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SYMPOSIUM - "IONIC AND RESPIRATORY INTERACTION IN AQUATIC ANIMALS" 425

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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. ASZ and BMES abstracts are so noted in upper right-hand corner.

VAGINAL BLOOD FLOW RESPONSE TO IMMERSION OF HAND IN ICE WATER. R.M. Abrams, M. Notelovitz* and C.J. Wilcox*, Depts. of OB-GYN and Dairy Science, University of Florida, Gainesville, FL 32610

Vaginal blood flow was evaluated in seven normal young women who were menstruating regularly and were on no medication. Subjects slept overnight in a quiet, temperature controlled (23C) room. Immediately upon awakening vaginal temperature was measured. A vaginal probe (J. Appl. Physiol. 33:144, 1972) was inserted and heat flow from the vaginal wall to the water-cooled (20-25C) probe was evaluated by recording continuously the mV output of 4 bismuth telluride heat flow discs embedded in the wall of the probe. Parameters evaluated each minute before, during and after a 4 minute period of hand immersion in an ice-water slush were: vaginal heat flow (HF) in $\mu V/\Delta T$ (vagina-water), systolic blood pressure (BP) (automatic sphygmomanometer), and pulse rate (PR) (toe photoelectric plethysmograph). Data were analyzed by method of least squares analysis of variance which included patient and time in the statistical model. No recognizable change in pre-immersion values could be detected in any of the response variables. HF, BP and PR mean pre-immersion levels were 266.9 $\mu V/C$, 100.4 mmHg, and 67/min. After immersion, significant increases occurred ($p < .01$); mean peak responses were attained at 2.4, 3.4, and 0.9 minutes and averaged 270.0 $\mu V/C$, 115.8 mmHg, and 69.8/min. In control experiments employing a vaginal thermocouple alone, there were no detectable changes in vaginal temperature during hand immersion. In view of an earlier demonstration that HF bears a qualitative relationship to vaginal blood flow, these results suggest that vaginal blood flow increases in women in response to a standard cold pressor stimulus. (Supported by NIH Grants HD-08229 and RR-00082.)

THE DEVELOPMENT OF BLOOD BUFFERING CAPACITY IN THE CHICKEN EMBRYO. Ralph A. Ackerman* and Hermann Rahn. Dept. of Physiology, State Univ. of N.Y. at Buffalo, Buffalo, N.Y. 14214

Blood buffering capacities of 7- through 18-day chicken embryos were measured by the Astrup technique using two CO_2 in O_2 mixtures. Hemoglobin concentrations were derived from measured hematocrit values. Blood buffer values double from 8 - 10 slykes to 20 - 22 slykes from day 7 through day 18 of incubation, the most dramatic increase occurring between days 9 and 14, at which time the blood buffering capacity has reached adult levels. While hematocrit doubles from 15% to 32% between day 7 and day 18, hemoglobin concentration increases only from 5.6 to 9.3 g %. If the buffering capacity of embryonic chicken hemoglobin is similar to adult chicken or human hemoglobin, then hemoglobin accounts for a decreasing proportion of total blood buffering capacity as development proceeds. On day 7 about 85% of total buffering capacity can be attributed to hemoglobin, and 60% on day 18. This suggests a significant increase of non-hemoglobin buffer during development. The air cell P_{CO_2} and P_{O_2} were also determined for each egg, using techniques published earlier. The P_{CO_2} measured in the air cell can be used to estimate blood pH on the assumption that air cell CO_2 tension is near that of blood CO_2. It appears that blood pH peaks at 7.6 on day 11. Thereafter pH falls to 7.48 by day 15, where it remains constant through day 18. This is consistent with the findings of others. (Supported in part by NIH Fellowship 1F32 HL0519-01.)

BEHAVIORAL REDUCTION OF PREOPTIC TEMPERATURE: RESPONSE THRESHOLDS. Eleanor R. Adair, John B. Pierce Fndn. Lab. and Yale Univ., New Haven, CT 06519.

Squirrel monkeys (Saimiri sciureus) can be trained to regulate preoptic/anterior hypothalamic temperature (T_{po}) behaviorally. Highly localized T_{po} control is achieved with a microheater inserted in an implanted thermode tube. The monkeys learn, in a 37°C environment with microheater temperature set at 53°C, to pull a rope for 15-sec respites from preoptic heating. Once learned, the rope-pulling response was found to be a function both of microheater (T_{htr}) and ambient (T_a) temperatures. The level of T_{htr} for initiation and cessation of behavioral responding ("on" and "off" behavioral threshold) was determined as a function of T_a (33°-37°C). In a constant T_a with the response rope always available. T_{htr} was slowly increased (at a rate of .32°C/min) to a maximum of 53-56°C, held at this level for 10 min, and then slowly decreased at the same rate. The onset, subsequent incidence, and offset of rope pulling to reduce T_{po} was recorded throughout, together with measures of preoptic, rectal and four representative skin temperatures (abdomen, tail, leg and foot). The T_{htr} at the "on" threshold was 42°C at T_a = 37°C and increased linearly to about 55°C at T_a = 33°C. Above the "on" threshold, response frequency increased as T_{htr} increased. In general, the "off" response threshold was similar to but slightly lower than the "on" threshold. The latter appeared to be correlated with the rate of change of foot skin temperature at T_a = 33°-35°C. (Supported by USPHS Grant NS-11517).

ADDITIVE OR NONADDITIVE INTERACTION OF CHEMORECEPTORS? J. M. Adams*, E. O. Attinger and F. M. Attinger*, Div. of Biomedical Engineering, University of Virginia, Charlottesville, Va. 22901

A Bilateral, isolated and donor-perfused Carotid sinus preperation (with hypoxic perfusate) was used in conjunction with Carbon Dioxide (CO_2) inhalation to separately or simultaneously stimulate the Carotid and Medullary chemoreceptors at two levels in six anesthetized dogs. Tidal volume, respiratory period and minute ventilation were measured by computer program from magnetic tape records of pneumotachograph output. Statistical test, using the Wilcox rank sum method, compared the sum of the percent changes of each of the variables for the separate stimuli with the percent change for the simultaneous stimuli. There was a significant ($p < .05$) difference only for tidal volume and only at the higher level of hypoxia in the Carotid sinus. A multivariate regression of the percent changes on the alveolar CO_2, arterial pH, perfusate partial pressure of oxygen and perfusate pH showed nonadditive interactions of tidal volume and minute ventilation. The difference between the Wilcox test and regression is due to the large variance of minute ventilation; this effect is reduced for the regression since a larger number of data points were used. These results indicate that the chemoreceptor effects are synergistic, not additive, for minute ventilation and that this is due to the tidal volume component and not to respiratory period.
(Supported by grant PHS 5 T01 GM 01919-05).

HYDRAULIC AND OSMOTIC EFFECTS ON SKIN ELECTRICAL PHENOMENA
Thomas Adams, Michael A. Steinmetz* and S. Richard Heisey. Dept. of Physiology, Michigan State University, East Lansing, MI 48824

Skin potential level (SPL), electrical conductance level (SCL) and their respective, evoked responses (SPR and SCR) were found to vary interdependently as functions of both the water and salt content of the epidermis. Electrical phenomena were recorded transcutaneously at the glabrous skin of the central footpad in the anesthetized (Na pent.; 36 $mg \cdot kg^{-1}$; IP) cat in response to a single test stimulus (8 V; 3 $impulses \cdot train^{-1}$) of the peripheral nerve supplying the hindfoot. Water content of the upper skin layers was adjusted by controlled sweat gland activity using electrical stimulation of the nerve ($f = 3 \cdot sec^{-1}$) in bursts of 10 secs, each followed by a test stimulus, for a total 100 sec period. Ionic concentration of the footpad skin was adjusted by soaking it with deionized water, isotonic (300 $mosm \cdot l^{-1}$) or hypertonic (600 $mosm \cdot l^{-1}$) NaCl solutions and drying it with a stream of dry air prior to each test. Against this background, SPR's and SCR's became progressively larger and rose from serially elevated SPL's and SCL's as sweat increasingly penetrated and infiltrated the skin. These effects were least for the deionized skin and were greatest for the skin previously salt loaded either by the isotonic or by the hypertonic solutions. Skin hydration affected all responses, whereas the effect of its salt content alone influenced SPR, SCL and SCR more than it did SPL. These data are interpreted as indicating that both the water and salt concentrations of the epidermis need to be considered for a quantitative interpretation of skin electrical phenomena. Since these effects are presumed to operate at the level of the stratum corneum more than they do in the sub-epidermis, its thickness and composition are likely to be additional, influential factors. (Research supported in part by funds from COM, MSU)

EFFECTS OF ZINC ON FATHEAD MINNOW CELL CULTURES. P.J. Adragna* and C.A. Privitera. Division of Biology, S.U.N.Y./Buffalo, Buffalo, New York 14214

Fathead minnow cells were cultured in varying concentrations of Zn^{++} (18-50 mg/l) for two separate time courses: short term (7 days) and long term (several months). The more concentrated the zinc in the growth medium, the less numerous were the cells growing in the culture. Cell size and cell volume increased dramatically when cells were grown in progressively higher zinc concentrations. Concomitantly cell protein content also increased (in both the soluble and insoluble fractions). Data obtained by atomic absorption studies indicated increased intracellular zinc content with higher Zn^{++} content in the growth medium. Electron micrographs reveal greater vacuolization on the part of cells exposed to high Zn^{++} concentrations. Enzyme assays suggest increased enzymic activity of some Zn^{++} metalloenzymes in those cells grown in higher zinc concentrations. These data further suggest that cells exposed to zinc as a stressor manifest profound and subtle morphological and physiological changes as adaptive mechanisms.

"SHORT LOOP" FEEDBACK CONTROL OF PROLACTIN. J.P. Advis*, T.R. Hall*, C.A. Hodson, G.P. Mueller* and J. Meites (SPON: Dr. R.A. Bernard). Dept. of Physiology, Michigan State Univ., East Lansing, MI 48824.

Prolactin has been shown to inhibit its own secretion by a "short loop" feedback mechanism (Vit. Horm. 30:165, 1972). Recent findings also indicate that this process involves stimulation of a hypothalamic dopamine-PIF system (Neuroendocrinology 9:100, 1972). In order to study the temporal effects of this mechanism, ovine prolactin (1 mg/rat); which does not cross-react in the rat prolactin-RIA, was given s.c. in two different experimental models: (a) three min restraint stress and (b) pimozide treatment (2 mg/kg), with male rats. Four hrs following injection of ovine prolactin basal levels of serum prolactin were significantly reduced. Restraint stress elevated serum prolactin levels 10-fold; pretreatment with ovine prolactin blocked 50% of this rise when given 4 hrs, but not 1 or 12 hrs, prior to the stress. Blockade of dopamine receptors by the administration of pimozide produced an 8-fold rise in serum prolactin levels by 2 and 4 hrs after injection. Ovine prolactin given in combination with pimozide partially blocked ($P<0.05$) the stimulation of prolactin due to pimozide at 2 and 4 hrs. These findings show that the "short loop" feedback inhibition of prolactin release requires more than 1 hr but less than 4 hrs to become active. Failure of pimozide to completely eliminate the feedback of prolactin suggests that additional non-dopaminergic mechanisms are involved. (Supported in part by NIH grant AM 04784).

VENTILATORY RESPONSES OF AWAKE RATS TO ACID-BASE DISTURBANCES IN BRAIN ECF. D. Aggarwal*, J.A. Dempsey and E.B. Olson, Jr.*. Dept. of Preventive Medicine, University of Wisconsin, Madison, WI 53706.

This study was performed to investigate the suitability of awake albino rats as a model for studying ventilatory responses to acid-base changes in brain and to other known and suspected stimuli in the brain ECF. Rats were studied awake and unrestrained. V and arterial blood composition were measured, while the lateral ventricle was being perfused (at a rate equal to the rat's own production rate) with mock CSF solutions of varying composition via chronically implanted guide tube in the lateral ventricle. While breathing room air at rest, the rat has: Hct=43.5 $\pm$ 2.1; PaO_2=85.3 $\pm$ 2.9; $PaCO_2$=38.7 $\pm$ 1.1; pH_a=7.439 $\pm$ .013; $HCO_{3_a}^-$=25.8 $\pm$ 1.0; f=82 $\pm$ 10; V_T=2.2 $\pm$ .4 ml and $\dot{V}$=74 ml/min/100 gm body weight. While perfusing the lateral ventricle with normal mock CSF ($[HCO_3^-]$=26.8) no ventilatory changes were obtained. On decreasing perfusate HCO_3^- (5-10 mEq/L), $\dot{V}$ increased markedly through both, f and V_T and arterial hypocapnia was significant. No ventilatory depression occurred with moderate increases in perfusate HCO_3^- (40 mEq/L). Perfusate HCO_3^- of 4 to 5 times normal was required to produce significant hypoventilation and hypercapnia. Hence, like awake goat (Pappenheimer, AJP 208:436) and man, the gain of the rat's H^+ chemoreceptors differ greatly above and below the eupnic point. A pulsed ventricular injection (0.1 ml) of high and low HCO_3^- solutions produced marked and rapid hypo- and hyperventilation respectively. $\dot{V}$ returned to control levels within 30 minutes. In summary, awake, unrestrained, chronically implanted rats appear to be a highly suitable model for the study of potential mediators of ventilatory regulation acting via the brain ECF. (Supported by NIH Grants 15469 and 00149.)

GLYCEROL AND ALANINE METABOLISM IN THE HIBERNATING BLACK BEAR. David A. Ahlquist,* Ralph A. Nelson, James D. Jones* and Ralph D. Ellefson.* Mayo Medical School, Rochester, MN 55901

Factors that permit maintenance of normal levels of plasma protein, amino acids, and glucose in hibernation were studied. Both before and during hibernation, intravenous injection of either ^{14}C-glycerol or ^{14}C-alanine was followed by serial collections of blood, urine, and expired gases. Mass and isotope quantitations were then performed. From the active phase to the end of 1 month of hibernation, the mean respiratory quotient decreased from 0.78 to 0.69, the mean blood urea from 34 to 20 mg/dl, and the mean weight loss was only 10%. Relative to the active phase, the following changes were found in torpor with both isotopes: specific activity of plasma glucose, lactate, pyruvate, protein, and lipid esters increased, but no label was detected in urea; of the labeled amino acids, ^{14}C-alanine alone exhibited increased half-life; and considerable reduction in expired $^{14}C\text{-}CO_2$ was noted. In active and hibernating bears receiving ^{14}C-glycerol, free and protein-bound amino acids containing the label included alanine, serine, glutamine, and asparagine. Results imply that the following metabolic adaptations occur in the hibernating bear: (1) glycerol is the primary nonrecycled substrate for gluconeogenesis and is a carbon source for the synthesis of nonessential amino acids; (2) alanine functions in recycling the carbons from glucose and the nitrogen from protein metabolism; (3) rapid protein turnover takes place with minimal urea formation; (4) glycolytic intermediates are prevented from oxidation to CO_2 in the tricarboxylic acid cycle; and (5) hepatic esterification of fatty acids is increased. (Supported by grant #SPF-8469 from Northwest Area Foundation.)

AN IMMEDIATE RESPONSE TO ALLOXAN BY ISOLATED ISLETS OF LANGERHANS.
J.O. Akpan*, J.R. Oliver* and P.H. Wright, Department of Pharmacology, Indiana University School of Medicine, Indianapolis, Indiana 46202

Following brief exposure to alloxan, isolated islets of Langerhans fail to secrete insulin in response to stimulation with glucose. To study more immediate effects of alloxan, isolated rat islets (100/chamber) were perifused with a bicarbonate-buffered medium (pH, 7.4; 1.0 ml/min) containing glucose in low concentration (30 mg/100 ml). When, after a control period of about 20 minutes, alloxan (25 mg/100 ml) was added to the perifused medium for 6 minutes, insulin was immediately but only transiently released. This effect was consistently obtained with islets from both fed and fasting rats. On exposure to glucose in high concentration (500 mg/100 ml) 14 minutes later, no insulin was secreted. If mannoheptulose, 2-deoxyglucose or 3-O-methyl glucose (500 mg/100 ml) was added to the medium in addition to alloxan, no immediate release of insulin was observed and the islets subsequently responded normally to glucose. None of these three sugars affected insulin secretion when perifused alone but one did affect subsequent response of the islets to glucose; after exposure to 3-O-methyl glucose, glucose induced no immediate release (First Phase) but normal subsequent (Second Phase) secretion. The immediate stimulant effect of alloxan appeared to be similar to that induced by Tolbutamide (200 µg/ml) but in this case none of the above sugars had any inhibitory effect. It is concluded that alloxan, in addition to its ultimate effects upon beta cells, causes immediate release of insulin by a mechanism which differs from those caused immediately by glucose or Tolbutamide. It also appears that the two phases of insulin release induced by glucose may not involve the same mechanisms (Supported by the Upjohn Company, Kalamazoo, Michigan).

EFFECTS OF ATRIAL PACING ON METABOLIC GRADIENTS IN THE CANINE LEFT VENTRICLE.
T.B. Allison* and J.W. Holsinger, Jr. V.A. Hospital, Newington, CT 06111 and Dept. Pharmacology & Medicine, U. Connecticut Health Center, Farmington, CT 06032.

The effects of increased heart rate on myocardial metabolism was examined. Dogs were anesthetized with Nembutal (30 mg/kg, iv), intubated and respiration supported with a positive pressure respirator. Blood gases and pH were maintained at physiologic levels. After sternotomy, a pacing electrode was sewn to the right atrium near the SA node and hearts paced (P) for 15 minutes at 252±2 beats/min. Nonpaced (NP) dogs underwent the same procedure except for pacing. At the end of the pacing or control period, a transmural biopsy was obtained through the posteriolateral wall of the left ventricle. This was dropped into liquid N_2 immediately and frozen. Epicardial fat and blood vessels were trimmed off and the outer 3mm taken (O); any residual papillary muscle was removed and the inner 3mm taken (I). Phosphocreatine (PCr), ATP, lactate (LAC) and glycogen (GLY) were extracted and analyzed. Values are expressed as µm/g dry wt, except for GLY, µm C_6/g dry wt.

	PCr		ATP		LAC		GLY	
	O	I	O	I	O	I	O	I
NP (6)	42.3	32.6	27.4	22.3	4.40	7.79	174.8	214.5
	±1.6	±1.9	±0.7	±0.8	±0.13	±0.28	±17.4	±10.3
P (6)	43.0	32.6	26.8	21.1	4.38	7.49	180.0	227.5
	±3.5	±2.5	±0.2	±0.3	±0.17	±0.24	±8.3	±15.8

Although there were significant ($P<0.001$) transmural differences for each metabolite, there were no significant ($P>0.5$) differences in any of the metabolic parameters when comparing NP to P. These data support the hypothesis that tachycardia does not result in any significant ischemia, particularly in the subendocardium where the potential for ischemia is the greatest.

ESTROGENS AND PROTECTION AGAINST CIRCULATORY SHOCK. Burton M. Altura. SUNY Downstate Medical Center, Brooklyn, N.Y. 11203.

Although it is generally believed that female mammals are more resistant to a number of diseases and stresses than are male mammals, this information is fragmentary. The present study was designed to determine whether sex and administration of synthetic estrogenic hormones could influence: 1) survival of rats (male and female) to different forms of lethal circulatory trauma (e.g. LD_{10-100}); 2) the tone of splanchnic microvessels of rats subjected to lethal forms of experimental shock (i.e., drum trauma and bowel ischemia); and 3) the blood pressure responses post-trauma. The results indicate that: a) inbred females are significantly more resistant to Noble-Collip drum trauma (NCDT) and bowel ischemia (BI) than are males of the same strain; b) estradiol pre-treatment of males, using either acute, massive (1, 10 mg/kg) or multiple, low dose (10, 100 μg/kg) regimens, confers trauma resistance on such animals; c) untreated female as well as estradiol-treated males exhibit significantly higher arterial blood pressures post-trauma than do untreated male rats; d) direct, in vivo microscopic observation of rat mesenteric vessels indicates that, in the late stages of lethal BI or NCDT, the untreated females as well as the estradiol-treated males exhibit significantly less dilatation (e.g. 50% less) of microscopic capacitance vessels (i.e., venules) than do untreated male rats. The data reported herein could be used to suggest that estrogenic hormones may play pivotal roles in: 1) the amelioration of organism's reaction to systemic stress and shock; and 2) control of peripheral vascular functions. (Supported by USPHS NHLI Grants 18002 and 18015.)

ASZ (DCPB)

MORPHINE ACTIONS ON ISOLATED VASCULAR SMOOTH MUSCLES. B.T. Altura* and B.M. Altura, SUNY Downstate Medical Center, Brooklyn, NY 11203.

Little information currently exists with regard to the possible direct actions of narcotics on blood vessels. The present studies, using isolated rat aortic strips (RAS) and portal veins (PV), were undertaken to: 1) determine whether certain concentrations of morphine sulfate (MS) induce direct actions on RAS and PV; 2) study the effects of MS ($3-30 \times 10^{-5}$M) on reactivity to epinephrine (E), KCl (K^+), angiotensin (AT) and serotonin (5HT); 3) gain some insight into how these effects are brought about. The results indicate that MS can: a) induce contractions of RAS which are dependent upon $[Ca^{++}]_o$, cannot be blocked by amine pharmacologic antagonists but can be prevented by naloxone (NL) ($6-14 \times 10^{-6}$M); b) enhance the amplitude of the spontaneous mechanical responses in PV; c) dose-dependently attenuate contractions induced by E, K^+, AT and 5HT; and d) noncompetitively shift the dose-response curves (DRC) of these agents to the right. Other experiments indicate: a) NL (up to 6×10^{-5}M) cannot induce contraction of RAS or PV but can in high doses ($1-6 \times 10^{-5}$M) reduce spontaneous mechanical activity in PV; b) prostaglandin E_1 (0.5-2μg/ml) did not prevent MS-induced contractions of RAS; c) ethanol (100-170mM), rather than enhancing the MS antagonism of drug-induced contractions, abolished these actions; and d) MS (up to 5×10^{-4}M) did not attenuate Ca^{++}-induced contractions of K^+-depolarized RAS. These data suggest: 1) although these diverse actions of MS on RAS and PV appear to be directed toward movement of cellular Ca^{++}, they differ from the interactions previously reported for ethanol (Anesth. 44: 311, 1976) and barbiturates (Am. J. Physiol. 229: 1635, 1975) with Ca^{++} on these vascular smooth muscles (VSM); 2) analgesic agents may act differently from anesthetic drugs on VSM; and 3) there may be a MS receptor in VSM. (Supported in part by USPHS NHLI Grant 18015 and NIMH Grant 26236.)

BASAL BLOOD PRESSURES, PLASMA CATECHOLAMINES AND RENIN PROFILES IN UNANESTHETIZED MONKEYS. E.T. Angelakos, A. Gould*, A. Sternberg* and M. Warnick*. Hahnemann Medical College, Philadelphia, PA. 19102.

Over one hundred African Green Monkeys (C. Aethiops) of two subspecies Grivets (G) and Vervets (V) were evaluated. Arterial blood pressures (BP) were measured over a 2-5 day period directly from the cannulated tail artery in unanesthetized animals conditioned to partial restraint. Basal BP's were obtained. Plasma catecholamines (PCA), renin activity (PRA), renin substrate (PRS) and renin concentration were measured at the same time. Blood volumes, urinary catecholamines and glucose tolerance curves were also measured. The data was used to identify animals with hypertension for selective breeding. On the average the V subspecies had higher BP than did the G. In both, BP in males (M) was higher than in females (F). PRA showed a bimodal distribution. The mean values of PCA, PRA and PRS were M>F and V>G. The PCA and PRA values indicate that the animals were not stressed when basal BP's were taken. Ketamine anesthesia altered BP differently in different animals although group mean values were similar. There appears to be a correlation between basal BP, PCA and PRA in the unanesthetized state.

THE HYPOCALCEMIC EFFECTS OF GLUCAGON AND PANCREATIC TISSUE HOMOGENATE IN THE DOG. Hubert E. Appert, Michio Sowa* and John M. Howard*, Medical College of Ohio at Toledo, Toledo, Ohio 43614

Glucagon and pancreatic homogenates to be tested for hypocalcemic effects were injected either intravenously or intraperitoneally in thyroparathyroid-intact and in thyroparathyroidectomized dogs. Pancreatic tissue was homogenized in a Waring blender, filtered through cheese cloth and centrifuged at 15,000 x g for 15 minutes. The supernatant obtained after centrifugation was passed through an Amicon PM-30 filter membrane which retains materials having a molecular weight of 40,000 or greater. Intravenous glucagon (0.05 mg/kg body weight) caused a drop in serum calcium of 0.7 (±0.2 S.E.) mg/100 ml at five hours after its administration in thyroparathyroid-intact dogs but had no effect in thyroparathyroidectomized dogs. On the other hand, the pancreatic homogenate retained by the Amicon PM-30 filter was equally effective in causing hypocalcemia (a drop of 1.6 (±0.2 S.E.) mg/100 ml) in both thyroparathyroidectomized dogs and in thyroparathyroid-intact dogs. Furthermore, the intravenous infusion of PM-30 retained pancreatic homogenate fraction had a hypocalcemic effect which was equal to or greater than when it was given intraperitoneally. These observations suggest that the pancreas contains a factor distinct from glucagon which may be responsible for the hypocalcemia observed during pancreatitis. The fact that the pancreatic homogenate was as effective when given intravenously as intraperitoneally suggests that some mechanism other than the intraperitoneal deposition of calcium soaps of fatty acids was involved in producing the hypocalcemic effect.

(Supported by NIH Grant #AM 17789)

THE ACTIVITY AND SOLUBILITY OF PARTICULATE FORMS OF AMINOACYL-t-RNA LIGASES FROM SKELETAL MUSCLE OF MICE: EFFECTS OF DIABETES AND INSULIN. C. Arbeeny* and W. Stirewalt* (SPON: A. K. Sinha). Dept. of Physiology, CMDNJ-Rutgers Medical School, Piscataway, N.J. 08854.

The activities and sedimentation properties of leucyl-, methionyl-, threonyl-, and glutamyl-t-RNA ligases of dialyzed and nondialyzed postribosomal supernatant fractions (PRS) of skeletal muscles from diabetic and insulin-treated diabetic mice have been compared. No differences in total activity or the distribution of activity in fractions of sucrose gradients were observed between dialyzed PRS of muscle isolated from the two groups of animals. However, while ligase activities in the nondialyzed PRS from untreated diabetic mice were stable and remained in solution for several days, up to 70% of the activity of ligases in the nondialyzed PRS from diabetic mice injected with insulin 90 min before killing became associated with a precipitate containing less than 2% of the total protein in the fraction. A concentrated dialysate of the PRS from muscle of insulin-treated animals effected a similar selective precipitation of ligase activities in the PRS of muscle from untreated diabetic animals. The effector of the solubility changes in less than 10,000 MW and has not been identified. The absence of the precipitation factor in muscles of diabetic mice and its appearance after insulin treatment suggests that its identity may provide clues to the intracellular events mediating the anabolic effects of the hormone on muscle.
(Supported by grant GRS-CMDNJ-Rutgers Medical School).

EFFECTS OF SMALL-PARTICLE AEROSOLS OF RIMANTADINE AND RIBAVIRIN ON ARTERIAL BLOOD pH, GAS TENSIONS, AND LUNG WATER CONTENT OF A2 INFLUENZA-INFECTED MICE. J. B. Arensman,* J. W. Dominik,* C. T. Liu, and D. E. Hilmas* (SPON: P. G. Canonico). USA Med. Res. Inst. of Infectious Diseases, Fort Detrick, Md. 21701

The respiratory pathophysiology of A2 influenza infection was studied in mice treated with small-particle aerosols (SPA) of rimantadine or ribavirin. Untreated infections in mice result in a survival rate of 35% or less, and are characterized by (1) severe hypoventilation ($\downarrow P_{O_2}$ and $\uparrow P_{CO_2}$), (2) compensated respiratory acidosis ($\uparrow P_{CO_2}$, $\uparrow HCO_3^-$, with normal pH), (3) pulmonary edema (↑ratio of wet/dry lung weight), and (4) hypothermia. SPA of rimantadine (presented dose of 8 mg/kg/day for 4 days) initiated 72 hr after virus challenge of mice, using SPA, significantly improved survival rate (85%) but failed to alter the hypoventilation, respiratory acidosis, pulmonary edema, hypothermia, lung virus titers, or lung pathology found in infected, untreated mice. SPA of ribavirin (presented dose of 40 mg/kg/day for 4 days) initiated 6 hr after SPA exposure of mice to virus significantly improved survival rate (95%), and reduced lung virus titers and lung pathology. Gas exchange and pulmonary edema in ribavirin-treated, infected mice were significantly improved over those of infected, untreated controls. The improved survival rate induced by SPA of rimantadine cannot be ascribed to improvements in lung functions. In contrast, however, it appeared that SPA of ribavirin improved survival rate by reducing major lung pathology and pulmonary dysfunction. This was most likely mediated through the antiviral effects of ribavirin.

TOWARD A PARSIMONIOUS DESCRIPTION OF COMPLEX SYSTEMS. E.O. Attinger, D. Henry*, M. Adams*, F.M. Attinger* and A. Anné. Div. of Biomedical Engineering, U. of Virginia, Charlottesville, VA 22901

If the essence of the behavior of complex hierarchically organized systems, namely the interactions between and within its part is to be recaptured from experimental data it becomes necessary to continuously monitor large numbers of variables. The exact role of these observable variables in terms of input-output relationships is often not understood, particularly since it may alter under different conditions of stress. It thus becomes desirable to seek more parsimonious descriptions of the system under study, in terms of intrinsic or latent variables which are smaller in number than the observed or manifest variables but may shed some light on the relative importance of the latter.

Using cluster- and principal component- analyses for the identification of latent variables which characterize the control hierarchy of the O_2 transport system we found that not more than 4 dimensions were necessary to account for most of the variance of the data. The validity of the method has been tested using a computer simulation.

Supported in part by PHS grant HL 11747 and GM01919.

IMPAIRED TIDAL VOLUME STABILIZATION FOLLOWING RIB CAGE DENERVATION IN MAN. K. Axen* and E.H. Bergofsky. Institute of Rehabilitation Medicine. 400 East 34th Street, New York, N.Y. 10016.

The ability to regulate tidal volume was quantified in 26 cervical cord injured patients by comparing the "effective" elastance (E'rs) observed during single breath inspiratory elastic loads to the passive respiratory elastance (Ers) measured separately with relaxed muscles. Eleven of these patients failed to sense any impediment to breathing during loading. This group, plus 4 of the remaining 15 subjects who consciously sensed loads as an obstruction, also failed to demonstrate any tidal volume compensation (i.e. E'rs $\leq$ Ers) under load conditions even though intrinsic properties of their intact diaphragm would, by themselves, mechanically serve to stabilize tidal volume and thus produce an "effective" elastance larger than passive elastance. Measurements of rib cage geometry revealed that paralyzed intercostal muscles permitted rib cage collapse under load conditions but this effect contributed only a small component (19 $\pm$4ml, mean $\pm$ SE) to the impaired defense of tidal volume. These data suggest that phrenic motoneuron output may have declined sufficiently during the loaded breath to nullify the mechanical contribution to the augmentation of E'rs afforded by intrinsic properties of the diaphragm. This hypothesis finds support from our observation that the subjects with an absent defense of tidal volume (E'rs $\leq$ Ers) also shortened their inspiratory duration by more than any mechanically explainable amount (to 63 $\pm$ 4% of control, mean $\pm$ SE) thus suggesting a premature termination of the phrenic motoneuron output. These results suggest that, in addition to the compensatory mechanisms provided by intrinsic muscle properties, reflexes requiring an intact rib cage play an important role in the stabilization of tidal volume in spontaneously breathing man. (Supported by NIH, NINDS, NS 10164-A12A).

PREPARATION OF ISOLATED MAMMALIAN SMOOTH MUSCLE CELLS.

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We hoped to find a mammalian preparation which, like Bufo marinus stomach (Bagby, et.al. 1971. Nature 234:351-352), yielded relaxed, extended smooth muscle cells which responded to electrical stimulation.

Male guinea pigs were killed and the vasa deferentia, taenia coli and strips of circular duodenal muscle were removed and minced with scissors. The muscle pieces were incubated at 31°C in 0.1% collagenase (Worthington CLS Type II) in physiological saline. After 30-45 min. without agitation, the supernatant was discarded. Fresh enzyme mixture was added and muscle pieces were agitated frequently during a 15 min. period by gently drawing them in and out of a pipet. The supernatant containing cells was removed, and tissue pieces were recycled through the 15 min. digestion-agitation procedure several times. Cells suitable for contraction studies were obtained in 1-1 1/2 hours. Contractions to electrical stimulus were recorded by a system previously described (Klipple and Bagby, 1974. J. Micros. 101:211-213).

Although some success was obtained with all three muscles, vas deferens gave the most consistent results. In all cases it was necessary to use cells as soon as possible after isolation since cells began to "round up" shortly after isolation, with increased temperature, centrifugation, and excessive agitation hastening this process. Viability is low and cells do not remain extended long, but we believe that, with care, much useful information about the contractile process in mammalian smooth muscle may be obtained from these cells. (Supported by grant GB 36433 from NSF and HL-18077 from NIH).

PULMONARY VASCULAR RESISTANCE IN A MECHANICAL CANINE ASTHMA MODEL.

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Previous results from our laboratory demonstrated a lack of changes in pulmonary vascular resistance (PVR) in experimental canine asthma associated with severe arterial hypoxemia 15-30 minutes after antigen challenge. In contrast, a significant increase in PVR (mean of 80%) was demonstrated when animals breathed 10% O_2 resulting in comparable degrees of hypoxemia. Since the release of chemical mediators or the non-uniformity of alveolar hypoxia may explain the absence of the hypoxic pulmonary vasoconstrictor response, we repeated the measurements in a mechanical asthma model. Regional airway obstruction was simulated by placing plastic beads into lobar and segmental airways of anesthetized dogs. PVR was obtained by placing pressure catheters into the pulmonary artery and left atrium and measuring cardiac output by the dye dilution technique. Serial measurements were made of arterial blood gases, respiratory resistance (R_{rs}) with a forced oscillation technique, functional residual capacity (FRC) by helium dilution and static lung compliance (C_{st}) using an esophageal balloon. While there were no changes in heart rate, systemic arterial pressure and cardiac output 15-30 minutes after the beginning of bead placement, mean PVR (± SD), increased from 4.9 $cmH_2O/L/min$ (± 1.1) to 9.8 $cmH_2O/L/min$ (± 1.8), $p < 0.001$ ($n = 6$). Mean arterial pO_2 decreased from 99.4 (± 7.7) to 48.6 mmHg (± 3.6); pH was kept constant with intravenous bicarbonate administration. R_{rs} increased whereas FRC and C_{st} remained unchanged. The lack of changes in PVR in antigen induced asthma and the increase of PVR in a mechanical asthma model suggests that chemical mediators released in the asthmatic response may prevent the hypoxic pulmonary vasoconstrictor response. (Supported in part by NIH Grant HL-10622.

