH-T01-HL05979-02S1, and Florida Heart Association 74-AG-2)

ERYTHROCYTE SIZE AND CALCIUM CONTENT IN BLOOD OF ACTIVE LIMBS WITH SUBMACIMAL AND MAXIMAL EXERCISE. W. van Beaumont, Dept. of Physiology, St.Louis University School of Medicine,St.Louis,Mo. 63104 and J.E.Greenleaf, Ames Research Center, Moffett Field,California, 94035.

Five male and one female volunteer subjects performed 10 min arm exercises at various intensities in a cool environment (22-24 ^{0}C). Quadruplicate hematocrit, hemoglobin determinations and red blood cell counts were made from duplicate pre-exercise and immediate (≤2 m) and delayed (+ 20 min) post-exercise antecubital venous blood samples. In spite of variable changes in plasma osmolarity (5-28 mOsm/L), blood pCO_2 (7-42 mm Hg) , blood pO_2 (1-27 mm Hg) and pH (.04-.40) the mean corpuscular volume (MCV) did not change beyond that which was measured in resting subjects over an 8 hour period. Consequently , calculating the shifts of plasma fluid resulting from the exercise by the Hct or the combined Hct-Hb changes, gave identical values . From the simultaneously measured changes in plasma calcium concentration it could be calculated that the plasma calcium content decreased significantly in the blood of the active limbs, but much less than the plasma content of sodium or chloride ions. It appears that size and valency play a significant role in the ion shifts observed during and after physical exertion.

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ALTERATION OF ELECTROLYTE TRANSPORT BY AN ANESTHETIC NOBLE GAS. Paul S. Van Nice*and William R. Galey* (SPON: Gerald K. Weiss). University of New Mexico School of Medicine, Albuquerque, N.M. 87131.

High partial pressures of inert gases have narcotic effects on diverse organisms and tissues, and the elucidation of how these simple molecules induce general anesthesia should provide insight into the mechanism of anesthetic action at the molecular level. Our study examines the interaction between the noble gas argon, which is relatively inert chemically, and a simple membrane system, the human erythrocyte.Previous studies (P.Seeman,1972,Pharm.Rev. 24:583) have shown the suitability of the erythrocyte as a model for anesthetic action. We describe the effects of high partial pressures of argon on the transport of sodium and potassium across the membranes of human red blood cells. Since hydrostatic pressures greater than 25 atmospheres (ATA) have been shown to antagonize anesthesia, and since helium lacks narcotic potency in the pressure range of our experiments (15-100 ATA), red cells are subjected to pressures of helium equal to those of argon, as a control for the pressure effect. Both control and experimental cell suspensions are maintained in pressurized chambers at 37°C and sampled at intervals. Permeability rate constants are calculated for both influx and efflux of ^{22}Na and ^{42}K at various pressures of gases and in the presence or absence of 10^{-4}M oubain. Our data indicate that the rate constants for Na^{+} and K^{+} fluxes increase with raised partial pressures of argon. These higher permeability coefficients associated with high partial pressures appear to be the result of an increase in the passive permeability of the plasma membrane and may be the basis for argon's anesthetic effects.

EFFECTS OF DEUTERIUM OXIDE AND SEVERAL NON-ELECTROLYTES ON RESTING AND DEVELOPED TENSION IN HEART MUSCLE. F.F. Vargas* and J.A. Johnson, Dept. Physiology, University of Minnesota, Minneapolis, Mn. 55455

Contractile force, electrogram, water movement and vascular resistance were measured in the isolated perfused rabbit heart. The hearts were perfused with Ringer solutions in which H_2O had been replaced by D_2O or to which sucrose, glycerol, urea, ethylene-glycol or formamide had been added. D_2O Ringers produced a partial or complete loss of tension while the electrical activity was only slightly modified. This E-C uncoupling could not be corrected by caffeine or isoproterenol. Raising Ca^{2+} concentration to 10 mM reestablished the developed tension. The non-electrolytes tested inhibited developed tension. This effect showed a linear dependence on the water loss from the heart. The developed tension remained low in the presence of the test solute. Only urea produced a transient drop followed by a marked tension increase. Resting tension was lowered by D_2O and raised by sucrose and urea. It was not modified by the other non-electrolytes. The effects of the non-electrolytes seem to be related to their permeabilities in the heart muscle cells. Permeability coefficients estimated from the volume changes correlate well with the above reported effects of the different molecules. On returning to normal Ringers after perfusion with urea or glycerol containing Ringers a complete loss of tension was observed. This may be caused by swelling and increased K^+ permeability of the heart cells.
(Supported by NIH Grant HL 14835.)

TOXIC MECHANISMS OF STROPHANTHIDIN IN CARDIAC PURKINJE FIBERS. M. Vassalle, Dept. Physiology, State University of New York, Downstate Medical Center, Brooklyn, N.Y. 11203

Canine Purkinje fibers were perfused in a tissue bath and transmembrane potential were recorded by a microelectrode technique. The fibers were exposed to strophanthidin (10^{-6}M). Strophanthidin accelerated diastolic depolarization and induced oscillations. The enhanced diastolic depolarization was responsible for the initial acceleration and the attainment of threshold by oscillations for the abrupt increase in rate of discharge. The maximum diastolic potential decreased and fast rhythms due to small action potentials developed at the plateau level. High calcium slowed the rate of discharge of normal action potential but increased that of small action potentials. Low calcium had an opposite effect. In high potassium no signs of toxicity appeared, but on returning to normal $[K]_o$ arrhythmias developed. High potassium stopped the small action potentials by progressively reducing their amplitude. Tetrodotoxin antagonized the arrhythmias whether the action potentials were normal or small. Overdrive accelerated the small action potentials if drive was short and suppressed them if drive was long. The mechanism of suppression was a more rapid onset of stage of inexcitability. Short drives could induce fast rhythms. Small action potentials were little affected by acetylcholine and were depressed by Verapamil. These and other results suggest that strophanthidin causes an accelerated discharge by steepening diastolic depolarization, by developing oscillations superimposed to diastolic depolarization and by development of small action potentials in the plateau region. The arrhythmogenic manifestations of strophanthidin can occur in the absence of a poisoning of the sodium potassium pump and different currents may be involved in the different types of rhythms. (Supported by grant HL-13924 from N.I.H.).

EFFECTS OF ANESTHETICS ON BAROREFLEX CONTROL. Stephen F. Vatner, W. Thomas Manders*, Robert J. McRitchie* and Eugene Braunwald. Dept. Med., Harvard Med. Sch. and Peter Bent Brigham Hospital. Boston, Ma. 02115.

In order to examine the extent to which various anesthetics alter reflex control of arterial pressure(AP), the effects of nitroglycerin, 24 μg/kg, i.v. and hemorrhage were examined in conscious dogs before and after recovery from either bilateral section of carotid sinus(CS) nerves and CS and aortic nerves (denervated) and in intact dogs anesthetized on separate days with pentobarbital Na, 30 mg/kg, 1.5% halothane in O_2 and alpha chloralose, 120 mg/kg. Hemorrhage, 25 ml/kg, reduced mean AP 13 ± 5 mmHg in intact conscious dogs, 26 ± 4 mmHg after chloralose, 32 ± 4 mmHg after halothane, 48 ± 5 mmHg after pentobarbital and 25 ± 5 mmHg after CS nerve section and 56 ± 4 mmHg in conscious denervated dogs. Nitroglycerin induced a similar differential reduction in AP and increased heart rate 77 ± 5 beats/min(bpm) in intact conscious dogs, 63 ± 8 bpm after chloralose, 38 ± 7 bpm after pentobarbital, 6 ± 2 bpm after halothane, 49 ± 7 bpm after CS nerve section and 1 ± 1 bpm in denervated conscious dogs. The change in bpm per mmHg reduction in mean AP was used as another index of baroreflex sensitivity. After nitroglycerin this index averaged 3.2 ± .3 in intact conscious dogs, 1.8 ± .3 after chloralose, 0.9 ± .2 after pentobarbital, 0.2 ± .1 after halothane, 1.5 ± .3 after CS nerve section and 0.08 ± .04 in denervated conscious dogs. Thus, all general anesthetics studied interfered significantly with baroreflex control. Pentobarbital altered the ability to maintain AP the most, whereas halothane attenuated reflex tachycardia the most. Administration of alpha chloralose altered reflex control by an amount approximately equivalent to section of both CS nerves in conscious dogs, while pentobarbital and halothane induced effects on reflex control intermediate between CS nerve section and denervation of all four major buffer nerves.

OUABAIN BINDING IN FROG MUSCLE. R.A.Venosa* and P.Horowicz. University of Rochester, School of Medicine & Dentistry, Dept. Physiology, Rochester, N. Y. 14642

Ouabain binding, using ^{3}H-ouabain, was measured in frog sartorius muscle for concentrations 1.29×10^{-7} to 7×10^{-5}M. The time course of binding was followed by exposing 8 muscles (4 pairs) to a given concentration of ouabain for different periods of time. At the end of the exposure, all muscles were washed for 1 hr in a ouabain-free Ringer's fluid. An estimate of ^{3}H-ouabain remaining in the extracellular space was obtained from the decline of radioactivity in samples collected during the washout. This estimate was subtracted from the total activity found in the muscles. A single exponential function of time adequately describes the binding kinetics. As the ouabain concentration increases the time constant of binding progressively shortens and at 7×10^{-5}M appears limited by diffusion in the extracellular space. The binding of the cardioglycoside as a function of its concentration in normal Ringer's fluid saturates at about 221±12 pM/g (22 experiments). Taking a surface to weight ratio of 552 cm^2/g of muscle this is equivalent to a density of 2415±130 molecules/μm^2 of surface membrane area. The binding sites are half-saturated at about 2.4×10^{-7}M ouabain. 'Detubulation' by treatment with 400 mM glycerol does not alter measurably the extent of binding suggesting that the density of the Na^+ pumping sites in the 'transverse' tubular system of muscle fibers is substantially lower than on the surface membrane.
(Supported by USPHS Grant #5 RO1 NS 10981).

ACCUMULATION OF ^{3}H-NOREPINEPHRINE IN C-6 GLIAL CELLS IN CULTURE. Antonia Vernadakis, Depts. of Psychiatry and Pharmacology, Univ. of Colorado Medical School, Denver, Colorado 80220

Glial cells derived from a rat astrocytoma have been used as cell model to study uptake properties of neurohumors in glial cells. In this study we report the accumulation of ^{3}H-norepinephrine (^{3}H-NE) in C-6 glial cells under various experimental conditions. Cells were cultured in F-12 media plus 10% fetal calf serum at 37°C in 95% air and 5% CO_2. In some cultures dibutyryl cyclic AMP (DBcAMP), 10^{-3}M, was added 24 and 48 hrs after plating. DBcAMP induced morphological transformation in the cells. On the 3rd day after plating, control and DBcAMP-treated cultures were changed to serum-free media and cortisol, 5.5 X 10^{-5}M, was added for 1 hr or 4 hrs. At the end of hormone treatment, cultures were changed to oxygenated Krebs-Henseleit buffer and were incubated with ^{3}H-NE, 10^{-6}M, for 15', 30', 60' at 37°C. After this incubation period, the cells were washed 3X, harvested and cells were counted with a hemocytometer. NE was extracted with ethanol:triton (0.5% triton) and radioactivity was counted. Accumulation of ^{3}H-NE (dpms/10^{6} cells) was cell density (cells/mm^{2}) dependent: high accumulation at low cell density and decreasing accumulation with increasing cell density. In DBcAMP-treated cultures, ^{3}H-NE accumulation was significantly higher than controls of similar cell density. Cortisol treatment significantly decreased ^{3}H-NE accumulation. These data support other findings that cortisol inhibits the uptake of NE in glial cells and thus may regulate the concentration of NE at the intersynaptic space. (Supported by National Fdn., Milheim Fdn., and Res. Sci. Development Award KO2 MH-42479 from NIMH, NIH).

PREVENTION OF ADRIAMYCIN INDUCED CARDIAC ARRHYTHMIAS WITH CARNITINE. J. A. Vick*, S. L. DeFelice* and C. C. Hassett. Biomedical Laboratory, Edgewood Arsenal, M.D. 21010 and Bio-Bascis International, N.Y. 10011.

Adriamycin is a anti-cancer drug which has been used in the treatment of acute leukemias and lymphomas. Patients receiving this drug for long periods of time have shown an unusually high incidence of cardiac toxicity. This side effect has somewhat limited the use of the drug. Isolated perfused Langendorff heart preparations were used to experimentally reproduce the cardiac effects of Adriamycin and to test drugs which might be used in preventing this toxicity. Hearts were surgically excised from anesthetized mongrel dogs and perfused with heparinized autologous blood. EKG, heart rate, force of contraction, coronary perfusion pressure and coronary blood flow were continuously monitored. Adriamycin was injected directly into the coronary circulation and consistently produced arrhythmias, decreased heart rate and force of contraction and a sharply elevated coronary perfusion pressure. All of the 20 control hearts given Adriamycin failed within 30 min. A second group of 20 hearts were pretreated 5 min prior to Adriamycin with 100 to 500 mg of Carnitine. In 50% of the hearts no toxicity was observed during the 4 hr observation period. In the remaining 10 heart preparations there were significant elevations in coronary vascular resistance following Adriamycin; however no arrhythmias or changes in force or rate were noted. Ten Rhesus monkeys were also used in this study. Five were given only Adriamycin and were observed to develop severe arrhythmias. Four of 5 pretreated with 500 mg Carnitine showed no toxicity to the drug. It appears that Carnitine may be useful in preventing the cardiac toxicity so often observed following long-term Adriamycin therapy.

LOCATION AND STIMULATION OF RAPIDLY-ADAPTING AIRWAY RECEPTORS IN DOGS WITH A FIBEROPTIC BRONCHOSCOPE. E. Vidruk*, H. L. Hahn*, J.A. Nadel, and S.R. Sampson. Univ. of California, San Francisco, California 94143.

The rate of discharge of canine rapidly-adapting airway receptors is increased by histamine administered by aerosol or intravascularly. As the increased activity either coincides with or follows an increase in intratracheal pressure, it is not known whether the histamine effect on receptor activity is exerted directly in the airway containing the receptor or secondarily as a result of histamine-induced changes in total lung mechanics. To investigate this problem, we applied histamine directly to the mucosa with the aid of a fiberoptic bronchoscope passed into the airways containing these receptors, while single fiber recordings were made from small slips dissected off the otherwise intact vagus nerve in dogs anesthetized with chloralose-urethane. The location of each receptor was determined by mechanical stimulation with a small catheter inserted into the airway via the fiberoptic bronchoscope. Application of 0.1% histamine (0.1-1.0 ml) through the catheter to the area of the receptor caused a marked increase in afferent fiber activity in the absence of any change in intratracheal pressure. The increase in activity occurred throughout the respiratory cycle and persisted for several minutes unless it was reversed by hyperinflation of the lungs; the same volume of 0.9% NaCl occasionally produced only a brief burst of activity during application. Local application of 1% lidocaine (as little as 0.1 ml) completely and reversibly blocked receptor activity. We conclude that the histamine-induced increase in activity of rapidly-adapting airway receptors can occur as a result of direct effects in the region of the receptor. (Supported in part by NIH grants HL-14201, HL-00448 and HL-06285).

CYCLIC AMP MEDIATED PHOSPHORYLATION OF CARDIAC TROPONIN GIVES GREATER Ca^{++} SENSITIVITY OF ACTOMYOSIN ATPASE. C. Villar-Palasi* and R. Rubio, Dept. Pharmacology & Physiology, Univ. of Virginia Medical Center, Charlottesville, Virginia 22901.