REGIONAL DISTRIBUTION OF PULMONARY EXTRAVASCULAR WATER. E.M. Baile*, P.D. Pare* and J.C. Hogg. Dept. of Pathology, McGill University, Montreal, Canada. H3A 2B4

Since hydrostatic capillary pressure increases down the lung due to the effect of gravity while oncotic pressure remains the same, it is reasonable to expect that more fluid leaves the capillaries in the dependent lung regions. Collection of fluid in the bronchovascular space has been postulated as a possible mechanism for increased vascular resistance in this region, but there have been few measurements relating regional pulmonary extravascular water (PEWr) to regional blood flow ($\dot{Q}r$). In the present study we developed a method of measuring PEWr and were able to relate these measurements to blood flow in small samples of lung tissue. In 5 intact, upright, anesthetized dogs we measured mean pulmonary artery and left atrial pressures and cardiac output and injected Cr51-tagged RBCs and Tc 99m-labelled macroaggregates of albumin. The dogs were killed, frozen solid and the thorax cut into 2-cm horizontal slices. Samples were taken peripherally from each lung slice and we obtained volume, wet-to-dry weight ratio (W/D), Cr and Tc counts/g lung. By measuring W/D and Cr counts/ml systemic blood we calculated the amount of blood and blood water/g lung; subtracting blood water from total water gave PEWr/g lung. $\dot{Q}r$ was determined by distribution of the labelled macroaggregates. Results were expressed per g dry tissue from apex to base. $\dot{Q}r$ increased rapidly to 40% lung height and then decreased; blood volume increased to 50% lung height and then showed little change; PEWr decreased progressively down the lung. We conclude that perivascular fluid collection is an unlikely cause of increased vascular resistance at the lung base as the extravascular water was least in this region. The reasons for the increase in PEWr at the lung top and the fraction of the PEWr that is part of the exchangeable pool remains to be determined.

INTRACELLULAR RECORDS FROM TROCHLEAR MOTONEURONS AND AXONS OF IDENTIFIED SECONDARY VESTIBULAR NEURONS DURING EYE MOVEMENT IN THE ALERT CAT. R. Baker and M. Gresty*. Div. Neurobiol., Univ. Ia., Iowa City, Ia. 52242

Synaptic events in the trochlear nucleus were recorded with glass microelectrodes during spontaneous eye movement in the alert cat. Following either ipsi- (Vi) or contralateral (Vc) vestibular nerve stimulation the latency, amplitude and time course of the extracellular field potential depth profiles and intracellular postsynaptic potentials were the same as those previously described in the pentobarbital anesthetized cat. The disynaptic Vi (IPSP) and Vc (EPSP) were modulated during vertical eye movement indicating postsynaptic effects at the vestibular and/or motoneuronal level. Condition-test Vi or Vc stimulation revealed the presence of a strong inhibitory pathway which is likely to be cerebellar in origin. Intracellular records from monosynaptically (<1msec) activated axons of vestibular neurons isolated within the trochlear nucleus showed a characteristic modulation during all phases of voluntary eye movements. Vi neurons were clearly related to all changes in vertical eye position with "on" direction upward and "off" downward. Vc neurons exhibited similar but oppositely directed responses. Eye movement (saccadic) sensitivity was asymmetrical for both Vi and Vc neurons. Saccades into the "off" direction produced pauses beginning prior to and equal to the duration of the saccades; however, saccades into the "on" direction were not accompanied by a burst of activity. Even so, Vi and Vc activity was already altered near to, or in some cases, prior to the onset of saccades. These results demonstrate that a class of identified secondary vestibular neurons terminating directly on a sub-group of oculomotoneurons are regulated during all changes in vertical gaze. We conclude that activity in vestibular nuclei neurons contributes to all eye movements even though they are not produced by labyrinthine activation.

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EFFECT OF CO_2 ON PULMONARY VAGAL AFFERENTS IN DOGS. R.B. Banzett*, H.M. Coleridge and J.C.G. Coleridge. Cardiovas. Res. Inst. UCSF, San Francisco, CA 94143

We have attempted to identify the vagal afferents responsible for the pulmonary CO_2 reflex (Banzett et al. Physiologist 18:130, 1975). In anesthetized dogs with open chest the right and left lungs were ventilated separately. The left pulmonary artery was occluded; circulation to the right lung was intact. We examined the response of 4 types of afferent vagal ending when CO_2 was added to the O_2ventilating the left lung. Mean impulse frequency of slowly adapting stretch receptors decreased 40% ($P<.05$) when $FICO_2$ was raised from 0 to 0.03. Successively smaller reductions in firing occurred when $FICO_2$ was increased to 0.05 and then to 0.07. These effects were not diminished when bronchial smooth muscle tone was reduced by hyperinflation or by bronchodilator drugs, thus they were not secondary to mechanical changes in the lung. Activity of rapidly adapting (irritant) receptors also was reduced by adding CO_2 to the left lung, but the effect of further increases in CO_2 was variable. Activity of two types of C-fiber ending ('pulmonary' and 'bronchial') was reduced when $FICO_2$ was raised to 0.03 but the effect was not sustained when CO_2 was raised further. The slope of the CO_2-response curve of the slowly adapting stretch receptors was inversely proportional to the slope of the reflex response described previously. Stretch receptors inhibit breathing; vagal cooling to 7-8°C blocks both their afferent fibers and the pulmonary CO_2 reflex. We believe that changes in stretch receptor activity account for the reflex increase in ventilatory drive that occurs when CO_2 is added to the unperfused lung. (Supported by NIH grants HL-06285 and HL-05251).

A STOCHASTIC FORMULATION FOR DUAL-LIMIT BEHAVIORAL THERMOREGULATION IN LIZARDS. B.J. Barber* and E.C. Crawford, Jr. School of Biological Sciences, University of Kentucky, Lexington, Ky. 40506

Heath (The Physiologist. 13(4), 399-410, 1970) has proposed that thermoregulatory behavior of lizards is controlled by maximum and minimum limit temperatures (high and low set-points) separated by a non-thermoregulatory zone. On precursory examination this hypothesis seems incompatible with the unimodal distribution of body temperatures of lizards in the field and in continous thermal gradient experiments. Evidence from two-temperature selection experiments indicate that the high and low limit temperatures are stochastically distributed. Based on this observation we have formulated a stochastic mathematical model of the system, which predicts the distribution of body temperatures of lizards confined in a linear temperature gradient. According to the model, an increase in the variance of the limit temperatures results in decrease in the variance of the unimodel distribution of body temperatures in a continuous gradient. As the variance of the lower limit increases relative to that of the upper limit the model predicts a negatively skewed distribution of body temperatures, a common observation in continuous gradient experiments.
(Supported by NSF grant PCM 74-19054)

OPTIMAL THIAMIN FOR HUMAN GROWTH AND PERINATAL SURVIVAL. J. N. Barker, Dept. Physiol. & Rehab. Med., New York Univ. Sch. Med., N. Y., N. Y.

Although thiamin specialists have suggested and provided some proof that usual U.S. thiamin intakes may be suboptimal for pregnancy and infancy, a linkage between thiamin intake (TI) and the unusually high incidences of perinatal mortality and low birth weight in the U.S. has not been suspected. Evidence will be presented showing that these are linked to thiamin status over a range which exceeds USRDA by at least a factor of 2. (1) The slope of the regression line for TI and perinatal mortality for multinational data is -10 deaths/1000 live births per mg daily thiamin intake, over a range of 0.5-2.2 mg. Mean U. S. intakes and RDA of 1.1 mg/day are thus associated with a predicted high perinatal mortality, representing about 30% total. (2) Extrapolation to zero mortality at 3.5 mg/day suggests that optimal intake is between 2.2-3.5 mg/day, levels seldom observed in U.S. dietary surveys. (3) Birth weight is proportional to maternal blood thiamin concentrations over the range 40-90 ng/ml, varying from minimal acceptable to above average by that method of analysis. Impaired placental exchange is implicated. The lowest birth weights are less than 2.5 kg and associated with mortalities of 140/1000. (4) Postneonatal mortality has the same relation to TI as perinatal, suggesting that deficiencies arising in utero continue to endanger life after birth. While correlation does not prove causation, (5) infants dying of the Sudden Infant Death Syndrome and those dying of infantile beriberi share more than 60 identities, including physiologic, biochemical, pathologic and epidemiologic aspects; impaired brain growth and microvascular aberrations are observed. It is suggested that thiamin requirements be reassessed in terms of specific goals to be achieved, i.e., living infants with optimally developed brains. Nutritionists also emphasize this need.
(Supported by RSA RT-1 R2 and Kimmelman Fund)

TIME AND SPACE RESOLVED REDOX CHANGES IN PERFUSED HEART. C. Barlow and B. Chance. Johnson Research Foundation, University of Pennsylvania Medical School, Philadelphia, PA 19174, USA

Time resolution of oxygen delivery in cardiac tissue has been suggested by previous reports of fluctuations of oxy, deoxymyoglobin concentrations and of tissue pO_2 measurements as recorded by microplatinum electrodes during contraction relaxation cycles indicating increased oxygen delivery in early systole (Chance et al., Fed. Proc. 33, 425, 1974), a result that is supported by cinemaphotography of flow through blood vessels (Tillmans et al., Circ. Res. 34, 561, 1974) and time resolved pyridine nucleotide kinetics in perfused rat heart (Barlow et al., Fed. Proc. 34, 336, 1975)*. Flash illumination of the perfused rat and rabbit heart with 360 nm radiation extends to the beating heart the NADH fluorophotography technique applied previously to the brain (Ji et al., Brain Res. In press.), and reveals "island anoxias" over the surface of the left ventricle in coronary artery occlusions, arteriole blockage and low flow ischemias. Complete blockage of regional coronary circulation by coronary artery occlusion resulted in a region of uniformly high NADH fluorescence with well defined sharp border defining the abrupt change in oxygen tension from the normoxic to the anoxic zone. Low flow ischemia resulted in the appearance of many small well-defined anoxic regions which both multiply in number and grow in size. The use of color film to record the fluorescence emission allows simultaneous recording of NADH fluorescence and the fluorescence of a dye which remains in the coronary circulation and helps define the circulation pattern in the heart.
(Supported by USPHS Grants HL-02396, HL-18726, and HL-15,835)
*For a summary, see B. Chance, Circulation Research, in press.

EFFECTS OF VALSALVA AND MÜLLER MANEUVERS ON BREATH HOLDING TIME. D. Bartlett, Jr., Dept. of Physiology, Dartmouth Medical School, Hanover, N.H. 03755.

Rigg, et al.(Clin. Sci. 47:193-199, 1974) reported that an inspiratory effort against an occluded airway (Müller maneuver), initiated at the breaking point of voluntary breath holding, enables the subject to prolong the breath hold considerably. They suggested that relief of discomfort may derive from afferents from inspiratory muscles or from a change in the pattern of vagal afferent information owing to intrapulmonary shifts of regional lung volume. An alternative explanation is suggested by the demonstration of numerous slowly adapting stretch receptors in the extrathoracic trachea of the dog (Bartlett, et al., J. Physiol., in press). These vagally innervated receptors respond to both distending and collapsing pressures; if they are responsible for the relief provided by inspiratory efforts, then expiratory efforts (Valsalva maneuvers) should be equally effective. To examine this question, breath holding at FRC was studied in six healthy, seated subjects. Sustained inspiratory or expiratory effort was initiated at a command 5 seconds before the anticipated breaking point, determined in previous trials. The subject tried to maintain a target mouth pressure of -20 or +20 cmH_2O, displayed on an oscilloscope, for the remainder of the breath hold. The results show clearly that both types of maneuver are effective in prolonging breath holding time. However, the results of control experiments, which appear not to have been carried out in previous breath holding studies, suggest that the effects of these maneuvers, and of other respiratory acts as well, may be non-specific. (Supported by grant HL 70129 from NHLI.)

STIMULATION OF THE PENTOSE CYCLE BY PARAQUAT IN ISOLATED PERFUSED RAT LUNGS. D.J.P. Bassett* and A.B. Fisher, Dept. of Physiol., University of Pennsylvania School of Medicine, Philadelphia, Pa. 19174.

Previous studies have suggested that the pulmonary toxicity of paraquat (PQ) may be related to alterations of lung metabolism. In this study, we measured the effects of perfusion with paraquat on the glucose metabolism and pentose cycle flux of isolated rat lungs. Lungs were ventilated with air - 5% CO_2 and perfused in a recirculating system with Krebs-Ringer bicarbonate buffer, pH 7.4, containing 5.5 mM glucose and 3% fatty acid-free bovine serum albumin. Glucose utilization was estimated by the production of ^3H_2O from [5-^{3}H] glucose. Total CO_2 production was measured with [U-^{14}C] glucose. Pentose cycle activity was calculated from specific $^{14}CO_2$ yields during separate perfusions with [1-^{14}C] or [6-^{14}C] glucose. In control perfusions, the pentose pathway represented 13% of a glucose utilization of 44±3 μmoles/hr/g dry wt. In μmoles/hr/g dry wt, total CO_2 production was 70±6 and lactate plus pyruvate production was 42±4 with a L/P of 11. Total CO_2 production was progressively stimulated with increasing perfusate PQ concentration up to 1.5 mM. At this PQ concentration, glucose utilization increased 32%, lactate plus pyruvate production increased 28% with no significant change in L/P, and total CO_2 production increased 105%. Partition of the CO_2 derived from glucose indicated 163% increase in production via the pentose pathway while mitochondrial CO_2 production did not change significantly. These studies show marked stimulation of the pentose cycle in the presence of PQ indicating increased turnover of cytoplasmic NADPH. Reduction of PQ by NADPH may generate reactive species that result in toxic lung injury. Supported by HL 15061.

TRANSPULMONARY PRESSURE AND FLUID TRANSUDATION IN ISOLATED PERFUSED DOG LOBE. *G. Batra, W. Mitzner (Spon.: D. Proctor). The Johns Hopkins University, Department of Environmental Medicine, Baltimore, Maryland 21205.

We have studied the effect of lung inflation on the rate of extravascular fluid accumulation ($\dot{W}$) under constant flow and constant pressure conditions. Vascular pressures were zero referenced to the bottom of the lung and pressures were all measured in cm H_2O relative to pleural pressure (atmospheric in these experiments). In 7 ventilated lobes a control state was established with mean values of pulmonary artery pressure (Ppa) = 27, pulmonary venous pressure = 15, mean transpulmonary pressure (Ptp) =4, flow = 412 ml/min, and an initial $\dot{W}$ of 17 g/h/100 g initial lobe weight. Inflation of the lung to a mean Ptp of 16.3 cm H_2O at constant intravascular pressure required a reduction in flow to 125 ml/min. Under these conditions the $\dot{W}$ was reduced by 34%. Inflation of the lung to the same Ptp with constant flow caused the Ppa to rise to 39 cm H_2O. In this case the $\dot{W}$ was increased by 120%. In order to obtain data regarding the relative permeabilities of arterial versus venous regions, the lobes were perfused in both normal and retrograde directions. We found no significant differences in the results for retrograde flow, although there was a tendency for $\dot{W}$ to be slightly lower in the retrograde condition. Our results indicate that inflation of the lung has variable effects on $\dot{W}$. On one hand, an increase in Ptp will decrease $\dot{W}$ when alveolar pressure exceeds venous pressure (zone 2) and vascular pressures are kept constant. On the other hand, the same increase in Ptp will increase $\dot{W}$ if flow is kept constant.
(Supported By: NIH Research Grant HL 18350, HL 05453 and Johns Hopkins University General Funds).

ROLE OF RESPIRATORY NEURONS IN A STIMULATED INFLATION REFLEX. H.L. Batsel. V.A. Hospital, Long Beach, CA. 90822.

Extracellular activity of 109 bulbar respiratory neurons was recorded in 30 anesthetized cats in which weak, 300 Hz stimulation of intact cervical vagus was utilized to mimic the inflation reflex (terminating inspiration and creating apnea). Twenty-four of 40 inspiratory neurons located ventrolateral to fasciculus solitarius were promptly inhibited by stimulation of the ipsilateral vagus. The remaining 16 inspiratory units were tonically activated by ipsilateral vagal stimulation. Six out of 10 of these inspiratory neurons were active during apnea resulting from maintained lung inflation. Low frequency stimulation of ipsilateral vagus drove these neurons at stable, short latency (2.5 to 15 msec). Thus these neurons have characteristics of R-$\mathscr{I}$ inspiratory neurons. Stimulation of the contralateral vagus so as to mimic the inflation reflex resulted in prompt inhibition of the same inspiratory neurons that were activated by ipsilateral stimulation. Inspiratory neurons (N=36) located in the area of nucleus ambiguus were rapidly inhibited when inspiration was terminated by stimulating either vagus. Thirteen out of 28 expiratory neurons were inhibited by ipsilateral vagal stimulation, but all of those were accelerated by stimulation of the contralateral vagus. Five latent expiratory neurons and a few active expiratory neurons were rapidly activated by stimulating either vagus. Inhibition of R-$\mathscr{I}$ inspiratory neurons by contralateral vagal stimulation raises serious question about their role as inhibitors of other inspiratory neurons. Since there is near total inhibition of inspiratory neurons in remote areas of the medulla, the source of the inhibition may have some other anatomical site.

FUNCTIONAL STUDIES ON HEMOGLOBIN FROM HIGHLAND MAMMALS AND BIRDS. C.Bauer* and D.Petschow* (SPON: M.Delivoria-Papadopoulos). Physiolog.Inst.MHH, 3 Hannover, Germany.

Unlike man, whose blood exhibits a decreased oxygen affinity upon exposure to hypoxic hypoxia, animals dwelling at high altitude have generally an increased O_2 affinity. In order to gain insights in the mechanism of this respiratory property we have measured P_{50} (P_{O_2} at Hb = HbO_2) in blood and hemoglobin (Hb) solutions as well as the concentration of organic phosphates in the erythrocytes from the bar-headed goose (Anser indicus) and the guanaco (Lama guanicoe) who usually reside at high altitude. P_{50} values (37 °, pH 7,4, pCO_2 = 40 mm Hg) were 29,7 and 22,5 mm Hg for the bar-headed goose and the guanaco respectively, whilst two goose species living at sea-level (B.canadensis and A.anser) had P_{50} values which were about 10 mm Hg higher than that of the bar-headed goose. As the concentration of inositol pentaphosphate (IPP) and other phosphate esters was similar in the erythrocytes of the three goose species we conclude that the low P_{50} in the blood of the bar-headed goose is caused by a reduced interaction of the Hb with IPP. This conclusion is corroborated by O_2-binding studies on purified Hb-solutions in the absence and presence of inositol hexaphosphate. A similar mechanism serves to explain the low P_{50} of guanaco blood compared to human blood (P_{50} = 27 mm Hg) as guanaco Hb reacts very weakly with 2,3 bisphosphoglycerate (DPG) and the concentrations of DPG in guanaco and human red blood cells are alike.

FUNCTIONAL CONTRIBUTION OF THE RIGHT AND LEFT VAGI TO GASTRIC ACID SECRETION IN THE CAT. Raymond F. Bauer* and Frank P. Brooks. Dept. Physiology, University of Pennsylvania, Philadelphia, Penna. 19174

Previous comparisons of acid output during electrical stimulation of the right and left vagal trunks failed to show significant differences; however acid outputs were low in relation to maximal secretory capacity in cats. We have compared the mean acid output (AO) and mean peak acid output (PAO) during electrical stimulation of the right, left and both vagal trunks in the neck of cats anesthetized with chloralose-urethan. In 12 male cats weighing 3-4.5 kg the vagi were stimulated at 5 Hz, 1 mAmp and 4 mSec (previously shown to produce up to 80% of the maximal acid response to pentagastrin) (Bauer and Brooks. Fed. Proc. 35:217, 1976). Stimulation of the right vagus produced a PAO (Mean ± SE) of 0.282 ± 0.060 mEq/15 min. Stimulation of the left vagus produced 0.607 ± 0.099 mEq/15 min and stimulation of both simultaneously 0.735 ± 0.094 mEq/15 min. In 8 of 12 cats PAO occurred with bilateral stimulation, and in 4 of 12 with left vagal stimulation. Ten of the 12 cats showed a greater AO with left vagal stimulation compared to right vagal stimulation. The PAO during bilateral stimulation did not differ significantly from that during left vagal stimulation. PAO during bilateral stimulation was significantly greater from that during right vagal stimulation. We conclude that under the conditions of our experiments PAO is obtained with bilateral stimulation and that the left vagus makes a greater contribution to the stimulation of acid secretion. (Supported by USPHS. NIH Grants 2R01 AM14563 and 5F22 AM01378-02.)

MECHANISMS OF INSECT FREEZING TOLERANCE. J. G. Baust[1] and R. E. Morrissey[2], Dept. of Biology, University of Houston, Houston, Tx 77004[1] and Dept. of Zoology, University of Washington, Seattle, WA 98105[2].

The cryoprotective role of natural "antifreeze" compounds (i.e., glycerol, sorbitol, etc.) has been reported in insects; yet due to the variability of experimental design in acclimation studies, results have been paradoxical. Freezing tolerance is mediated through extended supercooling (SC) attendant to the synthesis of cryoprotectants such that the hydroxyl (water binding) equivalent exceeds 1.2 molar.

Ontogenetically, the gall fly (Eurosta solidagensis) utilizes this mechanism in the third instar larval stage (freezing tolerant) but not other stages which are freezing susceptible. The latter group relies on SC extensions during cold exposures. SC extensions are not adequate in third instar larvae, but a temperature-dependent, three phase cryoprotectant accumulation pattern is apparent. Hemolymph glycerol peaks at 0.6M by early winter (0 to -10° C), sorbitol at 0.3M following freezing (-10 to -20° C) and trehalose at 300mg% (-20 to -40° C). The activity of glycerol kinase, sorbitol dehydrogenase and trehalase are maximized at peak cryoprotectant levels. The arctic beetle (Pterostichus brevicornis) employs a single phase cryoprotectant system following initial freezing exposure. Glycerol synthesis is maintained to -60° C. Hemolymph levels fluctuate during ambient temperature cycling below the SC point.
(Supported by grant BMS75-23605 from NSF.)

PROLACTIN (PRL) SECRETION DURING THE DELAY INTERVAL PRECEDING LONG-DELAY PSEUDOPREGNANCY IN THE RAT. Judith E. Beach*, Lee Tyrey*, and John W. Everett. Departments of Physiology, Obstetrics and Gynecology, and Anatomy, Duke University, Durham, NC 27710.

Earlier reports from this laboratory showed that cervical stimulation (CS) at 1400 hr diestrus day 2 induced a pseudopregnancy (PSP) after the succeeding estrus (short-delay PSP). No significant elevation of PRL over control values from cyclic rats occurred until immediately after the normal proestrous PRL surge, 37 hr after CS. Thereafter, both nocturnal and diurnal surges of PRL were evident late in the periods of dark and light, beginning on the morning after estrus. These surge patterns were similar to those occurring in normal PSP induced by CS at 1400 hr on estrus or diestrus day 1. By contrast, in the case of longer delay when a full cycle intervenes between the stimulus and the onset of PSP, the present study shows a comparatively rapid appearance, during the delay interval, of twice-daily PRL surges resembling those of normal PSP. Long-delay PSP was induced (ca. 60%) in 4-day cycling rats (Charles River CD) by electrical stimulation of the hypothalamus on the third day of ovulation blockade with sodium pentobarbital. For the first 3 days after stereotaxic procedures, serial blood samples ($\leq$3/24 hr) were taken from freely moving, stimulated or sham-stimulated rats by means of a heart catheter. In those rats that later manifested a long-delay PSP, twice-daily surges of PRL began during the first morning after the stimulation, with the nocturnal peaks on the second and third day of the delay interval reaching higher levels than any of the diurnal surges. Sham-stimulated rats and those which continued to cycle following stimulation exhibited no such PRL surges. (Supported by NSF grant BMS 70-00603 and BMS 75-14052).

EFFECTS OF DEVELOPMENT AND RENAL COMPENSATORY GROWTH ON CHOLINE METABOLISM. G.H. Bean* and L.M. Lowenstein, Depts. of Medicine and Physiology, Boston University Medical Center, Boston, Mass. 02118

Renal compensatory growth is associated with an increase in choline incorporation into membrane phospholipids. Choline is metabolized by 2 major pathways: 1) phosphorylation by choline kinase (CK) to phosphorylcholine (PC) and thence into phospholipids, and 2) oxidation by choline oxidases (CO) to betaine. We studied the effect of renal compensatory growth on both choline metabolic pathways in 84 young and adult rats. Renal compensatory growth was initiated by uninephrectomy; the compensating kidneys were compared to kidneys from sham-operated and unoperated rats. Renal homogenates were incubated with ^{14}C-choline (6 μCi/ml) and CK and CO activities measured by the appearance of PC and betaine and identified by paper chromatography and radioactivity measurements.

Kidneys of fetal rats contained CK but no CO activity. During the first month of life, CO activity appeared and increased linearly ($r=0.97$) so that by 1 month, the activities of both enzyme systems were equal. Throughout this first month, the sum of radioactive choline incorporated into PC and into betaine remained generally constant, at 3780 ± 100 (S.E.) cpm/mg protein/min.

Compensating kidneys of rats 1 month old showed a 30% increase in CK activity ($p<0.001$) ($n=14$). This increase was present following 2, 24, and 48 hours of compensatory growth. CO activity was not affected.

These results indicate that renal CK and CO activities are inversely related during early normal development. During compensatory growth, choline pathways are shifted so that increased amounts of PC are formed, probably for increased membrane synthesis.

CALCIUM REVERSAL OF THE SYMPATHOLYTIC EFFECT OF POTASSIUM. Orren Beaty* and David E. Donald. Mayo Clinic and Foundation, Rochester, Minnesota 55901.

The vasoconstrictive response to sympathetic nerve stimulation, during the first minutes of rhythmic skeletal muscle contraction is 50% of the steady state response obtained after 16 minutes of exercise. At the time of this initial depression of the response to sympathetic nerve stimulation, interstitial muscle potassium (K^+) is elevated. In the rhythmically contracting gracilis muscle perfused at constant flow, intraarterial infusion of calcium (Ca^{+2}) which increased plasma venous Ca^{+2} from a control of 12.6 to 17.7 mg/100 ml abolished the initial depression of the vasoconstrictive responses to sympathetic nerve stimulation. In the dog hindlimb perfused at constant flow and exercised for at least 30 minutes, the vasoconstrictive response to sympathetic nerve stimulation was reduced by 34% on increasing venous K^+ from 5.5 to 7.5 mEq/l. The addition of Ca^{+2} to the K^+ infusate to produce an ionic ratio similar to normal dog blood not only eliminated this sympatholytic effect of K^+ but augmented the vasoconstrictive response by 22%. The infusion of only Ca^{+2} to the exercising hindlimb did not alter the response to sympathetic nerve stimulation. These data are consistent with the view that during exercise the initial depression of the vasoconstrictive response to sympathetic nerve stimulation results from a transient interference with the transport of Ca^{+2} into the smooth muscle cell. This phenomenon is thought to result from an imbalance of the normal Ca^{+2}/K^+ ratio due to the release of K^+ from contracting skeletal muscle. (Supported by grant HL6143 from NIH).

SUBLIMINAL COMMUNICATION: ONE YEAR'S EXPERIENCE USING VIDEOTAPED VISUAL SUBLIMINAL STIMULI IN A BEHAVIOR MODIFICATION WEIGHT CONTROL PROGRAM. H.C. Becker, J.F. Jewell* and D.L. Neely*. Behavioral Engineering Corporation, 3701 Houma Blvd., Metairie, La. 70002

Subliminal Communication is a term coined by the authors to denote the presentation of meaningful audio and/or visual stimuli to individuals or groups at an intensity level below that of conscious, reportable awareness. This technique has been used for a year in the author's behavior modification weight control program in color videotapes, combined with live counseling, presented to groups of weight control participants in a 12-week, one session per week course. The videotapes contained a variety of instructional material on proper nutrition, relaxation techniques, positive reinforcers for adaptive eating behavior and mild aversives for the maladaptive. Participants learned to discriminate stimuli that trigger overeating, and to respond within the context of a new purpose of food. Most participants reported that they feel the subliminal stimuli helped them learn discriminative behavior in the presence of food -- not only nutritious, healthful food, but also junk food, thus shaping new adaptive responses to compelling food cues, and fading in three protein-rich meals daily with thorough chewing of each mouthful. Salient scientific and technical considerations central to the insertion of subliminal stimuli into color videotapes will be presented.

IN VIVO MEASUREMENT OF BLOOD-BRAIN TRANSPORT OF GLUCOSE. M.R.Bedford* K.B. Larson* and M.E. Raichle. Div. of Radiation Sciences, Washington University School of Medicine, St. Louis, Mo. 63110

Blood-brain barrier transport of glucose was studied in vivo in rhesus monkeys by a new method based on use of ^{11}C-labeled glucose. The time course of the tracer subsequent to its rapid injection into the carotid artery was followed by external monitoring of the 511-keV radiation from the head. Because recirculating tracer contributes significantly to the monitored radiation, a means of accounting for its presence was developed employing a second injection of labeled glucose into the superior vena cava. The method also made use of a vascular reference tracer, ^{15}O-labeled carboxyhemoglobin. The short-lived positron emitters ^{11}C and ^{15}O, with half lives of 20.4 min. and 123 sec., respectively, were made with a cyclotron in close proximity. Analysis of the data was based on a mathematical model of a system in which tracer not extracted into brain tissue on its first passage can reappear by recirculation in subsequent passages. Transport between blood and tissue was modeled on the basis of a Krogh capillary-tissue cylinder to represent the brain microvasculature. The model permitted the first-passage fractional extraction of glucose, E, to be derived from the data. The unidirectional rate of glucose transport, Φ_+, was then calculated from the relation $\Phi_+ = EC_aF$. Here, C_a is the arterial blood glucose concentration and F is the relative cerebral blood flow. The latter was measured from the clearance rate of ^{15}O-labeled water following intracarotid injection. The observed variation of Φ_+ over an arterial blood glucose concentration range of 62-582 mg/100 ml exhibited the saturation behavior characteristic of facilitated diffusion. Fitting the results from 19 trials to the Michaelis-Menten equation yielded an apparent K_m of 7.91±.95 mM and a V_{max} of 1.37±.08 μmole/(min g).

THE EFFECT OF 6-HYDROXYDOPAMINE IN VIVO ON DOPAMINE-β-HYDROXYLASE AND CYTOCHROME OXIDASE ACTIVITIES IN BROWN ADIPOSE TISSUE OF NEW-BORN RATS. W.A. Behrens* and F. Depocas (SPON. J. Cowan). Div. of Biological Sciences, Natl Research Council of Canada, Ottawa, Canada K1A 0R6.

Dopamine-β-hydroxylase a known marker of sympathetic endings is present in interscapular brown adipose tissue (IBAT) of 2 day-old rats. Its total activity increases 3-4 times by the 20th day of postnatal life. Cytochrome oxidase the total activity of which can be taken as an index of the oxidative capacity of a tissue increases 30 fold in the IBAT between day 2 and day 20. Daily subcutaneous administration of 150 μg 6-hydroxydopamine (6-OHDA) per g body weight, during 10 days, starting at 2 days of age, prevented the normal increases in activity of both enzymes with age. Eight days after stopping 6-OHDA treatment the activities of both enzymes were still very low. Development of oxidative capacity of brown adipose tissue thus appears to require concurrent development of sympathetic innervation.

DELAY AND DISPERSION DUE TO VENOUS VASCULAR TRANSIT IN HEART AND SKELETAL MUSCLE. F.L. Belloni, Y. Hazeyama*, and H.V. Sparks. The University of Michigan, Ann Arbor, Michigan 48109.

During transients, the time course of venous effluent concentration changes reflects, in part, the delay and dispersive effects of vascular transit between tissue and the venous measurement site. To estimate these venous transit effects, we measured the distributions of (1) transorgan transit times (integral = dye arrival) using as a tracer an intravascular dye measured with a densitometer and (2) pre-capillary transit times (integral = microsphere arrival) using radioactive microspheres counted with a portable scintillation crystal placed over the tissue with collimation and shielding to prevent detection of microspheres in major vessels. (1) Isolated calf muscles and (2) left main coronary arteries of anesthetized dogs were perfused at constant flow with blood. Tracers were injected as close arterial boluses. We assumed a multiple parallel pathway model with a pre-capillary and a capillary-venous component for each path. A fixed fraction of each transorgan transit time was ascribed to the capillary-venous component of the pathway representing that transit time. This fraction was chosen by iterative trials so that, by using the resulting calculated distribution of capillary-venous transit times as a transfer function, the microsphere arrival curve was transformed into the best possible approximation to the dye arrival curve. Based on these calculations, it was determined that over 90% of the delay and dispersion seen in transorgan vascular transit can be ascribed to capillary and venous channels in heart and skeletal muscle. (Supported by USPHS grants HL-14516 and HL-16760.).

Effects of Tobacco Smoke Exposure on the Circulatory Responses to Bilateral Carotid Occlusion. Charles H. Bennett, and Daniel R. Richardson, Department of Physiology and Biophysics, University of Kentucky School of Medicine, Lexington, Kentucky 40506

The purpose of these studies was to test the hypothesis that tobacco smoke exposure alters the neural reflex component of arterial pressure regulation. One group of rats was exposed daily to tobacco smoke from five reference cigarettes for a period of three to four months, while a second group was sham treated. At the end of the treatment period, the animals were anesthetized with urethan following which systemic arterial blood pressure responses to bilateral carotid occlusion were measured. It was observed that the smoke exposed animals experienced significantly greater increases in arterial blood pressure than the sham treated animals over a 40s post-occlusion period. Pre-occlusion systemic arterial pressure measurements in these two groups were not significantly different. It was also observed that the time required to reach maximal pressor responses following carotid occlusion was significantly less in the smoke treated animals. These results indicate that tobacco smoke exposure sensitizes the baroreceptor reflex pathway to alterations in arterial blood pressure. (Supported by the University of Kentucky Tobacco and Health Research Institute, contract no. 24016.)

EFFECTS OF DEUTERIUM OXIDE, LOW TEMPERATURE, AND LIGHT ON CIRCADIAN OUTPUT OF THE POPULATION OF OSCILLATORS IN THE EYE OF APLYSIA. J.A. Benson* and J.W. Jacklet. Dept. of Biol. Sci., State University of New York at Albany, NY 12222.

The isolated eye of Aplysia californica has been cultured for 14 days, allowing continuous monitoring of compound action potentials (CAP's) in the optic nerve. In constant darkness (DD) at 15°C, the eye exhibited a circadian rhythm of CAP output. Deuterium oxide (D_2O) lengthened the period of the rhythm linearly from 26.7 hrs for controls to 33.7 hrs in 50% D_2O culture medium. 60% D_2O stopped the rhythm at its upper phase point after one cycle. Constant light applied to the eye for many hours (e.g. 108 hrs at 1100 lux) damped the rhythm until it stopped at its lower phase point. Returning the eye to DD reinitiated the rhythm. Reduction of constant temperature level lengthened the period non-linearly. Cold pulses of 4°C for more than 12 hrs stopped the rhythm at its lower phase point. The rhythm was reinitiated when the eye was returned to 15°C. When 12 hr cold pulses were applied symmetrically spanning the rhythm peak, pulses of 9°C or above had little effect on the rhythm while those at 4°C or below stopped it. Pulses between 6.5° and 8.5°C in some cases caused the subsequent CAP output rhythm to split into two components which oscillated out of phase with one another for several cycles, until they came back into phase to form a normal rhythm. Such rhythm splitting is additional evidence that the circadian clock in the eye of Aplysia comprises a population of coupled oscillators. (Supported by NIH NS 08443 to J.W.J.)

VASCULAR REACTIVITY IN THE DOCA HYPERTENSIVE PIG. Kathleen H. Berecek and David F. Bohr. Dept. of Physiology, Univ. of Michigan, Ann Arbor, MI 48109.

The development of altered vascular reactivity was characterized in the DOCA hypertensive pig. Chester White and Yorkshire boars, 8-12 weeks of age, were uninephrectomized and instrumented with an electromagnetic flowprobe on the ascending aorta and tygon catheters in the aorta and thoracic vena cava. Approximately 2 weeks after surgery, silicone strips impregnated with DOCA (100 mg/Kg) were implanted subcutaneously. 5-10 days after implantation MAP started to rise reaching stable hypertensive levels of approximately 150 mm Hg in 1 month. Vascular reactivity to angiotensin and to norepinephrine (NE) were determined in 2 different studies: 1) Changes in total peripheral resistance in response to graded i.v. infusions of these vasoconstrictors were calculated from recordings of MAP and cardiac output. Studies at intervals during the control period and after DOCA implantation demonstrated significant increases in sensitivity (decreased threshold) and reactivity within 1 week following implantation (n=6) which persisted throughout a 1-month post-implantation period. 2) Terminal hindlimb perfusion studies showed that hypertensive vascular beds (n=3) had significantly greater ($p < .005$) resistances than controls (n=7) both before and after maximal dilation with papaverine. In response to i.a. injections of NE (.01-192 μg) hypertensive pigs (n=6) demonstrated significantly greater maximum pressor responses, shifts in the dose-response curves to the left, and lower vasoconstrictor thresholds than controls (n=8). It is concluded that resistance vessels in the hypertensive pig demonstrate changes in both structure and smooth muscle function; the latter do not appear to be secondary to increased wall stress. (Supported by USPHS, NHLI Grant HL-03756.)

EFFECT OF DIACETYLMONOXIME ON AUTOMATICITY IN CARDIAC PURKINJE FIBERS. J.L. Bergey* and A.R. Freeman, Dept. of Physiol., Temple Univ. Sch. of Med., Phila., Pa. 19140.

It has been reported by this laboratory that diacetylmonoxime (DAM) specifically abolishes the plateau of the cardiac Purkinje fiber action potential (AP) in a concentration-dependent manner. We suggest that this effect may be due to a chemical reversal of phosphate monoester formation resulting from activity of a cyclic AMP-dependent Kinase, which is associated with the beta adrenergic system. This study was extended to include the effect of DAM on automaticity in Purkinje fibers (PF). DAM (10-20mM) reduces or abolishes automaticity in PF demonstrating spontaneous phase 4 depolarization (P4D). This is accomplished by a concentration-dependent decrease in the slope of P4D and a decrease in the absolute magnitude of depolarization following stimulation of arrested fibers. Loss of automaticity occurs at concentrations of DAM that do not abolish the plateau. In the presence of DAM (10 mm), theophylline (1-4 mM) or epinephrine reverse the effects of DAM by (lower concentration) increasing the slope and magnitude of depolarization following stimulation, with higher concentrations restoring automaticity. However, still higher concentrations of DAM (20 mM) further antagonized these effects of theophylline or epinephrine. It is suggested that cyclic AMP-dependent Kinase activity is responsible for P4D as well as maintainance of the plateau, although separate sites of action may be implied by the differential sensitivity of those two phases of electrical activity to blockade by DAM.

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AUTONOMIC INFLUENCE ON LUNG COMPLIANCE IN CATS. D.R. Bergren* and D.L. Beckman. Dept. Physiology, Univ. North Dakota, Grand Forks, 58201 and East Carolina Univ., Greenville, N.C. 27834.

Previous reports have shown that mechanical CNS injury by captive bolt and also stellate ganglion stimulation in cats resulted in a low lung compliance, high minimum surface tension and increased intra-alveolar cholesterol. The purpose of the present study was to determine whether these lung changes were of sympathetic origin. Four cats per treatment group were anesthetized with ketamine, the stellate isolated and an esophageal balloon inserted. A tracheal cannula was attached to a pneumotachograph, the signal from which was integrated to give tidal volume. Isoproterenol (0.2 mg/cat iv) was administered to insure maximal airway dilation. Initial lung compliance was 9.5 ± 2.6 (SE) ml/cm H_2O in untreated controls, 8.0 ± 2.4 in a phenoxybenzamine pretreated group, 11.9 ± 3.9 in a phentolamine pretreated group and 14.6 ± 1.6 in a reserpine pretreated group. During stellate stimulation compliance fell in the untreated controls to 6.5 ± 1.5 ($P < 0.01$) but in the pretreated groups increased slightly to 8.3 ± 2.2, 13.3 ± 9.4 and 15.2 ± 1.8, respectively. This pretreatment also prevented a stellate-induced significantly increased minimum surface tension and intra-alveolar cholesterol. Results from the present study indicate causal involvement of sympathetic alpha receptors in the compliance decrease associated with this stellate ganglion stimulation. (Supported by NIH Training Grant No. 3 T01 HL05939-01A1.)

CENTRAL DEPRESSION OF RESPIRATION BY AMMONIA. R.A. Berkman*, A.G. Rosenberg*, P.J. Feustel*, and R.E. Dutton (Spon: J.C. Newell). Dept. of Physiol., Albany Medical College, Albany, NY 12208.

A significant depression of ventilatory sensitivity to CO_2 inhalation has been observed by us as a result of 4 times control elevation of arterial ammonia levels (Fed Proc 35:718,1976). The present study was undertaken to determine the influence of a similar elevation of the arterial ammonia level on the ventilatory response to hypoxia and the ventilatory sensitivity to hypercapnia after sino-aortic denervation. Sixteen dogs were anesthetized with Na pentobarbital, 25 mg/kg. In 8 dogs ammonia elevation itself resulted in an increase in room air ventilation and a decrease in Pa_{CO_2} from 40.1±1.1 to 34.2±1.6 mmHg ($P<.05$). Inhalation of 12.5% O_2 and 6% O_2 with end-tidal CO_2 held constant resulted in an increase in ventilation over control, expressed as a change in ventilation ratio (ΔVR), of 2.5±0.5 and 10.5±2.3, respectively. After ammonia elevation, the ΔVR's decreased to 0.7±0.3 and 3.9±0.7. In another 8 sino-aortic denervated dogs, ammonia elevation resulted in a decrease in room air control ventilation with an increase in Pa_{CO_2} from 40.8±0.7 to 45.6±2.6 mmHg. Inhalation of 6% and 10% CO_2 in air resulted in ΔVR's of 1.5±0.2 and 6.1±0.9, respectively, before ammonia. After ammonia elevation these decreased to 0.6±0.2 and 2.8±0.5, respectively. In both the intact hypoxic and sino-aortic denervated hypercapnic inhalation experiments, changes in airway occlusion pressures one hundred milliseconds after inhalation reflected the changes in VR's. The results of these experiments suggest that the maintenance of ventilation in the hyperammonemic state is better in the presence of intact peripheral chemoreceptors, and that ammonia elevation produces respiratory depression that is at least in part due to depression of the central chemoreceptors. (Supported by NIH Grant HL-12564)

THE CHEMICAL AND PHYSIOLOGICAL PROPERTIES OF AN ACYL-MODIFIED OCTAPEPTIDE OF CCK. J.M. Berkowitz, J. Fara, M. Praissman†, Nassau Cty Med Ctr, East Meadow, N.Y. and SUNY Stony Brook, N.Y.

While studying the binding properties of the physiologically active C-terminal octapeptide (OP) of CCK, we found the peptide was modified by what appeared to be non-specific proteolyic agents released from the tissue. In an effort to resolve this problem an acyl moiety was introduced on the free N-terminal amino group. 0.2 micromole of OP was exposed to an equimolar quantity of tritium-labeled acetic anhydride. Unreacted acetic anhydride was separated from OP by column chromatography. Acylated OP (A-OP) was then separated from unreacted OP by thin layer isoelectric focusing in a pH 2.5 to 4.0 gradient. Acylation did not affect the immunochemical properties of OP as both forms (OP and A-OP) were equally effective in displacing I-125 labeled gastrin from an antibody that recognizes both OP and gastrin. Dose-response curves were developed with cat gall-bladder tissue for isometric tension development with both A-OP and OP. Tension responses to A-OP were identical to those found with the unmodified OP on a molar basis. When A-OP was incubated with cat gall-bladder tissue or placed in solutions that had been previously exposed to this tissue there was no decline in immunoreactive OP concentration. This was sharp contrast to the one-third loss in immunoreactive concentration of the unmodified OP when exposed to the same conditions. It thus appears that acylation of OP protects it from non-specific proteolytic agents which can destroy its immunochemical properties. These results also suggest that the free N-terminal amino group of OP is not critical for either its physiological or immunological properties.

TRANSEPITHELIAL POTENTIALS ACROSS ISOLATED PROXIMAL AND DISTAL TUBULES OF REPTILIAN NEPHRONS. Klaus W. Beyenbach* and William H. Dantzler, Dept. Physiology, Coll. Medicine, Univ. Arizona, Tucson, Az. 85724.

Transepithelial electrical potentials (p.d.) of proximal and distal tubules of the garter snake Thamnophis were measured in vitro through microperfusion pipettes, 8-12 μ inner diameter. In the presence of Na-Ringer (151 mM/L Na) in bath and lumen, maximum proximal p.d.'s measure -0.66 ± 0.13 mV (24), and distal p.d.'s are -36.6 ± 6.6 mV (13), (sign of lumen; mean ± S.E., number of tubules). Choline-Ringer (128 mM/L choline) on both sides of the epithelium reduces proximal p.d.'s to -0.46 ± 0.05 mV (6) and distal p.d.'s to values ranging from -3.5 to +1.6 mV. This distal p.d. remains unchanged when choline-Ringer in the bath is replaced with Na-Ringer; however, K-Ringer (100 mM/L K) in the bath reduces the distal p.d. towards zero when Na-Ringer is in the lumen, and renders the lumen positive by 6 to 11 mV when perfused with choline-Ringer. In contrast, the presence of Na in the distal lumen illicits marked changes in transtubular p.d. Changing lumenal perfusate from choline- to Na-Ringer raises the p.d. from -3 to -42 mV. This increase in p.d. occurs regardless of the presence of Na in the bath and is further augmented when luminal Cl is replaced with methyl sulfate. However, lumenal perfusion with Na-Ringer, 75mM Na-Ringer (isosmotic), or Cl-free Na-Ringer results in transient increases in p.d. which are dissipated within 45-130 minutes. Thus, while ion substitutions in bath and lumen are consistent with known permselectivities of distal peritubular and lumenal membranes to K and Na respectively, the time course of the transepithelial p.d. across the reptilian distal tubule during Na perfusion is at variance with stable p.d.'s measured across distal tubules of higher vertebrates. (NSF PCM 75-09918; NIH HL 05884; postdoctoral fellowship NKF)

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COMPARISON OF MECHANOPHYSIOLOGICAL RESPONSES DURING RUNNING AND JUMPING IN MAN. A. Bhattacharya, E.P. McCutcheon, J.E. Greenleaf, and E. Shvartz*. Biomedical Research Div., NASA-Ames Research Center, Moffett Field, CA 94035.

Acceleration profiles and their modes of generation were determined during treadmill and trampoline studies. Seven adults (mean age: 22.7 ± 4.7 S.D. yrs) were exposed to 10 to 6 min. of level treadmill running at 4 speeds (4.8 to 11.3 Km/hr.), and trampoline jumping at 4 heights (18 to 94 cm) for 5 min. The values of peak acceleration (A_h, at the forehead; A_b, at the lumbosacral region; and A_a, at the ankle), heart rate (HR), and oxygen consumption ($\dot{V}O_2$) increased progressively with both increased running speed and jumping height. With running A_a (range 3 to 12 G) always exceeded A_h and A_b (range .8 to 3.9, and .9 to 5 G, respectively) and G-profile included higher frequency components than those of jumping. Corresponding ranges of $\dot{V}O_2$ and HR were .8 to 3L/min and 90 to 180 bpm, respectively. With jumping, G levels were more symmetrically distributed (A_a=3 to 7 G, A_b=3.9 to 6 G, A_h=3 to 5.6 G); $\dot{V}O_2$ and HR ranges were 1.1 to 2.5 L/min and 102 to 175 bpm, respectively. The relationship of HR to $\dot{V}O_2$ was the same for both exercise types. However, the relationship of these two variables to G differed; in some subjects, equivalent $\dot{V}O_2$ levels were produced by higher G with jumping (max. difference +68%). These results indicate that for a equivalent metabolic cost jumping can provide higher stimulii to the gravireceptors, essential for maintaining proper cardiovascular (CV) and muscular tones. These observations may have significant impact on the choice of 'acceleration-profile' and its frequency spectrum needed for a CV and muscular conditioning program to avert deconditioning known to occur, during immobilization or bed rest or inactivity, due to lack of gravireceptor stimulation.

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ANALYSIS OF THE EFFECTS OF SIMULTANEOUS TIME-VARYING PULMONARY CAPILLARY BLOOD FLOW AND VOLUME ON GAS EXCHANGE. A. Bidani, E.D. Crandall* and R.W. Flumerfelt*, U of Penn, Phila., PA and U of Houston, Houston, TX.

Blood flow into the pulmonary capillaries and the volume of blood within the capillary bed are both pulsatile with the cardiac cycle. Previous theoretical approaches to determine the separate effects of these time-varying parameters in the lung have led to the conclusion that the pulsations result in an impairment in diffusional gas exchange between alveoli and capillary blood when compared to the case of constant flow and volume. To investigate the possibility that coupling between two parameters might lead to enhancement of gas exchange ("parametric pumping"), we have developed a quantitative model of diffusional exchange in the lung that incorporates simultaneous cardiac-induced blood flow and volume changes in the pulmonary capillaries. The alveoli are considered to be a lumped well-mixed compartment whereas the capillary bed is described as a distributed parameter system with spatial variation in gas contents considered in the flow direction alone. For normal man breathing room air at rest, the computed results agree well with previous predictions for the constant flow case and for the case of pulsatile flow alone. When coupled time-varying pulmonary capillary flow and volume are included, using the best data available in the literature to define these parameters, diffusional gas exchange is significantly improved over the case of pulsatile flow alone and closely approximates that obtained for the constant flow case. These results suggest that gas exchange during coupled flow and volume pulsations as they exist in the lung capillaries may not only be equally efficient to that theoretically obtainable under conditions of constant flow, but may, under certain physiologic and pathologic conditions, augment diffusional transport of the respiratory gases in the lung. (Supported by NHLI 7027, RCDA HL00134, AHA 75-992 and ALA.)

HIBERNATION INDUCTION OF THE GOLDEN HAMSTER. D.A. Bishop* and J.G. Minor. Dept. of Biology, University of Missouri - Kansas City, Kansas City, Missouri 64110

Despite the widespread use of the golden hamster in hibernation studies, few protocols have been published on methods to reliably induce its hibernation. It is our purpose to outline a protocol we recommend for hibernation induction. Males were caged separately at 24°C and held on a light cycle (LD 12:12) for 3 weeks with lab chow and water supplied ad lib. Following this adjustment period, the photoperiod was reduced over 4 days to 2 hours light per day. This regime was held for 3 weeks before the animals were placed in the cold. One week prior to exposure, apple was substituted for the hamster's water supply. After less than 3.5 weeks of cold exposure (6°C) (LD 2:22), initial bouts of hibernation were observed in winter (January) and spring (April) colonies. By 7 weeks of cold exposure, 54% of the winter colony had undergone bouts of hibernation, while in the spring colony, 40% had initiated hibernation. As often reported, testicular regression was found in those animals placed in reduced light. That this is important in hibernation induction is evident from the smaller average testes weight obtained from those hamsters sacrificed while hibernating (0.88 gms / 100 gms body weight) as compared with those sacrificed without entering hibernation (1.46 gms / 100 gms body weight). This links the decrease in gonadal function often associated with reduced photoperiods with the increased ease of hibernation inducibility. We feel we have established a highly reliable protocol for inducing hibernation in the golden hamster.

ROLE OF VAGAL AFFERENTS ON THE ARTERIAL BLOOD PRESSURE RESPONSES TO HEMORRHAGE IN RABBITS. V.S. Bishop, H.I. Chen*, D.F. Peterson and H.O. Stinnett.* The Univ. of Texas Health Science Center at San Antonio, San Antonio, Texas 78284

The role of vagal afferents in the circulatory adjustments during hemorrhage were studied in rabbits anesthetized with chloralose and urethane. Hemorrhage (H) of 10, 20 and 30 ml caused an increase in heart rate (HR) (12, 24 and 28 b/min, respectively) which accompanied a fall in systemic arterial pressure (SAP) (7.5, 16.2 and 26.6 mmHg, respectively). Cervical vagotomy or vagal cold block (V) increased SAP by 4.4 mmHg. Subsequent H of 10, 20 and 30 ml produced a smaller fall in SAP than before V (4.6, 11.2 and 20.0 mmHg, respectively). In 4 animals H of 20 ml produced a fall in SAP of 18.3 mmHg. However, V during H increased SAP by 11.4 mmHg. The SAP following reperfusion was only 5.1 mmHg above that before vagotomy. After sinoaortic denervation (SAD) hemorrhage of 30 ml caused a fall in SAP of 68.3 mmHg. Vagotomy following SAD increased SAP by 14.6 mmHg. Hemorrhage of 30 ml after SAD + V caused a fall in SAP of 50.5 mmHg which was significantly less than the decline before vagotomy. In 4 animals with SAD, H of 20 ml caused a fall in SAP of 50 mmHg (123 to 73 mmHg). Vagotomy during this subsequent hemorrhage increased SAP from 73.0 to 99.6 mmHg. Retransfusion increased SAP to 139.0 mmHg, a 16.0 mmHg increase above control. Thus, these results provide additional evidence against a buffering function of vagal afferents in the rabbit. (Supported by National Institutes of Health grant #HL12415 and AFOSR #73-2525).

HYPOXIC TOLERANCE AND VENTILATORY RESPONSE IN THE BAR-HEADED GOOSE. Craig Patrick Black*, S. Marsh Tenney, and Ann R. Paulsen*. Dept. of Physiology, Dartmouth Medical School, Hanover, N.H. 03755.

The Bar-headed Goose (Anser indicus) crosses the Himalayas twice yearly during migration. Observations of these birds flying at over 23,000 ft on numerous occasions and over the summit of Everest (29,028 ft) at least once suggest that this species may be unusually tolerant of hypoxia. The ventilatory control system was studied by determining responses of frequency (f), tidal volume (V_T), and ventilation ($\dot{V}_E$) in conscious, unacclimatized, unrestrained birds to graded hypoxia (F_{IO_2} equivalent to 10, 20, 25, 30, 35, 38, and 40 thousand feet). For comparative purposes, identical measurements were made on the Canada Goose (Branta canadensis), a strong flier facing no high-altitude migratory barriers, and on the domestic Peking Duck, a weak flier. $\dot{V}_E$ increased above resting, normoxic levels with decreasing F_{IO_2} in all three species. Both V_T and f increased predictably in the two geese, but their response was erratic in the duck. Maximum $\dot{V}_E$ occurred at F_{IO_2} = 0.042-0.045 in the duck (4.1 X resting ventilation), at 0.042-0.052 in the Canada Goose (21 X resting), and at 0.032-0.038 in the Bar-headed Goose (9.2 X resting). Below these respective levels, $\dot{V}_E$ was depressed in all three species, although the Bar-headed Goose has tolerated F_{IO_2} as low as 0.028 (40,000 ft) for up to 15 min. These results suggest that the hypoxic conditions encountered on the unique high-altitude migratory route of the Bar-headed Goose have selected for increased tolerance of hypoxia in this species. (Supported by grant HL 02888-20 from PHS.)

RENIN SECRETION AFTER OUABAIN IN SHEEP. Edward H. Blaine, Dept. of Physiology, Univ. of Pittsburgh School of Med., Pittsburgh, PA 15261.

Furosemide stimulates renin secretion in the absence of volume depletion in conscious sheep during renal arterial infusion of papaverine (Blaine, Physiologist 18:143, 1975). If ouabain and furosemide inhibit the same ion transport process within the kidney, then it would be expected that both substances would increase renin release. Four conscious and 4 chlorolose-anesthetized sheep were uninephrectomized and the contralateral kidney surgically denervated. These animals were studied during continuous renal arterial infusion of papaverine to block the vascular receptor for renin release. Isovolemia was maintained by continuous replacement of urine volume with normal saline. In the conscious animals, papaverine (7mg/min) alone always produced a decrease in Na excretion ($U_{Na}V$) while in anesthetized sheep, an increase was always observed. Ouabain (approximately 0.75 mg) administered into the renal artery over 10 min produced a marked increase in $U_{Na}V$ during the ensuing 60 min (mean $\pm$ SEM difference from papaverine alone infusion, conscious 529 $\pm$ 119; anesthetized 625 $\pm$ 125 uEq/min). Renin secretion did not increase in either group after ouabain (conscious -65 $\pm$ 170; anesthetized 44 $\pm$ 158 ng AI equivalents/min). These data suggest that the mechanism of action of ouabain and furosemide differ, at least at the macula densa, and that renin secretion might be responsive to inhibition of transcellular NaCl transport and not to inhibition of homocellular Na-K exchange (Proverbio, et al, Biochim Biophys Acta 211:327, 1970). Supported by USPHS grant HL 16483.

REVERSAL OF POSTANESTHETIC DELIRIUM AND PROLONGED ANESTHESIA WITH PHYSOSTIGMINE. A.L. Bleyaert,* S.S. Read,* P.M. Oczypok,* and R.B.F. Smith* (SPON: E.M. Nemoto). Dept. of Anesthesiology/CCM Program, University of Pittsburgh Medical School, Eye and Ear Hospital, University Health Center, Pittsburgh, PA 15261.

Postanesthetic delirium and prolonged recovery from anesthesia often causes a serious problem. No adequate treatment is available. Physostigmine is known to reverse scopolamine delirium and some drug-induced coma. On the basis of this information, we administered physostigmine 0.025-0.05 mg/kg intravenously in 53 patients. These included 17 females, 35 males, 33 children, and 20 adults. Their ages ranged from 3 to 76 years (mean 16.7 years). Thirty-six patients were treated for acute restlessness, 11 for prolonged deep anesthesia, and 6 for acute airway problems during arousal. Preoperative medication was Vistaril 1 mg/kg, Nembutal 2 mg/kg, Valium 0.1 mg/kg, or a combination of these together with atropine 0.05 mg/kg. Anesthesia was induced with halothane or Surital (4 mg/kg) and maintained with halothane 1.5%, N_2O 50%, O_2 50%. All patients woke up within 3-15 minutes (mean 6.28 min.). Airway problems in all 6 patients were resolved in less than 3 minutes. Restlessness was cured in 92% of the patients and they became calm and cooperative. The other 8% woke up, were not delirious, but continued to need direct nursing supervision. Compared to a control group, there was a significant decrease in duration of agitation and awakening time. Some side effects such as bradycardia and vomiting were seen. Physostigmine crosses the blood-brain barrier and acts as an anticholinesterase. The clinical picture of reversal appears to be different from the effect of general analeptic drugs. The results suggest an interaction of sedatives and physostigmine at the central cholinergic synapses.

DIFFUSION THROUGH A DISTRIBUTED PORE SIZE MEMBRANE. G. Bloom and J.A. Johnson, Dept. of Physiology, University of Minnesota, Minneapolis, MN 55455

In a recent publication (Microvascular Research 10, 217, 1975) we treated osmosis through capillary membranes from a distributed pore size point of view. In this presentation we extend the theory to include diffusion through a distributed pore size membrane. We then apply this model to several different membranes including capillary membranes and the common cellulose acetate dialysis membrane. The procedure we use is basically as follows: 1. Assume diffusion through a channel to follow Fick's law but to be modified by entrance effects and by hydrodynamic wall-particle interactions. 2. Assume these channels to be log normally distributed with respect to size (cross sectional area of pore). 3. Integrate the resulting equation to obtain a permeability coefficient for the whole membrane. 4. Equate the theoretical expression to the measured permeability coefficient for a given solute in a given membrane. 5. Repeat this procedure for another size molecule, including the permeability coefficient obtained by extrapolating the log of experimentally determined permeability coefficients plotted vs. solute radius to zero radius. 6. We generate in this way several equations containing three unknowns one of which is the extrapolated permeability coefficient mentioned above. The other two unknowns are the mean and standard deviation of the assumed distribution. By plotting curves of possible standard deviation versus the mean for each substance and finding a place of crossing of the curves, we can obtain a unique mean and standard deviation of pore size which characterizes the membrane. 7. We have also developed a permeability ratio procedure which gives a mean and standard deviation without relying on the extrapolated permeability value mentioned above.

TRANSMURAL AUTOREGULATION OF CORONARY BLOOD FLOW. R.B. Boatwright*, H.F. Downey, F.A. Bashour, and P.E. Parker. Depts. of Physiol. and Med., Univ. Tex. Health Sci. Center and Cardiopulmonary Institute, Dallas, Texas 75235.

Autoregulation of coronary blood flow has been previously demonstrated, but the local autoregulatory capability of the coronary circulation has not been examined transmurally. To accomplish this, regional myocardial blood flow was measured (microsphere technique, 7-10 μ) in 17 anesthetized, open-chest dogs whose left common coronary artery was pump perfused. With coronary perfusion pressure (P) set equal to arterial pressure (97±2.2(SE) mmHg), flow (F) to epicardium (EPI) and endocardium (ENDO) averaged 1.13±.12 and 1.03±.12 ml/min/g, respectively. Results obtained with (a) elevated coronary perfusion pressures and flows and with (b) perfusion pressure held constant by adenosine infusion are expressed as percent of the control.

	n	P (mmHg)	P/Pcontrol %	F/Fcontrol (%) EPI	ENDO
a_1	9	149±1.3	154	112±8	157±22
a_2	17	196±1.8	202	151±11	234±28
b	4	97±2.5	100	216±23	141±15

When F was increased by elevated pressure, ENDO was preferentially perfused, but this gradient was reversed when F was increased by adenosine. It appears that EPI is more capable of autoregulation than ENDO.

(Supported by Southwestern Medical Foundation and Council For Tobacco Research - U.S.A., Inc.)

MODEL FOR STUDY OF LINK BETWEEN METABOLISM AND BLOOD FLOW IN SKELETAL MUSCLE. Emma L. Bockman and Jack E. McKenzie*. Dept. of Physiology, LSU Med. Ctr., 1542 Tulane Ave., New Orleans, La. 70112.

The purpose of this work was to develop skeletal muscle preparations that would take advantage of the basic metabolic differences of different fiber types to study the link between metabolic activity and blood flow. In the cat, the soleus is 90-100% intermediate fiber type (slow twitch, oxidative), and our study has shown the gracilis to be about 80% white fiber type (fast twitch, glycolytic). The circulation of the muscle was isolated by ligating all vessels except those supplying the muscle being studied. Venous overflow was diverted through a drop counter for measuring blood flow. The nerve to the muscle was stimulated through a platinum electrode at optimum voltage and duration. Both soleus and gracilis muscles exhibited active hyperemia. The control blood flow was 4.0±0.6 (SE) ml/min/100 g (N=5) for the soleus and 2.9±0.5 ml/min/100 g (N=6) for the gracilis. After 20 min of contraction at 0.25 Hz, blood flow was 7.0±1.40 ml/min/100 g for soleus and 5.7±1.8 ml/min/100 g for gracilis. Twenty minutes after contractions ceased, blood flow was 3.9±0.9 ml/min/100 g for the soleus and 2.3±0.4 ml/min/100 g for gracilis. Neither the soleus nor gracilis muscles fatigued during 20 min of stimulation at 0.25 Hz. Soleus muscles maintained their tension development up to frequencies which caused tetanus, while the gracilis muscles fatigued at much lower frequencies. The degree of active hyperemia in the soleus muscles was related to stimulation frequency. These two muscle preparations should prove useful in determining the relative contributions such agents as K^+, osmolarity, and adenosine and how each relates to the metabolism of the muscle. (Supported by grant HL 17932).

EFFECTS OF SYMPATHETIC NERVE STIMULATION ON DIRECTLY MEASURED PRESSURES IN RAT INTESTINAL MUSCLE. H.G. Bohlen* and R.W. Gore. Dept. Physiology, University of Arizona, Tucson, Ariz. 85724

Pressures throughout the microcirculation are assumed to change during sympathetically-induced vasoconstriction. However, the magnitude, direction and location of these pressure changes in arterioles and venules have not been measured. The purpose of the present study was to determine where the major shift in the pressure distribution occurs as the frequency of direct sympathetic stimulation is increased. To accomplish this, micropressures and diameters were simultaneously measured in consecutive segments of the microcirculation of rat intestinal muscle during control conditions, and during direct nerve stimulation at frequencies of 4, 8 and 16 Hz. Stimulation at 4 Hz caused constriction of both arterioles and venules, but only the pressures in small venules decreased. At a stimulation frequency of 8 Hz, pressures throughout the microcirculation decreased with the major reduction occurring in capillaries, small arterioles and venules. Vasoconstriction of large arterioles during stimulation at 16 Hz decreased pressures in the intermediate-sized arterioles from a normal of 42 mmHg to about 16 mmHg, even though systemic arterial pressure remained constant (90-100 mmHg). The data indicate that as the frequency of sympathetic nerve stimulation is increased, the major change in the pressure distribution shifts from venules to small arterioles to larger arterioles. At a stimulation frequency of 16 Hz, the large arterioles assume the dominant role in control of the pressure distribution and, presumably, vascular resistance. (Supported by NIH Grants HL-13437 and HL-17421.)

CARDIOVASCULAR AND RENAL FUNCTION IN SHEEP WITH SEVERE THERMAL INJURY. C.T. Bohs*, H.F.Carvajal*, T.H. Miller*, H.A. Linares* and D.L. Traber. Dept. of Anesthesiol., Univ. Texas Med. Br. and Div. of Anesthesiol., Pedi. Neph. & Path., Shriners Burns Inst., Galveston, Texas 77550.

A model has been developed to study the chronic response to thermal injury in unanesthetized (UA) sheep. Using aseptic technique, anesthetized range ewes were catheterized for cardiovascular and hematological measurements. The bladder was catheterized 3 days later and control studies performed in UA sheep. The animals then received a third degree flame burn (under anesthesia) over 40% of their calculated body surface area. Fluid resuscitation was begun 1 hour post burn (pb)and continued throughout the study. Variables monitored twice daily for 4 days pb included cardiac index (CI); mean arterial, pulmonary arterial and central venous pressures; heart rate (HR); arterial blood gases and pH; serum proteins and electrolytes; hematocrit; hemoglobin; glomerular filtration rate; fractional K+ and Na+ excretion; urine osmolarity and electrolytes; blood glucose levels and plasma volume. The sheep were then sacrificed and autopsy performed. Full thickness third degree burn was confirmed by histological examination of skin specimens from the burned area. During the first 48 hours pb total peripheral resistance (TPR) and CI were stable; at 4 days pb, however, CI had increased 48% above control while TPR had decreased by 29%. The increased CI may have been due in part to a progressive increase in HR which went from a control level of 95 beats/min to 62% above control at 4 days pb. Urinary flow rate which had fallen to 1/3 of control at 24 hours pb was double the preburn value at 48 hours, a period when CI and TPR were not greatly altered. Urine production remained elevated above control through the 4th pb day. These findings are similar to those seen in burned patients and thus this animal model should be useful in studying therapeutic regimens to improve clinical morbidity and mortality.

CORRELATION BETWEEN SKELETAL MUSCLE VASCULAR DECOMPENSATION, O_2 EXTRACTION, CO_2 RELEASE AND ELECTROLYTE BALANCE IN SHOCK. R.F. Bond, E.S.Manning* and L.C.Peissner*,Dept. Physiology, Kirksville College of Osteopathic Medicine, Kirksville, MO. 63501.

Previous reports from this laboratory have demonstrated a significant degree of hindlimb skeletal muscle (SM)vasodilation coincident with entry into decompensatory shock induced by hemorrhage. The aim of the present investigation was to examine the relationship between this apparent vascular decompensation and the arterial/SM venous O_2,CO_2, Na^+ and K^+ differences during various stages of shock. Pentobarbitalized dogs were subjected to a shock protocol in which they were bled in 5 ml/Kg steps into a suspended reservoir until MAP was 35-40 mm Hg, and held at this pressure until signs of decompensation were apparent (i.e. 25% blood uptake and spontaneous increase in SM conductance). The results confirmed our earlier reports that skeletal muscle vascular conductance increased from 28% of prehemorrhage control during early shock to 122% of control at 25% blood uptake. This correlated well with a progressive increase in plasma K^+ from a control of 3.5 to 6.2 meq/L and a slight increase in Na^+ from 142 meq/L to 146 meq/L. O_2 extraction, CO_2 release and pH data indicated skeletal muscle ischemia. The data suggests that the SM vascular decompensation may be at least in part the result of a direct inhibition of vascular smooth muscle by hypoxia, acidosis and hyperkalemia.
(Supported in part by AOA grant #74-98.)