It has been shown that cyclic (cAMP)-dependent protein kinase (PK) catalyzes the incorporation of ^{32}P from γ-labelled ATP into the purified inhibitory component of troponin (TNI). In addition, the phosphorylation of cardiac TNI occurs "in vivo", and its degree of phosphorylation increases in parallel with the inotropic effect of epinephrine (England, P. Febs. Letters 50:57, 1975). We found that phosphorylation of TNI causes a change in Ca^{++} sensitivity of cardiac actomyosin ATPase. The plot of Ca^{++}-ATPase activity of actomyosin vs. pCa was shifted to the left, i.e., greater sensitivity to Ca^{++} by the phosphorylation of troponin. Guinea pig heart actomyosin preincubated with γ-^{32}P-ATP, cAMP and PK resulted in a) an increased Ca^{++} sensitivity of the ATPase, and b) phosphorylation of a protein having a molecular weight of 28,000. This protein component may be either TNI or a light chain of myosin. To decide which one was responsible for the increased Ca^{++} sensitivity of actomyosin the following experiments on the reconstitution of actomyosin were performed using: 1) myosin plus F-actin-native tropomyosin (Faw) or 2) desensitized actomyosin plus native tropomyosin (NT). Previous incubation of cardiac Faw or NT with γ-^{32}P-ATP, cAMP and PK in both cases resulted in the phosphorylation of TNI and in a reconstituted actomyosin with a greater Ca^{++} sensitivity. In summary, phosphorylation of cardiac TNI by cAMP-dependent PK increases Ca^{++} sensitivity of cardiac actomyosin and this effect may be one of the mechanisms involved in the inotropic action of β-adrenergic agonists.

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AEROBIC POWER AND BODY FAT IN A MILITARY POPULATION. J. A. Vogel and J. F. Patton. U.S. Army Rsch. Inst. of Env Med., Natick, MA 01760

It has been suggested that physical fitness and specifically maximal aerobic power, is inferior in young adult men in the United States as opposed to Western Europe. We have determined actual maximal oxygen uptake ($\dot{V}O_2$ max) and body fat (BF) in two groups of soldiers between the age of 17 and 35. One group was unselected new assignees (group NA, n = 234) to an infantry division while the second group was randomly sampled after five months (group 5M, n = 165) in the division. $\dot{V}O_2$ max was determined on the treadmill by an interrupted technique with the Douglas bag procedure and % BF estimated from four skin folds. Mean ± SD for age, $\dot{V}O_2$ max and % BF, respectively, for group NA was 23.3 ± 5.3 years, 49.6 ± 7.0 ml/kg·min and 17.8 ± 5.7% and for group 5M was 22.9 ± 3.4 years, 52.3 ± 5.7 ml/kg·min and 16.6 ± 4.8%. $\dot{V}O_2$ max and % BF for group NA when divided into four age groups are shown in the following table (mean ± SD):

	Age group			
	17-20	20-25	25-30	30-35
n	73	95	38	23
$\dot{V}O_2$ max, ml/kg·min	53.3±5.0	50.0±6.7	46.5±6.7	43.8±6.3
% BF	15.8±4.1	17.9±6.1	19.3±5.9	20.0±5.8

Thus $\dot{V}O_2$ max decreased by approximately 20% and % BF increased by 25% over this age span. Correlation coefficient for $\dot{V}O_2$ max to age was r = -.55 and $\dot{V}O_2$ max to % BF was r = -.65. Five months of infantry division training eliminated most of the age related changes. It is concluded that these levels of aerobic power for young U.S. soldiers are as high as those reported for Western European Army populations.

EFFECTS OF BODY TEMPERATURE ON THE LEVEL OF RENAL FUNCTION IN HYPOTHERMIC HAMSTERS. W. A. Volkert,* G. E. Tempel,* and X. J. Musacchia (Spon: R. P. Breitenbach). Departments of Radiology and Physiology, and Dalton Research Center, University of Missouri, Columbia, MO 65201.

The applicability of the scintillation camera in observing renal function in hamsters at low body temperatures (T_{re} 6-15C) has been recently described. This methodology has been refined to enable quantification of glomerular filtration and tubular secretion at low body temperatures. Distribution of ^{99m}Tc-DTPA and ^{131}I-orthoiodohippurate was followed in hamsters positioned 8 inches below the orifice of a pinhole collimator of a Searle Analytical H.P. Scintillation camera hardwired to a PDP-11 computer. This system yields whole body distribution and percent of injected activity concentrated by the kidneys as a function of time following i.v. administration. It was shown that the kidneys are perfused at low body temperature, and that the degree of perfusion increases as the temperature increases. The rate of ^{131}I-orthoiodohippurate is only 3.2±2.5%/hr at T_{re} 6-8C, continually increasing to a value of 15.0±1.6%/hr at T_{re} 12-13C. There is a sharp rise in this rate at T_{re} 15C to 25-30%/hr. Concentration of ^{99m}Tc-DTPA, an agent predominantly filtered, is not measureable below T_{re} 13C, suggesting minimal or filtration at low temperatures. In a parallel series of experiments, mean arterial pressure showed a similar direct relationship to temperature. At T_{re} 7C, renal perfusion occurred at a pressure of 47.5±6 mmHg, increased to 75.5±6, and 93.0±4.4 mmHg at T_{re} 12 and 15C, respectively. The rapid rise in pressure explains, in part, the reported increase in filtration. These data indicate that renal secretory activity is functional, although to a minimal extent, in deeply hypothermic hamsters (T_{re} 6-12C). (Supported by NASA NGL 26-004-021 S10 and Dalton Res. Ctr.)

APPARENT TOLERANCE OF CENTRAL RESPIRATORY MECHANISMS TO ANTICHOLINESTERASE INTOXICATION. J.K.D. von Bredow*, N.L. Adams* and H.V. DeVera* (SPON: F.N. Craig). Biomedical Laboratory, Edgewood Arsenal Aberdeen Proving Ground, Md. 21010

The primary lethal effect of toxic amounts of lipid soluble anticholinesterase compounds is believed to be due to a depressant effect on the central respiratory mechanisms. Administration of a lethal dose of a lipid soluble anticholinesterase compound to an anesthetized cat preparation will induce an immediate halt in all central respiratory activity, however, repeated administration of sublethal doses induces a revised state which ultimately allows the administration of multilethal doses of the same or other anticholinesterase compound without a halt in the central respiratory activity. If the anticholinesterase compound is administered in small increments the phenomena can be induced by any route of administration. In spite of apparent adequate central respiratory activity the diaphragm and intercostal muscles do not respond to the electrical activity of the phrenic nerve. Therefore, although the central respiratory mechanisms can apparently become desensitized, the peripheral neuromuscular junction cannot adapt by any schedule of anticholinesterase compound administration. The apparent central desensitization but lack of peripheral adaptation may suggest that the central respiratory mechanism consists of several neuronal systems which can be reorganized during repeated sublethal exposures to anticholinesterase compounds.

CEREBRAL CAPILLARY TRANSPORT OF METHIONINE AND OTHER NEUTRAL AMINO ACIDS BY THE L TRANSPORT SYSTEM. Lester A. Wade* and Robert Katzman, Dept. of Neurology, Albert Einstein College of Medicine, Bronx, New York 10461.

Evidence has accumulated that transport of neutral amino acids across the blood-brain barrier may occur chiefly by the L (leucine) transport system. To determine whether the other major neutral amino acid system, the A (alanine) system, is functional at the cerebral capillary, the uptake of L-(3-^{14}C)methionine was investigated using the non-metabolizable synthetic amino acids BCH (2-aminonorbornane-2-carboxylic acid and MeAIB (α-(methylamino)-isobutyric acid), specific inhibitors of the L and A systems, respectively. The uptake of radioactively labeled neutral amino acids across the cerebral capillaries in vivo was measured in the rat by the carotid injection technique of Oldendorf. The total uptake of radioactive L-(3-^{14}C)methionine was composed of a saturable component and a nonsaturable component over a concentration range of 0.02 to 4 mM. At an injected concentration of 0.05 mM, similar to plasma levels, the nonsaturable component with a K_d of 0.014 min^{-1} accounted for less than 8% of the total methionine transport. Nonradioactive MeAIB at a concentration of 2 mM (40 times that of L-(3-^{14}C)methionine) had no effect. In contrast, the saturable transport of L-(3-^{14}C)methionine was inhibited by BCH with maximum inhibition estimated at 90%. The remaining 10% may be due to the variability of our system. We have similar findings for DOPA and isoleucine. Thus, we have been unable to demonstrate any transport across the cerebral capillaries by the A system. These data suggest that the neutral amino acids are predominantly transported by the L system at the cerebral capillaries.

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SEPARATE AND COMBINED EFFECTS OF ALTITUDE (3048 m) AND ELEVATED BLOOD CARBOXYHEMOGLOBIN (% HbCO) ON MAN'S WORK PERFORMANCE. J. A. Wagner, S. M. Horvath, and G. M. Andrew*. Inst. Environmental Stress, U.C.S.B., Santa Barbara, CA 93106

Six men (22-34 yrs) performed bicycle work (55% sea level $\dot{V}O_{2\ max}$) for 30 min in an altitude chamber under the following 4 conditions: I, simulated sea level (30.5% amb O_2, 523 torr P_{amb}) with 0.5 ± 0.0 % HbCO; II, simulated sea level with 4.2 ± 0.1 % HbCO; III, altitude (20.9% amb O_2, 523 torr P_{amb}) with 0.5 HbCO; and IV, altitude with 4.2 HbCO. During submaximal work under (I) conditions the subjects performed the work with a mean oxygen uptake ($\dot{V}O_2$) = 2.10 ± 0.13 L/min, minute ventilation ($\dot{V}E_{BTPS}$) = 53.6 ± 5.9 L/min, and heart rate (HR) = 138 ± 15 beats/min. The absolute $\dot{V}O_2$ was not altered during exposures (II, III, or IV): $\dot{V}E$ and HR remained unchanged during (II) but increased progressively with exposures III and IV. Cardiac output (nitrous oxide technique) was the same during (I) and (III), but was slightly lower during (II) and 23% higher during (IV). Arterial-venous O_2 differences reflected the changes in cardiac output, being slightly higher during (II) than during (I) and 20% lower during (IV). These observations suggest that during this submaximal work the hypoxic effects of carbon monoxide and altitude are quite different and not simply additive.

COMPARISON OF INERT GAS EXCHANGE IN SERIES AND PARALLEL MODELS OF THE LUNG. P.D. Wagner and J.W. Evans*. Depts. of Medicine and Mathematics, University of California San Diego, La Jolla, Ca 92037

Inert gas exchange has been calculated and compared in two two-compartmental models of the lung: 1) one with units ventilated in series 2) one with units ventilated in parallel. This was done for each model by expressing its mixed expired inert gas tension (P_E) as an algebraic function of inert gas solubility and the distributions of both ventilation and blood flow within the model. Then, the conditions were determined for P_E in the two models to be algebraically identical simultaneously for all inert gases. Under the simplest assumptions, namely, of inert gas exchange alone without accompanying O_2 or CO_2 exchange, a parallel lung could always be found so as to have identical gas exchange to that in any given series model. In this particular case the analysis could be extended from two to any number of compartments. The same result was obtained in the more complex situation of simultaneous inert and respiratory gas exchange, provided that the inspired inert gas tension (P_I) was zero. However, when P_I was greater than zero, it was never possible to find a parallel model with the same gas exchange as a given series model. It is concluded that under the usual conditions for measuring inert gas elimination (P_I=0), it is not possible on theoretical grounds to distinguish between series and parallel forms of ventilation-perfusion inequality with our previously described method (J. Appl. Physiol. 36:588-599, 1974). However such a distinction might become feasible if P_I were made greater than zero, and experimental errors were sufficiently small.

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AORTIC AND PERIPHERAL VASCULAR RESPONSES TO ASPHYXIA BEFORE AND AFTER ALPHA-ADRENERGIC BLOCKADE. W. E. Walker* and W. R. Milnor, Dept. of Physiology, Johns Hopkins University School of Medicine, Baltimore, Md.

Experiments were performed in five mongrel dogs (av. wt. 21 kg), anesthetized with pentobarbital and paralyzed with succinylcholine. Each was subjected to a two-minute period of asphyxia (A) by stopping the ventilator, both before and after alpha-adrenergic blockade (AAB) with phenoxybenzamine 1.5 mg/kg IV. Pulsatile aortic root flow (Q_{AO}) and pressure (P_{AO}) were recorded continuously. Characteristic aortic impedance (Z_O) was estimated as the average input impedance modulus between 2 and 12 hz, input resistance (R_{IN}) was $\overline{P}_{AO}/\overline{Q}_{AO}$ and both the steady and pulsatile (W_{osc}) components of external power were calculated. After 2 mins asphyxia, arterial blood measurements (in 3 dogs) averaged pO_2 = 20 mm Hg, pCO_2 = 48 mm Hg, pH = 7.32. The results were as follows (averages ± S.E.M.):

	$\overline{P}_{AO}$ mm Hg	$\overline{Q}_{AO}$ ml sec^{-1}	R_{IN} dsc^{-5}	Z_O dsc^{-5}	W_{osc} %
Control	102 ± 3	34 ± 4	4225 ± 360	144 ± 10	10 ± 0.3
Asphyxia	113 ± 6	36 ± 6	4730 ± 540	148 ± 9	13 ± 0.4
Control (AAB)	82 ± 6	44 ± 8	3135 ± 645	135 ± 6	15 ± 0.3
Asphyxia (AAB)	44 ± 4	36 ± 6	1770 ± 135	191 ± 10	43 ± 0.8

There was little change in Z_O and W_{osc} % with A before AAB, but after AAB there was a significant increase over control both in Z_O and W_{osc} % suggesting that the aorta had become stiffer. Similar changes in resistance have been observed by many investigators, and indicate alpha-adrenergic activation of arteriolar smooth muscle. The increased impedance with hypoxia after AAB, however, suggests that the response of aortic smooth muscle is not mediated by alpha-adrenergic receptors.

CLOSING VOLUME IN ANESTHETIZED SUBJECTS. C.L.Waltemath* and N.Bergman, Dept. of Anesthesiology, Univ. of Oregon Med.Schl., Portland, OR 97201

Closing volume (CV) was measured in supine anesthetized patients who were paralyzed, artificially ventilated and receiving nitrogen-free gas. A pressure-volume curve for the total respiratory system from residual volume (RV) to total lung capacity (TLC) was initially obtained in each subject. Vital capacity (VC) was defined as the volume between the point where no further gas could be aspirated from the lung and the abrupt decrease in slope of the pressure-volume curve at its upper end. To measure CV, the lungs were aspirated to RV. A 500 ml bolus of air was injected followed by inflation to TLC with oxygen. After 3-5 sec at TLC deflation back to RV was performed. Both inflation and deflation occurred at a constant flow of 0.2-0.3 l/sec delivered by a 7000 ml syringe controlled by a linear drive mechanism. During deflation exhaled N_2 concentration, expiratory flow rate and transthoracic pressure were displayed as functions of exhaled volume on a storage oscilloscope. Volume of gas added to or removed from the lungs was measured by simultaneously determining volume of gas moving between the gas-tight cylinder behind the piston and a spirometer. VC measured during anesthesia was always larger than that determined or predicted in the conscious state. In seven anesthetized subjects magnitude of CV expressed as percentage VC was comparable to values reported by others for conscious subjects of identical age. In this small group CV coincided with functional residual capacity at about age 40. Adaptation of CV measurement for use in apneic subjects provides a technique for studying closure of lung units in anesthetized patients and during artificial ventilation of patients in respiratory failure.

ZINC LOCALIZATION AND TURNOVER IN RATS: PRELIMINARY REPORT. J. WANG,* M. KIRCHER,* and R.N. PIERSON, JR. St. Luke's Hospital Center NYC 10025

Zinc metabolism as measured by plasma concentration is abnormal in alcoholism and in certain disease status. This study developed organ uptake and turnover data for 17 organs and for certain sub-cellular fractions in the rat, using ^{65}Zn, as a baseline for subsequent studies in the rat model for alcohol toxicity and malnutrition.

Mature (280 - 320 g) male Sprague-Dawley rats were sacrificed 1,7, and 14 days after intravenous ^{65}Zn. Complete urine and fecal excretion was monitored, and ^{65}Zn content in skin, muscle, liver, spleen, kidney, heart, lung, fat, intestine, stomach, brain, gonads, thyroid, bladder, prostate, bone, marrow, plasma, and RBC was measured at each time interval. In liver and muscle, cell sap (CS) and cell sap free (CSF)fractions were separated; in CS and plasma, soluble protein-bound zinc (PB Zn) was further characterized by polyacrylamide gel electrophoresis.

Zn retention is 92, 67, and 59% at 1, 7, and 14 days after I.V. dosing Bone, muscle, skin, and liver contain 47.1% of tracer at 14 days. Liver turnover is rapid, followed by rise in plasma and muscle PB Zn, and muscle CSF Zn, indicating hepatic incorporation of Zn into proteins. Electrophoresis showed muscle and liver CS Zn binding to species of 80,000, 92,000 and 131,000 daltons. Net turnover is slow in muscle, fat, prostate, gonad, bone, brain; intermediate in intestine, stomach, thyroid; and fast in skin, liver, lung, kidney and spleen.

Instrumental capability to measure Zn to levels of 0.1µg/ml by AA spectroscopy, and ^{65}Zn (T 1/2 245 days) to 2 nanocuries/ml permit specific activity levels to be determined, and therefore space size and organ turnovers to be measured, under physiological conditions and with safe and convenient doses of radioactive tracer well suited to study biological parameters.

MODULATION BY ANGIOTENSIN OF BAROREFLEXIVE DEPRESSION OF TOTAL BODY OXYGEN CONSUMPTION AND HEART RATE.
N. Wasserstrum and J.A. Herd, Dept. Physiology, Harvard Medical School, Boston, MA 02115

Unanesthetized squirrel monkeys exposed to an ambient temperature of 10°C showed elevations in total body oxygen consumption ($\dot{V}O_2$), systemic arterial blood pressure (BP), and heart rate (HR) above values recorded at 28°C. Further elevation of BP in the cold by intravenous infusion of phenylephrine (5-50 $\mu g/kg \cdot min$) was accompanied by reduction in both $\dot{V}O_2$ and HR, and the changes in $\dot{V}O_2$ were proportional to those in HR. When BP was raised by intravenous infusion of angiotensin (0.05-1.0 $\mu g/kg \cdot min$), large elevations in BP were again accompanied by reductions in HR and $\dot{V}O_2$. However, for equivalent elevations in BP, the depressions in both HR and $\dot{V}O_2$ were much smaller with angiotensin that they were with phenylephrine. Previous studies in this laboratory have demonstrated that in response to experimental elevation of BP, reflexes originating at the sino-aortic baroreceptors depress not only HR but also $\dot{V}O_2$. The present results suggest that angiotensin modulates baroreflexive responses to elevation in BP. The reductions in HR and $\dot{V}O_2$ that ordinarily occur in response to baroreceptor stimulation may be modified by an action of angiotensin on the central nervous system.

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STUDIES OF TWO KIDNEY RENOVASCULAR HYPERTENSION IN THE DOG. B.E. Watkins* and J.O. Davis (SPON: W.M. Hart). Dept. Physiology, University of Missouri School of Medicine, Columbia, Missouri 65201

Hypertension was produced in 10 dogs by plicating one renal artery to reduce renal blood flow by 80% while leaving the opposite kidney intact. Mean arterial pressure (MAP) increased from 116±3 (SEM) to 144±5 mm Hg ($P<.001$) by the second day after plication. All dogs had elevated plasma renin activity (PRA) and increased water turnover for 6 days after plication. Sodium was retained during the first 3 days and the increase in total body Na was maintained for 10-20 days. In two of the dogs MAP fell after 40 and 65 days and marked atrophy of the plicated kidney was observed during laparotomy. In 3 other animals, MAP fell to normal after 60-80 days, coincident with development of pericapsular collaterals. Ligation of these collaterals re-established the hypertension for as long as 2 months when the study was terminated. Two other dogs had elevated MAP for 24 and 28 days when the observations were ended. The remaining 3 dogs had MAP which returned to normal between 10 and 14 days after plication in association with renal atrophy. The effect of angiotensin II (A-II) blockade on blood pressure was studied in 5 dogs which had been hypertensive for 1 month. Infusion of 1-sar-8-ala-angiotensin II did not alter MAP or PRA in the Na replete state. In the same animals during Na depletion, the already elevated PRA rose four-fold during A-II blockade while MAP fell from 136±5 to 106±9 mm Hg ($P<.005$). Saline replacement during A-II blockade increased MAP to 127±9 mm Hg ($P<.01$) while PRA dropped by 50% ($P<.05$). With cessation of the infusion, MAP increased to 153±3 mm Hg ($P<.05$) in spite of continued decline of PRA. These studies indicate that A-II is supportive in maintenance of 2 kidney hypertension in dogs during Na depletion.

EFFECTS OF SOME INSECTICIDES ON THE SHORT-CIRCUIT CURRENT AND RESISTANCE OF ISOLATED FROG SKIN. G.D. Webb and R.W. Sharp, Dept. of Physiology and Biophysics, University of Vermont College of Medicine, Burlington, VT 05401.

Previous work in our laboratory has shown that DDT blocks Na-K ATPase in the intact electroplaque of the electric eel (Niemi and Webb, Fed. Proc. 31:395, 1972). In the present study, a number of insecticides were screened for possible effects on active transport of Na and K. The isolated frog skin preparation was used because the short-circuit current (SCC) is easily measured and is believed to usually represent the active transport of Na. Paired right and left pieces of abdominal skin from large specimens of Rana pipiens were mounted in Ussing-type chambers modified for minimization of edge damage. In each experiment the effect of a 60 minute exposure of both sides of the skin to 2×10^{-4} M insecticide in Ringer containing 1% N,N-dimethylformamide (DMF) was compared to the control skin which was simultaneously exposed to 1% DMF-Ringer. We found that DDT, aldrin, γ-chlordane, and endrin had very little effect on the SCC of the frog skin. Carbaryl and dieldrin increased the SCC while simultaneously decreasing the resistance, suggesting that Na may have been entering the transporting cells more readily at the outer membrane, a hypothesis we are now testing. Nonachlor decreased the SCC while increasing the resistance, suggesting that Na may have been entering the transporting cells more slowly, thus slowing the Na pump. Lindane, the smallest molecule tested, increased both the SCC and the resistance, suggesting a possible stimulatory effect directly on the Na-K transport mechanism. The lack of any significant effect of DDT, which is known to block Na-K ATPase in a variety of preparations, suggests that the frog skin may have permeability barriers which prevent large molecules from reaching the active Na-K ATPase. Supported by USPHS Grant #RO1 00885-02.

A NEW TERM FOR THE BODY HEAT (ENERGY) BALANCE EQUATION. Paul Webb. Webb Associates, Yellow Springs, Ohio 45387.

Direct and indirect calorimetry measure all the terms except heat storage ($\triangle H$, for change in enthalpy) and work (W) in the standard body heat balance equation: $\triangle H = M-(\pm R\pm C\pm K\pm E) - W$. We have used continuous direct and indirect calorimetry, plus conventional ergometry during exercise, to derive values for $\triangle H$ every hour of 24-hr experiment days. The values of $\triangle H$ for single hours have varied between 95 and -163 kcal ($\bar{x} = 4.7$ kcal ± 30.1, $n = 312$), yet body temperature data failed to vary accordingly. For full 24-hr periods, the standard heat balance has given believable values for $\triangle H$ only when a subject rested in a chair all day and lay down to sleep at night. The equation has given huge values for $\triangle H$ in other situations (work, sleeplessness, and a 24-hr food deficit); $\triangle H$ in 24 hours has ranged from 958 kcal to -363 kcal, with little change in surface and deep body temperatures. It would seem that there is a term missing. If metabolic free energy (M) is equivalent to Gibbs' free energy, then an appropriate equation for energy balance (not heat balance) would be: $\triangle H = M-(\pm R\pm C\pm K\pm E)-W-T\triangle S$, where $T\triangle S$ is the absolute temperature (T) times the net sum of imported and exported entropy ($\triangle S$) of an open system. There is evidence for the $T\triangle S$ term (energy storage?) not only in our own data but in other human calorimetric studies from 1903 to the present. The new term might represent differences between endergonic and exergonic reactions, or something like a metabolic cost of mobilizing fuel stored in the body.

RELATIVE CAPABILITIES OF DIFFERENT PREGANGLIONIC INPUTS TO THE IMG TO CONTROL COLONIC MOTILITY. W. A. Weems* and J. H. Szurszewski, Mayo Clinic and Foundation, Rochester, Minnesota 55901.

Neurons in the inferior mesenteric ganglion (IMG) of guinea pigs receive neural input from the central nervous system, proximal viscera, colonic mechanoreceptors and pelvic regions. Experiments were designed to evaluate the relative ability of each of these inputs to independently alter colonic motility. In vitro experiments were conducted on IMG-colon preparations. Nerve trunks attached to the IMG were placed on platinum electrodes to permit electrical stimulation. Intracellular electrodes were used to monitor electrical activity of IMG neurons. Colonic motility was measured by recording intralumanal pressure. Using single stimuli, 96% of the neurons tested received the greatest synaptic input from the colonic nerve. Intermesenteric nerve stimulation produced the next largest synaptic response in 95% of the neurons tested and single inferior splanchnic nerves the least in 65% of the neurons tested. In the majority of neurons, maximal stimulation of either an inferior splanchnic or hypogastric nerve did not produce action potentials. Colonic motility was inhibited when the intermesenteric nerve was stimulated at frequencies as low as 1-7 Hz. When an inferior splanchnic or hypogastric nerve was stimulated, greater frequencies were required to alter motility. Mechanoreceptor input via colonic nerves was insufficient to alter motility. It is concluded that factors such as temporal distribution of input and organization of neural circuitry prevent colonic inhibition from being directly related to the maximum synaptic response of a given preganglionic input. (Supported by grant AM-17632 NIH and Minnesota Heart Association.)

EFFECT OF INDOMETHACIN ON FUNCTIONAL AND POST-OCCLUSIVE DILATION IN THE CANINE GRACILIS MUSCLE. R. Weiner, E.J. Messina, J. Rodenburg* and G. Kaley, Dept. Physiol., N.Y. Med. Col., Valhalla, N.Y. 10595

In order to evaluate further the role of prostaglandins in the regulation of skeletal muscle blood flow we examined the influence of indomethacin, a prostaglandin synthetase inhibitor, on the vasodilation which accompanies exercise and follows release of arterial occlusion. The vascularly isolated, denervated gracilis muscle of anesthetized dogs was perfused with a constant inflow of arterial blood by means of a pump. In a group of 10 dogs, functional vasodilation induced by a 1 min. period of muscle contraction was measured prior to (control) and following 10 min. infusion of indomethacin (100 μg/kg/min, i.a.). Vasodilator responses, reproducible for 2 to 3 hrs, were assessed by measuring the peak fall in pressure (ΔP) and the duration of the response. Control values (mean $\pm$ SE) for these parameters were -50.3 $\pm$ 4.8 mm Hg and 294 $\pm$ 63 seconds, respectively. Indomethacin significantly inhibited ΔP by 15% and shortened the duration of the dilation by 40% when compared to control reactions. In another group of 10 dogs, vasodilation evoked by a 2 min. period of arterial occlusion was evaluated before and following indomethacin. Significant inhibition of the post-occlusive dilation, as evidenced by a 40% reduction in the duration of the response was found in the dogs receiving indomethacin when compared to control responses (367 $\pm$ 73 sec.). In both groups of animals, indomethacin had no significant effect on resting (basal) vascular resistance. Overall these data lend additional support for the contention that prostaglandins contribute to local adjustments in vascular smooth muscle tone in skeletal muscle. (Supported by a grant from the National Heart and Lung Institute, HE-12342).

INVERSE CORRELATION BETWEEN ANAEROBIC THRESHOLD AND JUMPING ABILITY. P.C. Weiser*, G.P. Caffrey*, J.V. Weil*, and R.F. Grover. University of Colorado Medical Center, Denver, Colorado, 80220, and University of Denver, Denver, Colorado 80210

During graded exercise, anaerobic threshold has been defined as the level of O_2 uptake at which metabolic acidosis occurs, and this provides an added stimulus to ventilation. An oxygen demand greater than the available O_2 delivery has been suggested as the mechanism for the metabolic acidosis. An alternative mechanism could be a consequence of recruiting fast twitch, glycolytic lactate-producing (type 2) muscle fibers rather than slow twitch, oxidative (type 1) fibers. To test for this alternative mechanism, a vertical jump was used as an estimator of type 2 fiber predominance and compared to the anaerobic threshold. Eleven physically active women from 22 to 42 years were studied. $\dot{V}O_2$ max was determined with a continuous, graded treadmill test. Anaerobic threshold was taken as the highest O_2 uptake on the linear portion of the $\dot{V}_E$-$\dot{V}O_2$ curve and ranged from 52.0 to 81.2% $\dot{V}O_2$ max. Vertical jump was measured and ranged from 27 to 61 cm. Anaerobic threshold was not correlated with $\dot{V}O_2$ max. However, anaerobic threshold was highly inversely correlated with vertical jump ($r = -.93$; $p < .01$). It is suggested that individuals with higher jumping ability due to a presumed preponderance of glycolytic fibers also have a lower anaerobic threshold. Hence, the pattern of muscle fiber type may be an important determinant of anaerobic threshold. (Supported by NIH grants HL14985 and HL05973.)

EFFECTS OF SELF DETERMINED INTRAVENOUS INFUSIONS ON THE SATIATION OF SODIUM APPETITE OF SODIUM DEFICIENT SHEEP. R. S. Weisinger*, D. A. Denton* and M. J. McKinley* (Spon: I. Darian-Smith). Howard Florey Institute, University of Melbourne, Vic. 3052, Australia.

Sheep with parotid fistulae continually lose large volumes of sodium (Na) rich saliva. After 24-48 hr Na deprivation, these animals rapidly and commensurately replace Na deficits of 150-800 mEq over 3-10 min. Previous studies have shown there is a time lag in the response of salt appetite to a change of body Na balance produced by systemic infusion. A sudden rise of cerebral arterial [Na] during 7 min prior to and the first 7 min of presentation of $NaHCO_3$ solution did not reduce intake during 15 min of access. To study further this problem, sheep with parotid fistulae were trained to bar press for 2 hr daily in order to obtain Na. As control condition, either 10 ml or 50 ml of 300 mEq/l $NaHCO_3$ was delivered to a cup in the animal's cage. Patterns of voluntary Na intake were established for 4 animals under each condition, and the number of deliveries between conditions was significantly different by 20 min (50 ml = 16.8 ± 1.1 (SEM) vs 10 ml = 37.1 ± 4.6, $p<0.001$, paired t-test). Then intravenous infusion of NaCl solution (6 ml in 10 sec) was paired with the 10 ml delivery, i.e., each delivery consisted of 10 ml (cup) and 6 ml (I.V.). The results indicated that with 15 mEq Na per delivery (50 ml (cup), or 10 ml (cup) + 6 ml of 2M NaCl (I.V.)), Na acquisition was substantially finished by 20-30 min. With 3-3.9 mEq Na per delivery (10 ml (cup) or 10 ml (cup) + 6 ml of 0.15M NaCl (I.V.)), Na acquisition persisted at a high rate for 90-120 min. In 12 experiments, sheep worked for significantly fewer deliveries by 20 min when the I.V. infusion was 2M NaCl (18.2 ± 2.6) than when it was 0.15M NaCl (32.0 ± 4.5) ($p<0.05$, paired t-test). Therefore, self determined, large bursts of I.V. Na were effective in satiation of Na appetite.