SUDDEN INFANT DEATH SYNDROME: A WORKING HYPOTHESIS. R.A. Bonner*, E.T. Angelakos, P. Baizer*, C. Munroe* and R. Sapawi* (SPON: C.V. Nelson). Biomedical Research Institute, Univ. of Maine, Portland, Me. 04102.

The infant domestic pig, one day to eight weeks of age, is currently being researched as a possible suitable animal model in which to study a Sudden Infant Death-like syndrome. The mechanism(s) involved in the respiratory and cardiovascular reflex responses to normally non-life-threatening stimuli which often result in death are being researched. Reflex induced apnea leading to bradycardia, arrhythmias, hypotension and death has resulted from simple postural alteration (lateral to supine), slight head and neck flexion producing snoring, laryngeal manipulation or temporary nasal occlusion (30-45 sec.). Findings have indicated that the SID-like response in the infant pigs may be age related. Quantitative fluorometric analysis for biogenic amines within specific areas of the central nervous system (cervical cord, medulla, pons and hypothalamus) was performed in 45 control animals aged one day to six weeks. Results have revealed a gradual maturation of the amine levels which appear to plateau near three weeks of age. A relatively large standard deviation found in most areas of the brain analyzed has tentatively been attributed to variations in the individual rates of maturation. It is believed that there are a wide variety of normally non-life-threatening stimuli which travel to the central cardiorespiratory control centers. When the afferent impulses stimulate the central regulatory centers, the resulting efferent response is either immature, inappropriate or insufficient resulting in life-threatening apnea which is soon followed by bradycardia, hypotension, atrio-ventricular blocks and death. The ultimate faulty link in SIDS may be that of improper neurotransmission within the central regulatory centers.

RESPIRATORY TIDAL VOLUME (V_T) RESPONSE TO A STEP CHANGE IN ARTERIAL BLOOD pH EFFECTED ISOCAPNICALLY FOLLOWING PERIPHERAL CHEMODENERVATION IN THE CAT. H.L. Borison, S. Gonsalves*† and L.E. McCarthy*. Dartmouth Med. Sch., Hanover, NH 03755.

Sudden shifts in $[H_a^+]$ were produced by controlled i.v. infusions of $NaHCO_3$ (1.0 N) and HCl (0.5 N) while pH_a was monitored continuously with a General Electric indwelling electrode in the abdominal aorta. P_ACO_2 was controlled at a constant level concurrently. In unanesthetized mid-brain decerebrate cats as well as in pentobarbitalized brain-intact cats, a step change in pH_a of 0.2-0.4 unit yielded the following V_T response dynamics irrespective of the stimulus-response direction. Under all experimental conditions, minimal onset latency varied between 5 and 10 sec and was not measurably longer than the $\Delta[H_a^+]$ transit time from the inferior vena cava to the arterial iliac bifurcation. Before peripheral denervation, the response half-time $t\frac{1}{2}(V_T)$ = 10 to 20 sec. This value was not notably affected by vagotomy. However, subsequent carotid sinus nerve section resulted in a ten-fold prolongation in response half-time, i.e., $t\frac{1}{2}(V_T)$ = 100 to 200 sec. It is concluded that the respiratory center promptly senses change in $[H_a^+]$ and that the neural responsiveness of the V_T controller is facilitated by simultaneous change in peripheral chemoreceptor input. (Supported by USPHS Grant NS 04456) †Pre-doctoral Fellow of the Ryan Foundation.

THE ELEMENTAL MICROENVIRONMENTS OF SPERMATOZOA IN THE FEMALE MOUSE FOLLOWING COITUS. Raymond M. Borland*, Sulekha Hazra*, John D. Biggers* and Claude P. Lechene, Harvard Medical School, Boston, Mass. 02115.

Micropuncture and electron probe microanalysis were used to determine the concentrations of Na, Cl, K, Ca, Mg, S and P in picoliter volumes of 1) the first or liquid fraction of the mouse ejaculate, 2) proestrous uterine and ampullary fluids, and 3) post-coital uterine and ampullary fluids in the mouse. Since ejaculation occurs directly into the lumen of the uterine cornua, post-coital uterine fluid is the first microenvironment of sperm following coitus. This fluid is characterized by a high concentration of K (32mM) but low concentrations of Na (114 mM), Cl (115 mM) and Ca (1 mM) relative to mouse serum. Elemental analyses of the liquid ejaculate and proestrous uterine fluid demonstrate that the liquid ejaculate is the main modifier of proestrous uterine fluid in the formation of post-coital uterine fluid. In passing from post-coital uterine fluid to the ampulla, the site of fertilization, spermatozoa experience changes in the concentrations of only two elements: Cl and Ca significantly increase. The concentrations of Na, Cl, Ca, K and S in post-coital ampullary fluid are intermediate in value to the concentrations of these elements in proestrous ampullary and post-coital uterine fluids. These data may indicate that flow of uterine fluid up the oviduct is an important determinant of the microenvironment of sperm in the ampulla. Regardless of the mechanisms controlling the elemental microenvironments of sperm in the uterus and oviduct, both microenvironments are characterized by low concentrations of Na and high concentrations of K. Similar Na and K concentrations have been reported to be optimal for capacitation of epididymal rat spermatozoa in vitro (Toyoda and Chang, 1974) and may play a similar role in the mouse in vivo.

SEGMENTAL VENTRICULAR FUNCTION AND CORONARY FLOW DURING AND AFTER ACUTE CORONARY OCCLUSION IN DOGS. Z. Bosnjak*, E.J. Zuperku*, R.L. Coon, H. Singh*, and J.P. Kampine*. (SPON: H.F. Edelhauser) The Med. Col. of Wisc. and Wood VA Ctr., Milwaukee, Wisconsin 53226.

Segmental coronary artery occlusion produces a decrease in segmental ventricular function in the occluded area and increase in ventricular function away from the occluded area. Fifteen mongrel dogs were anesthetized with sodium thiopental 20-25 mg/kg and halothane in O_2 (0.5-1.0% inspired concentration). Left ventricular pressure, and segmental ventricular ECG, contractile force and myocardial length were measured in the areas of the ventricle supplied by the left anterior descending (LAD) and left circumflex (LC) coronary arteries. Snares were placed at the origins of the LAD and LC arteries and measurements of segmental ventricular function were made before and after occlusions for varying periods of time (15, 30, 60 and 90 sec). The studies were repeated (60 sec. occlusions) during and after stellate ganglion and thoracic vagal stimulation (1 volt, .6 ms, 10 p/sec.). In five animals LAD and LC blood flows were measured with electromagnetic flow probes. A 30% increase in contractile force ($P<.01$) during 50 occlusions in the area of the myocardium away from the occlusion was observed, as well as increase in coronary flow (98% of 50 occlusions). During the occlusions, left and right stellate ganglion stimulation increased the ventricular function in distant myocardium above control values. No effect or decrease in ventricular function was observed when the left or right thoracic vagus was stimulated. Denervation had similar results. Post occlusion increase in contractile force of over 80% ($P<.01$) was consistently observed. The maximum increase in contractile force did not coincide with the maximum hyperemic response. (Supported in part by the Wisconsin Heart Association and NIH Grant HL 16511-01A2).

AN ALTERNATE METHOD OF ESTIMATING LEFT VENTRICULAR EJECTION FRACTION (SV/EDV). J. Boyle, III, Dept. Physiology, New Jersey Medical School, Newark, New Jersey 07103.

Since muscle tissue is essentially incompressible and since the ventricular muscle mass is constant from beat to beat the ventricular myocardium can be used as a plethysmograph. It will be shown that $SV/EDV = 1-(h_d/h_s)^x$ where h_d is end diastolic wall thickness, h_s is end systolic wall thickness and x is a function of ventricular geometric shape. Utilizing angiographic (angio) data ($n = 47$) from Circ. Res. 13:91, 1963; Fed. Proc. 28:1344, 1969; Circ. 39: 455, 1965; Circ. 44:548, 1971; x was found to be 1.78, consistent with a spheroidal shape. Angio SV and h were used to calculate EDV from the above formula and compared to angio EDV. Comparison of the 2 estimates of EDV revealed no significant differences between the means ($P > .40$) and a correlation coefficient (r) of 0.91. Data from normal individuals or those with valve lesions ($n = 35$) revealed an r of 0.97 and a standard error (SEE) of 21 cc, while data from patients with diagnoses compatible with ventricular asynergy gave an r of 0.64 and a SEE of 67 cc. Determination of h at the end of isovolumic relaxation may improve the accuracy of the method in the presence of asynergy. Although the data used were derived from angio studies h could be measured just as accurately using ultrasound. The proposed method appears to estimate EDV more accurately than previous methods using ultrasound. I wish to thank the authors and publishers of the cited papers for permission to use the data.

INTERACTION OF TRANSCAPILLARY STARLING FORCES IN THE ISOLATED AND INTACT DOG FORELIMB. R.A. Brace. Dept. Physiology & Biophysics, Univ. Miss. Med. Cntr., Jackson, MS 39216

The effects of isolation on the four Starling forces were determined in the forelimb which was isolated using standard electrocautery techniques. Colloid osmotic pressure of the interstitial fluid as estimated from lymph (πif) was decreased by an average of 1.5 mm Hg in the isolated forelimb compared with the same limb prior to isolation while colloid osmotic pressure of the plasma (πp) did not change. Interstitial fluid pressure (Pif) as measured with the implanted capsule technique was 3 to 6 mm Hg higher following isolation than in the intact limb, depending partly upon whether the limb was denervated. Isogravimetric capillary pressure (Pci) averaged 16.5 mm Hg or about 2.5 mm Hg lower than πp in the isolated limb. Since the measured values of the 4 Starling forces summed to zero in the isolated limb, the changes in πif and Pif can be used to estimate Pci in the intact limb before isolation. This approach indicates that Pci ranges between 8 mm Hg and 12 mm Hg in the intact dog forelimb. True capillary pressure would be slightly greater than Pci since there is normally a net capillary filtration of fluid which is carried away by the lymphatic system. These studies point to two important differences between the intact and isolated limb: First, Pci is close to πp in the isolated limb while Pci in the intact limb appears to be equal to approximately 50% of πp, i.e., about 9 mm Hg lower than πp. Second, Pif is positive in the isolated limb whereas Pif is negative in the intact limb. (Supported by NIH grant HL 11678).

RENAL RESPONSE OF THE STARLING (STURNUS VULGARIS) TO AN INTRAVENOUS SALT-LOAD. Eldon J. Braun. Dept. Physiology, Coll. Med., Univ. Ariz., Tucson. 85724

The nephron population in the avian kidney consists of nephrons resembling those found in reptilian kidneys (RT) and nephrons resembling those found in mammalian kidneys (MT). When desert quail were salt-loaded in a previous study (AJP 222) the total-kidney GFR fell. This fall in GFR was caused by a reduction in the number of filtering RT nephrons. In the present study, total-kidney function and single nephron glomerular filtration rates (SNGFRs) were measured in the starling, a bird with a much broader distribution (than the quail) but one restricted by the availability of drinking water. In control studies (I.V. infusion of 2.5% mannitol) the starlings had a total-kidney GFR of 2.88 ml/kg per min and a urine flow of 0.169 ml/kg per min. During the control-infusion the starlings reabsorbed 93% of the filtered water whereas the quail reabsorbed 78%. The starling reabsorbed 99.4% and the quail 94.0% of the filtered Na^+ during the mannitol infusion. As previously done with the desert quail, the SNGFRs were evaluated in the starling using the sodium ferrocyanide constant infusion technique. Following the control infusion the MT nephrons were filtering at 15.6$\pm$.75 nl/min ($\bar{x}\pm$SE) and the RT at 7.0$\pm$.35 nl/min. These values are not significantly different from corresponding values for the desert quail (MT, 14.4$\pm$.79; RT, 6.4$\pm$.20). When salt-loaded the mean SNGFRs for the starling increased to 28.0$\pm$1.25 for MT and 14.4$\pm$1.10 nl/min for the RT nephrons. Previous values for the quail were MT 12.7nl/min and the RT nephrons stopped filtering during salt-load. These studies indicate that the starling retains more water than the quail during the control mannitol infusion. However, when stressed osmotically the starling tends to excrete the osmotic load at the expense of plasma water. NSF BMS 75-10105.

RAT RENAL CLEARANCE PROCEDURE. F. T. Brennan*, G. Sosnowski*, W. Mann*, L. Sulat* and V. Wiebelhaus* (SPON: Dr. A. Bender). Smith Kline & French Labs., Philadelphia, PA 19101

A rat renal clearance procedure was developed in which 3% mannitol in 0.9% NaCl was infused at 0.08 ml/min into the femoral vein. Glomerular filtration rate (GFR) and effective renal plasma flow (RPF) were determined by clearance of infusions of 1.5 μCi/ml ^{14}C-Inulin and 2.5 μCi/ml of ^{3}H-PAH. Urine flow through seven 20 min clearance periods averaged 0.022 ± .003 ml/min. GFR was 0.90 ± .02 and RPF averaged 2.67 ml/min/100 g. Na^+ excretion ranged between 4 and 10 and K^+ output varied between 20 and 40 μEq/20 min. The Na^+/K^+ ratio was 0.18 and the In/PAH clearance ratio was 0.34. Triamterene increased Na^+ output to 34 μEq/20 min and reduced K^+ excretion (Na^+/K^+ ratio = 11.6) without affecting urine vol., GFR or RPF. Hydrochlorothiazide significantly increased urine volume (0.021 to 0.039 ml/min), had no effect on GFR or RPF and elevated Na^+ excretion from 2 to 102 μEq/20 min. K^+ excretion increased from 23 to 135 and Cl^- output rose from 7 to 163 μEq/20 min. Acetazoleamide was the most natriuretic compound tested. When urine volume increased from 0.018 to 0.069 ml/min., Na^+ excretion rose from 2 to 466 μEq/20 min. K^+ excretion also was pronounced and essentially little Cl^- was excreted. The compound had no effect on GFR or RPF. Furosemide had a marked effect on urine volume (0.021 to 0.153 ml/min) despite a slightly lowered (but not statistically significant) GFR and RPF. Na^+ excretion was increased from 4 to 372 μEq/20 min. K^+ output was moderately elevated and Cl^- excretion almost matched Na^+ excretion. None of the standards tested affected the clearance ratio. GFR and RPF values in the described test are at the approximate middle of the "normal" range for the rat in order that compounds which might increase these parameters can be evaluated.

EFFECT OF INDUCED THROMBOCYTOPENIA IN EXPERIMENTAL CIRCULATORY SHOCK. G. Alan Bridenbaugh*, John T. Flynn and Allan M. Lefer. Dept. of Physiology, Jefferson Med. College, Thomas Jefferson Univ., Philadelphia, PA 19107. (Spon: R. P. Gilbert)

Thrombocytopenia was induced in pentobarbital anesthetized dogs by perfusion of blood through columns packed with 1 mm diameter glass beads. This procedure resulted in a 79% decrease in platelet count, but did not alter mean arterial blood pressure (MABP), portal venous pressure (PVP), superior mesenteric artery flow (SMAF), plasma cathepsin D activity and prostaglandin E and $F_{2\alpha}$ concentrations. Splanchnic artery occlusion (SAO) shock was induced in thrombocytopenic and sham thrombocytopenic dogs by occlusion of the celiac, and superior and inferior mesenteric arteries for 2 hours followed by release of the clamps. The marked decreases in MABP and SMAF seen after release of the clamps were not altered by thrombocytopenia. Also, the increase in PVP plasma cathepsin D activity and PGE and $PGF_{2\alpha}$ concentrations were similar in both SAO shock groups. Therefore, platelets did not significantly contribute to the plasma accumulation of cathepsin D or prostaglandins in SAO shock. Neither did thrombocytopenia modify the plasma accumulation of a myocardial depressant factor (MDF) in SAO shock; MDF activity averaged 55 to 56 MDF units in both SAO shock groups. Platelet counts in the sham thrombocytopenic animals gradually decreased 23% during shock while the thrombocytopenic group was stable at low levels (i.e., 40 to 50 x $10^3/mm^3$). Thrombocytopenia significantly attenuated the early (i.e., first 15 min) post-release increase in screen filtration pressure, indicative of reduced formation of platelet aggregates in response to the shock state. These data suggest that neither platelet release of humoral substances nor platelet aggregation are major mechanisms in the pathophysiology of SAO shock in dogs. (Supported in part by NIH Grant No. HL-17745).

THE CORRELLATION OF X-RAY FINDINGS SUGGESTIVE OF EMPHYSEMA WITH ABNORMALITIES OF TESTS OF DISTRIBUTION BY THE FORCED EQUILIBRATING EXPIRATION (FEE),TIME TOWARDS EQUILIBRATING (TTE) AND FOWLER SINGLE BREATH PLATEAU TEST(FSBT).A.W.Brody,A.Dowell*,S.G.Kellog* and J.K.Conboy*, Pulmonary Section,Dept.Med. and Dept.Radiol.,Creighton Univ.Med. Center,St.Joseph's Hosp.,Omaha,Neb. 68108.

The FEE and the TTE are tests different from and usually somewhat less sensitive than the FSBT in the detection of unevenness of ventilation(Am J Med 1970 48:424;Am Rev Resp Dis 1970,102:525). The FSBT is recorded during the 1st breath of a closed circuit rebreathing procedure to determine the FRC;the TTE is recorded during the continued equilibration and is somewhat analagous to the Cournand 7 min. washout;and the FEE is the N_2 concentration recorded without interrupting the equilibration during a forced expiration to 500 cc below the end-tidal level performed at 2 min. after the start. The correllations of abnormalities of these tests with abnormalities of the x-rays was studied in 85 patients with lung disease. The study had been undertaken because of a high correllation of abnormality of the TTE and FEE with the degree of obstruction, combined with an absence of moderate or severe abnormalities of the FEE in asthma. In this study, significant abnormality of the FEE almost always, and of the TTE usually was associated with the x-ray finding of significant Bullae in patients with obstructive dysfunction. Significant abnormality of the FEE was not present in patients with "asthma", or "bronchitis" without either the finding of "hyperinflation" or "blebs" by x-ray. Maldistribution of these types does occur in a group of patients with restrictive dysfunction with gross regional differences by x-ray, a finding that further clarifies the abnormalities detected by these tests.

INFLUENCE OF AUTONOMIC NERVOUS SYSTEM STIMULATION ON THE PROTECTIVE ZONE. W.W. Brooks* R.L. Verrier and B. Lown*. Cardiovasc. Res. Lab., Dept. of Nutrition, Harvard School of Public Health, Boston, M.A. 02115

The influence of sympathetic and parasympathetic stimulation on the vulnerable period (VP) have been extensively studied. The effect of such stimulation on the protective zone (PZ), however, is unknown. When a fibrillatory stimulus delivered during the VP is followed by a second stimulus which engages the PZ, ventricular fibrillation (VF) is prevented. The present study was undertaken to define the influence of left stellate ganglion stimulation (LSGS) and vagal nerve stimulation (VNS) on the PZ. Experiments were conducted in 24 chloralose-anesthetized dogs. A transvenous bipolar catheter was placed in the apex of the right ventricle for pacing (214 beats/min) and delivering test stimuli. The repetitive extrasystole (RE) threshold was employed as an index of ventricular vulnerability to fibrillation. RE threshold was determined by scanning the vulnerable period (VP) with a single 5 msec stimulus. The borders of the PZ were defined by delivering an increasing number of stimuli at 10 msec intervals following S_1. During LSGS the RE threshold decreased from 26 ± 4 ma to 16 ± 4 ma ($P < 0.02$) and the VP nadir shifted 13 ± 2 msec earlier into diastole ($P < 0.01$). LSGS produced a corresponding 21 ± 3 msec shift of the PZ earlier in the cardiac cycle but did not alter its duration. In contrast, VNS increased the RE threshold from 20 ± 4 ma to 25 ± 4 ma ($P < .05$) and shifted the VP nadir 11 ± 4 msec later into diastole. VNS shifted the PZ 19 ± 5 msec later into diastole and significantly increased its duration by 17 ± 3 msec ($P < 0.02$). It is concluded: 1) that LSGS and VNS can substantially alter both the PZ and the RE threshold, 2) these effects must be considered when ventricular vulnerability is assessed with trains of stimuli which traverse the PZ as well as the VP.

ATP-INDUCED SWELLING OF DOG ERYTHROCYTES:THE ROLES OF Na AND CELLULAR METABOLISM. A.M.Brown* and A.L.Obaid* (SPON: A.Kleinzeller). Dept. of Physiology G4, University of Pennsylvania, Philadelphia, PA 19174.

Dog erythrocytes incubated in isotonic, Ca-free saline containing 0.5mM ATP swell rapidly compared with cells incubated without ATP,(25% increase in cell water in 2h). This ATP-accelerated, net isotonic uptake of water and bulk ions still occurred on substitution of Li^+ for extracellular Na^+ and was accompanied by increased net influx of Li^+ and net efflux of Na^+,demonstrating increased permeability of the cell to bulk cations. Even the additional replacement by Li^+ of 95% of the intracellular Na^+ did not stop the swelling caused by ATP. Depletion of more than 90% of the cell ATP, by preincubation of the cells for 1h with iodoacetate + 2-deoxyglucose (each 5mM), also did not prevent the ATP-induced swelling of the cells and did not alter the pattern of changes in cell bulk ion content that accompany the swelling.Decreases in cell ATP level occurred both in normal and in depleted cells during the swelling. However, both the cell swelling and the increased bidirectional cation movements caused by external ATP were inhibited by Ruthenium Red (0.1mM), cell swelling being reduced by about 40%. Thus, the effect of external ATP on the cell water content depends neither on cellular metabolism nor on the presence of a specific bulk cation, i.e. Na^+. Both these and other data are consistent with the concept of a Na^+-independent interaction of external ATP with the cell membrane producing increased permeability of the membrane to bulk cations. Cellular fluid uptake would then be the consequence of a passive inward net flux of permeant bulk cation(s) driven by the Donnan effect of impermeant anions within the cell. Since water and Cl^- are more permeable than cations, this swelling would be rate-limited by the cation permeability and so accelerated in the presence of external ATP. (Supported by grants 12619 and 15441 from NIH.)

HISTAMINE EFFECT ON LOWER ESOPHAGEAL SPHINCTER SMOOTH MUSCLE. F.C. Brown, A. Dubois and D.O. Castell, Internal Medicine Service, National Naval Medical Center and Uniformed Services University, Bethesda, Md.

Renewed interest has been generated in the role of histamine in gastrointestinal physiology by the discovery of two distinct classes of histamine receptors, designated H_1 and H_2. Because of the potential use of compounds which block H_2 receptor sites in patients with acid-peptic diseases a better understanding of histamine effects on lower esophageal sphincter (LES) smooth muscle is important. We have studied the LES response to histamine and to H_1 and H_2 receptor blocking agents in the awake restraint-chair adapted baboon. H_2 receptor blockade with cimetidine at doses which markedly inhibit gastric acid output did not alter basal LES pressure or the response of the LES to a wide range of doses of histamine, pentagastrin, or bethanechol. H_1 receptor blockade with chlorpheniramine did not alter basal LES pressure but did abolish the response of the LES to exogenous histamine. Although histamine receptors are important in gastric secretion, they appear to have no identifiable role in the maintenance of basal LES smooth muscle tone in the baboon. The results suggest the presence of a stimulatory H_1 receptor on LES smooth muscle but provide no evidence for presence of an H_2 receptor. As opposed to the parietal cell, the smooth muscle response to pentagastrin and bethanechol does not require an associated H_2 receptor.

ALDOSTERONE INDUCES THE SYNTHESIS OF MESSENGER RNA IN MUCOSAL CELLS OF THE TOADS URINARY BLADDER. James A. Brown, Jr.* and Walter N.Scott, Dept. of Physiology, Mt. Sinai School of Medicine, New York, New York.

We previously demonstrated that aldosterone (Aldo) induces the synthesis of protein in the mitochondria-rich (MR) cell of the intact toads urinary bladder (PNAS 72:4056, 1975). We have now examined the effects of Aldo upon the synthesis of RNA. MR and granular (G) cells were separated by density gradient centrifugation, each divided into three aliquots, and the effects of Aldo and of Aldo+spironolactone upon the incorporation of ^{3}H-uridine into RNA studied. The cells were incubated at room temperature for 2 hr, the cells disrupted by pressure homogenization, and the nuclei recovered by centrifugation. The supernatant was chromatographed on a poly(U)-sepharose column for recovery of the mRNA. This fraction gave the following results:

	^{3}H-Uridine (cpm/ug DNA)		
	Control	Aldo	Aldo+Spiro
MR cells	1976	53,450	1238
G cells	1521	1506	--

The amount of label incorporated into RNA corresponded to the relative sensitivities of the tissues to Aldo. Labeled ribonucleoprotein recovered from the poly(U) column was sedimented on continuous gradients of sucrose and yielded a broad peak between 7S and 30S. Similar experiments in which the label was incorporated into the RNA before the mucosal cells were removed from the bladders and separated gave similar results, though the amount of label incorporated was smaller. We conclude that Aldo induces the synthesis of RNA and of protein in the MR cells in the course of its effect(s) upon the tissue.

Supported by the American Heart Association and NSF.

Prostaglandin $F_{2\alpha}$ by Intravenous Infusion: Effects on Normal Subjects and Asthmatics. R. Brown*, R.H. Ingram, Jr. and E.R. McFadden, Jr. Department of Medicine, Peter Bent Brigham Hospital and Harvard Medical School, Boston, MA 02115

In order to evaluate the pulmonary effects of Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), a secondary mediator of the type I allergic reaction, this agent was given at a dose of 1.0-1.5 µgm Kg/min by intravenous infusion to four normal subjects and to five young subjects with asthma. Lung volumes with subdivisions, maximal expiratory flow curves with air and after a wash-in of an 80% helium - 20% oxygen mixture and static deflational transpulmonary pressure-volume relationships were assessed before and during the infusions. There were no between group differences in any of the lung function measurements made before infusion. During the infusions both normal subjects and asthmatics had similar increases in residual volume and decreases in both vital capacity and maximal expiratory flow rates at iso-lung volumes. However there were two response differences between groups: 1) there was a consistent and significant decrease in the ratio of maximal expiratory flow ($\dot{V}max$) with helium-oxygen to $\dot{V}max$ with air in the asthmatics but not in normals; 2) all 5 asthmatics had a decrease in elastic recoil pressure at isovolumes, whereas only one normal had such a change. These results indicate that although the response of asthmatics to $PGF_{2\alpha}$ is similar in magnitude to that of normals when pre-infusion lung function is similar, the site and/or mechanism of the response may differ.

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LINEAR A.C. ELECTRODE POLARIZATION DUE TO SPECIFICALLY ADSORBED HALOGEN IONS AT DIFFERENT EQUILIBRIUM STATES. M. Brownstein*, R.B. Beard*, and H. Carim* (SPON. S. Takashima) Drexel University, Biomedical Engineering and Science Program, Philadelphia, Pennsylvania 19104

Electrode polarization at metal electrode interfaces produces a potential drop which can be represented as electrical impedances. A.C. electrode polarization which has been analyzed on the basis of the rate determining mechanism of the oxygen electrode has been found to follow the frequency dependency predicted by an adsorption of electroactive species. When the potential is varied at platinum and palladium electrode interfaces at a set pH and frequency the electrode impedance varies according to changes in species at the electrode according to Pourbaix diagrams. Measurements which have been taken in distilled water are compared with those taken in physiological saline and other adsorbed background ions. There is a marked change in the electrode impedance on passing through different equilibrium states on the Pourbaix diagrams.The tendency of metal ions to form stable complexes depending on the relative coordinating affinities of non metal groups has been used by Ahrland and Pearson to classify metals and specifically adsorped halogen ions. The influence of the relative coordinating affinities of biological significant ligand atoms on the electrode polarization of platinum and palladium are considered at various equilibrium states.

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SERUM LH AND FSH IN YOUNG AND OLD MALE RATS IN RESPONSE TO SINGLE OR MULTIPLE INJECTIONS OF GnRH. J.F. Bruni*, H.H. Huang*, S. Marshall* and J. Meites (SPON: E.P. Reineke). Department of Physiology, Michigan State University, East Lansing, MI 48824

Serum LH and FSH were measured by RIA in 4 month and 21 month old male Wistar rats following a single injection of 450 ng GnRH/100 gm body wt. (BW) or during a series of 9 injections of 50 ng/100 gm BW given initially 5 and 25 min after blood collection and at 30 min intervals thereafter. Blood samples were taken at time 0, 20 min, 1 hr, 2 hr, 3 hr and 4 hr following GnRH injections. Serum LH in young and old male rats increased from basal levels of 18±1 ng/ml and 8±1 ng/ml ($P<.01$), respectively, to peak levels of 498±40 and 274±35 ng/ml ($P<.01$) 1 hr after injection. FSH also reached a peak 1 hr after the single injection, from basal levels of 305±7 ng/ml and 188±20 ng/ml ($P<.01$) to 794±24 and 532±25 ng/ml in the young and old rats, respectively ($P<.01$). Similarly after 9 multiple injections of 50 ng/100 gm BW, LH reached a peak 3 hrs after injections of 1388±190 ng/ml in the young and 527±20 ng/ml in the old rats, ($P<.01$) and serum FSH climaxed 4 hrs after the serial injections to 1261±75 ng/ml and 793±27 ng/ml in the young and old animals, respectively. These data show that old male rats have lower basal levels of serum gonadotropins than the young males and pituitary LH and FSH are less responsive to GnRH stimulation than young male rats. (Aided in part by NIH Grant AG00416.)

MECHANISMS MEDIATING AN ALTITUDE INDUCED RESPIRATORY OSCILLATOR. P. Brusil,* R. Kronauer,* and T. Waggener.* School Public Health;Div. Eng.&Appl.Phys., Harvard Univ., Cambridge, Ma. 02138 (SPON: V. Fencl)

We have observed a strong altitude induced ventilatory oscillation with a characteristic period of 23 ±3 sec in 4 subjects out of 16. In these oscillations tidal volume, V_e, and breath duration, T_t, change in opposition thereby producing changes of ventilation, $\dot{V}_e$, larger than either component. The relative contributions to V_e from abdomen and rib cage anterior-posterior displacements average about 70% and 30% respectively, and during a deep breath the contribution from the abdomen is slightly enhanced. If we compare a deeper-than-average breath with an average breath, we find that although inspiratory duration, T_I, is larger the average inspiratory flow is also larger. Expiratory duration, T_e, for the deeper breath is shorter and the average expiratory flow is much larger. These results suggest that excursions of V_e are mediated largely by active expiration. Such behavior is contrary to the Bradley et al (1) model in which drive to $\dot{V}_e$ increases V_e and simultaneously decreases both T_I and T_e proportionately. The strength and frequency of our observed oscillations are, however, remarkably similar to $\dot{V}_e$ oscillations seen in the model of Grodins et al (2) under somewhat different conditions of respiratory stress. Because of the short period of these oscillations the peripheral chemoreceptors are implicated. The sensitivity of these receptors is known to be enhanced at low oxygen tension and a classic high-loop-gain control instability is suggested.

1. Bradley et al. Biol. Cyber. 19:105-116, 1975.
2. Grodins et al. J. Appl. Physiol. 22:260-276, 1967.

(Supported by NIH Grant 1 R01 HL 16325-01A1 and Fellowship 1F 22 HL 01254-01.)

CHANGES IN REGIONAL CEREBRAL BLOOD FLOW (rCBF) DURING ENDOTOXIN SHOCK IN THE DOG. W.J. Bryan*, R.M. Daugherty, Jr., and T.E. Emerson, Jr. Depts. of Physiol. & Med., Mich. State Univ., E. Lansing, Mich. 48824

Previous studies from this laboratory show that total CBF is severely decreased during endotoxin shock in the dog (Physiologist 16:417, 1973; Fed. Proc. 35:794, 1976; Circ. Shock 3:21, 1976). The present study describes changes in rCBF in anesthetized, spontaneously breathing dogs during shock produced by i.v. injection of 2 mg/kg E. coli endotoxin. rCBF was measured using the radioactive particle distribution technique. Left ventricular injection of ^{85}Sr or ^{141}Ce was completed before and at 2 (N=10) or 4 (N=10) hrs of shock. The order of microsphere injection was randomized. Six control experiments were also completed. At 2 hrs of shock, aortic blood pressure decreased by 58% and rCBF changes were: pons, 33%↓; medulla, 29%↓; hypothalamus, 18%↓; thalamus, 40%↓; cortex, 42%↓; cerebellum, 38%↓; pituitary, 33%↓. At the 4th hr of shock, aortic blood pressure was decreased by 62% and rCBF changes were: pons, 56%↓; medulla, 57%↓; hypothalamus, 55%↓; thalamus, 64%↓; cortex, 65%↓; cerebellum, 61%↓; pituitary, 55%↓. Regional vascular resistances were significantly decreased in the pons, medulla, and hypothalamus, but were paradoxically unchanged in all other regions at both 2 & 4 hrs of shock. No changes occurred in the control group. This study supports our earlier studies in which only cerebral venous outflow was measured, and demonstrates that blood flow is severely and progressively decreased in all areas of the brain monitored. Coupled with our previous cerebral metabolic study in shock, the current study also suggests that O_2 and glucose delivery are severely compromised in areas of the brain important in systemic cardiovascular and respiratory control. (Supported by the Mich. Heart Assoc. and NIH-MSU General Research Support Fund)

ANTIHYPERTENSIVE FACTORS IN NORMAL AND SPONTANEOUSLY HYPERTENSIVE RAT KIDNEYS. Harriet A. Burge*, Jean A. Gaymer*, Elizabeth C. Clark*, and S. W. Hoobler, Division of Hypertension, Dept. of Internal Medicine, University of Michigan Medical Center, Ann Arbor, MI 48109

A comparison of the acute antihypertensive effects of spontaneously hypertensive rat (SHR) and normal rat kidneys transplanted into one-kidney renal hypertensive rat (1-KGH) has shown that SHR kidneys have significantly less antihypertensive capability than normal kidneys (ΔBP -30 mm Hg $\pm$ 6.5 SEM with normal kidneys; -10 mm Hg $\pm$ 2.5 SEM with SHR kidneys; $p<0.001$). Extracts of SHR kidney papillae injected intravenously into normal, angiotensin II-blocked (1 sar-8-ala-angiotensin II) assay rats produced significantly less acute depressor response than extracts of normal kidney papillae (ΔBP -23.7 mm Hg $\pm$ 6.6 SEM with SHR papillae; -40.6 mm Hg $\pm$ 3.9 SEM with normal papillae; $p<0.01$). The SHR kidney therefore lacks the acute antihypertensive capability of normal kidneys in a transplant situation, and contains significantly less extractable depressor activity. (Supported in part by grants from the Michigan Heart Association and HL-15710 from NHLI.)