CHANGES IN pH AND PCO_2 IN CEREBROSPINAL FLUID, ARTERIAL AND JUGULAR BULB BLOOD, IN MAN, AFTER 5 DAYS AT P_B 447 TORR. R.B. Weiskopf, R.A. Gabel, and V. Fencl. US Army Res Inst of Env Med, Natick, MA 01760 and Depts of Anes, P B Brigham Hosp and Harvard Med Sch, Boston, MA 02115

In six healthy young male volunteers, lumbar cerebrospinal fluid (LCSF), jugular bulb (IJ) and arterial (ART) blood were anaerobically sampled, pH and PCO_2 measured at sea level (SL) and after 5 days in a hypobaric chamber at P_B 447 torr (A). pH in intracranial CSF (CCSF) was estimated from LCSF [HCO_3^-] and from an estimate of cerebral tissue PCO_2: $[(PaCO_2 + P_{IJ}CO_2)/2]+1$. Mean values of pH, PCO_2 and [HCO_3^-] at A were significantly different ($P<0.02$) from those at SL (±SE):

	pH		PCO_2		[HCO_3^-]	
	SL	A	SL	A	SL	A
ART	7.396 ±.005	7.450 ±.010	41.0 ±1.1	28.3 ±1.2	24.8 ±0.4	19.7 ±0.5
IJ	7.344 ±.002	7.410 ±.010	50.2 ±0.6	33.6 ±0.8	26.8 ±0.3	21.3 ±0.8
LCSF	7.297 ±.005	7.327 ±.007	49.3 ±0.9	35.2 ±0.9	22.7 ±0.4	17.7 ±0.5
CCSF	7.318 ±.008	7.375 ±.014	46.6 ±0.8	31.9 ±1.0	22.7 ±0.4	17.7 ±0.5

pH in CSF was more alkaline at A than at SL, both as measured directly in LCSF, and as estimated for CCSF. The decrease in [HCO_3^-] was similar in CSF and in blood plasma (ART 5.1, IJ 5.5, LCSF 5.0 mM/L). These findings do not support the hypothesis that CSF pH is maintained normal by active transport of HCO_3^- during acclimatization to altitude.

DELINEATION OF THE DISTRIBUTION OF A LANTHANIDE (^{147}Pm) IN VASCULAR SMOOTH MUSCLE. George B. Weiss and Frank R. Goodman*. Department of Pharmacology, University of Texas Southwestern Medical School, Dallas, Texas 75235

In order to ascertain whether trivalent rare earth ions such as lanthanum (La^{3+}) penetrate the cell membrane under physiological conditions, the extracellular and cellular distribution of promethium (^{147}Pm), a carrier-free "analogue" of La^{3+}, was examined in rabbit aortic smooth muscle. Uptake of ^{147}Pm was inhibited by La^{3+} and other rare earth ions (neodymium, lutetium) only when the Pm:rare earth concentration ratio exceeded $1:10^6$. However, Ca^{2+} had no effect on ^{147}Pm uptake. Efflux of ^{147}Pm was transiently increased by 1.5 mM La^{3+}, and exposure to 0.05 mM ethylenediamine tetraacetic acid (EDTA) elicited an increased ^{147}Pm efflux with both transient and maintained components. The magnitude of the EDTA-induced increase in ^{147}Pm efflux was similar over a 30-fold range of EDTA concentrations (0.05-1.5 mM); the limiting factor for ^{147}Pm efflux is the rate of ^{147}Pm desorption rather than the EDTA concentration. Loss of ^{147}Pm in the presence of 0.5 mM EDTA could be described in terms of two washout components (one of which was the extracellular space). Uptake of ^{147}Pm was inhibited by lowering the incubation solution temperature to 0°C or by procaine. Metabolic inhibitors (iodoacetate and dinitrophenol) did not decrease either uptake or efflux of ^{147}Pm. Thus, ^{147}Pm distribution can be described in terms of a binding at and desorption from surface-accessible cellular sites. Significant quantities of ^{147}Pm do not appear to penetrate into and accumulate within the cell. (Supported by USPHS grant HL-14775.)

REGIONAL VENOUS OXYGEN SATURATION IN THE DOG HEART. Harvey R. Weiss and A. K. Sinha. C.M.D.N.J.-Rutgers Medical School, Department of Physiology, Piscataway, New Jersey 08854.

Regional oxygen saturation ($\%HbO_2$) of the frozen dog heart was measured in arteries and veins of the septum and left and right ventricular free walls. Hearts removed from anesthetized open chested dogs were frozen in liquid nitrogen chilled propane. Using a three wavelength (560,523,506 nm) microspectrophotometric method and 30 μ sections from the frozen heart, $\%HbO_2$ was determined in vessels ranging in diameter from 20 μ to 500 μ. No differences were observed in average venous $\%HbO_2$ between the right, left or septal walls. The mean venous $\%HbO_2$ was 21%. No gradients were observed in the base to apex plane of the heart in venous $\%HbO_2$. There was a large difference with depth in the left ventricular free wall. The subepicardial (superficial) venous $\%HbO_2$ averaged 26% and the subendocardial was 14%. These differences are similar to those observed with measurements of tissue Po_2. There were no observable differences in arterial $\%HbO_2$ which averaged 86.2% for these dogs. These findings support the hypotheses that the supply-demand relation for oxygen is more precarious in the subendocardial region of the left ventricle than in the rest of the heart. This study was supported in part by USPHS Grant HL-16134 and a grant-in-aid of the American Heart Assoc., N.J. Affiliate.

VASCULAR RESPONSES IN SKELETAL MUSCLE TO HYPOXIA AND ASPHYXIA. M.L. Weissman*, E.H. Rubinstein, and R.R. Sonnenschein, Dept. Physiology, U.C.L.A. School of Medicine, Los Angeles, Ca. 90024.

Vascular responses in the cat's skinned hind limb (paw tied off) to short term systemic hypoxia, hypercapnia, and asphyxia were characterized. Anesthetized, atropinized, paralyzed, mechanically respired cats were ventilated for 2-4 minutes with combinations from among seven test gases (7-21% O_2, 0 or 10% CO_2) while femoral artery flow was monitored. All gases produced a rise in arterial pressure and increased femoral resistance; asphyxic gases produced the greatest resistance increases, with decreased flow. Longer term responses to moderate asphyxia (10% O_2 + 10% CO_2; PaO_2=32-45, $PaCO_2$=60-80)were similarly assessed. 10-20 minutes of asphyxia produced pressor responses and sustained femoral resistance increases in most animals. Following lumbar sympathectomy plus peripheral denervation, moderate asphyxia produced an initial passive rise in flow followed by a gradually developing constriction; adrenalectomy did not alter this response pattern. With lumbar sympathectomy plus electrical pacing of the distal cut end of the sympathetic chain to re-establish the normal control flow level, moderate asphyxia produced a passive, sustained rise in flow. Intra-arterial infusion of phenoxybenzamine into the peripherally denervated skinned hind limb converted the previously observed constriction into a large sustained dilatation. Our results suggest that asphyxia may induce a local release of norepinephrine from the peripheral sympathetic nerve terminals in skeletal muscle. Another possibility is that a humoral agent of non-adrenal origin is released, which either excites peripheral α-receptors or excites other receptors blocked by phenoxybenzamine.

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ACIDOSIS ACTIVATION OF THE PITUITARY-ADRENAL-RENAL GLUTAMINASE I AXIS. T.C. Welbourne, Dept. Medicine, Université de Montréal, Montréal, P.Q. Canada.

My previous studies demonstrated the adrenal glands were necessary for acidosis activation of the mitochondrial glutaminase I pathway. The present studies were undertaken to determine if corticosterone levels are elevated in acidotic rats and if so, whether acidosis stimulates the adrenal glands directly or via the pituitary-adrenal axis. Metabolic acidosis induced by NH_4Cl, either acute or chronic, increased corticosterone levels 200 to 230 per cent in intact rats. Acute metabolic acidosis did not activate the mitochondrial pathway in adrenalectomized rats nor was there any increase in the corticosterone levels. Neither was the corticosterone levels elevated in hypophysectomized rats nor did activation of the mitochondrial pathway occur in response to acidosis. Therefore acidosis does not stimulate the adrenal gland directly rather it requires the intact pituitary. Administering exogenous adrenocorticotrophin to hypophysectomized rats resulted in an elevation of the plasma corticosterone levels and activation of the mitochondrial pathway. The pituitary-adrenal cortex-renal glutaminase I axis apparently operates as a functional unit in the homeostatic response to metabolic acidosis.

DENSITY DEPENDENCE OF MAXIMAL EXPIRATORY FLOW IN NORMAL SUBJECTS BEFORE AND AFTER ATROPINE AND ISOPROTERENOL. J.J. Wellman,* E.R. McFadden and R.H. Ingram, Jr.* (SPON: D.J. Strieder). Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass. 02115

Both atropine and isoproterenol dilate airways in normal subjects. Atropine blocks postganglionic cholinergic neural pathways and isoproterenol acts directly on smooth muscle, presumably by beta receptor stimulation. In order to explore the site of bronchodilation we have studied the density dependence of maximal expiratory flow ($\dot{V}_{max}$) in normal subjects. Plethysmographic maximal expiratory flow volume (MEFV) curves were obtained with the subjects breathing air (A) and after the lungs were washed out with an 80% He-20% oxygen mixture (He). Density dependence of $\dot{V}_{max}$ was expressed as a ratio of $\dot{V}_{max}$ He to $\dot{V}_{max}$ A at the same lung volumes in the mid vital capacity (VC) range. The results are reported for 8 subjects before and after the respective bronchodilators. There was a similar increase in $\dot{V}_{max}$ A at 50% VC after both bronchodilators (atropine 4.90 L/sec to 6.07 L/sec [means]); isoproterenol 4.84 L/sec to 5.90 L/sec [means]). After atropine the decrease in density dependence (1.46 to 1.20 [means]) in association with an increase in $\dot{V}_{max}$ A suggests an increase in the relative contribution of small airways to flow limitation. This could be due to either a more peripheral movement of the equal pressure point (EPP) or preferential dilatation of larger airways within the same upstream segment. The increase in density dependence after isoproterenol (1.41 to 1.64 [means]) suggests an increase in the relative contribution of large airways to flow limitation. This could be due either to a more mouthward movement of the EPP or relatively greater dilatation of smaller airways of the same upstream segment. We conclude that the two bronchodilators differ not only in neuropharmacologic terms but also in the mechanism of increases in $\dot{V}max$.

CHOLINE UPTAKE AND METABOLISM IN PLACENTA. Frank Welsch, Dept. of Pharmacology, Michigan State University, East Lansing, Michigan 48824.

Free choline (Ch) is one of the substrates for choline acetyltransferase (ChAc) in the biosynthesis of acetylcholine (ACh). The latter two occur in high concentrations in noninnervated human placenta where ACh is believed to be involved in the regulation of transport. Therefore it was of interest to study the fate of Ch in this tissue. Methyl-^{3}H-labelled Ch (^{3}H-Ch) was taken up into fragments of human term placenta *in vitro* by a process which fulfilled common criteria for active transport and was competitively inhibited by hemicholineum-3. Upon entry into the placenta cells ^{3}H-Ch was rapidly metabolized. Following a 5 min incubation with 5 μM ^{3}H-Ch 95% of the radioactivity in a homogenate was acid soluble (a.s.) while 5% remained in the acid insoluble (a.i.) portion. After 30 min the distribution was 88% and 12% respectively. Paper high voltage electrophoretic analysis of the a.s. material showed that after 5 min 55% of the ^{3}H had a mobility equal to authentic Ch, 35% equal to ACh, 6% to phosphorylcholine (PhCh) and 1% to betaine (Bet.). After 20 min it was 25% in Ch, 60% in ACh, 10% in PhCh and 2% in Bet. A chloroform-methanol extract from the a.i. residue revealed a linear increase of ^{3}H content from 0-30 min of incubation suggesting incorporation of ^{3}H-Ch into phospholipids. The results showed that the synthesis of ACh was the major pathway into which free Ch entered.

The existence of a very active ChAc has also been established in the placenta of the rhesus monkey by means of a specific radiometric assay combined with specific inhibitors of this enzyme. This supported a previous observation (C.O. Hebb and D. Ratkovic, J. Physiol. 163, 307, 1962) that significant concentrations of ChAc were present in the placentae of higher primates only. (Supported by NIH HD 07091.)

NOCTURNAL DEPRESSION OF THERMOREGULATORY THRESHOLDS. C.B. Wenger*, M. F. Roberts*, E.R. Nadel, and J.A.J. Stolwijk. John B. Pierce Fdn. Laboratory and Yale Univ. School of Medicine, New Haven, Ct. 06519.

Six subjects exercised on a bicycle ergometer at 60-70% of maximal aerobic power in an ambient temperature of 25°C. Experiments on each subject were conducted at night (3:00-6:00 a.m.) and in the early afternoon. Sweating rate ($\dot{m}_{sw}$) beneath a capsule on the chest was measured with resistance hygrometry. Forearm blood flow (BF), with a local skin temperature of about 35°C, was measured with electrocapacitance plethysmography. Esophageal temperature (T_{es}) was measured with a thermocouple at the level of the left atrium, and mean skin temperature ($\bar{T}_{sk}$) was computed from a weighted average of temperatures at three sites. Central thermoregulatory drive (CD), reflecting the relative contributions of T_{es} and $\bar{T}_{sk}$ to the control of $\dot{m}_{sw}$ and BF, was computed as $T_{es} + .125\ (\bar{T}_{sk} - 33°C)$. During the night, thresholds for sweating and vasodilation were shifted toward lower CD, but the slopes of the $\dot{m}_{sw}$:CD and BF:CD relations were unchanged from their daytime values. In any given subject, thresholds for sweating and vasodilation were shifted about equally. These shifts averaged 0.6°C (range: 0.2 - 1.1°C) for $\dot{m}_{sw}$ and 0.7°C (range: 0.2 - 1.2°C) for BF.

MECHANISM OF RECRUITMENT OF PULMONARY CAPILLARIES. John B. West, Alan M. Schneider* and Mark M. Mitchell*, Depts. of Medicine and Applied Mechanics and Engineering Sciences, University of California San Diego, La Jolla, California 92037.

Measurements of the number of open capillaries in rapidly frozen dog lungs have shown that many new capillary segments open up when the pulmonary arterial pressures is raised from low levels (J. Appl. Physiol. 32: 346-356, 1972). Since the capillary bed consists of a dense network of interconnected segments, we have studied by means of a computer simulation the behavior of a network of blood vessels in which a small critical pressure is required across each element for flow to occur. The critical pressures and resistances were randomly chosen from distributions. We found that recruitment (that is onset of flow) occurred over a large range of "arterial" pressures, and that relatively high arterial pressures were required before all elements were conducting. As a consequence the pressure-flow curve of the network was non-linear even when the individual elements had no "distensibility". Intermittent and reverse flow were commonly seen in some elements as the arterial pressure was raised in steps. The critical pressures required for such behavior in the human pulmonary microcirculation were calculated to be extremely small, of the order of 0.02 cm water. Pressures of this magnitude might result from sticking of red cells to capillary walls or to each other. We conclude that the properties of such a network may explain the patchiness of flow in the pulmonary microcirculation and the large range of arterial pressures over which recruitment is observed to occur.

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CAROTID BODY (CB) PO_2 DURING PERFUSION AND/OR SUPERFUSION WITH CELL-FREE SOLUTIONS (CFS). W.J. Whalen and P. Nair*, Dept. Research, St. Vincent Charity Hospital, Cleveland, Ohio 44115.

Tissue Po_2 (TPo_2) profiles were obtained in the CB of the anesthetized cat by means of a micro O_2 electrode during blood-perfusion (control) and, in series A, during perfusion with physiological CFS, (pH 7.35 - 7.45; glucose 5mM/L) equilibrated with air. Saline equilibrated with air or N_2 flowed over the CB. The $\bar{x}$ control TPo_2 values from 316 locations in 14 cats ranged from 10 - 104 mmHg ($\bar{x}$ = 72 ± 4 S.E.). During subsequent air-CFS perfusion the values from 593 locations ranged from 62 - 175 mmHg ($\bar{x}$ = 133 ± 3 S.E.). TPo_2 measurements were essentially independent of the O_2 in the superfusing solution, and of time (2-3 hours). In 4 additional experiments, (series B) perfusion with 100% O_2-CFS during the first 1 + hours yielded very high values for TPo_2 (300-500 mmHg). Subsequent TPo_2 values during air-CFS perfusion were not different from those in series A. In series C (6 cats) the CB was cleared of blood with air-CFS, perfusion stopped, and the CB superfused for 2-3 hours with solutions equilibrated with various gas mixtures. Results indicate that superfusion with solutions equilibrated with 50% O_2 (flow 6-8 ml/min) is adequate to maintain core Po_2 above 5 mmHg. We conclude that most studies on the artificially perfused or superfused CB can not be invalidated on the basis that the preparations were hypoxic. Supported in part by grant no. HL 13134 from USPHS.

L-(^{3}H)PROLYL-LEUCYL-GLYCINAMIDE (MIF) READILY PENETRATES THE BLOOD-BRAIN-BARRIER. Christopher Whalley*, Ruven Greenberg, Roderich Walter , Abba J. Kastin, and David Coy*. Dept. of Physiology, Univ. of Illinois Med. School, Chicago, Ill. 60680 and V. A. Hospital and Tulane Univ. School of Medicine, New Orleans, La. 70146.

There have been a number of examples of CNS behavioral effects subsequent to the parenteral administration of MIF. High levels of radioactivity have been demonstrated in the pineal and in the anterior and posterior pituitary regions of the brain of rats and mice by autoradiography and by direct measurement at 2 minutes and 10 minutes after i.v. injection of labelled MIF (Dupont et al., J. Endocr. 64, 243, 1975). We now report that MIF readily penetrates the Blood-Brain-Barrier after intra-carotid injection into rats by the Oldendorf procedure (Brain Res. 24, 372, 1970). Thus the MIF label readily enters the brain and presumably it could act at many brain sites. We have also measured its uptake into synaptosomes prepared from the whole brain and from hypothalamus, brain-stem and cerebral cortex of the rat. There is no evidence of a high affinity uptake except for a slight but not significantly increased uptake into hypothalamic synaptosomes. In similar studies, (^{14}C)arginine-vasopressin is highly impermeable to the Blood-Brain-Barrier; nor is there evidence for its uptake by a sodium-dependent system into synaptosomes.

EVIDENCE FOR A CO_2-MEDIATED PULMONARY CHEMOREFLEX IN DOG. B.J. Whipp, D.J. Huntsman* and K. Wasserman. Div. of Resp. Physiology and Medicine Harbor General Hospital-UCLA School of Medicine, Torrance, CA 90509.

We previously described an isocapnic hyperpnea which followed within a few seconds increases in cardiac output or CO_2 flux to the lungs. This response occurred even in the absence of the carotid bodies and following cervical vagotomy. We attempted to characterize this response further, by injecting into the superior vena cava (SVC) of 24 lightly anesthetized dogs (chloralose-urethane), three materials capable of abruptly increasing P_{CO_2} in the pulmonary circulation and alveolar gas: a) $NaHCO_3$, b) HCl and, c) blood equilibrated with 100% CO_2. The time of the initial ventilation ($\dot{V}$) responses were compared with those of NaCN and lobeline injected at the same site. The initial $\dot{V}$ response to $NaHCO_3$, HCl or CO_2-laden blood usually occurred in the breath during or following the increase in P_ACO_2, an average of 6.8 secs after the infusion. The hyperpnea in response to NaCN and lobeline occurred after 11.4 secs. No difference was observed when these materials were injected into the left atrium. Control SVC injections of venous blood, normal saline and hypertonic urea had no effect on $\dot{V}$. However, hypertonic saline did increase $\dot{V}$. The response to HCO_3^- was not abolished by vagotomy in 6 of 10 dogs, or in 3 of 4 with both vagotomy and carotid body resection. The response to hypertonic saline was abolished, however. We conclude that in lightly anesthetized dogs, a CO_2-mediated pulmonary chemoreflex exists whose afferent limb appears not to be vagal. (Supported by NIH Grants HL-14967 and HL-11907).

MECHANISM OF ABNORMAL PARASYMPATHETIC CONTROL OF HEART RATE IN HEART FAILURE. Carl W. White*, Dwain L. Eckberg and Francois M. Abboud (SPON: E.O. Theilen). CV Center and CV Division, Dept. of Medicine, University of Iowa and VA Hospitals, Iowa City, Iowa 52242.

Abnormalities in parasympathetic control of heart rate response to stimulation of baroreceptors occur in cardiac hypertrophy and failure. Alterations in the efferent limb of the parasympathetic response might result from changes in the sensitivity of the sinus node to the neurotransmitter acetyl choline (ACh) or from impairment in the release of acetyl choline from the vagus. To test these alternatives we studied parasympathetic heart rate control in 9 dogs with chronic cardiac failure (HF) produced by tricuspid ablation and pulmonic stenosis and in a control group (C) of 5 sham-operated and 4 unoperated dogs. The sinus node artery was isolated and perfused with arterial blood at constant flow rate. Dose response curves to the infusion of 10-100 µg of ACh into the sinus node artery showed no impairment in the responsiveness of the sinus node in heart failure. However, decreases in heart rate produced by vagal nerve stimulation (NS 0.1-10 Hz) were less in heart failure than in the control group ($p<0.01$).

	Basal Rate (beats/min)	Δ Rate			
		ACh		NS	
		25 µg	50 µg	0.3 Hz	1 Hz
Control	179±12	-16±4	-38±9	-32±4	-54±5
Heart Failure	168±10	-14±5	-34±9	-19±4	-36±5

Alterations in parasympathetic control of heart rate in cardiac failure are not secondary to decreases in the sensitivity of the sinoatrial node, but may result in part from impaired neurotransmitter release.

HABITUATION AND DISHABITUATION OF SYNAPTIC RESPONSES IN RETICULOSPINAL CELLS OF LAMPREY. Warren O. Wickelgren, Dept. of Physiology, Univ. of Colorado Medical School, Denver, CO 80220.

A single, low-intensity electrical stimulus applied to any of the cranial nerves produced a brief synaptic response in Muller cells (reticulospinal neurones) in the brainstem of lamprey. Synaptic responses produced by simultaneous stimulation of two cranial nerves summed linearly, indicating that separate pathways exist from each cranial nerve to a Muller cell. Repetitive low-intensity stimulation of one cranial nerve produced a progressive decline in the synaptic response. The characteristics of this synaptic "habituation" were similar to those reported in other organisms. There was no effect of repetitive low-intensity stimulation of one cranial nerve upon the synaptic response produced by stimulation of another, reflecting the separateness of the pathways. A single strong stimulus to a cranial nerve produced a large synaptic response followed by a high-frequency "afterdischarge" of synaptic activity which declined over a period of many seconds. In addition, such a single strong stimulus to one cranial nerve was capable of increasing the amplitude of a habituated synaptic response evoked by stimulation of another nerve (dishabituation). It is suggested that neurons responsible for the afterdischarge activity in Muller cells represent a single, high-threshold pathway common to all cranial nerves and parallel to the separate pathways activated by low-intensity stimulation and subject to habituation. Activity persisting within this afterdischarge pathway could sum with weak input from low-intensity stimulation to permit effective transmission through it and account for the phenomenon of dishabituation observed here. (Supported by NIH grants NS 09661 and NS 50295).

REGIONAL VASCULAR RESPONSES TO THE SOMATOPRESSOR REFLEX. C. Wickliffe*, D. Nutter, and H. Crumly.* Emory University School of Medicine, Atlanta, Georgia. (Spon: Jack L. Kostyo)

The regional circulatory effects of somatopressor reflexes (SPR) evoked by high intensity stimulation of tibial and radial nerves were studied in chloralose anesthetized, vagotomized dogs. SPR responses were compared with carotid baropressor reflex (BPR) and chemopressor reflex (CPR, nicotine stimulation) responses. Six, isolated, innervated regional vascular beds (hindlimb venous, hindlimb skin and muscle, left renal, mesenteric, and left circumflex coronary) were studied by constant flow pump perfusion, where perfusion pressure represents vascular resistance.

SPR, BPR, and CPR produced a significant elevation of mean systemic arterial pressure in all preparations. The reflex effects on regional resistance are shown below as perfusion pressure (mm Hg).

Vascular bed	SPR Baseline - Peak	BPR Baseline - Peak	CPR Baseline - Peak
Hindlimb venous (n=5)	28 - 25(-11%)	26 - 25(- 4%)	23 - 18(-18%)†
Hindlimb skin (n=4)	150 - 172(15%)	157 - 191(22%)	163 -122(-25%)†
Hindlimb muscle (n=4)	93 - 131(41%)†	97 - 156(38%)†	105 -146(28%)†
Left renal (n=7)	149 - 174(17%)†	150 - 173(15%)†	153 -184(20%)†
Mesenteric (n=7)	137 - 153(12%)†	139 - 152(9%)†	138 -150(8%)

In 4 vagotomized dogs SPR, BPR, and CPR evoked a biphasic response in the coronary circulation, i.e. an initial constriction and secondary dilatation (SPR 134-144-108 mm Hg). Intact vagi had little effect on coronary responses to SPR (131-143-102) and BPR but CPR under these conditions produced only a vasodilator response.

The SPR results in modest venodilatation and constriction in the resistance vessels of skin, muscle, kidney, gut and heart. †P<.01 t test

THE RELATIONSHIP BETWEEN CORONARY SINUS OXYGEN TENSION, CORONARY FLOW, AND ADENOSINE. V. T. Wiedmeier and L. H. Spell*, Med. Coll. of Georgia, Augusta, Ga., 30902.

Adenosine release by the myocardium has been linked to a decrease in myocardial oxygen content and has been implicated in the concomitant increase in coronary flow. Epinephrine (EPI), norepinephrine (NOR) and histamine (HIS) increase myocardial oxygen consumption and coronary flow. Glycerol trinitrate (GTN), on the other hand, increases coronary flow but does not increase oxygen consumption. The purpose of the present study was to determine whether coronary sinus oxygen levels, which reflect myocardial cell pO_2, are closely associated with adenosine release. Isolated guinea pig hearts were perfused with Krebs-Henseleit solution (pH 7.4, 37°C) aerated with 95% O_2-5% CO_2. Coronary flow, contractile force, coronary sinus oxygen (CSO_2), and adenosine and its degradative products in perfusates, were measured before and after the infusion of 2×10^{-6} M EPI, NOR, HIS, or GTN. All four compounds produced significant increases in coronary flow. The catecholamines and HIS had a positive inotropic effect and caused a significant reduction in CSO_2 which was accompanied by increased levels of adenosine in the perfusates. GTN, on the other hand, did not change contractile force, increased CSO_2 levels and did not increase the rate of adenosine release. Changes in inosine and hypoxanthine, degradative products of adenosine metabolism, paralleled those of adenosine. These findings indicate that adenosine release is intimately associated with a reduction of CSO_2 and further, that adenosine is not a mediator in the vasodilation induced by GTN. Supported by Ga. Heart Assn. Grant-in-Aid.

A MATHEMATICAL ANALYSIS OF VENTILATION DURING STEADY STATE WORK. David L. Wiegman*, Sid Robinson, James S. Heersma*, and Stephen P. Tzankoff*. Dept. Anatomy & Physiology, Indiana University, Bloomington, IN 47401.

The neural and humoral factors (and their interactions) known to be involved in the regulation of ventilation ($\dot{V}$) were quantitated. The neural factor is the increase in $\dot{V}$ associated with muscle and joint movement and the humoral factors are P_{O_2}, P_{CO_2}, and pH. These factors were combined to determine if they can account for total $\dot{V}$ or if additional factors must be identified. Body temperature and the level of circulating catecholamines were not considered as factors since they do not change significantly in short-term, moderate work. Four well-trained young men performed a series of experiments on a bicycle ergometer at each of three P_{IO_2}'s: 89, 144, and 688 mmHg. At each P_{IO_2} each subject completed four separate experiments. The first was a 15-minute rest experiment and the last three were individual 8-minute work experiments pedaling at 300, 600, and 900 kg·m/min. One subject also completed two hypercapnic series (P_{ICO_2}= 18 and 31 mmHg). Measured parameters included breath-by-breath $\dot{V}$, arterial blood gases, blood lactate, alveolar air, respiratory exchange, and heart rate. $\dot{V}$ during the last minute of work and the first two minutes of recovery (which was analyzed to quantitate the neural factor) can be characterized as a small step decrease at the end of work (<15% of total $\dot{V}$) followed by an exponential decline. The neural, humoral, and interaction factors accounted for all of $\dot{V}$ in the hyperoxic condition, but during normoxia and hypoxia a significant ($P<.05$) part of $\dot{V}$ was not accounted for. Our hypothesis is that some of the interactions among the neural and humoral factors may be underestimated since each of these factors were evaluated while the other factors were held at relatively low values. Alternatively, other factors, such as activity of the Reticular Activating System, may be involved. (Supported by US-AMRDC contract MD-2449)

EFFECTS OF BLOOD VOLUME CHANGES ON RESPONSES TO VALSALVA-LIKE MANEUVERS (VLM) IN DOGS. P.L. Wilkinson*, D.F. Stowe*, J.V. Tyberg and W.W.Parmley. Cardiovascular Research Institute, Division of Cardiology and Department of Anesthesiology. University of California, San Francisco, California. 94143

To see if changes in blood volume affect responses to VLM we anesthetised five dogs with chloralose Urethane and incrementally infused them with blood-dextran. Before each increment we monitored changes in aortic pressure (P_{AO}), right atrial pressure and R-R interval in response to constant airway pressures of 30 and 40mm Hg for 12 seconds. Central blood volume was calculated from dye dilution cardiac output and transit time. Infusion was continued until either a "square wave response" to VLM or pulmonary edema occurred. Changes in P_{AO} during classical phase I of the maneuver were measured by: a) the decrease in systolic pressure, b) the decrease in pulse pressure, c) the slope of $\log_e P_{AO}$, and d) the maximum decrease in systolic pressure from pre-VLM levels during phases I and II.

Correlations between central blood volume and a) maximum decrease in systolic pressure, and b) decrease in pulse pressure yield a significant inverse relationship. The slope of R-R interval vs. systolic pressure during phase IV was linear and did not change significantly with different central blood volumes and cardiac outputs. Our results suggest that intermediate and "square wave" responses to the VLM are related to changes in central blood volume, and that baroreceptor sensitivity as assessed by the slope of the relationship between R-R interval and systolic pressure is not altered by changes in cardiac output and central blood volume.

COLD-INDUCED PULMONARY HYPERTENSION. D.H. Will, I.F. McMurtry, J.T. Reeves and R.F. Grover, Dept. Physiology and Biophysics, Colo. State Univ., Fort Collins, CO and CVP Laboratory, Univ. Colo. Med. Ctr., Denver, CO

Exposure to cold is known to cause systemic vasoconstriction but its effect on the pulmonary circulation is unknown. During the course of studies in cattle bred for "susceptibility" (S) and "resistance" (R) to hypoxic pulmonary hypertension it was discovered that cold caused a rise in pulmonary arterial pressure not unlike that produced by hypoxia, itself. In an environmental chamber at T-0°C for 24-48 hrs., S calves showed a greater rise in mean pulmonary arterial pressure (29 to 58 mmHg) than did R calves (25 to 40 mmHg). Cardiac output and pulmonary vascular resistance increased in both groups. There was also an increase in arterial PCO_2 (38 to 45 mmHg) and a decrease in arterial PO_2 which was greater in S (76 to 55 mmHg) than in R animals (78 to 67 mmHg). In both groups, O_2 administration for 20 min. reduced pulmonary arterial pressures to near control levels. Results suggest that cold increases pulmonary arterial pressure and vascular resistance in cattle, in part, through hypoventilation and hypoxia. Cold at high altitude may contribute to the development of brisket or high mountain disease in this species.
(Supported by Colorado Heart Association and grant HL-14985 from NHLI)

NOREPINEPHRINE UPTAKE IN THE LUNG. A RELATIONSHIP TO PULMONARY VASCULAR REACTIVITY? J.A. Will, P. Katomski*, D.D., Buss*, and D.H. Will. Depts. of Vet. Sci., Univ. of Wisconsin, Madison, WI 53706, and Physiology and biophysics, Colorado State Univ., Fort Collins, CO 80521

Species classified as having a pulmonary vasconstrictor response that is only mildly reactive to hypoxia such as man, cat and dog have norepinephrine (NE) uptakes (U) in the range of 20-25%(Gillis, et al, Circ. Res. 1972, Ginn and Vane, Nature 1968). Two species having highly reactive pulmonary vasoconstrictor responses to hypoxia were studied. Using methods similar to Gillis, 5 unanesthetized (UA) ponies had an U of 52%±10.46 SEM while 7 UA calves had an U of 43.28%±3.64 SEM. Exposure to acute hypoxia did not sig. alter the U of ^{3}H-NE in either species. ^{3}H-NE U was subsequently measured in two strains of cattle considered to be genetically susceptible (S) or resistant (R) to hypoxic pulmonary hypertension (PH) (Weir et al C.V. Res. 1974). The experimental group consisted of 1 and 2 yr. old animals of each strain that were born, raised, and studied at 1500 m altitude (P_{BP}=630 mmHg)

Age	R n	$P_{\overline{PA}}$	U	S n	$P_{\overline{PA}}$	U
1 yr	2	24	61.2	1	28	15.7
2 yr	2	27	14.2	2	67	66.9

These preliminary data suggest that U is an index of pulmonary vascular reactivity. Acute hypoxia does not appear to influence U in calves and ponies. In the chronically hypoxic cattle, PH is evident only in S at 2 yrs. R, or normal cattle, show a decrease in U while maintaining normal $P_{\overline{PA}}$. This may infer that an alteration in lung U of NE may play a role in the maintenance of normal $P_{\overline{PA}}$. Conversely, a defect in U or NE metabolism may be important in the development of PH.