PRESSURE NATRIURESIS: A MAJOR ROLE FOR ALTERED REABSORPTION IN THE LOOP OF HENLE. Thomas J. Burke, Dept. of Physiology, Univ. Colo. Medical Center, Denver, CO 80220

Within the autoregulatory range, decreased blood pressure (BP) is accompanied by enhanced renal sodium and water reabsorption; micropuncture and clearance studies were performed at spontaneous and reduced BP (aortic constriction) in anesthetized dogs. GFR and RBF (flowmeter) did not change as BP was reduced from 138 $\pm$ 4 to 110 $\pm$ 3 mm Hg. $U_{Na}V$ and V decreased ($P < .001$) from 41 $\pm$ 3 to 20 $\pm$ 2 μEq/min and from 0.39 $\pm$ .05 to 0.20 $\pm$ .03 ml/min, respectively. Distal (d) nephron filtration rate (NFR) was unchanged averaging 41 $\pm$ 3 and 42 $\pm$ 4 nl/min. However (d)TF/P inulin ratio increased from 2.71 $\pm$ .18 to 3.54 $\pm$ .30 and collection rate (v) decreased from 15 $\pm$ 1 to 12 $\pm$ 1 nl/min, reflecting enhanced reabsorption prior to the distal nephron. In order to evaluate any enhanced proximal (p) reabsorption, freeflow (no oil injection) collections and recollections were obtained. (p)TF/P inulin did not change (1.26 $\pm$ .10 vs 1.31 $\pm$ .13). Since plasma inulin did not change, the product $(p)TF_{in} \cdot (v)$ should equal the product $(d)TF_{in} \cdot (v)$ as NFR was autoregulated at 42 nl/min. With this approach, volume delivery to the loop (vl) could be estimated. At high BP, vl averaged 33 $\pm$ 4 nl/min; at low BP vl averaged 32 $\pm$ 5 nl/min indicating that the proximal nephron does not, but the loop does, contribute greatly to the enhanced salt and water reabsorption associated with acute BP decreases. (Supported by grant AM-17646 from NIAMD.)

KINETIC PROPERTIES OF A PULMONARY O_2, CO-CARRIER: THE FIXED-SITE VERSUS THE MOBILE CARRIER ANALOGY. B. Burns, Dept. Environmental Medicine, Johns Hopkins University, Baltimore, MD 21205.

We have previously reported experimental evidence in support of a membrane carrier for O_2 and CO in the lung (Drug Metab. Disp. 1:374, 1973; Chest 69(2):316, 1976; and "Lung Metabolism" pp. 159-184, Academic Press, 1975) and placenta (J. Appl. Physiol. 39(5):728, 1975 and Nature 240(5382):473, 1972). The carrier appears to enhance the passive diffusional transport of both O_2 and CO, and is sensitive to inhibition by a variety of drug substrates involved in cellular microsomal drug metabolism reactions; suggesting that a mixed function oxidase may somehow be involved as a carrier. One such oxidase is pulmonary cytochrome P-450, for which certain kinetic parameters (K_m, V_{max}) have been determined in-vitro for CO-binding. The half-saturation value (or P-50) is approximately 0.2-0.3 mm Hg P_{CO}. Estimation of the unknown carrier P-50 in-vivo, by measuring the saturable component of the rebreathing DL_{CO} at varying alveolar CO levels results in a nearly identical P-50 for CO. This relatively low P-50 would prevent the CO carrier from being very efficient for O_2 unless the relative affinity were much greater for CO (as with Hb) or the maximum velocity were much greater for O_2 than for CO. Alternatively, a separate carrier could function for O_2. If the carrier is P-450 then the fixed-site carrier could seem appropriate; however, the simpler mobile carrier kinetics can be incorporated if the carrier is assumed to be semi-fixed-site or mobile around a relatively fixed locus in the cell. Both models are able to satisfy the criteria for a facilitated diffusion system. (Supported by American Heart Assn. grant and USPHS grants HL-10342 and ES-00454.)

ENHANCEMENT OF HAND VASOCONSTRICTOR RESPONSE TO COLD BY HYPOVOLEMIA FROM 450 ml BLOOD DONATION. R.L. Burse*, R.W. Newman* and R.F. Goldman. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760

Heat loss rates from the hand under prolonged cold stress are, of necessity, proportional to the circulatory heat input. Blood flow to the hand is controlled by the degree of vasoconstrictor tone. Both cold stress itself and post-hemorrhagic hypovolemia are vasoconstrictive stimuli. To determine if the circulatory heat input to the hand in the cold is further reduced after mild hemorrhage, heat loss rates from the hand when immersed in 16°C water for 25 min were determined in 11 men before and after a 450 ml blood donation. Baseline heat loss rates were determined both with and without antecubital venipuncture (as a "sham donation" control) on successive days in counterbalanced order. On the following day, heat loss rates were determined within 1 hour after blood donation. The degree of hypovolemia (based on blood volume as estimated from body weight) ranged from 6-8%. There were no significant differences between any of the conditions in the heat lost during the first 15 min of hand cooling ($\bar{X} \pm 1$ S.E. = 21.59 ± 1.14 kJ), indicating no change in tissue heat storage prior to immersion. Heat lost ($\bar{X} \pm 1$ S.E.) during min 16 to 25 was 6.42 ± 1.25 kJ for the control condition, 7.55 ± 1.39 after venipuncture alone and 5.69 ± 0.89 after donation, representing rates of 10.7 ± 2.1, 12.6 ± 2.3 and 9.5 ± 1.5 W, respectively. Only the latter two values were significantly different ($P<.05$), suggesting that venipuncture by itself may be followed by a reactive vasodilatation, but venipuncture with 450 ml phlebotomy significantly enhances arterial vasoconstriction under moderate cold stress.

ANALYSES OF THE PHENOTYPIC EXPRESSION OF THE DYSTROPHIC GENE IN THE 129/ReJ dy/dy AND THE C57BL/6J $dy^{2J}dy^{2J}$ MICE. Jane Butler* and Ethel Cosmos, Dept. Neurosciences, McMaster Univ. Medical Centre, Hamilton, Ontario, Canada L8S 4J9.

A developmental study of the structure and of the histoenzymic analyses of the distal hind limb muscles of the 129/ReJ dy/dy mice indicates that the disease, hereditary muscular dystrophy, is expressed primarily in the fast twitch glycolytic fibers; the slow twitch oxidative fibers seem to be affected only secondarily. Physiological studies which indicate an increased half relaxation time of the heterogeneous tibialis anterior or of the gastrocnemius (Brust, 1966, Am. J. Physiol. 210: 445) can be attributed to the preferential loss of fast twitch glycolytic fibers. In contrast, similar muscles from the C57BL/6J $dy^{2J}dy^{2J}$ mice do not show the increased half relaxation time noted with muscles of the dy/dy strain (Harris and Montgomery, 1975, Exp. Neurol. 48: 569). Our histoenzymic and structural examination of hind limb muscles from the $dy^{2J}dy^{2J}$ mice indicates that the slow twitch oxidative fibers are primarily affected by the disease; the severe wasting noted early in the slow twitch soleus verifies the susceptibility of oxidative fibers to the disorder. These observations indicate that although the dystrophic locus is known to be identical in these two strains, the dy and dy^{2J} alleles result in different phenotypic expression as to fiber type involvement.

(Supported by a special grant from the Muscular Dystrophy Association, Inc.)

EFFECTS OF SOMATOSTATIN ON BLOOD GLUCOSE AND KETONE BODY LEVELS IN INTACT AND EVISCERATED RATS WITH FUNCTIONING LIVERS. R.H. Byrne, D.J. Nompleggi, E.R. Ramey* and J.C. Penhos*. (SPON: D.K. Kasbekar). Dept. of Physiology and Biophysics, Georgetown University Medical School, Washington, D.C. 20007

We examined the effects of somatostatin on hyperglycemia and hyperketonemia in an insulin and glucagon deficient rat model after first establishing the potency of our somatostatin preparation in fasted intact animals. Twenty-four hour fasted intact or eviscerated rats with functioning liver (24 hr. post-op.) were infused with somatostatin (1 ml.; 100 ug/ml.) for 30 min. via femoral vein cannula. Blood glucose and ketone body levels rose during somatostatin infusion in intact rats. Somatostatin infusion had no effect on the hyperglycemia and hyperketonemia present in the eviscerate preparation with functioning liver. Our results suggest that exogenous somatostatin affects blood glucose or ketone levels only when insulin and glucagon secreting cells are present. There is a further indication that in rats with normal alpha and beta cell function, high doses of somatostatin can produce significant inhibition of both insulin and glucagon secretion, resulting in hyperglycemia and hyperketonemia. These results have implications for the use of somatostatin in the treatment of diabetes.

(Supported by grant AM-16342 from AMDD.)

DIFFERENCES IN CENTRAL NERVOUS SYSTEM REGULATION OF BLOOD PRESSURE IN SPONTANEOUSLY HYPERTENSIVE AND MATCHED CONTROL RATS. J.C. Campbell,* D.S. Robinson* and D. Whitehorn. Depts. of Physiology and Pharmacology, Univ. of Vermont College of Medicine, Burlington 05401.

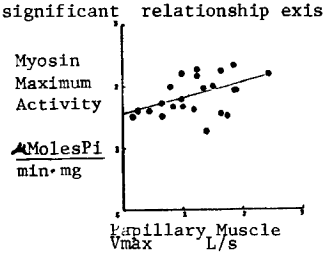
Recent studies have suggested differences in central nervous system blood pressure regulation between Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR). To determine if such differences can be demonstrated, changes in sympathetic activity (SA), recorded from the splanchnic nerve, were examined in 11 WKY and 11 SHR in response to stimulation of the posterior hypothalamus (PH) (+3.5AP, 0.5mm ML, + 3mm DV). The PH was stimulated at 20, 60 and 100 Hz for 3-second periods at a voltage twice that producing a just detectable (<5mm Hg) increase in blood pressure. The mean PH stimulating voltages were: WKY=11.2±1.1, SHR=9.4±1, ($P>.1$). Recorded activity was digitalized at 3KHz by a PDP 8/e computer, and was quantified by computing the average deviation about the mean for one-second periods. Activity during stimulation periods was compared with control recordings made three seconds prior to each stimulation and expressed as % of control. SHR showed greater increases in % control activity than WKY at all stimulation frequencies (100 Hz: WKY=174%±10.2, SHR=228%±9.6, $P<.01$; 60 Hz: WKY=164%±11.9, SHR=204%±11.6, $P<.05$; 20 Hz: WKY=113%±4.0, SHR=129%±8.0, $0.1>P>.05$). The relative and absolute increases in mean blood pressure during stimulation were greater for SHR than WKY at all frequencies but the differences were not statistically significant. This work demonstrates that SHR respond to PH stimulation with greater increases in splanchnic SA than WKY. This hypersensitivity of central regulatory systems to hypothalamic activation may be a contributing factor to the SHR hypertension.
(Supported by Vermont Heart Assn. Grant No. 333).

BONE FORMATION RATE IN EXPERIMENTAL DISUSE OSTEOPOROSIS IN MONKEYS (M. NEMESTRINA). Christopher Cann and Donald R. Young. Biomedical Research Division, NASA-Ames Research Center, Moffett Field, CA 94035.

Specific mechanisms underlying weightless and hypodynamic bone loss are obscure. A principal relationship which must be affected is the balance between bone formation and bone resorption rates. In order to better define the influence of those parameters on bone loss, and also to develop measurements in other species as a useful adjunct to human research, studies were undertaken with experimental monkeys. Tests were conducted with a total of 6 adult male monkeys, weighing 10-13kg, and approximately 10-12 yrs. of age to evaluate specifically bone formation rate during the development of disuse osteoporosis and osteopenia. Three animals were restrained in a semi-recumbent position for six months; three animals served as normal caged controls. Food intake (Purina) was held relatively constant at 200g/day for each animal. Using a Norland Bone Mineral Analyzer, bone mineral losses of 3.5 to 6% were seen in the mid-shaft of the tibia and in the distal radius. Bone loss was confirmed radiographically, with observation of thinning of the proximal tibial cortex and trabeculae in the calcaneus. Bone formation rate was determined using standard ^{47}Ca kinetics under metabolic balance conditions. After six months of restraint, accretion was 7.2-13.2 mg Ca/kg/day, compared to 3.2-4.1 mg Ca/kg/day in caged controls and 3-8 mg Ca/kg/day in normal adult humans. Fecal and urine calcium was 25-40% higher in restrained animals than in controls. Dietary calcium absorption decreases during restraint, and calcium turnover increases, implying a rise in bone resorption rate concommitant with the observed rise in bone accretion rate. Further studies dealing specifically with bone resorption are underway to define this more fully.

CARDIAC MUSCLE MAXIMUM MYOSIN ATPase ACTIVITY CORRELATED WITH MAXIMUM VELOCITY OF PAPILLARY MUSCLE SHORTENING. R.A. Carey*, A.A. Bove, R.L. Coulson*and J.F. Spann. Temple Univ. School of Medicine, Philadelphia, Pa. 19140.

Although it is important to understand the relationship between the velocity of muscle shortening and the velocity of ATP hydrolysis by myosin, the only established correlation has been in skeletal and smooth muscle from a variety of animal species. The present study established the relationship in cat myocardium under conditions known to alter the contractile function of heart muscle. Papillary muscle velocity of shortening was depressed by pressure overload hypertrophy and augmented by treatment with digitalis. Using a myograph to produce afterloaded isotonic contractions, the force-velocity relationship of papillary muscles from 24 hearts was described and the maximum velocity of shortening calculated from the Hill Equation. Maximum K-EDTA activated myosin ATPase activity was determined on the same myocardia. The regression coefficient was 0.26±0.10, the intercept was 1.56±0.13 and the correlation coefficient was 0.47 (n=24, $p<.01$) showing that a significant relationship exists between the maximum rate of ATP hydrolysis by myosin and the maximum velocity of muscle shortening under various states of contractile function. It was concluded that the velocity of muscle shortening is, in part, dependent on the myosin ATPase activity.



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A MECHANICAL CONTRIBUTION TO THE INHIBITION OF RENAL VASOCONSTRICTIONS BY REDUCED RENAL PERFUSION PRESSURE. D.E. Carlson* and L.P. Schramm. Dept. Biomed. Engr., Johns Hopkins Sch. of Med., Balto., Md. 21205

A model was formulated to test the hypothesis that the reduction in the speed of renal vasoconstrictions produced by reduced renal arterial pressure (RAP) is in part a mechanical property of the autoregulating renal vascular bed. Nine cats were anesthetized with chlorolose. Renal blood flow was measured electromagnetically, and RAP was controlled with a cuff on the descending aorta. The renal nerves were stimulated at several levels of RAP until renal vascular resistance (RVR) achieved a steady state. The ratio of the increase in RVR following the first 3 seconds of stimulation to the total steady state change in RVR was used as an index of the speed of vasoconstriction. A reduction in RAP from 134.0 ± 4.5 mmHg to 75 mmHg lowered this index by 68% ($P<0.01$). After administration of the prostaglandin inhibitor, indomethacin, a reduction in RAP from 129.4 ± 4.4 mmHg to 75 mmHg lowered the index by only 37% ($P<0.01$). The difference between the pre- and post-indomethacin data suggested that the reduction of the speed of renal vasoconstriction by reduced RAP was partially dependent on the intrarenal synthesis of prostaglandins. Our model suggested that the dependence of vascular resistance on the inverse fourth power of vessel diameter is the other major factor in the reduction of the speed of renal vasoconstriction at reduced RAP. As RAP was reduced, autoregulation caused a decrease in RVR and an increase in the diameter of intrarenal vessels. Because of the nonlinear resistance-diameter relationship, vasoconstrictions elicited in dilated kidneys at reduced RAP required larger decreases in vessel diameter and hence more time for execution than those elicited at control pressure in more constricted kidneys.

(Supported by NIH Grant HL16315.)

INFLUENCE OF GLUCOCORTICOID ON HEPATOCYTE RESPONSE TO SEVERE HYPOXIA IN THE PERFUSED CAT LIVER. Richard P. Carlson* and Allan M. Lefer. Dept. of Physiology, Jefferson Medical College, Thomas Jefferson Univ., Philadelphia, PA 19107. (Spon: S. A. D'Angelo)

Induction of hypoxia in perfused cat livers resulted in a significant release of cathepsin D into the perfusates, and a depressed rate of clearance of carbon particles by the reticuloendothelial system (RES). Methylprednisolone (10^{-3}M), equivalent to 30 mg/kg was added to the perfusate to determine if this glucocorticoid could preserve liver integrity during the induction of a hypoxic state similar to circulatory shock. Livers were perfused for 150 min with Krebs-Henseleit solution + 5% dextran and gassed with 95% O_2 + 5% CO_2 at pH 7.3 with 25 mM Hepes buffer. Hypoxia was induced by replacing the gas mixture with a mixture of 95% N_2 + 5% CO_2. In hypoxia, LDH and cathepsin D activity in the perfusate increased 11-fold and 3-fold respectively at 150 min. Methylprednisolone (MP) had only a very slight effect on LDH release, but significantly ($p<0.01$) inhibited cathepsin D release by 90% at 150 min. Liver flow was unchanged (i.e., no vasodilation or vasoconstriction occurred) during the perfusion period when MP was added to control or hypoxic livers, nor did MP significantly alter oxygen consumption in control or hypoxic perfused livers. Nevertheless, MP protected against the reduction in carbon clearance during hypoxia, without inducing blockade of colloidal carbon clearance in control livers. In this model, opsonization (i.e., addition of autologous plasma) did not improve the clearance of colloidal carbon above that observed in non-opsonized preparations. Massive pharmacologic doses of synthetic glucocorticoid did not impair RES clearance, produce vasodilation or alter oxygen consumption in perfused cat livers, but protected RES clearance and release of lysosomal hydrolases in hypoxic states. (Supported in part by NIH Grant No. HL-17688).

SIMILARITIES IN TIMING, AMPLITUDE AND DURATION OF SUCCESSIVE PROESTROUS LH SURGES IN INDIVIDUAL RATS. A.J. Carrillo* and C.H. Sawyer (SPON: R.A. Gorski). Dept. Anatomy and Brain Research Institute, UCLA, Los Angeles, Ca. 90024

The preovulatory LH surge is known to exhibit considerable variation in timing, amplitude and duration within a population of female rats. To test the variation in individual animals, from three to seven successive proestrous LH surges were recorded in each of five regular 4-day cycling rats fitted with chronic intravenous cannulas (Harms and Ojeda, J. Appl. Physiol. 36:391, 1974). The cannulas were flushed twice a day with 5% heparinized saline to maintain patency. On each successive proestrous day rats were sampled (0.5-0.6 ml blood hourly from 1400-2100) for radioimmunoassay of LH. Red blood cells were resuspended in saline and returned to the animals during the sampling period. The surgery of cannulation had no long-term effects on the regularity of the estrus cycle. Three rats did, however, show brief periods of anestrus, including one possible pseudopregnancy, followed by regular 4-day cycles. In each of three individual rats the successive proestrous plasma LH curves (4 in one and 3 each in the other two) showed remarkable internal consistency in shape, amplitude and timing, but they differed widely between animals - by as much as 2 hr in timing of "take offs" and peak amplitudes, with reduced amplitude associated with delayed LH surge. The other two animals, both with LH surges starting around 1600 hr (4 successive proestrous surges in one, 7 in the other), showed somewhat more internal variation. In one of them a "post-pseudopregnancy" proestrous surge was advanced two hr in timing and elevated to twice the mean peak amplitude of the cyclic LH surges in that rat. All animals checked for ovulation after the last proestrous surge had a full complement (7-14) of ova. (Supported by NIH and Ford Foundation)

CARDIOVASCULAR MEASUREMENTS IN DOGS WITH NORMAL LUNGS AND PULMONARY EDEMA ON IPPB AND PEEP. S.S. Cassidy* and C.H. Robertson, Jr.* (SPON: J.T. Willerson). Department of Medicine, Univ. Texas Health Science Center, Dallas, Texas.

The previously proposed mechanism of the fall in cardiac output (CO) in patients on positive pressure breathing (IPPB) and positive end expiratory pressure (PEEP) has been a reduction in ventricular filling pressure. Furthermore, it has been suggested that under these circumstances the pulmonary capillary wedge pressure (PCWP) may not accurately reflect the left atrial pressure (LAP). It is the purpose of this study to re-examine these issues. Twelve closed-chest, anesthesized, intubated, paralyzed dogs, six of which had pulmonary edema induced with oleic acid, were ventillated at 15 ml/kg tidal volume. Mean central venous pressure (CVP), PCWP, LAP, pulmonary artery pressure, pleural (Ppl) and airway (Paw) pressures were measured at 0, 5, 10, 15 cm H_2O PEEP. CO was measured, arterial blood gases were monitored, and ventilation regulated to maintain a constant P_{CO_2}.

	Normal				Pulmonary Edema			
cm H2O	IPPB	5	10	15	IPPB	5	10	15
Ppl	-0.9	1.1	3.4	4.7	1.2	2.8	5.0	7.3
LAP	6.2	7.7	10.8	13.7	2.9	4.8	7.1	10.5
PCWP	6.7	7.8	11.1	13.6	4.3	6.0	8.0	11.4
CVP	3.0	5.5	9.6	10.7	-0.2	2.6	5.3	8.7
CO	2.4	2.0	1.6	1.4	2.7	2.2	1.5	1.0

The PCWP accurately reflects the LAP in closed chest animals over a wide physiological range of vascular and airway pressures in normal and edematous lungs. Since the net right and left atrial filling pressures (CVP - Ppl and LAP - Ppl) remained unchanged at increasing levels of PEEP, the fall in CO cannot be explained by a decreased venous return.

CHANGES IN MEMBRANE STRUCTURE AND FUNCTION DURING CHICK EMBRYONIC ERYTHROPOIESIS. L.-N. Chan* and R.I. Sha'afi. The University of Connecticut Health Center, Farmington, Connecticut 06032

Changes in the pattern of membrane proteins and possible related functions during red cell development in chick (starting from 2½ day embryos to adults) have been studied. We have found considerable differences in the pattern of membrane proteins as well as in the relative amounts of individual components in isolated red cell membranes during the course of embryonic development. Of special interest is the increase in the relative amounts of two major polypeptides, bands 3 and 3.1 (M.W. 100,000 daltons), with increasing age of the cells. Associated with this change, we have found that both total and ouabain-inhibited Na efflux in intact red cells increased as the cells matured. In addition, there are significant alterations in the various components of membrane-bound enzymes with increasing age of the red blood cells. (Supported by NIH grant HL 19068, a Grant-in-Aid from the American Heart Association and a Basil O'Connor Starter Grant from the National Foundation-March of Dimes.)

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SPACE AND TIME RESOLVED SPECTROSCOPY OF OXYGEN CONCENTRATION IN CARDIAC TISSUE. B. Chance, S. Eleff*, W. Nadler*, C. Barlow* and B. Quistorff*, Johnson Research Foundation, University of Pennsylvania, Philadelphia, PA 19174.

Kinetic studies (Chance et al., Fed., Proc. 33 425, 1975) using spectrophotometric techniques and micro-platinum electrodes have found fluctuations of oxy-myoglobin and oxygen concentrations respectively during the contraction and relaxation cycles of the perfused rat heart. A computer controlled reflectance spectrophotometer has been built which can observe these changes as two-dimensional phenomenon over the surface of the left ventricle. This spectrophotometer contains a charged coupled device (CCD) which consists of a 100 by 100 photodiode array. The throughput rate of the data from the CCD into the computer memory is 30 msec., and is gated for systolic and diastolic intervals. The CCD method is now being used to study the intracellular oxygen concentration in perfused heart under various physiological conditions by monitoring the myoglobin spectra. Below its half saturation point of approximately 5μM O_2, myoglobin with its rapid response to changing oxygen concentration of 10 msec., affords both a highly sensitive and rapid oxygen indicator. A digital computer monitoring the left ventricular pressure initiates the CCD scanning and stores oxymyoglobin reflectance or transmission data during both the systolic and diastolic phases of contraction. The data may be summed over a large number of heart beats and processed to give the difference of oxygenation of myoglobin as a function of the phase of contraction and of distance along the ventricle in normal and infarcted rat heart models. (Supported by grant NIH- H1-18726.)

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EFFECT OF TAYLOR DISPERSION ON STRATIFIED INHOMOGENEITY. Hsin-kang Chang, Biomedical Engineering Unit and Department of Physiology, McGill University, Montreal H3G IY6, Canada.

The concept of Taylor dispersion has been used to explain the experimental findings that, contrary to what simple molecular diffusion theory would predict, more diffusible gases exhibit a greater degree of stratification during one breathing cycle. To investigate the validity of this qualitative explanation, a quantitative estimation based on the solution of convective-diffusion equation was made. Theoretical concentration profiles during one breathing cycle were obtained by using 1) molecular diffusion coefficient and 2) an effective diffusion coefficient modified from Taylor's original derivation. Over a reasonably wide range of frequencies and tidal volumes the use of Taylor dispersion coefficient was found to alter only slightly the concentration profiles, suggesting that this mechanism plays an insignificant role in pulmonary gas transport. Actual effect of Taylor dispersion is expected to be even less significant because: 1) velocity profiles in the airways are probably flatter than assumed in the calculations; 2) vortices which tend to eliminate radial concentration gradients were not accounted for; and 3) volume of airways in which Taylor dispersion is most likely to be significant is small compared to the volume of alveolar gas which is stratified. Thus it is doubtful that Taylor dispersion is responsible for the recent experimental findings mentioned above. To ascertain the role of Taylor dispersion in overall pulmonary gas transport, a detailed investigation of longitudinal dispersion downstream from an airway bifurcation appears most desirable.

ALTERATIONS OF THE METABOLIC POTENTIAL OF SKELETAL MUSCLE DURING COMPENSATORY HYPERTROPHY. V. Chen* and C.D. Ianuzzo, Depts. of Biology and Physical Education, York University, Toronto, Ontario M3J 1P3, Canada

The glycolytic and aerobic potentials, as indicated by the Vmax activities of phosphofructokinase (PFK) and succinate dehydrogenase (SDH) respectively, were determined in the plantaris muscle at 2,5, 15,30 and 60 days following the initiation of compensatory hypertrophy. Compensatory growth of the plantaris muscle was induced in male Sprague-Dawley albino rats (180-200 gm) by a total resectioning of the ipsilateral gastrocnemius muscle. The plantaris muscle from the sham-operated contralateral leg served as the control. By 2 days post-surgery there was a 38% increase in wet weight ($P<.01$) of the plantaris muscle with a corresponding decline in PFK (-37%) and SDH (-35%) activities ($P<.001$). Protein concentration of the hypertrophied muscle was also significantly reduced by 19%($P<.001$). Compensatory growth approached completion within 30 days (78%) with only a small non-significant increase occurring between the 30 and 60 day periods. PFK and SDH activities remained significantly lower ($P<.001$) than the control muscle for at least 15 days post-myectomy but returned to normal levels by the 30-day period. These findings indicate that during hypertrophy of skeletal muscle there is a commensurate decline in the glycolytic and aerobic potentials during the acute phase, which return to normal levels as compensatory growth reaches completion.

(Supported by a York University President's NRC grant)

RESPIRATORY HEAT AND WATER LOSS AND EXERCISE-INDUCED ASTHMA. W. Y. Chen*, D. J. Horton*, and J. F. Souhrada (SPON: A. R. Martin). Pulmonary Function Laboratory and Department of Medicine, National Jewish Hospital and Research Center, Denver, Colorado 80206

Exercise-induced asthma was studied in eight asthmatics using various conditions of inspired air during exercise. The exercise consisted of walking on a treadmill for 10 minutes, with a speed and grade elevation adjusted to achieve the target heart rate of approximately 90% of predicted maximum. Pulmonary function tests were performed pre- and post-exercise to determine exercise-induced asthma. With inspired air at 23°C and 15% relative humidity (RH), the post-exercise forced expiratory volume in one second (FEV_1), maximal mid-expiratory flow rate (MMEF), and specific airway conductance (SGaw) decreased to an average of 69%, 59%, and 38% of the pre-exercise baseline respectively. In contrast, the exercise-induced asthma was clearly prevented in all subjects by using inspired air at 37°C and 100% RH, when the post-exercise FEV_1, MMEF, and SGaw were 99%, 100%, and 91% of the baseline respectively. Inspiration of warm, dry air or humid, room air partially prevented exercise-induced asthma. The results indicate that the primary stimulus for exercise-induced asthma is the heat loss and/or water loss from the airways during exercise.

THE MECHANICS OF CORRUGATED COLLAGEN FIBRILS IN ARTERIES.
C. H. Chow* (SPON: J.C. Penhos). The Catholic University of America, School of Engineering, Washington, D.C. 20064

The nonlinear elastic characteristic of the arterial wall is treated as a composite structure of elastin with circumferentially aligned and lubricated collagen fibrils. The nonlinear characteristic of a pure elastin tube has been previously derived analytically and is shown to control the elastic characteristic of the artery at arterial pressure below 60mm Hg. At normal and high arterial pressures the nonlinear elastic characteristic is controlled by the pre-corrugated collagen fibrils. The mechanics of a pre-corrugated collagen fibril acting as a nonlinear spring is derived analytically and verified by a corrugated spring made of fine steel wire. The analysis further shows that the overall nonlinear elastic characteristic of the arterial wall can be simulated by a composite tube of rubber like elastin in combination with pre-corrugated collagen fibrils. This proves that the observed nonlinear elastic characteristic of the aortic wall is due mainly to the effect of both geometry and large deformation rather than an actual change in the physical properties of the basic materials. The calculated number density of collagen fibrils required to provide for the elastic characreristic of the aorta is found to be close to the actual density of approximately 10^9 fibrils/cm^2. It is hoped that this preliminary analysis will lead to a better understanding of the mechanics of the arteries under various pathological conditions.
(Supported by grant HE 12083-07 from U.S. Public Health Service.)

A COMPARISON OF CARDIAC MUSCLE pH VALUES OBTAINED WITH DMO AND NICOTINE, R. L. Clancy, R. A. Fenton* and N. C. Gonzalez. Dept. Physiology, Kansas Univ. Med. Ctr., Kansas City, Ks. 66103

It has been proposed that regions of differing pH's exist within cells. It can be shown theoretically that measurement of the intracellular pH (pH_i) with a weak acid will give a value closer to the region of the highest pH rather than the overall pH_i. Similarly,the pH_i obtained with a weak base will be closer to the region of the lowest pH_i rather than the overall pH_i. Experiments were carried out to determine the degree of pH_i heterogeneity in cardiac muscle using the radiolabeled weak organic acid 5,5-Dimethyloxazolidine-2,4-dione-^{14}C (DMO) and the radiolabeled weak organic base Nicotine-^{14}C (Nicotine). Isolated non-working rat hearts were perfused with a modified Krebs-Henseleit solution maintained at 37°C. Beta receptor blockade was produced by adding Sotalol to achieve a perfusate concentration of 10^{-4}M. The acid-base state of the perfusate was altered by changing the CO_2 tension. Under normocapnic conditions myocardial pH based on DMO measurements was 7.06±0.03. A value of 6.79±0.02 was obtained with Nicotine. Hypercapnia, venous CO_2 tension = 115 torr, resulted in a DMO pH_i value of 6.86±0.03 and a Nicotine pH_i value of 6.73±0.02. Addition of non-radiolabeled Nicotine (perfusate concentration = 2 mM) did not alter the DMO and Nicotine pH values under normocapnic or hypercapnic conditions. These results suggest that pH_i heterogeneity exists in rat cardiac muscle.

(Supported by NIH General Research Support Grant and Kansas Heart Association)

SUBSTRATE REQUIREMENTS FOR MAINTENANCE OF INTRACELLULAR K+ CONTENT OF THE ISOLATED PERFUSED RAT KIDNEY: SELECTIVE EFFECTS OF GLUCOSE AND LACTATE. Julius J. Cohen, Altamese J. Black*, Christine M. Gregg, Louise S. Merkens*, Orjan W. Peterson*, Marianna Zamlauski*, Dept. of Physiology, Univ. of Rochester, Rochester, N. Y. 14642.

Are there specific substrate requirements for maintenance of renal function and renal tissue composition? We are using the isolated perfused rat kidney as a model for determining which substrates are required for maintenance of renal function and renal tissue composition. Following 75 minutes of perfusion of the kidney with a Krebs Ringer Bicarbonate solution containing 60 mg/ml of substrate-free albumin to which no substrate was added, a loss of ∿30% of total kidney tissue K+ occurred. When 10 mM glucose or 10 mM glucose + insulin was present in the perfusate the renal tissue K+ loss was of the same magnitude as when no glucose was present. By contrast, when L(+)lactate, at initial concentrations of from 1 to 10 mM was added to the perfusate, no loss of renal tissue K+ occurred. There were no significant differences in the mean per cent water content, among the three groups of kidneys. Mean % Na+ reabsorption was increased from ∿55% without added substrate to 70% with glucose, and to 88% with lactate. Since addition of lactate but not glucose results in maintenance of intracellular K+ content of the kidney, while both substrates are oxidized (lactate oxidation > glucose oxidation), we conclude that lactate provides support for renal functions different from those supported by glucose. Supported by NIH, AM03602.

EVIDENCE THAT CALCIUM AND FREQUENCY SHORTEN THE ACTION POTENTIAL THROUGH INCREASES IN NET OUTWARD BACKGROUND CURRENT. T. J. Colatsky* and P. M. Hogan. Dept. of Physiol., State Univ. of N.Y. at Buffalo, Buffalo, N.Y. 14214.

The effects of increasing frequency and extracellular calcium, $[Ca]_o$, on action potential duration (APD) of canine Purkinje fibers were compared. APD decreased linearly with increases in frequency from 30-180/min at all $[Ca]_o$ tested (1.8 - 10.8 mM), and was reduced at a given frequency when $[Ca]_o$ was raised. Phase plane recordings of repolarization were found to be largely independent of changes in both rate and $[Ca]_o$. Similarly, estimates of the time constant for deactivation of i_x (τ_x) obtained using interval-duration analysis were unchanged by alterations in $[Ca]_o$ and frequency. These data suggest that frequency- and Ca-induced decreases in APD are not mediated by changes in i_x kinetics but through an increase in net outward background current. Manganese (3.6 mM) and verapamil (3-6 mg/ℓ) produced a marked slowing of τ_x and reduced the "effective peak outward current" obtained from phase portraits. Uniform modification of external surface charge was ruled out as the basis for slowing τ_x by determining membrane responsiveness curves in the same preparations. Mn^{++} and Ca^{++} shifted the curve in the depolarizing direction, while verapamil either produced no change or a hyperpolarizing shift. The Ca-antagonist property held in common by Mn and verapamil suggests that entry of Ca into the cell during the action potential may influence potassium conductance. It is concluded that increases in $[Ca]_o$ and frequency shorten the action potential by increasing net outward background current, mediated through changes in intracellular calcium. (Supported in part by USPH Grant HL 16135-03CVA and Henry M. Woodburn Fellowship Award.)

EXTRACTION OF ESTROGENS BY THE HIND LIMB OF THE DOG. EVIDENCE FOR REMOVAL BY THE LYMPHATICS. D.C. Collins, E.L. Bradley III*, and J.R.K. Preedy*. Depts. of Medicine and Surgery, Emory University School of Medicine, Atlanta, Ga. 30303.

The extraction of estrogens and other compounds by vascular regions and organs is usually considered to be due to metabolism. However, in certain areas it can also be attributed to removal by routes other than the vein(e.g. bile). We postulated that the lymphatics may be an alternate route for removal of compounds which could be a factor in the extraction from most areas of the body. To study this possibility ^{3}H-estrone(E_1)was infused in 5 dogs and the levels of total radioactivity, ^{3}H-E_1 and its metabolites estradiol-17β(E_2β), estrone sulfate(E_1S), estrone glucosiduronate(E_1G) and estradiol-17β glucosiduronate(E_2G) were measured in arterial(A) and femoral venous (FV) plasma, and the hind-limb extraction [100(1-FV/A)] calculated. The mean extractions (SE) were:Total 35(4), E_1 59(4), E_2 36(3), E_1S -11(4), E_1G 18(3), E_2G 20(4). These values indicate significant uptake of total radioactivity,E_1,E_2β, E_1G and E_2G, and net formation of E_1S. Although the uptakes of specific estrogens could be explained by metabolism in the hind limb,the uptake of total radioactivity could not. The best explanation is removal of estrogens by a route other than the vein, namely, the lymphatics. To test the role of the lymphatics, the thoracic lymph duct was cannulated and the infusion experiment described above repeated. The radioactive estrogens were shown to be present in the lymph within 10 min of the start of infusion and continues to rise to a level approximately one-half the plasma level at 140 min of infusion. Although the site of entry of radioactive estrogens into the thoracic duct lymph are as yet unknown,it is likely that the extraction of total radioactivity in the hind limb is due to the entry into the lymphatics.

TRANSCUTANEOUS EXCHANGE RATES FOR He, Ne, SF_6, CH_4, C_2H_4, N_2O and CO_2. J.M. Collins*, C.J. Lambertsen, J.A. Quinn*, Institute for Environmental Medicine and Department of Chemical and Biochemical Engineering, University of Pennsylvania, Philadelphia, Pa. 19174

Interest in the transcutaneous exchange of gases was stimulated by the phenomenon of isobaric counterdiffusion supersaturation [Graves et al., Science 179:582(1973), Lambertsen and Idicula, J. Appl. Physiol. 39:434(1975)]. We have measured specific flux rates for CO_2 and six inert gases outward across the skin of anesthetized pigs. Periodic gas samples were taken from a collection cup sealed on the lower abdominal region. Flux rates were calculated from the slope of the least squares line representing gas accumulation within the cup, normalized (except for CO_2) for the percentage of gas in the breathing mixture. These gases, chosen to cover a wide range of solubility and diffusivity, were studied simultaneously to minimize intra-animal variation. The skin temperature was controlled by heating the gas inside the cup. Flux rates were measured at skin temperatures of 34, 37, and 41 °C. Sample results are presented for 37°C skin temperature (SF_6 not measured at this temperature.) Flux units are cc/hr/M^2/ATA, except for CO_2 (cc/hr/M^2).

Gas	He	Ne	CH_4	C_2H_4	N_2O	CO_2
Flux	60	42	36	67	500	80

Both perfusion and diffusion control the rate of gas transfer across the skin, with metabolism an additional factor for CO_2. Models incorporating these processes are developed, and the effects of perfusion and diffusion as limiting cases are discussed.
(Supported by NIH grant HL-08899-12, ONR grant N00014-76-C-0248, and NASA grant NSG-9011.)

EFFECT OF STROPHANTHIDIN ON "PHOSPHAGEN" TURNOVER IN FROG STRIATED MUSCLE. R. J. Connett*, E. T. Hays*. Dept. Physiology, University of Rochester, Rochester, New York 14642. (Sponsor: C. R. Honig)

In freshly isolated frog sartorius muscles, sodium efflux is nearly equally divided between glycoside-sensitive and glycoside-insensitive fractions. In order to estimate the energy requirement for the glycoside-sensitive sodium extrusion in fresh muscle, the phosphagen contents were measured at various times after the poisoning of metabolism with cyanide and iodoacetate in the presence and absence of 3×10^{-5} M strophanthidin (stroph). Creatine phosphate (CrP), ATP, free creatine, ADP and AMP were determined. Since in no case was there a change in ADP contents the energy content ($\sim$P) was expressed as (CrP + 2ATP)/total creatine (Cr_T). The energy content fell linearly from 30 min to 2 hr. after metabolic poisoning in the presence or absence of stroph. The rate of fall in normal Ringer's fluid was 0.236μMoles "$\sim$P"/μMole $Cr_T \cdot hr$. This is equivalent to a P/O ratio of 2-3, well within normal muscle values. The sparing due to stroph is 0.045μMoles "$\sim$P"/$Cr_T \cdot hr$. In order to estimate the energy requirement of the external sodium sensitive strophanthidin-insensitive sodium efflux Na^+ in the Ringer's fluid was replaced by Li^+, Mg^{2+}, tris or guanidinium ions. When Mg^{2+} or Tris replaced Na^+ there was no change in the rate of energy turnover in the presence of stroph. Thus it appears that in freshly isolated frog striated muscle about 20% of the resting energy turnover is associated with glycoside-sensitive Na^+ efflux whereas the sodium sensitive glycoside-insensitive Na^+ efflux is not associated with significant energy turnover.

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Histochemistry of Non-alveolar Pulmonary Tissue. B.H. Cook, R.E. Parker, D.N. Granger, H.J. Granger, and A.E. Taylor. Dept. Physiology Univ. Miss. Med. Cntr., Jackson MS 39216.

Fresh biopsies of lung from 10 mongrel dogs were examined by standard histochemical techniques for 10 enzymes and 4 substrates. Rapidly frozen sections were evaluated for activities of glycolytic, Kreb's cycle, the hexose monophosphate shunt, lipolytic, respiratory chain and ATP-hydrolyzing enzymes as well as hydrophobic lipids and free fatty acids. Glycogen was demonstrated in fixed paraffin embedded sections. The histochemical profiles of bronchial epithelium, bronchial smooth muscle, and lung vasculature were evaluated for comparison purposes. Bronchial epithelium was found to be richly endowed with enzymes concerned with both synthesis and degradation of lipids with concomitant levels of substrate. In addition, some capacity was demonstrated for carbohydrate metabolism. Pulmonary arteries appeared to be generally more aerobic with respect to metabolic capacities than were small peribronchial arteries. Pulmonary veins showed lesser capacities for most types of metabolism than was demonstrated by the arterial system of the lung. Bronchial smooth muscle was found to possess the greatest anaerobic capabilities of the surveyed segments of the lung with similar capabilities for aerobic metabolism. Hydrophobic lipid and Gomori's "lipase" were found to be absent from all structures examined with the exception of bronchial epithelium. Herman-Padykula ATPase was found to be richest in vascular smooth muscle with lesser activity in bronchial smooth muscle and weak activity in bronchial epithelium. The histochemical approach has not delineated any great difference between the metabolic profiles of pulmonary and bronchial arteries which indicate that the lung vascular enzymes are more homogeneously distributed than other vascular beds previously studied.

Supported by Grant HL 11477.

EFFECT OF GLUCAN ADMINISTRATION ON IN VITRO RESPONSE OF SPLENIC LYMPHOCYTES TO T AND B CELL MITOGENS. J.A. Cook*, T.E. Stege*, and N.R. Di Luzio, Dept. of Physiology, Tulane University School of Medicine, New Orleans, La. 70112.

The administration of glucan, an agent developed in our laboratory, possesses the ability to produce profound proliferation and activation of macrophages as well as enhance cellular and humoral immunity. Glucan has also been shown to significantly inhibit tumor growth and metastasis. To evaluate possible mechanisms of the anti-tumor action of glucan, studies were undertaken to ascertain the effect of glucan administration on in vitro blastogenesis of spleen cells in response to T- and B- cell mitogens. Glucan was administered intraveneously (0.2 mg) to C57 BL/6J mice 6 and 3 days prior to sacrifice. Spleens were removed from glucan treated and control mice, and a suspension of 1 X 10^6 spleen cells were prepared in RPMI 1640 media with 10% Fetal calf serum, streptomycin (100ug/ml), and penicillin (100 units/ml). Phytohemagglutinin, Concanavalin A, or lipopolysaccharide from Escherichia coli 026:B6 were added as mitogenic compounds to the spleen cells. The cultures were incubated at 37 C° in 5% CO_2 and 95% air. After 48 hours of incubation the cells were pulsed with ^3H thymidine and 24 hours later incorporation of the label was evaluated. Spleen cells from glucan treated mice showed a significantly increased incorporation of ^3H thymidine relative to the control group in response to the T cell mitogen, Concanavalin A, and the B cell mitogen, lipopolysaccharide. These studies denote that glucan in addition to activating macrophages also enhances lymphocyte reactivity to mitogen-induced blastogenesis.

HEPATOCYTE AND MACROPHAGE FUNCTIONS IN REGENERATING LIVERS OF FASTING RATS. Robert P. Cornell, Division of Science, Northeast Missouri State University, Kirksville, Missouri, 63501.

The liver has two major cell populations--hepatocytes which carry out a variety of metabolic processes and macrophages which are responsible for phagocytosis of foreign material. The purpose of this investigation was to study the functional capacity of the two cell populations during liver regeneration. Male rats of the Holtzman strain (275 ± 10 g) were fasted overnight and then subjected to partial (70%) hepatectomy under light ether anesthesia. Sham control rats underwent midline laporotomy and both groups continued to fast with water ad libitum. Gluconeogenesis by hepatocytes was evaluated by radiotracer conversion of ^{14}C-alanine (4 μCi in 1.0 mmole iv) into blood glucose just following (0 hr) and at 48 hr post-surgery. Phagocytosis by hepatic macrophages was determined by clearance half-time of colloidal carbon (12 mg carbon/100 g body wt iv). The remaining liver lobes (right and caudate) after hepatectomy, which were 30.8% of the total liver, increased in weight by 64.0% at 48 hr. Conversely, body weight decreased by 11.8% at 48 hr. The table below presents the data for gluconeogenesis and phagocytosis.

Group	Blood ^{14}C-glucose (dpm x 10^4/ml)	Half-time (min)
Untreated control	1.41 ± 0.04	16.4 ± 2.8
Sham control at 0 hr	1.38 ± 0.05	18.5 ± 2.2
Partial hepex at 0 hr	1.03 ± 0.05	76.0 ± 13.3
Sham control at 48 hr	1.29 ± 0.04	16.3 ± 1.2
Partial hepex at 48 hr	1.28 ± 0.04	29.2 ± 6.6

Both untreated and sham controls at 0 hr were similar while partially hepatectomized rats at 0 hr demonstrated marked reduction of both hepatocyte and macrophage functions. Functional recovery at 48 hr was more complete for gluconeogenesis than for phagocytosis. This may reflect the regeneration rate following partial hepatectomy for the two cell populations.

AFFECT OF SALT ON THE WATER RESPONSE IN THE FROG. Janice A. Coté* and Michael B. Wang. Temple Univ. Sch. Med., Phila., Pa. 19140.

Application of distilled water to the tongue of the frog produced a characteristic neural response in single glossopharyngeal nerve fibers. Sodium, potassium, lithium, cesium, magnesium, barium and lysine, when added to the water in concentrations less than 0.01 molar, effectively inhibited the water response with the maximal inhibition occurring at a salt concentration of 0.01 molar. When applied in similar concentrations, however, calcium, ammonium, manganese, quinine hydrochloride, mannitol, sucrose and urea were unable to inhibit the response to water. These results suggest a mechanism to explain the water response. We propose that a receptor is maintained in an inactive state by binding cations. Maximal inactivation occurs when the cation concentration in the solution bathing the tongue is 0.01 molar. Since sodium is presumed to be the predominant ion in saliva, it is most likely the ion that is normally bound to the receptor. As distilled water is flowed over the tongue, the cation would be washed from the receptor allowing it to become active, thus, producing the water response. If low amounts of sodium, or any of the other cations that can substitute for it, are added to the water, some of the sites would remain filled. This would keep the receptor in a less active state and thus, decrease the neural response. Compounds which lack the ability to inhibit the water response, would presumably be incapable of binding to these cation receptor sites. (Supported in part by GIA grant # 700-050-67.)

LETHAL EFFECTS OF N_2O IN NEW ZEALAND WHITE RABBITS AT INCREASED AMBIENT PRESSURES. J.K.M. Cowley* (SPON: J.M. Clark). Institute for Environmental Medicine, University of Pennsylvania, Phila., Pa. 19174

There is little information concerning the toxic effects of N_2O at elevated pressures. This investigation was designed to study the dose-response characteristics of N_2O toxicity. 85 New Zealand White Rabbits (female 2.3±0.2 kg) were exposed to breathing mixtures containing N_2O+O_2 or N_2+O_2, at pressures between 1 and 11 ATA in a hyperbaric chamber. Group I, which included 60 rabbits, was exposed to 80% N_2O, 20% O_2 at 0.7 ATA increments from sea level to 4.4 ATA. 2 subgroups of 5 animals were exposed at each pressure with the temperature stable at 25±1°C for 8 hrs. or until no animals survived. Direct observations were made through large ports in the chamber. Respiratory frequency (f) was monitored. Significant observations included: excessive swallowing, respiratory difficulty, peripheral vasoconstriction, dilated pupils, frothy sputum and death. Autopsy showed gross pulmonary edema. The LD_{50} for an 8 hr. exposure was 1.7 ATA inspired P_{N_2O}. Group II, which consisted of 20 rabbits breathing air at 2 ATA and 4.4 ATA, showed none of the symptomatology of Group I and all animals survived the full 8 hrs. Group III, consisting of 5 rabbits exposed to normoxic N_2 in 1 ATA steps to a maximum of 11 ATA, did not develop any of the above symptoms. They did show a decrease in f of approximately 10%/ATA up to 6 ATA where the effect levelled off giving an apparent asymptote at 30% of control. The Group I rabbits showed some decrease in f at inspired pressures below 2 ATA N_2O, but showed a progressive increase in f above this pressure. Although the rabbit is particularly susceptible to drug-induced pulmonary edema, the severity of the condition suggests that these effects may also limit the use of N_2O in man during experimental hyperbaric exposures. (Supported by NIH grant HL-08899-12, ONR grant N00014-76-C-0248, and NASA grant NSG-9011.)

COMPARISON OF SERIES ELASTICITY IN ARTERIAL SMOOTH MUSCLE DETERMINED BY THREE METHODS. Robert H. Cox, Bockus Inst., and Dept. of Physiol., Univ. of Pa., Phila., Pa. 19146

The mechanical properties of elements functionally connected in series (SE) with contractile elements (CE) in iliac artery smooth muscle were studied by three methods: 1) periodic incremental release (PIR) during an isometric contraction, 2) afterloaded quick-release (AQR) from peak isometric response, and 3) complete controlled quick-release (CQR) from peak isometric response. Intact cylindrical segments of iliac arteries were taken from anesthetized dogs and mounted in vitro at their nominal in vivo length. Constant diameter (isometric) responses to norepinephrine were obtained at a tangential strain (0.61 ± 0.04) corresponding to the maximum isometric stress response ($1330 \pm 65 \times 10^3$ dynes/cm^2), i.e., L_o. PIR responses were obtained during isometric responses by superimposing pulse pressure steps of 5-10 mmHg for 300 msec at 2-4 Hz. AQR and CQR responses were obtained at the end of the isometric response by decreasing P quickly to a constant afterload. Responses were repeated several times in each segment to define the SE by all three methods. The rapid response portion of the AQR responses (SE recoil) for different afterloads followed the same trajectory in the pressure-diameter plane. Thus, AQR and CQR produced identical SE data. Maximum SE extension at peak isometric response was 0.023 ± 0.002 cm by PIR, and 0.027 ± 0.002 cm by AQR and CQR. When corrected for CE shortening, the latter value was 0.025 ± 0.002 cm. While larger than the former value they were not statistically different. In conclusion, the three methods yield the same quantitative description of the mechanical properties of the SE. Supported by USPHS Grant HL-17840.

ASZ(DCPB)

HEART AND GILL-BAILER COUPLING IN CRABS- EVIDENCE FOR UNILATERAL COORDINATION. P.E. Coyer, Dept. Zoology, University of Massachusetts, Amherst, Ma. 01002

Both gill-bailer and heart activities are controlled by rhythmic output from neuronal oscillators. The central mechanism coordinating patterns of branchial ventilation and heart beat involved in crab respiration is being investigated in semi-intact and intact preparations. In my early experiments, hydrostatic pressure changes resulting from movements of only one gill-bailer were monitored simultaneously with impedance differences associated with heart beat. Subsequently both gill-bailer and heart rhythms were determined using the impedance technique in intact specimens of Cancer irroratus. Simultaneous recordings of impedance changes and muscle potentials associated with the direction of gill-bailer movement established the reliability of the impedance pneumography technique. To determine phase relationships among the three rhythms, cycle by cycle analyses of the gill-bailer rhythms and heart beat were undertaken. I found periods of gill-bailer coordination unrelated to the heart beat and what is more interesting- coupling of the heart beat onto one gill-bailer rhythm at times when there is no coordination between gill-bailers. The hypothesis of cardiac ganglion modulation by neuronal signals emanating from the thoracic ganglion is being tested.
(Supported by a Grass Fellowship in Neurophysiology)

TENDON ORGAN RESPONSES DURING CROSSED EXTENSOR AND STRETCH REFLEXES. P.E. Crago*, J.C. Houk, and W.Z. Rymer*, The Johns Hopkins University Medical School, Baltimore, Maryland 21205.

Golgi tendon organs represent a major class of muscle stretch receptors being nearly as numerous as muscle spindles. Recent studies have established that the adequate stimulus for tendon organs is the force generated by the contraction of muscle fibers in series with the receptor. Nearly all of the muscle fibers (approximately 10) in series with the tendon organ are from different motor units, and these motor units are a mixture of types, based on mechanical properties. Thus, although a tendon organ seems to receive a random sample of motor unit activity the sample is quite small (approximately 0.1% of the total number of muscle fibers). Recently we have assessed the quality of the sample of total force more directly, by studying responses of tendon organs during naturally graded contractions. Discharge was monitored in dorsal root filaments of decerebrate cats as muscle force was graded by stretch of the soleus muscle or by a crossed-extension reflex. Nearly all of 30 tendon organs were recruited to discharge at muscle forces less than 10% of maximum. The relationship between steady-state discharge rate and muscle force was roughly linear (approximately 100 pps/Kgm-wt) for most receptors. The quality of the estimate of total muscle force provided by individual tendon organs was limited by the variability of response, but it was remarkably good considering the restricted character of the spatial sample of muscle force. The ensemble of all tendon organs in the muscle undoubtedly provides quite a reliable measure of muscle force.
(Supported by NIH NS 06828 and NIH 57 240.)

ASZ(DCPB)

PROLONGED EXERCISE AND ITS EFFECTS ON CORTICOSTERONE PRODUCTION IN THE MALE RAT. B. W. Craig. Wichita State University, Wichita, Kansas 67208

The effects of prolonged exercise (swimming) on corticosterone production in the male rat was studied over a ten week period. Groups of non-exercise controls and exercised animals were sacrificed at 0, 2, 4, 6, 8, and 10 weeks of exercise. The adrenal glands and plasma samples were removed and their corticosterone content determined. The initial response to exercise (2-4 weeks) was a large increase in plasma corticosterone and a decline in glandular levels. After six weeks of exercise there was a decrease in glandular and plasma concentrations. Prolonged exercise (8-10 weeks) resulted in increased plasma and glandular levels. It is concluded that short-term exercise represents a stress to the animal and the pituitary-adrenal axis responds by increasing corticosterone output. This demand for glucocorticoids stops once the system adapts to the exercise, and corticoid levels decline. With prolonged exercise the demand for corticosterone returns, and the concentrations of the steroid increase and are maintained to meet the needs of the animal.

SLOW pH CHANGES IN BLOOD IN VIVO DURING CARBONIC ANHYDRASE INHIBITION. E.D. Crandall, A. Bidani* and R.E. Forster, Dept. of Physiology, Univ. of Pennsylvania, PA 19174.

To investigate the hypothesis that slow pH changes take place in blood in vivo after it leaves an exchange capillary, we have developed a sensitive, temperature-controlled, rapidly-responding pH electrode assembly incorporating a pressure- and flow-insensitive reference electrode liquid junction. Carotid arterial blood from an anesthetized cat is withdrawn through the apparatus into a syringe. Syringe movement is then suddenly stopped. Temperature and pH of the blood in the electrode assembly are continuously recorded, both before and after blood withdrawal ceases. In control experiments, respiratory oscillations of 0.01-0.03 pH units were observed during withdrawal, but we failed to detect any pH change after stopping the flow. To inhibit selectively carbonic anhydrase activity available to plasma (e.g., due to lysis), benzolamide (CL 11,366) was administered IV (2mg/kg) and the experiments repeated 2-4 minutes later (case A). Respiratory oscillations were markedly diminished and pH became more alkaline by 0.02-0.05 pH units over 90 seconds after stopping flow. Experiments repeated 30-90 minutes after giving 50 mg/kg acetazolamide IV (case B) again showed markedly diminished respiratory oscillations but, after stopping the flow, plasma pH became more acid by 0.08-0.15 pH units over 90 seconds. The difference in the pH changes after withdrawal ceases lies in the fact that in B, erythrocytes leave the lung capillaries with a large excess of H^+ relative to plasma, whereas in A there is a relative depletion of erythrocyte H^+ when blood exits from the pulmonary capillaries. We conclude that disequilibrium for H^+ between red cells and plasma due to respiratory gas exchange can lead to marked shifts in the acid-base and blood gas status of blood in vivo after leaving an exchange capillary. (Supp.-NHLI 4108 & RCDA 0134; ALA 75992; ALA.)

INFLUENCE OF pH ON THE ELASTIC SHEAR MODULUS OF THE HUMAN ERYTHROCYTE MEMBRANE. E.D. Crandall, A. Osher* and R.E. Forster, Dept. of Physiol., Univ. of Penna., Phila., PA 19174 (SPON: T.G. Schnabel, Jr.).

Fresh human erythrocytes were suspended in many times their volume of a buffered saline-sucrose solution and titrated to a pH varying from 4.5 to 10.5 by the addition of small amounts of 0.1 N HCl or 0.1 N NaOH. Circular regions of the membrane of individual cells at a given pH were then deformed at 25 C by aspiration into a micropipette having an internal tip diameter of 1.0-1.5 microns. A membrane shear modulus μ was computed from the relationship between the length of the aspirated membrane and the deforming pressure according to a two-dimensional membrane model. The shear modulus of the membrane is a marked function of pH, increasing by several orders of magnitude as pH falls from 7.2 to 4.5. pH greater than 7.2 had little effect on elasticity. There is a remarkable dependence of μ on time after acidification, the increase occurring with a t90% measured in hours. The time course of the change in μ is similar to that computed for the change in intracellular pH using previously published values for OH^- permeability of human red cells. Addition of bicarbonate or CO_2 to the suspending medium accelerates the rate of change of μ. Shear modulus is not different whether $[Ca^{++}]$ in the original suspending medium is 0 mM or 1.5 mM. Control cells at pH 7.2 and 25 C showed little increase in μ over several days. These results suggest that membrane surface elasticity is a function of intracellular pH but is not directly affected by extracellular pH changes. This interpretation is consistent with the hypothesis that the elastic properties of the red cell membrane are in large part determined by a layer of structural proteins located in the cytoplasmic surface of the membrane, perhaps mediated by altered cross-linking or altered quarternary structure of the components of the layer due to titration of polar groups. (Supp. by RCDA HL00134 and AHA 75-992.)

SEX AND SPECIES DIFFERENCES IN PLATELET AGGREGATION AND OSMOTIC FRAGILITY OF WASHED RED BLOOD CELLS. B.H. Crane*, T.L. Maish*, E. Ramey, and P.W. Ramwell (SPON: M. Lorber). Dept. Physiology and Biophysics, Georgetown University Medical Center, Washington, D.C. 20007.

Blood was obtained from fasted men (age 23.7±2.9 S.D.) and women (age 20.8±2.5 S.D.) and from New Zealand rabbits (age 5-7 months). Heparinized samples were used for studies of red cells and citrated ones for platelet aggregation studies. In rabbits, but not in humans, mean cell volumes (MCV) increased significantly and similarly in both sexes during washing ($p < 0.01$ males; $p < 0.05$ females). Between 0.55% and 0.425% phosphate-buffered saline, washed red cells from male rabbits (N=9) were more fragile ($p < 0.01$) than those from females (N=9). In humans, however, washed red cells of women (N=17) were more fragile than those of men (N=16) between 0.475% and 0.425% saline ($p < 0.01$ at 0.475%; $p < 0.05$ at 0.45% and 0.425%), which represents the initial portion of the hemolysis curve and contains many older red cells (Marks, et al, Ann. N.Y. Acad. Sci. 75, 95, 1958). Platelet studies showed higher peak primary aggregation in women (N=18) than in men (N=16) at 0.5-1.0 µg ADP/ml ($p < 0.05$). The greatest difference, however, was at 0.25 µg ADP/ml ($p < 0.005$; N=7 for each sex). In humans, a negative correlation ($p < 0.01$) was noted between platelet aggregation and hematocrit (males: 46.5±1.8 S.D.; females: 40.8±2.7 S.D.), perhaps reflecting the inverse relationship between hematocrit and free plasma calcium levels in the presence of a constant amount of citrate. The fact that no sex difference was observed in aggregation of rabbit platelets (N=6 for each sex) may, therefore, be due at least in part to lack of a sex difference in hematocrit in this species.
(Supported by the Education Foundation of America and NHLI 11516)

EFFECTS OF LOW CARBOXYHEMOGLOBIN CONCENTRATIONS [COHb] ON AEROBIC WORK CAPACITY AND PHYSIOLOGICAL ADAPTATIONS TO EXHAUSTIVE EXERCISE. G.J. Cropp, P.C. Weiser* and C.G. Morrill*. Dept. Clin. Physiol., National Asthma Center, Denver, Colorado 80204.

Although high [COHb] are known to reduce aerobic work capacity, little information is available about physiological adaptations to exercise at low [COHb]. We studied 2 groups, each consisting of 6 normal men (22-45 yrs.), during incrementally increasing treadmill exercise. One group breathed on 2 separate occasions either air or CO in air causing the [COHb] to increase to 5.6%. The second group exercised under identical conditions, but with [COHb] at 9.8%. [COHb] was increased by administering an initial CO-bolus and then giving sufficient CO to maintain a stable [COHb]. As [COHb] increased, the aerobic work capacity ($\dot{V}O_2$ max) and the anaerobic threshold (AT) decreased significantly in proportion to increases in the [COHb]. Although $\dot{V}O_2$ max was reduced whenever [COHb] was increased, peak minute ventilation ($\dot{V}_E$), peak heart rates (HR) and peak venous lactates (La_V) were not significantly altered. At any given $\dot{V}O_2$ above the AT, $\dot{V}_E$, HR and La_V tended to be highest when [COHb] averaged 9.8%, intermediate when [COHb] was 5.6% and lowest during air breathing.

[COHb]	$\Delta\dot{V}O_2$ (max)	ΔAT	$\dot{V}_E$ (peak)	HR (peak)	La_V (peak)
5.6%	-5.1%	-9.4%	ns	ns	ns
9.8%	-9.8%	-19.8%	ns	ns	ns

Above the AT, $\dot{V}_E$ correlated well with increases in La_V, but not with changes in $\dot{V}O_2$. We conclude that even small increases in [COHb] reduce $\dot{V}O_2$ max significantly and alter the physiological adaptation to exercise.

(Supported by EPA Contract #68-02-2244)

EFFECT OF CHANGING THE DURATION OF INFLATION OF THE LUNG ON THE ASSOCIATED PHRENIC MOTONEURONE OUTPUT. B.A. Cross* and A. Guz* (SPON: M.I. Cohen). Dept. Medicine, Charing Cross Hospital Medical School, London W6 8RF, England.

Chloralose-anaesthetised dogs were paralyzed with gallamine and ventilated with a phrenic nerve controlled/triggered respirator. Activity from the C_5 phrenic root was integrated to give a signal which was used to trigger the respirator to deliver a fixed volume in the form of a ramp. The duration of inflation was initially adjusted to correspond to the inspiratory time (T_I) of the integrated phrenic signal. The duration of inflation was then either reduced or increased for one breath while keeping the tidal volume constant. When the increase or decrease of inflation duration exceeded 100-150 msec, the resultant increases in phrenic T_I and peak amplitude of the integrated signal were found to be inverse linear functions of the volume present in the lung above the end-expiratory level, at a time corresponding to the end of inspiration in the preceding (control) breath. The rate of lung inflation was unimportant. Expiratory time was prolonged only by increases in duration of inflation. The responses were abolished by vagotomy. These results demonstrate the dependence of phrenic motoneurone output on vagally-mediated volume information from the lungs during late inspiration.

ARTERIAL HYPOXIA AND OXYGEN DELIVERY TO RESTING SKELETAL MUSCLE. George J. Crystal* and Harvey R. Weiss. C.M.D.N.J. - Rutgers Medical School, Dept. Physiology, Piscataway, N.J. 08854

The relative roles of local and reflex responses to arterial hypoxia on the relationship between O_2 supply and demand were examined in the intact and denervated dog gracilis muscle. Hypoxia was induced by inhalation of various low O_2 gases. Muscle $\dot{V}O_2$ was determined from arterial flow and O_2 extraction. Relative tissue PO_2 was estimated polarographically and small vessel blood content was used to estimate open capillary density. Arterial hypoxia resulted in no significant change in muscle $\dot{V}O_2$, flow, or O_2 extraction, within the range 100-65% SaO_2, in both the intact and denervated preparations. Under more severe conditions neither muscle preparation showed the capacity to maintain $\dot{V}O_2$ at control levels. In both cases O_2 extraction was substantially reduced. Severe hypoxia resulted in a marked rise in flow to the denervated muscle. Resistance in the intact muscle was elevated with severe hypoxia. Relative tissue PO_2 declined linearly with decreasing SaO_2 and small vessel blood content increased. Data were in qualitative agreement with Krogh analysis predictions. It is concluded that vasomotor nerve discharge appears not to interfere with the capacity of muscle to support its resting metabolic needs in the face of acute arterial hypoxia. The results also suggest that these nerves act chiefly at arteriolar sites, and while largely nullified by local factors under moderate hypoxia, become unmasked only during severe arterial hypoxia. This study was supported in part by USPHS Grant HL-16134 and grant-in-aid of the American Heart Assoc., N.J. Affiliate.

ACUTE PULMONARY TOXICITY OF PRESSURIZED CONSUMER PRODUCTS AS DETERMINED BY BRONCHOPULMONARY LAVAGE. E. G. Damon and D. R. Phipps*, Inhalation Toxicology Research Institute, Lovelace Foundation, P.O. Box 5890, Albuquerque, New Mexico 87115

Relative acute pulmonary toxicity ratings were determined for nine pressurized consumer products. Varied concentrations of the residual ingredients, following venting of the propellants and volatile solvents from each product, were dissolved or suspended in isotonic saline and were introduced into the lungs of Syrian hamsters via bilateral broncho-pulmonary lavage. There was no mortality in controls lavaged with saline alone. Data on the mortality at seven days were subjected to parallel probit analysis and the lethal concentration for 50% mortality (LC_{50}) was determined for each product. The range of the LC_{50} values was 0.06-0.70%. A spray wood panel wax, a spray laundry aid, a spray wood panel cleaner, and a spray carpet cleaner produced mortality at lower concentrations than the remaining five consumer products, and thus appear to be the most toxic to the pulmonary system. The three least toxic products tested were a spray fabric protector, a spray dusting aid, and a spray enamel.

(Research performed under an Interagency Agreement between the Consumer Product Safety Commission and the U.S. Energy Research and Development Administration Contract E(29-2)-1013 in facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.)

MONITORING SUPERSATURATION IN BIOMEDICAL BYPASS PROCEDURES. B. G. D'Aoust, H. Seibold*, and R. White*, Virginia Mason Research Center, Seattle, Washington 98101.

When patients are treated by peritoneal dialysis or similar procedures where body fluids are separated from a tap water temperature bath by a gas permeable exchange membrane, there is a danger of supersaturation of the patient's dialysate because almost all pressurized water supplies are supersaturated with air. Levels vary depending on the temperature used; however, it is common to find supersaturations of 13% in tap water adjusted to 38°C by an appropriate hot/cold flow ratio. These levels are surprisingly stable, can cause bubble formation in free liquids and can be dangerous over a few hours. It is known that low level supersaturation can eventually be lethal to fish and other aquatic organisms continuously exposed to it. Hematologic and pathologic sequelae to vascular gas emboli have been demonstrated in divers and fish, and thus any degree of supersaturation is to be avoided. There are a number of simple means of eliminating the supersaturation; however, it is advisable to first quantify the problem since the ease of elimination depends non-linearly on the levels encountered, and the system in use. Simple instrumentation has been developed in our laboratory which allows continuous monitoring of total dissolved gas pressure in liquids or any flowing stream by simply inserting a sample "T" into the stream. Cost and construction are minimal for the basic system which uses available pressure transducers and electronics. It is being currently used in studies of hyperbaric decompression and supersaturation monitoring in natural waters.
(Supported by PHS Grant HL 14801 and EPA Grant R 804175010.)