THE EFFECT OF TETRODOTOXIN (TTX) UPON MESENTERIC VENOUS MEMBRANE POTENTIAL AND DIAMETER IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). W.J. Willems, M.W. Willems* and W.J. Stekiel, Dept. Physiology, Medical College of Wisconsin, Milwaukee, WI 53233.

Our objective was the estimation of the neural input to mesenteric veins in normal and SHR rats by measurement of the vascular smooth muscle (VSM) response to neural blockade. Paired groups of SHR and Wistar-Kyoto Normotensive (NT) rats, 14 to 17 weeks old, were anesthetized with sodium pentobarbital and catheterized for measurement of arterial blood pressure. An ileal loop was placed in a transilluminated Lucite perfusion chamber suffused with warm, buffered physiologic salt solution. In 5 animal pairs, small (200-500 μm) mesenteric vein diameters were measured with a Vicker's image-splitting eyepiece and 50 power optics before and after suffusion with 10^{-6} g./cc. TTX. In six animal pairs, intracellular membrane potential measurements were obtained in mesenteric venous VSM with flexibly mounted glass microelectrodes (35-80 Mohms). In 2 animal pairs, membrane potential measurements were also obtained after TTX suffusion. The data follows:

PAIRS	PARAMETER MEASURED	NT	SHR
5	Increase in diameter after TTX	13 ± 1.2 μm.	29 ± 5.7 μm.*
6	Membrane Potential	-59 ± 2.0 mv.	-39 ± 2.1 mv.*
2	Memb. Pot. Range after TTX	-55 to -72 mv.	-53 to 64 mv.

*Significantly different than NT ($p < .05$)

These results suggest that in mesenteric venous VSM of SHR rats: 1)a significantly greater neural influence is present, 2) the increased neural influence is associated with a significantly lower membrane polarization, and 3)the reduction of vasoconstrictor tone produced by neural blockade is associated with a membrane hyperpolarization. (Supported by Wisconsin Heart Association).

EFFECTS OF PARACHLOROPHENYLALANINE ON CIRCADIAN RHYTHM OF BODY TEMPERATURE IN THE RAT. B. A. Williams, G. N. McEwen, Jr.*, G. P. Moberg*, and J. L. Hanegan*. Biotechnology Division, Ames Research Center, Moffett Field, CA 94035.

Daily variations in body temperature were recorded every two minutes by telemetry from 5 rats maintained continuously at 22C in metabolic cages. Eight days of control data preceded I.P. injections of 300 mg/kg parachlorophenylalanine (pCPA), a specific inhibitor of tryptophan hydroxylase required for synthesis of 5-HT. 5-HT is known to be a transmitter for heat loss effectors in the rat. Initial response to the pCPA injection was an immediate drop in body temperature to -2.02 ± 0.52 S.D.C. Approximately 6 hours after this initial systemmic "shock" body temperature had increased to slightly over control levels. During the four days after injection, the daily body temperature rhythm had a decreased integrated amplitude, approximately 50% of control. The mean body temperatures were slightly higher which was the result of a significant elevation of the low mean temperature. The high mean temperatures were not significantly altered. This indicates an increase in activity "state" during the rats normal resting periods, but no increase during the normally active periods. By standard vector analysis techniques, control data fit a sine-curve while the body temperatures after injection did not fit. This indicates that I.P. injection of pCPA in the rat results in modification of heat-loss and/or heat production and alters normal body temperature rhythms. Although the mechanism of these alterations may be due to action of the thermoregulatory centers, other effector mechanisms such as activity, excitability or sleep-wakefulness might give similar results without any direct involvement of CNS thermoregulatory centers.

EFFECTS OF IONS ON AMYLASE RELEASE BY ISOLATED PANCREATIC ACINAR CELLS J.A. Williams, P.C. Cary* and B. Moffat* (SPON: R. Gallo). Dept. of Physiology, Univ. of California, San Francisco, CA. 94143

Isolated acinar cells have been prepared from mouse and guinea pig pancreas by use of collagenase, EGTA and mechanical shearing. Cells are intact by trypan blue exclusion and electron microscopy and contain normal intracellular levels of Na^+ (30-50mM) and K^+ (150-200mM). Amylase release was increased 100-300% in response to cholinergic agonists, caerulein and the Ca^{++} ionophore A23187. Neither omission of Ca^{++} or Na^+ from the medium reduced initial rates of bethanechol stimulated amylase release. The lack of inhibition when Na^+ is removed contrasts with data previously obtained using pancreatic fragments while the effect of omitting Ca^{++} is similar. After 15 min in Na^{++} free medium, however, stimulated amylase release was not significantly greater than that by control cells. As $^{22}Na^+$ efflux (loss of cell Na^+) occurred with a half-time of 3-5 min in both normal and Na^+ free medium, bethanechol stimulated amylase release appears dependent on intracellular rather than extracellular Na^+. Elevation of the concentration of K^+ in the medium ten-fold did not affect amylase release nor did replacement of CO_2-HCO_3^- by a Tris buffer system or replacement of Cl^- by isethionate. The effect of bethanechol on ion fluxes was studied since the depolarization measured in intact tissue is believed due to an increased Na^+ conductance. No effect was seen on the influx of $^{22}Na^+$ or the efflux of either $^{22}Na^+$ or $^{36}Cl^-$. Thus in the isolated pancreatic cell preparation there is no dependence of stimulated amylase release on any single ionic constituent of the medium or evidence for an increased membrane ionic conductance accompanying secretion (supported by NIH grant GM 19998 and a grant from the National Cystic Fibrosis Research Foundation).

RADIOIMMUNOASSAY OF OXYTOCIN. N. Wilson* and V.Y. Greenhouse* (SPON: J.A. Hinke). The University of British Columbia, Faculty of Medicine, Department of Physiology, Vancouver, B. C., Canada.

Iodinated oxytocin (^{125}I-OT) was prepared using thallium chloride iodination procedure. This procedure was adapted from that used by Commerford (Biochem. 10: 1993, 1971) and by Getz, Altenburg, and Saunders (Bioch. Biophys. Acta 287: 485, 1972) for iodination of nucleic acids. Purification of the iodinated hormone was accomplished on Sephadex G-15, and eluent fractions monitored for radioactivity and binding to excess antiserum. When chromatography was performed immediately following the iodination reaction, good separation of iodinated from uniodinated hormone was achieved. In this system OT was found to have a smaller elution volume than ^{125}I-OT. Similar separation could not be achieved on Sephadex G-10. Purified ^{125}I-OT was stable for at least one month when stored at 4°C. Storage at -20°C caused a faster decline in ability to bind to antiserum. Storage of iodination mixture prior to chromatography on Sephadex G-15 resulted in apparent polymerization of ^{125}I-OT. This phenomenon more pronounced at -20°C than at 4°C. Polymerized material was still able to participate in competitive binding system. The assay sensitivity was 10 femtomoles (fM). The antiserum used in this work did not crossreact with vasopressin or vasotocin in the 10-1000 fM range. It showed considerable crossreactivity with oxidized (performic acid) OT, with 4-ser, 8-ileu oxytocin and with the C-terminal tripeptide of OT. Measurements of immunoreactive OT were preceded by the extraction procedure of Robertson (J. Clin. Invest. 52: 2340, 1973). Plasma levels in normal human males and females were in the range of 100-200 fM/ml. Thallium chloride iodination was found to be equally suitable for arginine vasotocin, arginine and lysine vasopressins. (Supported by MRC MA-4887).

CILIARY PROPULSION IN TUBES: MEASUREMENT OF WALL DRAG REDUCTION BY MUCIN. H. Winet, Biophysical Fluid Mechanics Group, Engineering Science, California Institute of Technology, Pasadena, CA 91125

By utilizing a simple biological system, reduction of wall drag on cilia-propelled objects by mucin is shown to be due to lubrication near the wall and to a non-Newtonian viscosity reduction far from the wall. Multiple flash photographs were taken of self-propelled ciliated bodies swimming in a variety of concentrations—0-5%—of bovine submaxillary mucin (Sigma) through glass tubes of various bore diameters. Measurements of body velocities relative to velocities in 'unbounded' tubes (U/U_∞) and body clearances relative to average cilium length (C/r) were used to draw propulsion velocity profiles with C/r a function of U/U_∞. When resulting plots were compared with mucin-less controls, two regions of drag reduction appeared. In the first region, of thickness $0 < C/r \leq 1.5$, lubrication occurs as the non-slip condition at the wall is violated. In the second region $C/r \geq 3.5$ an optimized hydrodynamic affect for $1.7\% < \text{mucin}\% < 4.1\%$ is evident. Photomicrographs of the mucin suspensions show that the mucin gel clusters formed in concentrations between 0 and < 9.1% (w/v) are free to be propelled by cilia, a condition sufficient to lead to slippage near a wall. Clusters in suspensions which are optimal for the far region affect, in contrast, have the additional constraints of being large enough to allow collision and shearing of one another yet small enough to be propelled at ciliary shear rates. In general no wall drag reduction appears in the region $1.5 < C/r < 3.5$.

Transformation from a ciliated body in a non-ciliated tube to a non-ciliated body in a ciliated tube should no more than double the thicknesses of the two drag reduction regions. (Supported by NSF GK31161X & ONR N00014 67A 0094 0012)

SYNCHRONY OF PHYSIOLOGICAL RHYTHMS IS REGULATED BY SOCIAL ZEITGEBERS. C.M. Winget, J. Vernikos-Danellis and J.R. Beljan, Biomedical Research Division, NASA, Ames Research Center, Moffett Field, CA 94035 and School of Medicine, Wright State University, Dayton, Ohio 45431.

Although circadian rhythms in man are endogenous and persist under constant conditions, environmental correlates have been shown to synchronize physiological functions. The possibility that social stimuli may also have synchronizing properties was determined by analyzing the circadian rhythm characteristics of nine healthy male subjects confined singly or in groups of three under regulated or constant light conditions. Heart rate (HR), body temperature (BT), activity, urine volume, and urine excretion of certain metabolites were measured frequently each experimental day. The two groups of three subjects each were confined in rooms where the environment was regulated; the third group served as controls, were not confined, but were exposed to ambient experimental conditions. During the first 24-day control period when all three groups were in 16L:8D the BT and HR rhythms remained stable and circadian in the confined subjects, as they did in the controls throughout the study. The photoperiod was then changed to 24L:0D in both confinement rooms. Under these conditions period lengths increased and considerable phase shifting occurred in all six confined subjects. However, although the rate of this increase in period and phase shift was identical for the three subjects within a room they differed greatly between the two rooms. One confined group desynchronized with respect to sidereal time at the rate of 12 min/day whereas the other group shifted by 60 min/day, in spite of the fact that both groups were under identical environmental conditions. These free-running periods differed from those of the same subjects under the same conditions when confined singly. The data provide evidence that social interaction may act as a zeitgeber to synchronize endogenous rhythms.

GLUCOSE KINETICS AND CARDIOVASCULAR FUNCTION AFTER BURN TRAUMA IN GUINEA PIGS. R.R. Wolfe, D. Elahi, J.J. Spitzer, H.I. Miller, L.S.U. Medical Center, New Orleans, La. 70112.

Glucose turnover was measured in guinea pigs (gp) before and during burn shock by the primed constant rate infusion technique, using 6-H^3-glucose as the tracer. Shock was induced in temporarily anesthetized gp by immersion to one inch below the xphoid process for 3 sec, and was evidenced by a greater than 50% reduction in cardiac output (CO) at 90 min. The rate of appearance of glucose (Ra) was increased from 4.74 $\pm$ 0.31* mg/kg-min before burning to 9.09 $\pm$ 1.56* mg/kg-min at 90 min. Metabolic clearance rate (MCR) changed only slightly, and consequently the plasma glucose level (GLU) increased from 129 $\pm$ 8.2* to 200 $\pm$ 13.7*mg%. Ninety minutes after burning, 6.5 ml saline/hr was infused I.V. for 24 hours. After the saline resuscitation, CO was 20% higher than before burning. Ra remained elevated above the pre-value, and MCR was also slightly higher; GLU was 147 $\pm$ 4.0* mg%. Four days after burning, CO had fallen below the pre-value, Ra was more than twice the value before burning, and MCR was also higher. GLU was 150 $\pm$ 6.1*mg%. We concluded that hyperglycemia after burning was due to an increased hepatic glucose output and a failure of the MCR to increase to a similar extent. *SEM

(Supported by ONR Contract NR 202-018.)

EFFECTS OF EXERCISE, GUANETHIDINE OR ITS COMBINATION ON HEMODYNAMIC CHANGES IN ATHEROSCLEROTIC COCKERELS. H.Y.C. Wong, T.E. Nightingale*, S.N. David*, S.O. Orimilikwe* and J.A. Reinshagen*. Dept. of Physiology, Howard University College of Medicine, Washington, D.C., 20059 and USDA Poultry Research Laboratory, Georgetown, DE 19973.

Cardiovascular measurements were made on unanesthetized young White Leghorn cockerels which had been fed a plain mash (PM) or atherogenic diet (AD) consisting of 2% cholesterol plus 5% cottonseed oil added to mash. Treatments were: A. Diets only (control); B. Diets + exercise (EX); C. Diets + guanethidine (G); and D. Diets + EX + G. Exercise consisted of running in a circular treadmill for approximately 500 yds for 20 minutes twice daily for 5 consecutive days a week. Guanethidine was administered orally, 2.5 mg/day for 5 consecutive days a week. After 11 weeks the following results were obtained: (1). Only scattered statistically significant differences were noted in heart rates (HR) and blood pressures (systolic, diastolic, and mean), while cardiac output (CO), stroke volume (SV) and total peripheral resistance (TPR), were unchanged throughout; (2). Exercised cockerels on both PM and AD showed decreased CO, and increased TPR; (3). Birds treated with guanethidine had a slight increase in CO, with lower TPR; and (4). Combining exercise with guanethidine produced significant tachycardia in PM birds ($P < 0.05$), and hypertension in AD cockerels ($P < 0.05$), while CO was reduced (-37% and -13%) and TPR increased (+41% and +33%) in PM and AD birds respectively. Conclusion: Cardiovascular changes due to exercise were similar to mammalian data although guanethidine gave contradictory results, and the combined treatments were generally counterproductive. (Supported in part by grants #RR0816 and #1T02-050150-01 from NIH.)

MODULATION OF PROSTAGLANDIN BIOSYNTHESIS AND PROSTAGLANDIN E 9-KETO REDUCTASE BY BRADYKININ AND CYCLIC GUANOSINE 3',5'-MONOPHOSPHATE IN BOVINE MESENTERIC ARTERIES. P.Y-K Wong*, N.A. Terragno*, A. Terragno*, and J.C. McGiff. Dept. Pharmacology, Sect. Clinical Pharmacology, The Medical College of Wisconsin, Milwaukee, WI, 53233.