COMPARISONS OF TOTAL BODY WATER, WATER TURNOVER AND METABOLISM DURING COLD EXPOSURE IN THREE SPECIES OF RODENTS. Daniel R. Deavers*[1], Jack W. Hudson, and X.J. Musacchia, Section of Ecology and Systematics, Cornell University, Ithaca, N.Y. 14850 and Dalton Research Center, University of Missouri, Columbia, Mo. 65201.

At 20°C ambient temperature (T_a), the total body water (TBW), measured by ^3H_2O dilution, of the red-backed vole (Clethrionomys gapperi, 65.3% of body weight) and the white-footed mouse (Peromyscus leucopus, 62.3%) was similar to TBW of other mammals, but ground squirrels (Spermophilus tridecemlineatus) had markedly lower TBW (40.4%). Cold exposure (T_a 5°C) did not affect TBW of voles or mice. When given minimum water rations, mice and voles lost weight and TBW (ml) decreased, but percent body water increased. When given ad libitum water at 20°C, water turnover rate (WTR) of voles and mice was 13.8 and 6.2 ml/day, respectively, and minimum WTR was 7.8 and 3.5 ml/day, respectively. At 5°C ad libitum WTR of voles and mice was 1.5 and 1.4 times higher than at 20°C, respectively. At 5°C minimum WTR was 1.7 times higher than at 20°C for both species. Since increases in $\dot{V}O_2$ at 5°C compared to 20°C were of about the same magnitude as increases in WTR, it is suggested that increased metabolism may have caused increased WTR. This conclusion is also supported by data showing parallel reductions of $\dot{V}O_2$ and WTR of hibernating ground squirrels. WTR of cold exposed (T_a 7°C) normothermic squirrels was 14.5 ml/day, while that of hibernating squirrels was less than 0.2 ml/day. The reductions of $\dot{V}O_2$ of normothermic vs hibernating squirrels were of about the same magnitude as changes in WTR. Supported in part by NIH 15889, NSF 17002 and NASA NGL 26-004-021-S12.

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INFLUENCE OF LONG-TERM DOSAGE INFUSIONS OF ANGIOTENSIN II ON ARTERIAL PRESSURE, PLASMA ALDOSTERONE CONCENTRATION AND RENAL SODIUM EXCRETION. J.W. DeClue, A.W. Cowley, Jr., T.G. Coleman, R.E. McCaa, and A.C. Guyton. (Spon. D.B. Young). Dept. Physiology & Biophysics, Univ. Med. Cntr., Jackson, MS 39216

In a previous report evidence was presented for an action of angiotensin II (A-II) on the long-term control of renal sodium excretion. In 6 conscious dogs, when the i.v. dosage infusion rate of A-II was held constant at 5 ng/Kg/min for several days to weeks (A-II study) the steady-state level of MABP was found linearly related to the steady-state rate of i.v. isotonic sodium chloride intake. Thus, at steady-state sodium intakes of 5, 100, 300 and 600 mEq/day, MABP increased by 6, 18, 29 and 45%, respectively. In the absence of A-II infusion (normal group) continuous 24 hr recordings of MABP averaged less than a 5% total increase over this range of salt and volume intake. (FED. PROC. 35:397, 1976). In the present report we present the steady-state values of plasma aldosterone concentration (PA) associated with each of the above long-term rates of salt and volume intake and excretion. In the normal study PA averaged 23.8±4, 5.5±1, 7.0±2 and 5.8±1 ng% (±S.E., N=4), respectively. In the A-II study PA averaged 20.0±4, 6.4±1, 6.3±1, and 7.6±2 ng%, respectively. There were no statistically significant differences in PA at any given level of sodium intake between the two study groups. Therefore, when infused at low dosage rates, A-II promotes renal retention of salt and water; this effect, however, is compensated by the accompanying rise in MABP which promotes pressure diuresis and natriuresis. The effects of A-II to maintain renal salt and water retention despite elevations in MABP, were not dependent on any significant long-term elevation in PA. (Supported by NIH grant HL 11678).

EFFECTS OF PINEALECTOMY ON DAILY VARIATIONS OF LIVER AND PLASMA METABOLITES IN GOLDFISH. G. Delahunty and V.L. de Vlaming. Dept. Biology, Marquette University, Milwaukee, Wis. 53233

Diurnal variations of liver glycogen, liver lipid, plasma glucose and plasma total lipid occur in goldfish (Carassius auratus). Photoperiod and feeding time play an important role in controlling these daily metabolite rhythms. The effects of pinealectomy on these daily rhythms of liver and plasma metabolites were examined. In goldfish exposed to a 15.5L/8.5D photoperiod pinealectomy abolishes or alters the daily variations of plasma glucose and liver glycogen. Liver glycogen levels are normally lower in pinealectomized fish than in sham operated animals exposed to a 15.5L/8.5D photoperiod. Treatment of fish exposed to a 15.5L/8.5D photoperiod with melatonin increases liver glycogen levels. In liver slices (taken from fish maintained on a 15.5L/8.5D photoperiod) incubated without melatonin, glycogen levels increase, but decrease in liver slices incubated with melatonin. Since the in vitro and in vivo effects of melatonin on hepatic glycogen differ, our data indicate that the effects of the pineal on carbohydrate metabolism is not mediated solely by the direct action of this indolamine on the liver. Our results do suggest that the goldfish pineal participates in mediating the effects of photoperiod on daily variations in liver and plasma metabolites. (Supported by grants GB-41338 and PCM73-01434 A01 from NSF.)

THE EFFECT OF AGE ON FAT CELL SIZE DISTRIBUTION., F.D. DeMartinis, A.A. Francendese*, H.A. Bertrand* and N. Legradi*, Dept. of Physiology and Biochemistry, Medical College of Pennsylvania, Philadelphia, Pa. 19129.

In the course of studying the cellular characteristics of rat epididymal adipose tissue it became clear that a subpopulation of small fat cells exists in this depot in addition to the usual adipocyte population. Epididymal fat pads from male rats of the Fischer 344 strain were excised and digested using a collagenase technique. The resultant cell suspension was fixed with glutaraldehyde, stained with crystal violet and fat cell diameters measured by a modification of Di Girolamo's method (Am. J. Physiol. 221: 850-858, 1971). Frequency histograms of 300 cell diameters suggested a bimodal distribution existed within the adipocyte population. Frequency histograms of an additional 100 cells whose diameters fell between 6-35 microns confirmed that a subpopulation of small fat cells could be found within that size range. Examination of the adipocyte population in epididymal fat pads from rats 6 weeks to 28 months of age revealed a changing pattern. At 6 weeks of age a unimodal distribution of cell sizes was found but by 14 weeks of age a distinct bimodal distribution of fat cell diameters had become apparent and was present at all subsequent ages examined. These results demonstrate that a previously unrecognized subpopulation of small fat cells exists within the epididymal adipocyte population and that, once developed, this subpopulation persists throughout the animal's life. (Supported by NIH Grant HD-06267.)

LOCAL REGULATION OF CSF [HCO_3^-] DURING LONG-TERM HYPOCAPNIA IN MAN.
J.A. Dempsey, H.V. Forster, L.W. Chosy*, W.G. Reddan* and P.G. Hanson*. Dept. of Prev. Medicine, University of Wisconsin, Madison, WI 53706.

Our previous data showed: 1. that during chronic hypoxic hypocapnia in man and pony, %pH compensation is incomplete and identical in blood and CSF; and 2. that during 7 hrs of moderate hypocapnia in the anesth. dog almost all of the decrease in CSF [HCO_3^-] was prevented by preventing [HCO_3^-]$_a$ from falling via $NaHCO_3^-$ infusion. We hypothesized, then, that compensatory reductions in CSF [HCO_3^-] during chronic hypocapnia would be dependent upon a reduced [HCO_3^-]$_a$. In 10 normals, mild met. alk. was induced by daily $NaHCO_3^-$ ingestion or K+ depletion by thiazide diuretics. [HCO_3^-]$_a$ was maintained--uninterrupted--at 3-5 mEq/l > control for 5-10d at sea-level and 1-3 mEq/l > control as hypocapnia progressed over the initial 4-6d at 3200 m ($P_B \sim 517$). Combined mean data from both groups are tabled.

	ARTERIAL BLOOD				LUMBAR CSF		
	PO_2	PCO_2	[HCO_3^-]	pH	PCO_2	[HCO_3^-]	pH
Control-Sea level	91	40.1	24.7	7.403	51.9	25.4	7.319
+5-10d Met.Alk.	95	42.1	28.5	7.455	53.3	26.9	7.332
+4-6d-3200m+Met.Alk.	55	34.0	26.0	7.493	44.2	22.7	7.343

% CSF pH compensation in prolonged hypocapnia was identical (66%) in subjects with elevated [HCO_3^-]$_a$ (table) and those who acclimatized normally with low [HCO_3^-]$_a$ (not shown). Further study of 4 subjects in whom met. alk. was induced or stopped for 3-4d, following an initial 4-8d at 3200m, confirmed that changes in CSF [HCO_3^-] during prolonged hypocapnia followed changes in CSF P_{CO_2} rather than in [HCO_3^-]$_a$. Our hypothesis was not confirmed. While changes in [HCO_3^-]$_a$ are critical to CSF [HCO_3^-] regulation in short-term hypocapnia, some mechanism sensitive to brain hypocapnia appears as a dominant regulator in the chronic state. (Supported by NIH Grants 15469 and 00149.)

NORADRENALINE CONCENTRATION IN RAT PLASMA. RESTING LEVEL AND EFFECT OF MANIPULATION, DECAPITATION AND ANESTHESIA.
F. Depocas and W.A. Behrens*. Div. of Biological Sciences, Natl Research Council of Canada, Ottawa, Canada K1A 0R6.

Plasma from 20 warm-acclimated white rats (fed a semi-synthetic diet) implanted 5 days previously with an intra-aortic cannula and resting comfortably in an enclosed metabolism cage (Depocas and Masironi, Am. J. Physiol. 199: 1051, 1960) at 27°C contained 0.15 ± 0.01 ng noradrenaline per ml as measured with improved sensitivity by the radio-enzymatic method of Henry et al. (Life Sciences, 16: 375, 1975). Levels of noradrenaline in ng/ml measured after various treatments in groups of 4-5 rats were as follows: Manipulation: 0.63 ± 0.18, decapitation of the awake animal: 1.32 ± 0.25, 5 minutes after 3% halothane: 0.23 ± .01, decapitation under halothane: 0.40 ± 0.03. In 5 rats fed Purina Lab Chow at room temperature normal values were 0.11 ± 0.02 ng/ml and concentrations invariably increased with manipulation and decapitation. Recently published normal values obtained by this method are higher than the above by an order of magnitude. This would indicate that special precautions must be taken to ensure minimal sympathetic activity when resting plasma levels of noradrenaline are required.

PREVENTION OF EXPERIMENTAL GASTRIC STRESS BLEEDING BY INTRAVENOUS HYPERALIMENTATION. M. Deysine and D. Katzka*, Dept. of Surgery, Long Island Jewish-Hillside Medical Center, New Hyde Park, N.Y. 11040, SUNY at Stony Brook.

Clinical gastric stress bleeding (GSB) is associated with a high mortality and morbidity. The purpose of this project was to investigate the effect of intravenous hyperalimentation (IVH) on the incidence of GSB in an experimental model. Sixty adult rats were stressed by immobilization under a wire screen nailed to a board for one hour at 20°C, followed by one hour at 4°C of ambient temperature. During that time, 20 rats received no I.V. solutions, 20 received I.V. normal saline, and 20 received IVH (Freamine II). Both solutions were infused I.V. at a rate of 1.45/ml/100 gms/body weight/hour. At the end of the 2 hours, the rats were decapitated, their stomachs were removed, opened and photographed. The number of ulcers was counted on the specimen by an observer not aware of the protocol. In the control immobilized rats, 15 ± 3 S.D. ulcers were counted. In those immobilized receiving I.V. N/S, 16 ± 3 S.D. ulcers were counted. In contrast, in those immobilized receiving IVH, 4 ± 2 S.D. ulcers were counted. The difference between those receiving IVH and the other two groups (controls) was highly significant, $P < .001$. The progression of the lesion observed in animals sacrificed serially was that of a mucosal capillary hemorrhage progressing into mucosal ulcerations. These results demonstrate that under our experimental conditions, IVH can significantly diminish the incidence of gastric stress bleeding.

THE EFFECT OF METABOLIC INHIBITORS ON CALCIUM TRANSPORT IN MYELINATED NERVE OF FROG. F.P.J. Diecke, Stanley Greenberg* and Marguerite A. Stout*. Dept. of Physiol., CMDNJ-N.J. Medical School, Newark, N.J. 07103 and Dept. of Pharmacol., Ohio State Univ. Coll. of Medicine, Columbus, Ohio 43210.

The effect of the metabolic inhibitors, 2,4-Dinitrophenol, cyanide, mersalyl and azide, on ^{45}calcium influx and efflux from desheathed bundles of myelinated nerve of frog were investigated. Concentrations of 5×10^{-4} M DNP or mersalyl and 5×10^{-3} M azide or cyanide increase calcium efflux and influx significantly. Calcium efflux begins to increase within 30 min after application of the inhibitor and reaches a maximum after 60-90 min. The maximal observed increase of efflux ranged from 50 to 100% of the control efflux. A similar increase was observed for calcium influx in nerve bundles preincubated for 60 min in Ringer solution containing the metabolic inhibitor.

In parallel experiments we measured the change of ATP-concentration in desheathed nerve bundles under the influence of metabolic inhibitors. After a 60 min exposure to Ringer solution containing metabolic inhibitors the ATP-content decreased from a control value of 1.23 μMol/gram wet weight to 0.1-0.26 μMol/gram. With continued exposure the ATP-content continued to decrease rapidly. The results confirm the observation on squid giant axon (Blaustein and Hodgkin, 1969) that calcium transport increases with decreasing ATP-concentrations. However, the effects of low ATP-concentrations are by far smaller in vertebrate tissues such as myelinated nerve, cardiac muscle (Reuter and Seitz, 1968) and rabbit vagus nerve (Kalix, 1972) than in squid axon. (Supported by grant NS 05188 from NINCDS.)

CHANGES IN DISCHARGE RATE OF EPILEPTOGENIC FOCI DURING PASSIVE CHANGES IN INTRAVESICAL PRESSURE IN CAT. R.C. Dill,* J.A. Romiti,* J.A. Kusske,* and R.W. Porter. VAH, LONG BEACH, CA 90801

We recently reported that the spike discharge rate of cortical epileptiform activity in cats showed significant decreases 10 sec. prior to, during, and 10 sec. after spontaneous urinary bladder contractions. The goal of this study was to further investigate this relationship and to assess the relative roles played by sensory and motor activities. Cats with epileptogenic cortical foci induced by freezing or penicillin application were used. Spike discharges and passive changes in intravesical pressure induced by the instillation of saline into, or withdrawal from, the urinary bladder were recorded concomitantly. Each trial consisted of five successive periods grouped as follows: 1) bladder empty and pressure zero (control), 2) twenty ml of saline instilled, 3) bladder volume (twenty ml) held constant, 4) twenty ml of saline withdrawn, and 5) post-change periods after bladder emptied. Results showed clear and consistent alterations in spike discharge rate for the three time periods involving pressure changes. Thus, compared to control, decreases during period 2 and increases during periods 3-4 were found. It was concluded that, under the present conditions, passive increases in intravesical pressure produce a suppression of cortical epileptiform activity; whereas, decreases in pressure produce an enhancement of this spiking. Since the earlier study reports decreases in the rate of epileptiform spiking during all phases of active bladder contractions, it is suggested that activity related to the detrusor contraction may predominate or obliterate any change related only to passive decreases in pressure.

ASZ(DCPB)

CATECHOLAMINE-SENSITIVE ADENYLATE CYCLASE FOLLOWING BURN INJURY. C. DiRusso*, D. Malamud, J. Aprille*, and H. Bode*, Depts. Pediatrics and Surgery, Shriners Burns Inst., and Massachusetts General Hosp., Boston, MA 02114

Catecholamine levels and metabolism are chronically elevated as a consequence of burn injury, resulting in severe depletion of energy and protein stores. Since exposure of normal cells to catecholamines usually renders them refractory to further hormonal stimulation, this suggests that the cell mechanisms for self-regulating sensitivity to hormones are deficient in post-burn trauma. We studied adenylate cyclase (AC) activity in white adipose tissue of burned rats (20% third degree dorsal scald burn) compared with sham and normal animals. AC activity was determined in fat cell ghosts prepared from pooled epididymal fat pads. Enzyme activity was measured in the presence of isoproterenol (10^{-7} to 10^{-4}M) or NaF (10^{-2}M) and compared to basal activity. At five days post-burn, no change was observed in basal or NaF-stimulated AC activity. There was no difference in dose-response curves for isoproterenol-stimulated AC activity; half-maximal stimulation was reached at ~4.0×10^{-6}M. Similar results were found with liver and skeletal muscle preparations. In the burned animals urinary catecholamine excretion was increased 2.5 fold. Since AC did not become refractory to catecholamines, the data suggest elevated hormone levels might chronically stimulate cellular metabolic responses and thus contribute to post-burn hypermetabolism.
(Supported by NIH GM 21700)

BIOCHEMICAL PROPERTIES OF HEXOKINASE ISOZYMES IN PIG ERYTHROCYTES AND LEUKOCYTES. EARL DIXON. DEPT. PHYSIOL. AND PHARMACOL., SCH. VET. MED., TUSKEGEE INSTITUTE, AL. 36088

Four hexokinase isozymes are known to occur in various mammalian cells. Some controversy exist regarding the isozyme type found in the mammalian mature erythrocyte. Previous studies in our laboratory have shown that the mature erythrocyte of the pig possesses the Type III isozyme as the predominate specie. It was also shown that the apparent Km and Vmax values in respect to glucose for the isozyme changes as the animal matures.

In order to determine the isozyme component present in pig erythrocytes and leukocytes, a starch-gel electrophoresis technique was utilized to identify the number of enzyme species present. In enzyme preparations isolated from mature erythrocytes, the zymograms show a fast migrating isozyme in pigs that were approximately one year of age. Animals that were in the age range of 4 to 6 months exhibited both slow and fast mobility components but animals less than 4 months of age possessed a predominance of the slow mobility isozyme. Leukocytes taken from all age groups exhibited a single slow mobility isozyme which is believed to be Type I. These data tend to suggest that the pig possesses erythrocyte isozymes properties that have not been reported in other mammals. (Supported in part by research grants from the National Institutes of Health MBS-5 S06 RR08091-02; Hoffman-LaRoche, Inc., National Science Foundation GY-11073; and Research Cooperation).

EQUILIBRIUM AND KINETIC PROPERTIES OF TWO KANGAROO HEMOGLOBINS. Susanna J. Dodgson-Schneider* and Robert A.B. Holland*(SPON: R.F. Coburn). School of Physiology and Pharmacology, University of New South Wales, Kensington 2033, Australia.

The Australian grey kangaroo, *Macropus giganteus* has two hemoglobins designated Hb I and Hb II which differ only at position 2 in the β-chain. Residue 2 is glutamine in Hb I and histidine in Hb II. A given animal may be homozygous for Hb I or II or be heterozygous. As β 2-His is a binding site for 2,3-DPG, comparing these two hemoglobins will show the importance of the positively charged histidine at this site. P_{50} for oxygen was measured by the mixing method at 30°C for pH 7.4 in bis-tris buffer, with Hb concentration approximately 0.15 mM tetramer. In stripped hemoglobin P_{50} was 6.0 torr for each. As 2,3-DPG was added P_{50} for Hb II at first increased more rapidly than for Hb I and at equal concentrations of Hb_4 and 2,3-DPG the values were 13.2 and 10.0 torr respectively. Above this concentration of 2,3-DPG the P_{50} values converged, being 16 torr for both when DPG:Hb_4 reached 2:1. Kinetic constants for CO combination with deoxy Hb, and O_2 release from fully oxy Hb, were determined in a Durrum-Gibson stopped-flow spectrophotometer. Fresh Hb solutions were studied in 0.1 M phosphate buffer at pH 7.1, and stripped Hb in bis-tris at the same pH. At 37°C l' was 500 mM^{-1} sec^{-1} for fresh Hb I and Hb II. The value for stripped Hb was about 40% higher in each. At 37°C k_4 was 390-430 sec^{-1} for Hb I and II; stripping did not effect k_4. The results indicate that 2,3-DPG is better bound when β2 is the positively charged histidine than when it is the neutral glutamine, but that the differences may be obscured in phosphate buffer.

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INTRAPITUITARY POLYMERIC FORMS OF ^{14}C-RAT PROLACTIN SYNTHESIZED *IN VITRO*. O.C. Dombroske* and W.L. Frantz. Dept. Physiology, Michigan State University, East Lansing, MI 48824

Previously we have reported molecular size heterogeneity for intrapituitary and secreted rat prolactin (r-PRL) *in vitro*, using standard NIH radioimmunoassay (RIA). Synthesis of these forms was investigated here using discontinuous electrophoresis in polyacrylamide gels containing sodium dodecyl sulfate (SDS-disc PAGE). Adenohypophysial blocks from mature female rats were incubated with ^{14}C-amino acids for 15 min. in Earle's saline and chased in medium 199. At specified intervals, r-PRL was extracted by homogenization in alkaline buffer and centrifugation. Supernatants were separated by gel filtration on G-100 Sephadex. Individual fractions were precipitated with trichloroacetic acid (70% of a ^{125}I-r-PRL control was recovered by this method), dissolved in SDS, reduced with mercaptoethanol (ME), and resolved by SDS-disc PAGE on 10% gels. The position of ^{14}C-r-PRL and its separation from somatotrophin were ascertained by migration of the appropriate hormone standards. Liquid scintillation analysis of gel slices allows the construction of a time-dependent gel filtration profile of newly synthesized, intrapituitary r-PRL whose distribution is: (1) immediately after pulse labelling, 10% for a polymer in the void volume, 16% for a form of $\sim$ 60,000 daltons, 45% dimer, and 29% monomeric r-PRL; (2) by the third hour of chase, 5% gel-excluded polymer, 12% apparent trimer, 45% dimer, and 38% monomer. These data demonstrate the synthesis of large forms of r-PRL with transition from larger to smaller forms. Treatment of these polymers with ME yields a product which co-migrates with monomeric r-PRL in SDS-disc PAGE, suggesting that intermolecular disulfide bonds stabilize polymeric r-PRL. (Supported by NSF grant GB 30686)

DETERMINATIONS OF THE PERMEABILITY CHARACTERISTICS OF THE BASAL LAMELLA OF THE INTESTINAL WALL OF ASCARIS SUUM. Manus J. Donahue* and Calvin G. Beames, Jr., (SPON: G.P. Mayer). Dept. of Physiological Sciences, Oklahoma State University, Stillwater, OK 74074

The basal lamella (basement membrane) appears to be a ubiquitous support structure of epithelial and endothelial cells. In addition, it is believed to function as a physiological barrier to the movement of water, organic solutes and electrolytes. The intestine of Ascaris suum consists of a single layer of high columnar epithelial cells on a thick basal lamella. The cells of isolated ribbons of the intestine can be removed by ultra sonication and the remaining basement membrane is tough and relatively easy to manipulate. Sections of the membrane of 0.03 cm^2 are positioned between two chambers of a device for measuring diffusion rates. With this system, it is possible to determine the permeability of the membrane to a series of hydrophilic, non-ionic molecules of graded molecular size. A filtration coefficient of 18.1×10^{-12} cm^5/dyne-sec is measured by an osmotic gradient method, and a relative geometric pore area is calculated as 25 Å. The results permit evaluation of the role of the membrane as a physiological barrier. (Supported by NIH Grant AI-12783)

SUPERNORMAL CONDUCTION IN DOG RIGHT ATRIA. T.J. Doubt*, R.C. Truex*, and G. Ascanio. Depts. of Physiology & Anatomy, Temple University School of Medicine, Philadelphia, Pa. 19140

The effects of heart rate and pacemaker location were studied in 13 isolated blood-perfused dog right atria. Six electrode sites within the atrium were used for both recording and stimulation. A seventh site recorded activity at the tip of the right atrial appendage (RAA). In 65% of the pacing events (31 of 48) periods of supernormal conduction were noted at a mean rate of 214.2 $\pm$ 7.5 beats per minute. During each period one or more interelectrode intervals shortened by 5-24% (2.5-10.0 mSec.). Three basic types of supernormal responses could be identified. Type A had a selective interval decrease; primarily in conduction to the sinus node (SAN), superior atrial septum (SAS), and crista terminalis (CT). A Type B response had a uniform decrease in all the electrode intervals that suggested supernormality in the area of the pacing electrode. This response only occurred during pacing through the SAN, SAS, and CT electrodes. The Type C response involved non-uniform decreases in all the intervals. The largest changes occurred in conduction to the SAN, SAS, CT, and RAA sites. The RAA interval decreased in 50% of all supernormal periods. Electrodes located in the fossa ovalis (FO), coronary sinus (CS), and low atrial septum (LAS) revealed little evidence of supernormal conduction within these areas. These results suggest that areas exist within the superior right atrium that can enhance conduction during periods of rapid heart rates. (Supported by Grants: HE 5362, HL 08886, and HL 07047 from N.I.H.)

TRANSMURAL DISTRIBUTION OF CORONARY COLLATERAL BLOOD FLOW DURING RETROGRADE FLOW DIVERSION IN DOGS WITH CHRONIC CORONARY OCCLUSION. H.F. Downey, F.A. Bashour, P.E. Parker, I.S. Boutros*, and A.G. Williams*. Depts. of Physiol. and Med., Univ. Tex. Health Sci. Center and Cardiopulmonary Institute, Dallas, Texas 75235.

Opening a coronary artery to atmospheric pressure distal to an obstruction diverts collateral blood flow retrogradely. This study examined the quantity and transmural distribution of collateral blood flow to myocardium during retrograde flow diversion. Ameroid constrictors were surgically implanted on the left anterior descending coronary artery (LAD) of 5 dogs. Six to eight weeks later, regional myocardial blood flow was determined from tissue uptake of radioactive microspheres (7-10 μ) administered into the left atrium after anesthesia and thoracotomy. Before diversion of retrograde flow, mean arterial blood pressure (BP) averaged 110±5.4(SE) mmHg and collateral perfusion of the LAD region was .94±.17, .78±.08, and .69±.07 ml/min/g to the epicardial, mid-mural, and endocardial layers, respectively. Severing the LAD just distal to the occluder reduced BP to 89±7.1 mmHg and antegrade collateral flow to .52±1.0, .32±.07, and .23±.06 ml/min/g to these layers. Inspite of retrograde flow diversion, significant collateral flow reached the LAD region. This flow was preferentially distributed to the epicardium.
(Supported by Cardiology Fund and Southwestern Medical Foundation.)

EFFECTS OF HEAD OUT IMMERSION IN WATER AT 25, 30 AND 35 C ON CARDIAC OUTPUT DURING REST AND GRADED EXERCISE.

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Effects of submersion to the neck in 25, 30, and 35 C water on HR and SV (by electrical impedance) were studied in four athletic men at rest, at four submaximal work rates, and at $\dot{V}O_2$max. The subjects performed the same upright bicycling exercise in water as in 25 C air. At rest and during submaximal work, SV was on the average 10 to 20% higher in water than in air. The calculated $\dot{Q}$ and HR were linearly related to $\dot{V}O_2$, with the regression lines approximately parallel for all conditions. By comparison to air at a given submaximal $\dot{V}O_2$, HR was about 12 bpm lower in 25 and 30 C, but the same in 35 C, while $\dot{Q}$ was about the same, 1 l/min higher, and 2 to 3 l/min higher in 25, 30, and 35 C, respectively. The following data, expressed as differences from values in air, were obtained during maximal work in water:

	25 C	30 C	35 C
HR, bpm	− 14	− 13	− 1
SV, ml	+ 5	+ 17	+ 18
$\dot{Q}$, l/min	− 1.2	+ 0.9	+ 2.8

Within the observed range of rectal temperatures (37.1 to 38.0 C) $\dot{V}O_2$max was not significantly affected by immersion or water temperature despite wide differences in $\dot{Q}$. The 4.0 l/min increase in $\dot{Q}$ during maximal work in 35 vs. 25 C water must have been distributed to the skin or other organs of low O_2 extraction. Head-out immersion at various water temperatures appears to be a useful model for manipulating HR and SV during exercise as well as for resting.

EFFECT OF CHRONIC INTRAUTERINE HYPOXIA ON PULMONARY ARTERY PRESSURE IN NEONATAL LAMBS.

Willa H. Drummond* and John M. Bissonnette. University of Oregon Health Sciences Center, Portland, Oregon 97201

Ewes with known breeding dates were surgically prepared at 105-115 days gestation (term = 145 - 150 days) by insertion of catheters into a fetal femoral artery and into one of the main uterine arteries. In one group of animals, the maternal side of the placenta was embolized daily with 15 micron non-radioactive microspheres. Fetal arterial PO_2 (FA PO_2) in utero was monitored every 2 to 3 days for the remainder of gestation. When FA PO_2 fell to less than 18 torr, embolization was discontinued. Grouping data for the entire last third of gestation showed: embolized FA PO_2 = 20.9 ± 0.3 torr (mean ± SEM), controls = 24.2 ± 0.4 torr ($p < 0.01$); embolized pH = 7.36 ± 0.01, controls = 7.38 ± 0.01 ($p < 0.01$); embolized Hct = 35.0 ± 0.4, controls = 32.6 ± 0.6 ($p < 0.01$). Pulmonary artery catheterization was performed on the lambs after delivery at term. The relationship between mean pulmonary artery pressure ($\bar{P}_{PA}$) and arterial PO_2 over the range 15 - 80 torr was examined. There was a more pronounced inverse relationship between $\bar{P}_{PA}$ and FA PO_2 in the embolized group [$\bar{P}_{PA}$ (mm Hg) = 70.3 - 0.489 PO_2 (torr) ($R = 0.59$)] than the control group [$\bar{P}_{PA}$ = 50.5 - 0.352 PO_2 ($R = 0.52$)]. The pH did not differ between embolized (7.28 ± 0.01) and control (7.29 ± 0.01) newborn lambs. We conclude that chronic intrauterine hypoxic stress of a moderate degree is associated with increased responsiveness of the pulmonary circulation to hypoxia in the neonate.

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INHIBITION OF THE PURINERGIC RESPONSE BY PHENTOLAMINE AND 2-2'-PYRIDYLISATOGEN TOSYLATE(PIT). T. Dumsha* and R. Bennett* (SPON: J.I. White). Univ. of Md. Sch. of Dentistry, Baltimore, Md. 21201

The effects of electrical stimulation(S), noradrenalin(NA), and exogenous ATP have been studied in vitro on the guinea-pig taenia coli. A high K^+ (23.5mM) modified Krebs solution was used to suppress spontaneous activity at 35±1 C. Isometric muscle activity was recorded. In 5 experiments phentolamine(53uM) inhibited the relaxation response to NA, ATP, and S by 81±5%(SEM), 96±2%, and 85±6% respectively. Following a 45 minute washout period, the response to NA, ATP, and S (same conc. and voltage) was inhibited by 60±10%, 47±7%, and 68±12% respectively. These results suggest that phentolamine may be competitively inhibiting ATP receptor sites. In 8 experiments PIT(50uM) was found to inhibit the response to NA, ATP, and S by 30±20%, 94±2%, and 64±6% respectively. This preferential inhibition of the ATP induced relaxation response in the taenia coli also supports the "Purinergic Nerve" hypothesis and confirms the work of Spedding et al., (Br. J. Pharmac. 53:575).

EFFECT OF HEART RATE ON TRANSMURAL METABOLITE LEVELS IN THE LEFT VENTRICULAR MYOCARDIUM. R.B. Dunn*, K.M. Hickey*, and D.M. Griggs, Jr. Dept. Physiology, University of Missouri, Columbia, MO. 65201.

Others have reported that raising heart rate by atrial pacing results in 1) a redistribution of myocardial blood flow with the subendocardium receiving a smaller fraction of the total blood flow and 2) a reduction in subendocardial oxygen tension. We sought to determine whether the subendocardium would exhibit metabolic signs of an imbalance between oxygen supply and demand under these conditions. Open chested dogs were paced at 100, 150 or 200 bpm and a transmural tissue sample was obtained from the base of the beating left ventricle using a rapid sampling and freezing technique (<2 sec.). The outer, middle and inner thirds of the tissue sample were analyzed for creatine phosphate, adenosine triphosphate, and lactate. Creatine phosphate was noted to be slightly but significantly lower ($p<.05$) in the inner than in either the middle or outer regions at all three heart rates. However, the difference between the outer and the inner regions was not increased at the higher heart rates, and more specifically, the inner region creatine phosphate level was the same at all three heart rates. Transmural levels of adenosine triphosphate and lactate were uniform at all three heart rates and no differences were detected in any region at different heart rates. These data fail to demonstrate the development of an oxygen imbalance in the subendocardium as a function of heart rate between 100 and 200 bpm. (Supported by Grant HL 11876 from NHLI)

REGIONAL FFA AND GLUCOSE OXIDATION IN VENTRICULAR MYOCARDIAL TISSUE. *Beatrice C. Durham. William Likoff Cardiovascular Institute. Hahnemann Medical College, Philadelphia, Pa. 19102.*

This study was undertaken to determine if there existed differences in FFA or glucose (GL) oxidation in the right (RV), left (LV) ventricle or interventricular septum (IVS) of the rat. Ventricular tissue slices were incubated in the presence of either ^{14}C-palmitate or -GL for one hour, evolved $^{14}CO_2$ was determined and the oxidation rates calculated. At a GL concentration of 0.5 mM, oxidation by RV was significantly higher than by IVS or LV ($p<.001$). When GL concentration was increased sixty-fold, RV continued to oxidize significantly more GL than IVS ($p<.01$). The percent of the medium GL oxidized by LV and IVS was identical at both GL concentrations, but was almost twice as high in RV at the low GL concentration ($p<.001$), possibly indicating a greater requirement for GL in RV. At an FFA concentration of 2.4 mM, there was no difference between oxidation rates in RV and LV, although each was significantly higher than in IVS ($p<.01$). At an even higher FFA level (47.1 mM), LV oxidized one-third more substrate than either RV or IVS ($p<.05$). However, there was no significant difference in the percent of medium FFA oxidized by each region at the two concentrations. It would appear that even at very high FFA levels, linearity between concentration and oxidation is maintained in vitro. The results suggest enhanced regional GL oxidation by RV. A greater ability of LV to oxidize FFA at high concentrations is also seen. These findings could partially explain the relatively high rate of carbohydrate utilization seen in isolated, perfused hearts when compared to in vivo preparations which measure only left ventricular oxidation.