Microsomal fractions were obtained by homogenization of fresh bovine mesenteric arteries (BMA) in 50 mM KH_2PO_4 buffer, pH 7.4 followed by differential centrifugation. The microsomal pellet (105,000 g, 60 min) contained enzymes which converted 1-^{14}C arachidonic acid into prostaglandins (PGs) in the presence of glutathione (GSH, 4mM). The synthesis of PGs was stimulated by bradykinin (BK) and inhibited by meclofenamate. With GSH alone the PGs synthesized were in the following ratio: $PGE_2 > PGD_2 > PGF_{2\alpha}$ (1.6:1.3:1.0) BK increased the total PG production and changed the ratio to $PGE_2 > PGF_{2\alpha} > PGD_2$ (1.5:1.3:1.0). The microsomal supernatant contained the enzyme PGE-9-Keto reductase, and when incubated with $NADP^+$, it converted ^{3}H-PGE_2 to ^{3}H-$PGF_{2\alpha}$ in a time dependent manner. The pH optima of this enzyme was found to be 7.1. The conversion of ^{3}H-PGE_2 to ^{3}H-$PGF_{2\alpha}$ was stimulated by BK and cyclic guanosine 3',5'-monophosphate (cGMP). The kinetic studies indicated both BK and cGMP increased the Vm without affecting the apparent Km of the enzyme. These observations suggest that the locally synthesized prostaglandins in BMA not only can be modulated by the kallikrein-kinin system, but also by a cGMP-mediated system. (Supported by grants HLHD 16560 and HL 13624 and American and Wisconsin Heart Association Grants).

HEMOGLOBIN-OXYGEN AFFINITY AND RED CELL DPG IN OBESE RATS AND HUMANS. Stephen C. Wood, Wolfgang W. Schmidt-Nowara* and Paul M. Nagel*. Depts. of Physiology and Medicine, School of Medicine, University of New Mexico, Albuquerque, New Mexico 87131.

Obesity often results in cardiorespiratory dysfunction. This study examines the role of modified red cell function as an adaptation to obesity. Hemoglobin-oxygen affinity (measured as P_{50}, the oxygen tension of 50% saturated blood) and the concentration of 2,3 diphosphoglycerate (DPG) were measured in genetically obese (Zucker) rats and in obese humans without clinically manifest cardiopulmonary diseases Blood P_{50} (pH 7.4, 37°C) was significantly higher in the obese rats (body weight = 509 ± 57 g) than in their lean litter mates (body weight = 263 ± 26 g) with average values of 38.9 vs. 34.2 mm Hg. There was a corresponding significant difference in red cell DPG levels with a molar ratio of DPG/Hb of 1.47 for obese and 1.16 for normal rats. There was no significant difference in either hematocrit or oxygen capacity. Similar results were obtained in parallel studies with humans. In 11 obese adults (183 % of ideal body weight) the average P_{50} (pH 7.4, 37°C) was 31.2 mm Hg compared with 28.5 mm Hg for 11 control subjects (98 % of ideal body weight). There was no significant difference in O_2 capacity of normal and obese subjects. Although the DPG level was elevated in the obese subjects (DPG/Hb = 1.04 vs. 0.97 for controls) the difference is not statistically significant. The results suggest that alterations of hemoglobin-oxygen affinity may be a sensitive indicator of cardiorespiratory stress. (Supported by NIH Grant HL-18026.)

FETAL AND NEONATAL CARDIOPULMONARY RESPONSE TO HISTAMINE. J. R. Woods, Jr.*, C. R. Brinkman, III and N. S. Assali, UCLA School of Medicine, Dept. Obstetrics and Gynecology, Los Angeles, California 90024.

Previous studies in nonpregnant ewes have shown that intravenous histamine results in fall in systemic pressure and some regional blood flows, while intraarterial injection produces increase in regional blood flow and decreased resistance. These results were attributed to H^1 and H^2 receptors in the heart and peripheral circulation on the basis of select blockade with Benadryl (H^1) and Metiamide (H^2). Present studies examined histamine action and its blockers on fetal and neonatal lambs. Near-term fetuses and newborn lambs were instrumented for measurement of arterial and pulmonary pressure, main pulmonary artery, ductus (fetus) and ascending aortic flows. Fetuses were studied with ductus open and clamped. Newborns were tested from 3-70 days old. Results show: a) in fetus, histamine results in marked fall in ductus flow and increase in ascending aortic and pulmonary flows; systemic and pulmonary pressures decreased. With ductus closed, the histamine induced pulmonary vasodilatation was blocked by Benadryl; b) in neonate, histamine produced pulmonary vasoconstriction similar to adult which was blocked by Benadryl; c) when neonatal pulmonary vascular resistance was raised by hypoxia (6-10% O_2), histamine produced pulmonary vasodilatation, followed by vasoconstriction; Benadryl blocked only the latter component of this biphasic response. Conclusion: 1) present data confirm previous observations that pulmonary response to vasoactive agents depends on the status of pulmonary resistance in resting condition; 2) H^1 receptor is probably dominant in pulmonary vascular bed; 3) histamine produced profound ductus constriction in fetus which may or may not be secondary to pulmonary vasodilatation. (Supported by NIH grants HL-01755 and HL-13634.)

AN INITIAL EVALUATION OF A THERMAL DIFFUSION PROBE (TDP) FOR MEASURING TISSUE BLOOD FLOW. M. Woods,* A.H. Harken,* T.A. Balasubramaniam,* H.F. Bowman* (SPON: R.J.T. Joy), Walter Reed Army Institute of Research, Washington, D.C. 20012 and Massachusetts Institute of Technology, Cambridge, Mass. 02139

The TDP technique employs a thermistor bead as both temperature sensor and heat source. When the TDP is immersed in a tissue, the power (V_{ss}^2) dissipated to maintain a constant temperature step (ΔT) above the tissue is dependent upon tissue thermal conductivity (k). In turn, k is dependent upon the imposed ΔT, intrinsic tissue k, and tissue blood flow (w). The TDP was inserted in the gracilis muscle of four isolated canine hindlimbs. Limbs were perfused with a membrane lung system which allowed control of limb w, temperature, arterial oxygen content, and arterial pH. The relationship of V_{ss}^2 to total limb w was evaluated over a range of 100-200 cc/min. Findings are summarized in the table.

DOG	r^2	P	REGRESSION EQUATION
1	.97	<0.01	$V_{ss}^2 = 2.12 + 0.025\ w$
2	.98	<0.01	$V_{ss}^2 = 1.13 + 0.0218\ w$
3	.98	<0.01	$V_{ss}^2 = 2.65 + 0.0103\ w$
4	.87	<0.01	$V_{ss}^2 = 0.23 + 0.0238\ w$

A statistical comparison of the four regression lines indicated that they could not be regarded as the same. However, for each dog V_{ss}^2 had a direct and significant relationship to total limb w over a range of 100-200 cc/min. Insofar as the relationship between V_{ss}^2 and k is known and a tissue thermal model can isolate w in cc/min·vol of tissue, these findings suggest that the TDP can be developed to quantify blood flow in small volumes of tissue.

AN EXPERIMENTAL MODEL FOR ATRIAL FIBRILLATION. Billy K. Yeh, Arthur J. Gosselin* and John W. Lister. Miami Heart Institute, Miami Beach, Florida 33140

Five greyhound dogs weighing from 50-70 lbs, anesthetized with sodium pentobarbital (35 mg/kg i.v.), were maintained on controlled ventilation. Mid-sternotomy and pericardiotomy were performed and the heart exposed. Bipolar plunge electrodes were inserted into the area of the sinus node. The electrodes were utilized either for stimulation or recording. In each experiment, a surface electrocardiogram, His bundle electrograms, and arterial blood pressures were continually and simultaneously monitored. One thousand units of sodium heparin was administered i.v. to each dog and then a curved 25 gauge needle was inserted into the left main coronary artery. No apparent signs of myocardial injury or hemodynamic deterioration were noticed with the introduction of the needle. In all experiments within five to twenty minutes after the needle insertion atrial fibrillation developed. Pacing from the area of the sinus node at rates greater than the intrinsic rate accelerated the time of onset of atrial fibrillation. Neither removal of the needle from the left main coronary artery after the onset of atrial fibrillation nor mechanical stretch of the atria terminated the atrial fibrillation; electric cardioversion only transiently restored normal sinus rhythm. This animal model for atrial fibrillation can be reliably reproduced and may be used for the experimental study of the electrophysiologic, hemodynamic and pharmacologic aspects of atrial fibrillation.

BLOCKADE OF TOLAZOLINE BY CIMETIDINE. T.O. Yellin* and J.G. Wofford* (SPON: H.H. Freedman). Gastroenterology Unit, Biomedical Research Dept. ICI United States Inc., Wilmington, Delaware 19897.

Tolazoline, the well-known alpha-adrenergic blocking agent, was recently identified as a partial histamine H2-receptor agonist in gastric fistula dogs and in guinea pig atria, in vitro (Nature 253, 561, 1975). Intravenous infusions of tolazoline stimulated acid secretion, increased heart rate and lowered blood pressure in anesthetized, gastric fistula cats. These effects of tolazoline were antagonized by metiamide and a new H2-receptor blocker, cimetidine (J Int Med Res 3, 68, 1975). But the spasmogenic action of tolazoline on guinea pig ileum was blocked by atropine and not by H1 or H2 antagonists. Against continuous infusions of tolazoline (40 μmol/kg hr), metiamide, 5 and 10 μmol/kg i.v., reduced total acid output (70 μEq/min) by 55 and 80% (peak), respectively. The fall in acid secretion was mirrored by a rise in blood pressure; simultaneously, heart rate decreased. In the absence of an H1-blocker, cimetidine, 10 μmol/kg i.v., abolished the hypotensive activity of tolazoline but not that of histamine. This provides evidence that tolazoline is a direct-acting H2 agonist, not a histamine releaser. As judged by norepinephrine reversal, complete alpha-adrenergic blockade remained in force even as the tolazoline-induced fall in diastolic blood pressure was completely antagonized by cimetidine. Moreover, in cat blood pressure experiments using single i.v. doses of tolazoline (2.5-40 μmol/kg), metiamide, 5 μmol/kg, produced a parallel, four-fold shift of the dose-response curve. Thus, tolazoline can be classified as an H2-histaminergic agonist in the cat. Our results suggest that the therapeutic utility and some of the clinical side-effects of tolazoline may be due to activation of histamine H2-receptors by the drug.

MODEL EXPERIMENTS ON FAHRAEUS EFFECT. R. T. Yen* and Y. C. Fung, (SPON: M. Intaglietta) Dept. AMES Bioengineering, University of California, San Diego, La Jolla, California 92037

It is known that if whole blood is allowed to flow from a large reservoir into a small circular cylindrical tube, the hematocrit in the tube is smaller. This is interpreted as a feature of a particular flow. We find that this relationship is not monotonic in a model experiment in which gelatin particles (circular disks) are suspended in a silicone fluid to simulate the blood. When the diameter of the undeformed cell is equal to or greater than the tube diameter, the volume fraction of the cells in the tubes increases to a value equal to or greater than that in the reservoir. Thus Fahraeus effect (1929) has a point of inversion.

Cokelet and Barbee (1970) have claimed that the flow conditions upstream from the capillary tube entrance are not responsible for the Fahraeus effect. We however find that the hematocrit in the tube could be greatly influenced by the flow condition at the entrance of the tube. If the tube is perpendicular to the main direction of flow in the reservoir (as is the case in Cokelet's experiment, or in artery-capillary junction), the velocity of flow in the reservoir affects the hematocrit in the tube.

In the model experiment, although the Reynolds number is matched, the flexibility of the red blood cells is not. Thus the model results cannot be applied directly to the whole blood (physiological conditions). Nevertheless the inversion of Fahraeus effect is of interest, and may have application to those pathological cases in which the red cells are hardened.(Supported by Grant HL-17731-01)

STEADY-STATE RESPONSES TO CHANGES IN ALDOSTERONE LEVELS. D.B. Young and A.C. Guyton. Dept. Physiology & Biophysics, Univ. Miss. Sch. Med., Jackson, MS 39216

To determine the responses of the fluid volume and electrolyte control system to different fixed levels of aldosterone, a group of 5 dogs was adrenalectomized and given aldosterone replacement at 4 fixed levels. Aldosterone was administered i.v. from a portable infusion pump worn by the dogs 24 hr/day. The levels of infusion were varied in 4 steps from 16 to 219 µg/day. The animals were maintained at one level for from 2 to 3 weeks until all measured variables were stable. Data is presented in the following table:

Aldo infusion rate µg/day	Plasma Na mEq/L	Plasma K mEq/L	Arterial Pressure	Plasma Renin Act. ng/ml/hr	22Na space ml
16 ± 1	134 ± 2	4.96±0.10	103 ± 3	9.6±1.8	6342±387
48 ± 3	140 ± 2	4.07±0.15	95 ± 3	2.1±0.5	7284±842
91 ± 4	144 ± 2	3.68±0.13	110 ± 3	0.15±0.05	8043±735
219 ± 10	145 ± 1	2.95±0.13	120 ± 1	0.04±0.01	7732±495

These data demonstrate that: 1) at normal to high levels, aldosterone has little effect on plasma Na concentration, 2) at all levels aldosterone is of prime importance in controlling plasma potassium concentration; 3) aldosterone is capable of profoundly altering fluid balance and related variables such as plasma renin activity and arterial pressure. Supported by NIH grant HL 11678.

QUANTITATIVE RELATIONSHIP BETWEEN TRANSMITTERS RELEASE AND ELECTRICITY PASSING THROUGH NERVES Wei Young and John A. Parker* ,Chemical Research Projects Office, Ames Research Center, NASA, Moffett Field, California 94035

The vagal inhibitory and sympathetic excitatory effects in vagal and sympathetic heart preparations were used as a quantitative assay for the release of acetylcholine and epinephrine in the isolated nerve heart system. The heart was perfused with Ringer's solution. The nerve was stimulated with a pair of platinum electrodes through a Grass S-8B stimulator. Fundamentally the nerve ending is equivalent to the anode and the active sites of the receptor act as if the cathode. Thus the vagal sympathetic heart system is essentially a microcoulometer. The number of transmitters liberated at nerve endings by the passage of an electric current is proportional to the total charge that has passed through the nerve fiber. The mass of transmitters liberated at nerve endings by the passage of an electric current is proportional to the chemical equivalent of the transmitters. The chemical equivalent for acetylcholine is determined to be 1.43×10^{-3} g per coulomb and that for epinephrine is 1.87×10^{-3} g per coulomb. For the first time, the Faraday's law is extended to the biological systems.

ADRENAL AND PLASMA CORTICOSTERONE LEVELS OF PARTIALLY HEPATECTOMIZED MALE RATS. M.Yu,* Linda Witek* and S.F. Marotta (SPON: R.F.LOIZZI). Dept. Physiology and Research Resources Laboratory, University of Illinois at the Medical Center, Chicago, Ill. 60680.

Metabolic degradation of steroids by the liver and possible hepatic involvement in the negative feedback control of adrenocortical secretion prompted studies on the effects of partial hepatectomy and hepatic restoration on adrenal and plasma corticosterone (Cpd.B) levels. Male rats (180-200gm) were divided into 3 groups as follows: unoperated, sham-operated and partially hepatectomized rats. The animals, which were housed at 22°C on a 12L:12D schedule with food and water ad lib., were sacrificed by decapitation at 0800 hr. on various days after hepatectomy. The data show that, for unoperated and sham-operated rats, adrenal (41 vs 42 mg) and liver (11 vs 10 gm) weights, plasma (4.6 vs 4.9 μg/100mml) and adrenal (.46 vs .51 μg/adr) Cpd.B levels, and plasma proteins (5.1 vs 5.1 gm/100ml) did not differ significantly from each other throughout the experiment (14 days.) In hepatectomized rats liver weights on days 1,2,3, and 4 were 35,50,75 and 80%, respectively, of the control groups, and returned to essentially control weights at 2 weeks. Plasma Cpd.B levels were elevated on day 1 (17.9 μg/100ml) and by days 2-4(9.1 μg/100ml) returned to slightly above control levels. Adrenal Cpd.B levels and weights were highest shortly after hepatectomy and then declined in parallel during the next few days. Plasma protein levels were depressed (3.7 gm/100ml) following hepatectomy and then gradually increased proportionately (r=.85) with liver restoration and inversely (r=.61) with plasma Cpd.B levels. These results show that a 50% reduction in liver capacity causes only slight elevations in adrenal and plasma Cpd.B concentrations, suggesting that factors other than the liver play a major role in the regulation of plasma Cpd.B levels in hepatectomized rats.
(Supported by PHS NU - 5020)

TRANSPORT OF SUGARS ACROSS THE RETINA PIGMENT EPITHELIUM. J.A.Zadunaisky.Depts.Physiology & Ophthalmology, New York University Medical Center, New York, N.Y. 10016

The retina pigment epithelium (REP) consists of one cell layer interposed between the blood vessels of the choroid and the neural retina. The junctional complexes between the RPE cells are the site of the blood-retina barrier. Because the nutrition of the outer retina depends on blood supply of metabolites, unidirectional fluxes of 3-0-methyl glucose (^{3}H), D-glucose (^{14}C), urea (^{14}C), and mannitol (^{14}C) were measured across the isolated pigment epithelium of the frog (R.catesbeiana) placed as a membrane in order to detect passive or active mode of passage. Resting potential and resistance were measured and fluxes determined in paired tissues from same or different eyes. There was a net flux of 3-0-methyl glucose and D-glucose from blood to retina and no net flux of urea or mannitol. Values obtained were: 3-0-methyl glucose: Jin 1.181 ± 0.182 (SEM) N=16; Jout 0.187 ± 0.22 N=19. D-glucose: 0.776 ± 0.075 N=10 and 0.508 ± 0.062 N=7. Mannitol 0.156 ± 0.067 and 0.136 ± 0.066 N=6 and urea 0.267 ± 0.058 and 0.303 ± 0.031 N=5. Statistically significant net fluxes were only those of the first two sugars examined. Phloritzin and n-ethyl maleimide reduced completely the net fluxes of the sugars. Counter flow acceleration by D-glucose on the 3-0-methyl glucose in flux was found. The electrical resistances of the tissues were between 1300 and 2500 ohms and the potentials from 5 to 15 mV. The net sugar transports described are related to retinal nutrition.

IOWA WRESTLING STUDY: WEIGHT LOSS AND URINARY PROFILES OF COLLEGIATE WRESTLERS. E.J. Zambraski*, D.T. Foster*, P.M. Gross* and C.M. Tipton, Exercise Physiology Laboratory, University of Iowa, Iowa City, IA 52242

We have previously documented that most high school state finalists lose between 9-13% of their preseason body weight by methods associated with food deprivation, fluid restrictions, and dehydration. Prematch urinary data from these individuals indicated that a general condition of dehydration was present. To determine whether similar changes were occurring in collegiate wrestlers, a longitudinal study was conducted with various members of the 1975 University of Iowa NCAA championship team. Body weight changes from September to December indicated a mean loss of 6%, while skinfold totals (6 sites) changed from a mean of 58 mm to 37 mm. During a four-month period, mean weight losses of 10.2, 9.5, 8.0, 7.5, and 7.0 lbs occurred in intervals of 12, 4, 3, 2, and 1 day, respectively. Basal urines analyzed weekly throughout the season usually contained 2-3 times the potassium excreted during the preseason. Analyses of urines at various times during a 2-day time period prior to weigh-in demonstrated a .003 increase in specific gravity, 160 mosm/l increase in osmolarity, .10 decrease in pH, 45.3 Meq/l decrease in Na^+ concentration, and a 71.3 Meq/l increase in K^+ concentration. These changes indicate that the wrestlers were dehydrated prior to competition. Total urinary electrolyte loss during the 2 days amounted to 3.7% of estimated total body Na^+ stores and 3.0% of total body K^+ stores. Although the members of this team repeatedly demonstrated a high performance level, these data illustrate that the patterns of weight loss are similar to what has been observed in high school wrestlers.

(Supported in part by funds from the Iowa Academy of Science and the University of Iowa Graduate College.)

DETERMINATION OF THE METABOLIC COST OF THE TOTAL WALKING PATTERN. M.Y. Zarrugh* (SPON: H.J. Ralston). Biomechanics Lab., Univ. California, Berkeley, Ca. 94720

Energy expenditure in walking is usually expressed as a function of walking speed. However, it has been shown (Zarrugh, M.Y., et al., Europ. J. Appl. Physiol. 33:293-306, 1974) that this form applies only to the optimal step length/step rate patterns freely adopted by human subjects, and that one must use both the step length and step rate to predict the energy expenditure of the suboptimal combinations of step lengths and step rates. The experimental evidence on 10 subjects indicates that the energy demand for any step length and step rate can be obtained by conducting two experiments. In the first, the subject is allowed to freely choose his own walking pattern to achieve a set of prescribed speeds. The speed is kept constant in the second experiment but the subject is forced to adopt a range of set step rates. The results of the two experiments combined yield enough data to evaluate the three parameters in the energy cost relationship of the total pattern.

(Supported by Veterans Administration Contract VAV 101 134)

RENAL FUNCTION OF LIMIT FED AND AD LIBITUM FED MINIATURE SWINE. M.L. Zatzman, H.A. Swartz*, K.H. Hicklin* and M.E. Tumbleson* (SPON: H.E. Dale). Dept. Physiology, Univ. of Mo. Medical Center, Dept. Veterinary Anatomy-Physiology and Sinclair Comparative Medicine Research Farm, Univ. of Mo., Columbia, Mo. 65201.

Measurements of glomerular filtration rate, effective renal plasma flow and glucose tubular maximum were made with ad libitum fed (obese) and limit fed Sinclair (S-1) miniature gilts 32 to 62 months of age. Inulin (GFR) and para-aminohippurate (ERPF) clearances were 1.01 ± 0.074 and 5.19 ± 0.357 ml min^{-1} kg^{-1}, respectively, with no difference demonstrated between the two groups. Glucose Tm was better related to total body weight than to fat-free body weight of the animals, and demonstrated a significant difference between the two groups: ad libitum fed Tm_G 1.92 ± 0.14 mg min^{-1} kg^{-1}, limit fed Tm_G 1.19 ± 0.10 $p < .001$. It was concluded that obesity mimiced the effects of hypertrophy in that Tm_G increased to a greater extent with body weight than GFR.

RENIN SECRETORY RESPONSES DURING CONTROLLED CO_2 INHALATION IN DOGS. J.E. Zehr, K.D. Kurz*, and H. Fuji*, Dept. Physiology & Biophysics, University of Illinois, Urbana, IL 61801.

Renin secretion was studied in chloralose anesthetized dogs undergoing controlled CO_2 inhalation with resultant respiratory acidosis. Minute ventilation was held constant throughout by controlling tidal volume and ventilatory rate with concomitant neuromuscular paralysis. In 8 dogs graded inhalation of 4, 8 and 12% CO_2 in air resulted in prompt increments in renin secretion. Renal blood flow (electromagnetic flowmeter) and arterial pressure were moderately reduced (15%) while renin secretion was elevated by more than 300% during 12% inhalation. Secretion rates returned to control levels following re-establishment of ventilation with air. Marked respiratory acidosis and hypercapnia were evidenced, reaching peak arterial pH's and PCO_2's of 7.03 and 90 mm Hg respectively. In order to test the influence of compromised renal hemodynamics on the renin response, 8 unilaterally nephrectomized dogs were tested prior to and again following renal vascular paralysis with intrarenal papaverine infusion. Renal vascular paralysis failed to block the renin secretory response to CO_2 inhalation. The role of the renal sympathetics was tested in 6 dogs who had undergone unilateral renal denervation several days prior to the experiments. Simultaneous, bilateral renin secretion studied during 12% CO_2 inhalation indicated that renin secretion was blunted but not blocked by renal denervation. Renin secretion from the denervated kidney was elevated more than 2X within 10 minutes while there was a greater than 3X increase from the innervated kidney. It is suggested that renin secretion is elevated during acute respiratory acidosis and that the response is a complex sympathetic activation involving both renal sympathetic and adrenal medullary mediated mechanisms. (Supported by NIH Grant HL-15307 and a Grant from the Illinois Heart Association.)

Active K transport in primary cell cultures of renal cortical cells from a hibernating and non-hibernating species of mammal. R. Zeidler* and J. S. Willis. University of Illinois, Urbana, 61801.

We reported previously that monolayer cultures of cells grown from kidney cortex of hibernators (hamsters, ground squirrels) retain K at 5°C whereas those from a non-hibernator (guinea pig) do not. Unidirectional flux determinations of ^{42}K showed a greater decrease in efflux with cooling in the hibernator cells than in the guinea pig cells. With some relatively minor exceptions ouabain-sensitive influx was reduced to about the same extent in the two groups. In the present study we examined kinetics of K influx in ground squirrel cells and guinea pig cells. K influx is a saturating function of K in the medium and although Vmax is greatly reduced by cooling, $K_{\frac{1}{2}}$ is not changed in cells of either species. Decreasing cell K (and increasing cell Na) by exposure to K free medium has a slight effect of stimulating K influx at 37°C in cells of both species and the magnitude of the effect is unchanged at 5°C for cells of guinea pigs. Cells of ground squirrel, however, are about four times as responsive to loss of K at 5°C as at 37°C, with the result that with their 10-15% loss of K at 5°C, they are pumping about twice as fast as they would with unchanged cell [K] and yet could pump at a rate still two times greater if their cell [K] were further reduced. In contrast the K pump rate of transport seen in untreated guinea pig cells at 5°C represents about the maximum efforts of those cells. Thus, while the actual steady rate of ouabain-sensitive K influx is about the same in the two species, there are differences in the cells of the hibernator which contribute to their ability to retain K at low temperature. Supported by USPH GM 11494.

SOFT LASER SCANNING DENSITOMETRY IN DETERMINING THE MOLECULAR HETEROGENEITY OF SERUM AND URINARY OSOMUCOID IN INJURY. R.A. Zeineh*, A.A. Hakim, and K. Abdul-Karim*, The Chicago Medical School, University of Illinois at the Medical Center, Chicago, Ill. 60680, and Arab Development Institute, Tripoli, LAR.

Multiple molecular species of urinary and serum proteins are of basic physiological significance. Although several procedures have been employed, none of them carry the resolving capacity of Immunocore electrophoresis (ICEP). The present communication reports on the multiple molecular forms of orosomucoid in the serum and urine of normal and injured dogs. In the normal state, samples were collected daily over a 21 day period. Injury was then produced by single standard dose of 0.1 ml of turpentine per kilogram body weight injected subcutaneously in the left glutal region. Serum and urine were taken daily and submitted to ICEP against mono specific antiserum for orosomucoid. (Zeineh, et al., Amer. J. Physiol., 222, 1326-1332, 1972). After immunoelectrophoresis the various forms of urinary orosomucoid were assessed by soft laser scanning densitometry (SLSD). ICEP combined with SLSD have a high resolving power and formulate a sensitive method for detecting protein variants. Three precipitin bands of orosomucoid appeared on ICEP in injured urine. In injury the level of serum orosomucoid increased and the ICEP pattern, number and band was quantitated by SLSD. The information obtained is rather complicated for interpretation and remains to be evaluated.

PINEAL FUNCTION WITHIN THE CIRCADIAN SYSTEM OF THE HOUSE SPARROW. Natille H. Zimmerman*and Michael Menaker, Dept. Zoology, University of Texas, Austin, Texas 78712

Surgical removal of the pineal organ abolishes the free running circadian rhythm of activity in the House Sparrow(Passer domesticus). Experiments were performed in which the pineal was left in situ but its neural connections were interrupted. Surgical disruption of neural output from the pineal does not abolish the free running rhythm in constant darkness suggesting that pineal influence on the circadian system is exerted hormonally. Chemical sympathectomy with 6-OHDA does not abolish the free running rhythm of activity. Thus the role of the pineal within the circadian system of sparrows does not depend on its being neurally coupled to a driving oscillator located elsewhere. Furthermore, transplantation of pineal tissue into the anterior chamber of the eye rapidly reestablishes rhythmicity in pinealectomized sparrows and also transfers the phase of the donor bird's rhythm to the recipient. These results strongly suggest that the pineal is acting as a self sustained oscillator driving the overt rhythm of locomotor activity.
(Supported by NIH grants MH12476, HD03803, and C.D.A. HD09327.)

PROLACTIN RESPONSE TO PRECIPITATED MORPHINE ABSTINENCE IN THE RAT. E. Zimmermann and C.N. Pang,* Dept. Anatomy and Brain Research Institute, UCLA School of Medicine, Los Angeles, CA 90024

Previous studies in this laboratory showed that morphine administration to naive rats causes a brief but marked increased secretion of prolactin and corticosterone (B) and that administration of naloxone to morphine-dependent rats causes increased B release. To determine the effect of precipitated morphine abstinence on circulating prolactin levels, adult male rats (Simonsen) were implanted subcutaneously with 3 morphine pellets (75 mg free base each). Controls received placebo pellets. Seventy-two hr later, 4 mg/kg naloxone or saline were injected i.p. and blood samples were obtained by rapid decapitation 30 min thereafter. Plasma levels of prolactin, determined by radioimmunoassay, were elevated ($p<0.05$) in naloxone-treated rats compared to saline-injected controls. In another study, rats bearing 2 subcutaneous morphine pellets for 72 hr received naloxone (4 mg/kg) or dexamethasone (100µg/kg) intraperitoneally. Compared to placebo-implanted controls, both naloxone-treated and dexamethasone-treated rats showed increased ($p<0.05$) plasma levels of prolactin 30 min later. These findings indicate that precipitated abstinence in morphine-dependent male rats is characterized by increased secretion of pituitary prolactin and that dexamethasone may antagonize neuroendocrine effects of morphine. Moreover, these results suggest that mechanisms underlying secretion of prolactin respond similarly to morphine administration and withdrawal.
(Supported by USPHS grant DA-826 and the Ford Foundation.)

HEMODYNAMIC EFFECTS OF INTRA-ARTERIAL CATECHOLAMINES IN THE PRIMATE STOMACH. M.J. Zinner,* J.C. Kerr,* D.G. Reynolds, Div Surg, Walter Reed Army Institute of Research, Washington, D.C. 20012

In a previous report epinephrine (E) was shown to cause vasoconstriction with autoregulatory escape when infused into the right gastric artery (GA) of dogs while in the left GA, E produced predominantly a dilator response. Norepinephrine (NE) caused constriction in both circulations with gradual autoregulatory escape and isoproterenol (I) caused dilation. The present study presents data on the effect of intra-arterial infusion of these catecholamines, at a dose of 0.05 μg/kg·min, in 10 anesthetized baboons. Total gastric blood flow (GBF) was measured electromagnetically by placing a flow transducer on the celiac artery of animals that were splenectomized and had hepatic artery ligation. Control GBF was 3.7 ± 0.3 ml/min·kg. E elicited a sustained decrease in GBF to 1.2 ± 0.3 ml/min·kg ($p < .05$) by 3 minutes of infusion with no sign of autoregulatory escape. NE produced a similar response. I produced a sustained increase in GBF to 5.6 ± 0.6 ml/min·kg. Following termination of the E and NE infusions at 10 minutes GBF returned to control values without the postinfusion dilation reported in the canine circulation. Alpha adrenergic receptor blockade (phenoxybenzamine, 1.5 mg/kg, IV) significantly attenuated the constrictor responses to both E and NE, without reversing the response of E infusion to dilation as reported in the canine gastric circulation. Beta adrenergic receptor blockade (propranolol 0.5 mg/kg, IV) significantly attenuated the dilator response to I without altering the responses to E and NE. E and NE appear to be relatively pure alpha adrenergic agonists in the baboon's gastric circulation while I exerts purely a beta adrenergic receptor influence on this vascular bed.

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