OXYGEN TRANSPORT CHARACTERISTICS OF A BLOOD PERFUSED WORKING ISOLATED RAT HEART. M.A. Duvelleroy* J.L. Martin* M. Duruble* and B. Teisseire*. (SPON: M.B. Laver). Dept. Biophysics, Faculté de Médecine Lariboisière Saint-Louis, Paris, France.

We describe a method for perfusion of a working isolated rat heart with washed pig erythrocytes suspended in Krebs-Henseleit HCO_3^- containing bovine albumine. The preparation is stable for three hours. Coronary blood flow (CBF), aortic flow (AF), external work (W), and myocardial oxygen consumption ($M\dot{V}O_2$) were measured as the oxygen transport characteristics of the perfusate were varied. As hematocrit decreased from 40% to 30%, 20%, and 0%, CBF had the following values: 3.5 ± .5, 5.4 ± .7, 6.6 ± .8, 12.6 ± .7 ml, and AF, 68 ± 9, 75 ± 8, 66 ± 6, and 32 ± 2 (ml/min g wet ventricle). Coronary sinus P_{O_2} (CSP_{O_2}) was highest with a red cell free perfusate. Change of Pa_{O_2} from 450 to 60 mm Hg, with arterial O_2 content constant, was associated with an increase of CBF of 30%. Change of P_{50} from 25 to 10 mm Hg was associated with either a drop of $M\dot{V}O_2$ of 25%, when CBF did not increase or by an increase of CBF of 30% when $M\dot{V}O_2$ remained unchanged. Shift of the HbO_2 dissociation curve to the left was always followed by a decrease of CSP_{O_2} and an increase of CS_{O_2} content. The results suggest that distribution of capillary perfusion compensates for the effect on an increase of oxygen affinity on oxygen delivery.

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THE EXPONENTIATED EXPONENTIAL--A VERSATILE DESCRIPTOR OF ASYMMETRIC SIGMOID PROCESSES. Dexter M. Easton, Jeffrey A. Kugel and Eugene L. Roberts, Dept. Biol. Sci., Fl. State U., Tallahassee, Fl. 32306.

Survival and growth curves of populations of cells or of individuals have been commonly described by the Compertz equation, an exponentiated exponential. The canonical form is $N=\bar{N}exp-bexpkt$, where k is + for survival, - for growth. The equation describes an asymmetric sigmoid relation in contrast to the logistic and certain hyperbolic functions which are symmetric. In the equation, k is the specifying proportionality ("rate") constant, while b sets the position of the curve along the abscissa. The curve constants are easily estimated by hand and refined by a curve-fitting program. The present results show the application of the equation to several diverse phenomena, including the time course of an action potential, K^+ conductance of the axon membrane during voltage clamp, recovery cycle of nerve, the intensity-response relation of a nerve to electrical stimulation, and of receptors to their adequate stimuli. With the help of its second derivative, it describes the Na^+ conductance of axon membrane under voltage clamp and the size distribution of axons of the olfactory nerve. The oxyhemoglobin dissociation curve as well as the time course of hemolysis of blood cells follows the growth equation. Any exponential process in which the proportionality term is not a constant but changes exponentially with the independent variable is a good candidate for Gompertzian treatment. (Aided by Psychobiology Program, F.S.U.).

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THE OSMOTIC MINIPUMP: A NEW TOOL FOR STUDYING THE ACTIONS OF DRUGS AND HORMONES IN THE STEADY STATE. Ben Eckenhoff, Sy Hoff*, F. Theeuwes, & Su Il Yum. ALZA Research, Palo Alto, California

The osmotic minipump is a cylindrical device (25mm by 6.5mm diameter) for fluid delivery which can be implanted subcutaneously or intraperitoneally in animals as small as the mouse, for parenteral administration of bioactive agents at constant rates for periods up to 7 days. The pump consists of deformable drug reservoir, which is coated with an osmotic agent which, in turn, is coated by a rate-controlling semiperimeable membrane, providing the external surface of the minipump. The membrane, a cellulosic, is bicompatible. When the minipump is placed within living animals, water moves osmotically into the osmotic agent at a rate controlled by the membrane. The membrane is rigid, hence the entrance of water displaces material from the reservoir, which collapses gradually with time, pumping contents out of the minipump. The minipump reservoir is filled by the user, its volume is 170 microliters. The reservoir is compatible with water, physiological salt solutions, polyethylene glycols, propylene glycol, and with dilute aqueous ethanol (up to 5 percent w/w/). The duration of delivery depends on the type of membrane. Two systems have been fabricated and tested, delivering at 1 ml/hr. for 7 days, and 2.4ml/hr. for 3 days. The implanted minipump can also be connected to a small catheter (0.8 mm ID) for either systemic delivery or local administration of agents intravenously, intracisternally, or to tissue sites, e.g., specific brain centers.

HYPOCALCIURIC EFFECT OF LONG-TERM POLYTHIAZIDE TREATMENT IN INTACT AND THYROPARATHYROIDECTOMIZED RATS. B.R. Edwards and P. Stern*. Dept. of Physiology, Dartmouth Medical School, Hanover, NH 03755.

Experiments were performed on 11 intact and 10 chronically thyroparathyroidectomized (TPTX) rats. The rats were placed in metabolism cages with free access to food and distilled water. Following several days of adaptation to this environment, sequential 24h urine collections and tail vein blood samples (every 48h) were obtained. After 3 control days, polythiazide (PTZ) was given for 6 days (0.1 mg/100g.24h p.o.). In intact rats, sodium excretion (UnaV) was increased on day 1 of PTZ (680 ± 40 SE vs 548 ± 28 μEq/100g.24h; $P < .05$) but returned to or below control levels thereafter. Calcium excretion (UcaV) was markedly reduced on day 1 of PTZ (12.1 ± 1.3 vs 26.5 ± 5.6μEq/100g.24h $P < .02$) and remained depressed thereafter. In TPTX rats, UnaV was increased only on day 2 of PTZ (670 ± 35 vs 562 ± 28 μEq/100g.24h; $P < .05$) whereas UcaV fell on day 1 (18.4 ± 1.4 vs 43.0 ± 7.0 μEq/100g.24h; $P < .01$) and remained depressed thereafter. Circulating PTH seems not to be a necessary requirement for the hypocalciuric response to PTZ. In TPTX rats, hypocalciuria occurred before any natriuresis was evident. Peak changes in body weight, as an estimate of changes in fluid volume, were small (-2% in intact, $P < .05$; +3% in TPTX, $P < .02$). Thus, at least in TPTX rats, the hypocalciuria was not associated with demonstrable volume depletion. These results suggest that some other mechanism is needed to explain the hypocalciuric effect of PTZ - perhaps a more direct effect on tubular reabsorption of calcium.

THE ACTION OF THE OCTAPEPTIDE OF CHOLECYSTOKININ ON INSULIN AND GLUCAGON RELEASE IN THE ANESTHETIZED DOG. L.E. Edwards, C.T. Edwards* and N.J. Hutton*. Department of Physiology, Medical College of Virginia, Richmond, Virginia 23298.

This investigation was designed to add to our knowledge of the control of intermediary metabolism by the G.I. hormones. In an earlier study we showed that pentagastrin stimulated the release of insulin and glucagon in such a way as to initiate anabolism before food is absorbed. In this study OP-CCK was infused into six anesthetized dogs and the portal plasma levels of glucose, glucagon and insulin were measured. After two one-half hour control periods, each animal was perfused with the octapeptide of cholecystokinin for one half-hour period and then followed for another two and one-half hours. OP-CCK stimulated the release of both insulin and glucagon. A sharp rise in the glucose levels accompanied the onset of the changes seen in the levels of insulin and glucagon. This was followed by a fall to a level below the control that lasted until the end of the recovery period. A biphasic increase in the I/G ratio was produced by the OP-CCK. This response was predominately anabolic. These results are in keeping with the idea that CCK contributes to the control of intermediary metabolism.

EFFECTS OF HYPOCAPNIA ON CORONARY VASCULAR RESISTANCE IN THE DOG. I.C. Ehrhart* and C. W. Smith. Depts. of Physiology, Medical College of Georgia, Augusta, Ga., 30902 and The Ohio State University, Columbus, Ohio, 43210.

Pulsatile coronary blood flow was measured with a velocity sensitive catheter-tip flowmeter in closed-chest urethane-chloralose anesthetized dogs. The animals were mechanically ventilated with 95% O_2-5% CO_2 in the control period and 100% O_2 in the experimental period. Within 3 minutes of the change to 100% O_2, the P_{CO_2} decreased from 45 to 20 mm Hg while the pH increased from 7.28 to 7.48. Late diastolic coronary vascular resistance was decreased throughout the 8 minute hypocapnic period. Late diastolic aortic pressure was decreased during the first 5 minutes of the hypocapnic period but coronary blood flow was unchanged. Following beta-adrenergic blockade (propranolol 1 mg/Kg i.v.) neither late diastolic pressure, coronary vascular resistance nor coronary blood flow were changed in response to hypocapnia. Heart rate was increased at 3 and 5 minutes during hypocapnia both before and after propranolol. These results indicate that whole body hypocapnia decreases both late diastolic aortic pressure and late diastolic coronary vascular resistance in the anesthetized animal. Furthermore, these hypocapnic responses can be eliminated by beta-adrenergic blockade.

ORGAN BLOOD FLOW AND MICROSPHERE SHUNTING IN THE TURKEY. S. Einzig*, J.J. Leonard*, R.V. Lucas*, Jr., D.A. Gerasch*, G.R. Noren*, M.R. Tripp* and I.J. Fox. Depts. of Physiology and Pediatrics, Univ. of Minn., Minneapolis, M.N. 55455

Regional blood flow (RBF) measurements (arterial reference sample technic) were made in 5 supine, closed-chested, male, broad-breasted white 9.8 ± 0.4 (± SEM) Kg turkeys, intubated and breathing spontaneously under methoxyflurane anesthesia with O_2 enrichment: temp. 41.4 ± .3 C, hematocrit 48 ± 1% and arterial blood pH 7.37 ± .2, pCO_2 54 ± 5 mm Hg, pO_2 246 ± 26 mm Hg. Simultaneous left ventricular (LV) injection of 1.33 ± .13 · 10^6 15μ ^{85}Sr and 4.57 ± .54 · 10^6 8μ ^{46}Sc labeled spheres did not change mean aortic pressure, mean pulmonary artery pressure or heart rate from their control values of 140 ± 14 mm Hg, 15 ± 1 mm Hg and 222 ± 11 beats/min respectively. Cardiac index values for the 8 and 15μ spheres were similar, 137 ± 14 and 128 ± 15 ml/Kg/min, respectively ($p > .05$). Total shunting across the systemic circulation, expressed as % of cardiac output, averaged 6.6 ± 2.4 and 33 ± 1.7% for the 15 and 8μ spheres, respectively, ($p < .001$). 15μ sphere flows (ml/gm/min) and the 8μ/15μ flow ratio (shunt fraction) were respectively for the following organs: LV (including septum) 1.54 ± .19, 0.92 ± .01; skin 0.17 ± .03, 0.48 ± .05; kidneys 3.88 ± .60, 0.31 ± .03; gall bladder 2.86 ± .56, 0.31 ± .03; spleen 6.02 ± 1.10, 0.58 ± 09; esophagus 0.56 ± .13, 0.63 ± .03; mid-small intestine 1.88 ± .48, 0.42 ± .06; colon 2.61 ± .19, 0.26 ± .02; testes 0.22 ± .02, 0.35 ± .02. 8μ spheres significantly ($p < .05$) underestimated 15μ sphere flow in all the above tissues. Skeletal muscle had a similar flow by both spheres, 0.026 ± .004, 0.94 ± .05, $p < .4$. The liver shunt fraction was 1.43 ± .19, which may represent trapping of 8μ spheres shunted into the portal circulation. Subendocardial:subepicardial RBF ratios of 1.43 ± .05 and 1.24 ± .06 for the 15 and 8 μ spheres respectively, were significantly different ($p < .01$).

COMPARISON OF GLUCOSE- AND FAT-INDUCED INSULIN RELEASE: ROLE OF GASTRIC INHIBITORY POLYPEPTIDE (GIP). D. Elahi, D.K. Andersen*, G.S. Raizes*, J.D. Tobin* and R. Andres. Gerontol.Res.Ctr.,NIA,NIH,Balto.,MD 21224

While the insulinotropic effect of oral glucose is well recognized, insulin release after fat ingestion is seen only in the presence of hyperglycemia. GIP release has been shown to be stimulated by both oral glucose(OG) and fat(OF). We therefore compared the role of OG- and OF-induced GIP release in insulin secretion. 14 normal men were studied using the glucose clamp technique (J.Clin.Invest. 53:1481,1974) which produced a square wave of hyperglycemia 125 mg/dl above basal for 3 hr. 40 g/m^2 OG or OF (emulsified corn oil) was ingested at 60 min, and blood glucose was held stable. Plasma immunoreactive GIP (IR-GIP) remained unchanged by IV glucose alone, but rose after oral stimuli. Plasma immunoreactive insulin (IRI) rose after oral stimuli above the elevated levels produced by hyperglycemia alone. Results:

	-----IR-GIP Response------			-------IRI Response--------		
Oral	Initial Resp.	Peak Resp.		Initial Resp.	Peak Resp.	
Stimulus	Time	Time	%Incr	Time	Time	%Incr
Glucose	10'	30-40'	432	10'	30-50'	226
Fat	25'	50-85'	131	25'	65-90'	197

Despite differences in the IR-GIP response, the magnitude of the IRI release after OG and OF was nearly identical. We conclude (1) During hyperglycemia, IRI responses to both stimuli parallel the respective GIP curves, confirming their functional relationship; (2) Delayed gastric emptying may account for the delay in GIP and IRI release after fat ingestion, but in light of the delay in GIP release, a source for prolonged gastric emptying other than gastric inhibitory polypeptide is suggested; (3) Despite similar degrees of IRI response to equal doses of OG and OF, differences in the degree of GIP release suggest increased beta-cell sensitivity to the GIP produced by fat. BMES

THREE DIMENSIONAL DECONVOLUTION OF REDOX STATES OF SEQUENTIAL BRAIN TISSUE SECTIONS. S Eleff*, B. Quistorff* and B. Chance, Johnson Research Foundation, University of Pennsylvania, Philadelphia, PA 19174

With the increasing application of two-dimensional optical scanning technology to morphological and biochemical studies, the quest for three-dimensional image reconstruction becomes a crucial issue. The ratio of flavoprotein and pyridine nucleotide fluorescence in brain and heart studies, affords an indication of the redox state of the intracellular mitochondria (Chance et al., Proceedings of the APS meeting, Anaheim, April 1976). A deconvolution problem arises in trying to reconstruct a three-dimensional image from the sequential sections. The 366 and 460 nm excitation lights may excite fluorescence to a depth of 0.5 mm. Because of this, the data collected from a generic slice whose thickness is 100 μ is in reality a weighted sum of the fluorescence due to all tissue sections which are still present and within a penetration depth which is sufficiently shallow to allow an experimentally noticeable change in the observed fluorescence value. The contribution from successive slices approaches zero exponentially and hence the theoretically infinite sum converges. Applying the Lambert-Beer law allows a mathematical formulation of this series to take on meaningful physical significance. Appropriate substitutions reduces this series to a set of N equations and 2N unknowns relating fluorescence reading, F, to the absorbtion coefficient, α, and quantum yield, Φ. The final equation is: $F_{k-1} - \alpha_k^2 F_k = \alpha_k^2 \Phi_k$ where the subscripts refer to the uppermost slice which is still present. Experimental determination of the α's will allow the reconstruction of a three-dimensional redox picture of the brain. (Supported by grant NIH-NS 10939.)

NUTRITIONAL REQUIREMENTS OF EASTERN BOX TURTLES (TERRAPENE CAROLINA CAROLINA). R. W. Elghammer* and R. E. Johnson, Dept. of Biology, Knox College, Galesburg, Illinois 61401

Preferences for different types of food have been studied in eastern box turtles (Terrapene carolina carolina) to assess their nutritional requirements and the metabolic mixture. Eighteen animals were studied for one year. They were kept in an environmentally controlled room which maintained temperatures of 27°C by day and 22°C by night. They were housed on bark in pairs in plastic cages with unlimited water. The light cycle was 12 h dark and 12 h light. Each Monday a base diet consisting of two parts raw ground beef, one part raw ground beef liver, and one part beef bone meal, beef fat, and beef bone marrow (supplemented with cod liver oil and a pediatric vitamin formula) was offered, 14 g per animal. Each Thursday a single food was made available for 24 h. The amounts eaten and food types were recorded. They represented meat products, fruits, vegetables, cereals, or a mixture of these. The box turtle has very specific dietary preferences. All cooked food was rejected, as were all cereal products and all commercially prepared animal foods. They did accept the base diet, raw chopped beef, ripe bananas and strawberries. The eastern box turtle appears to be a preferential carnivore. At the start the mean body weight was 400 g; after 12 months it was 468 g. All eighteen animals survived a full year and thrived on a mean weekly intake of 1.8g protein, 0.2 g carbohydrate and 2.0 g fat, supplemented with minerals and vitamins. This form is ideal for certain studies because the metabolic mixture can be specified accurately.
(Supported by the Knox College Biology Dept.)

ASZ(DCPB)

EFFECTS OF X-IRRADIATION ON ECLOSION IN DEVELOPING TOBACCO HORNWORMS, MANDUCA SEXTA. M.J. Ely and A.M. Jungreis, Department of Zoology, University of Tennessee, Knoxville, TN 37916.

Control of eclosion in M. sexta (lab reared at 23-25°C on LD 18:6) was investigated by utilizing the ED_{50} (X-ray exposure dose required to prevent eclosion in 50% of the animals) throughout pharate adult (PA) development as a measure of radiation sensitivity (RS). An initial period (Days 0-6) of nearly constant RS (ED_{50}=13.0-14.4 KR) was followed by a brief period of increased RS (D 6.5-7.75: minimal ED_{50}=8.23KR). Thereafter, a pronounced linear decrease in RS was noted through the day of eclosion (D 8: ED_{50}=19KR; D 22: ED_{50}=75KR). Selectively shielding PAs during X-irradiation demonstrated the absence of RS regions in the abdomen and their presence in the head-thorax. The association between ecdysone and the increased radiosensitivity on D 7 was studied. PAs administered β-ecdysone on D 1, D 4 and D 12 and irradiated 6, 24 and 48 hours post-injection experienced significant increases in RS. We propose that RS exhibited by M. sexta on D 7 is in part dependent upon the titer of ecdysone in hemolymph. The role of the brain as a RS region was also determined in D 10 PAs by selectively transplanting irradiated (I) and non-irradiated (NI) brains into I and NI animals. In NI animals, brain exchange or cutting the connectives to the brain resulted in only 45% eclosion success, while placing an ED_{100} I brain in the abdomen of an intact, NI animal failed to prevent eclosion. Using ED_{100} animals, NI brains transplanted to the heads or abdomens of intact animals or into animals debrained after irradiation could not induce eclosion. The presence of a RS component in addition to the brain is therefore proposed. Supported by NSF Grant PCM 75-23456 and Biomedical Sciences Support Grant #07088.

CEREBRAL HEMODYNAMIC EFFECTS OF CLOSE INTRA-ARTERIAL INFUSION OR CSF PERFUSION WITH CATECHOLAMINES IN THE ANESTHETIZED DOG. Thomas E. Emerson, Jr., Todd P. Burns*, and Richard M. Raymond*. Dept. of Physiol., Mich. State Univ., East Lansing, Mich. 48824

Although it has been demonstrated that catecholamines constrict the conducting vessels of the pial vasculature, their effects on total brain blood flow remain controversial. Cerebral venous outflow (CBF) was measured from the sinus confluens with the lateral sinuses occluded. Epinephrine (Epi.; N=10) or norepinephrine (NorEpi.; N=10) was infused at sequentially greater rates into the common carotid arteries (i.a.). Infusion rates for each were 2, 5, 10 & 20 μg/min. These amines were also introduced into the CSF system by sequentially increasing the conc. of each in mock CSF perfusate. Conc. of Epi (N=8) or NorEpi (N=7) were 0.1, 1.0 & 10 μg/ml. Complete exposure of the entire brain surface, sulci, circle of Willis and ventricles to the perfusate has been confirmed using India ink. At the highest i.a. rate, Epi caused a 12% decrease in CBF, a 23% increase in cerebral vascular resistance (CVR) and no change in arterial blood pressure (ABP) or P_ACO_2. CSF perfusion with Epi caused a 12% decrease in CBF, a 13% increase in CVR, and no effect on ABP or P_ACO_2 at the 10 μg/ml conc. NorEpi infused i.a. decreased CBF ($P<0.05$) and increased CVR ($P<0.05$) at each infusion rate, the greatest effect being a 7% decrease in CBF and a 17% increase in CVR, with no effect on ABP or P_ACO_2 at the 20 μg/min rate. CSF NorEpi increased ABP and CVR 11% each but did not effect CBF or P_ACO_2 at the 1 & 10 μg/ml conc. Finally, it is important to mention that individual results were inconsistent with both amines, i.e., CVR increased in some, decreased in a couple, and did not change in others. In conclusion, these data support the view that catecholamines are vasoactive in the cerebral vasculature, but that their effects on total CBF are much less than seen in other systemic organs. (Supported by Mich. Heart Assoc.)

CHARACTERIZATION OF ISOLATED RENIN GRANULES. N. L. Emmett* and J. B. Myers. Dept. Biology, Atlanta University, Atlanta, GA 30314

A considerable part of the renin in rat kidneys is bound in cytoplasmic granules which are recovered in the large granule fraction. Recent results indicate that these granules form a separate group of particles, entirely distinct from other cellular organelles. The ability to isolate intact granules provided a method for examining some of their properties and contributed toward an understanding of renin release. In this study a systematic analysis of the granule fraction stability under various experimental conditions in vitro has been made. Osmotic activation was studied as a function of the sucrose concentration of the suspension medium. Variability in granule resistance was indicated. It was assumed that this type of renin release was an osmotic phenomenon. Granules incubated at different pH (4.0 - 8.0) appeared to be more stable in the range of pH 6.0 - 7.0. Thermal activation of the granule fraction incubated at high temperature was ascribed to an autocatlytic change in the granule membrane. Attention was drawn to the observed solubilizing and stabilizing effects of certain ions. Granule stability increased with increasing concentrations of potassium, sodium, phosphate and magnesium. As could be expected, agents that affect membrane stability were also effective in stimulating renin release. Treating the isolated renin granule fraction in the manner described was accompanied by a release of renin into solution. Obviously, these properties are the characteristics that are reflective of granule release of renin in the hypertensive state, in which the renin-angiotensin mechanism is operative.

ELECTRICAL POTENTIALS IN THE RAT LUNG. J. Engelberg and J. Radin*, Dept. Physiology & Biophysics, University of Kentucky Medical Center, Lexington, KY 40506

The trachea, pulmonary artery, and left atrium were cannulated, and the isolated lungs floated, trachea oriented downward, on a layer of paraffin oil in an incubated chamber at 37°C. With the trachea partially filled with fluid, to establish electrical continuity, the electrical potential of the tracheal fluid, and of the pleural surface were measured with respect to the fluid in the vascular bed. With phosphate-buffered Ringer solution in the trachea, in the vascular bed and on the pleural surface, the alveolo-capillary potential, and the capillo-pleural potential were found to be on the order of -9 and -4mv, respectively. These potentials were greatly reduced or abolished by low temperature, lack of oxygen, cyanide, and ouabain, suggesting that they were generated by an energy-dependent transport of ions. When isotonic sodium chloride solution was used in place of Ringer solution, potentials similar to the above were obtained. However, when choline was substituted for sodium, or sulfate was substituted for chloride, the potentials were abolished. This suggests that both sodium and chloride ion, but no other ions, are necessary for the genesis of these potentials.

In the intact rat the alveolo-capillary potential (measured between the inside of the trachea and the blood in the carotid artery) was on the order of -8mv; with the chest open the capillo-pleural potential (measured between the blood in the carotid artery and the pleural surface of the lungs) was on the order of -3mv.

ASZ(DCPB)

EVOLUTIONARY ASPECTS OF PANCREATIC ISLET FUNCTION. A. Epple, T.L. Lewis* and S.B. Miller*, Anatomy Department, Thomas Jefferson University, Philadelphia, PA. 19107.

Since recent publications indicate that the role of the islet organ in birds and non-amniotes may be different from that in mammals, we studied the effects of pancreatectomy (TPX) and hypophysectomy (THX) in the yellow American eel, Anguilla rostrata. In this species, TPX causes: (a) either non-specific or transitory hyperglycemia, combined with an opposite trend of liver glycogen, and no clear effect on muscle glycogen; (b) hyperaminoacidemia; (c) no clear effect on serum FFA and adipose tissue, and a drop in serum cholesterol; (d) a drop of the hematocrit. With the exception of cholesterol (which showed a tendency to decrease), THX had effects similar to those in mammals: a tendency to, or significantly lowered values of serum glucose, liver and muscle glycogen, and serum amino acids. Serum FFA, liver FA and abdominal fat stores appear unaffected. When transferred to sea water, TPX eels (but not operated controls) show a very poor survival rate, which seems to be connected with muscle dehydration (but not with liver dehydration). THX eels survive well in both fresh and sea water. THX-TPX eels survive only in 1/3 sea water. An integration with the results of other studies suggests: (1) In "lower" vertebrates, insulin seems to be much less important for the intermediary metabolism than in mammals. (2) The islet organ of lower vertebrates has a dual function in both intermediary metabolism and osmoregulation. (3) At least with respect to intermediary metabolism, the pituitary is phylogenetically much more conservative than the islet organ.

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DISTRIBUTION OF RESPIRATORY MUSCLE BLOOD FLOW DURING EXPIRATORY RESISTANCE. W.L. Eschenbacher*, C. H. Robertson, Jr.*, and R.L. Johnson, Jr. Department of Medicine, Univ. Texas Health Science Center, Dallas, Texas.

The pattern of distribution of blood flow among respiratory muscle represents a good index of the pattern of distribution of work done by the individual muscles. We have used a radioactively-labeled microsphere technique to measure the blood flow to each respiratory muscle in dogs during quiet breathing and at graded expiratory resistances. Inspiratory and expiratory pressure-volume (PdV) work was measured by computer integration of change in thoracic gas volume and esophageal pressure. Cardiac output (indocyanine dye dilution) and blood pressure were monitored.

During quiet breathing only blood flow to the diaphragm (.15 ml/gm/min) was significantly higher than the range of values for the other respiratory and control muscles (.03-.09 ml/gm/min), and only inspiratory PdV work was accomplished. As expiratory resistance was increased there was a progressive rise in expiratory PdV work and blood flow increased in the transverse abdominal, internal oblique, internal intercostal and external oblique muscles, but not in the rectus abdominis or ileocostalis muscles ($p<.05$). There was a modest increase in inspiratory PdV work and blood flow to the diaphragm and external intercostals, but not to any other inspiratory or control muscles. There were minor decreases in blood pressure and cardiac output. Respiratory rate decreased significantly and tidal volume increased but there was a net fall in minute volume so that carbon dioxide retention occurred.

OVERDRIVE SUPPRESSION OF ATRIAL AND JUNCTIONAL PACEMAKERS DURING SYMPATHETIC ACTIVATION. David E. Euler*, S. B. Jones, E. L. Hardie* and W.C. Randall. Department of Physiology, Loyola University Stritch School of Medicine, Maywood, Illinois 60153.

The response of SA nodal, AV junctional and ectopic atrial pacemakers to sympathetic stimulation was studied in thoracotomized dogs anesthetized with sodium pentobarbital. AV junctional pacemakers were produced by acute surgical removal of the sulcus terminalis while ectopic atrial pacemakers were produced by chronic removal of the sulcus terminalis. Stimulation of the right or left ansa subclavia in dogs with an intact SA node resulted in a smooth acceleration of the atrial rate and a smooth deceleration after the stimulus was removed. Sympathetic stimulation in dogs with AV junctional or ectopic atrial pacemakers resulted in a smooth acceleration in rate frequently accompanied by a shift in pacemaker site as evidenced by a change in P wave morphology in the electrocardiogram. Furthermore, termination of stimulus was followed by a pause lasting up to several seconds before the control rate was restored. Similar pauses were obtained by electrically driving the atria at rates comparable to those seen during sympathetic stimulation. The prolonged pauses of ectopic pacemakers following sympathetic activation can be explained on the basis of overdrive suppression of the dominant ectopic pacemaker by a latent pacemaker excited by local release of norepinephrine during the sympathetic stimulation. The difference in the response of the SA node and ectopic pacemakers to sympathetic stimulation is a function of their relative susceptibility to overdrive suppression. (Supported by NIH Grant HL 08682).

SEASONAL DIFFERENCES IN GLUCOSE-6-PHOSPHATE DEHYDROGENASE ACTIVITY IN THE COCKROACH, LEUCOPHAEA MADERAE.
John Fabianek and Leon L. Pierre*. Dept. Life Sciences, New York Tech, 888 Seventh Ave. New York, N.Y. 10019. (Spon: Alfred L. Copley).

Spectrophotometric investigation(Beckman DU) of Glucose-6-phosphate dehydrogenase activity in materials of the symbionts and fat bodies of the cockroach, Leucophaea maderae was performed according to the methods of Faulkner 1956(B.J. 64: 402-436) and Prota 1961 (J.N.Y.Ent. Soc.49:59-67).

Symbiont materials showed Spring-time (March-June) activity of 1.150 and those of normal adult and nymphal materials showed respective activities of 0.681 and 0.473. Corresponding activities of aposymbiotic insects were 0.689 and 0.652 respectively. Summertime (July-October) activity of symbiont materials were 1.159 and those of the normal adults and nymphs showed activities of 1.072 and 0.836 respectively. The respective corresponding activities of the aposymbiotic insect materials were 1.130 and 1.050.

The fore-going results indicate that during the cooler months,the metabolism of the insect is toned down. However, metabolism speeds up during the warmer days when the insect is more active.

VELOCITY PROFILES AND SHEAR STRESSES IN ARTIFICIAL VALVES UNDER STEADY FLOW CONDITIONS. Herman Falsetti and Richard Swope*, Cardiovascular Center, Dept. of Internal Medicine, University of Iowa, Iowa City, Iowa 52242.

Artificial valves (Bjork-Shiley, Starr-Edwards and Beall) were mounted and tested in a model left ventricle-aorta. A hot film anemometer system was used to measure point velocities distal to the valves under steady flow conditions of 3, 6 and 8 liters/min. Velocity profiles, turbulent intensities and turbulent shear stresses were calculated at three locations: 1, 2 and 4 aortic diameters downstream of the valve.

Velocity fields with no valves showed a typical flat velocity profile with no appreciable turbulence or shear stress. Placing the prosthetic valve in the system caused gross distortion of the velocity profile. The profiles demonstrated disturbed flow as well as negative flow. Spectral analysis of these velocity wave forms showed significant Fourier series components 100 HZ and above. Comparison of the three tested valves showed that all have relatively small laminar shear stresses at the wall, but turbulent shear stresses were high, from 200 to 600 dynes/cm^2. These turbulent stresses are similar to those reported to cause endothelial damage and hemolysis. Although there is a large difference in velocity profiles, there appears to be little difference in stresses between the Bjork-Shiley and Starr-Edwards valves. These two valves generate lower stresses than the Beall valve. Distal propagation of turbulence is most severe for the Beall valve.

In summary, this study shows that under steady flow conditions artificial valves generate disturbed flows with high levels of shear stress.

A REGIONALLY LINEAR MODEL OF NEURON INTERACTION. Belmont G. Farley, Dept. of Computer and Information Sciences, Temple Univ., Philadelphia, pa. 19122.

This paper discusses systems of interacting neurons having the following general model properties: (1) Neurons are represented by their membrane voltage in one or more compartments; (2) interaction between compartments is by linear electrotonus or by synaptic "excitation"; (3) Interaction produced by action potentials is represented by excitation which is a function of average impulse rate; (4) the effect of synaptic excitation is to produce a membrane voltage rate-of-change proportional to the value of the incoming excitation; (5) Excitation outgoing from a compartment is a fixed linear function of membrane voltage between certain voltage thresholds. Upon crossing such a threshold, the linear function may change. This model leads to a system of non-linear differential-difference equations whose variables are the membrane voltages of compartments. Behavior, however, is linear within the regions of the variable-space bounded by the membrane voltage thresholds, so that linear solutions can be "patched" together at these boundaries. Since the interaction between neurons is represented by continuous functions, the model applies, within its approximations, to neural interaction with or without "action potentials." Analytic and computer studies show that particular model systems can: (1) Simulate any logical function; (2) Support controlled wave propagation in both linear and non-linear modes; (3) Produce a variety of controlled, time-dependent, parallel outputs, as in motor behavior; (4) Respond decisively to classes of time-dependent, parallel inputs, as in recognition behavior; (5) "Record" impressed inputs for a period of time, as in short-term memory.

BMES

PRESSURE-FLOW LOOPS IN EXPERIMENTAL ARTERIAL STENOSIS. D.J. Farrar*, G.S. Malindzak, Jr., G. Johnson, Jr.*, and H.S. Hsiao*. Dept. of Physiology, Bowman Gray School of Medicine, Winston-Salem, N.C., and Depts. of Physiology and Surgery, U.N. Carolina, Chapel Hill, N.C.

Pulsatile pressure (P) and flow ($\dot{Q}$) were measured 3 cm proximal to a graded arterial stenosis produced experimentally in the femoral arteries of 12 mongrel dogs. Pressure-flow loops were generated at each of 5 levels of stenosis from the pressure pulse versus the corresponding flow pulse for single cardiac cycles. The pulse impedance (Z_P) a) was defined as the slope of the major axis of the loop, and b) was computed as the ratio of peak-to-peak pressure to peak-to-peak flow. At the same time, the femoral artery input impedance (Z_{IN}) was determined by Fourier analysis of the same P and $\dot{Q}$ pulses. The large vessel impedance (Z_L) was previously shown to be directly related to the hydraulic resistance of the stenosis (Fed. Proc. 35(3):448,1976), and was computed as the average Z_{IN} modulus from 3 to 19 Hz. At each level of stenosis, measurements were made at steady state (SS) and at peak vasodilated flow produced by intra-arterial bolus injection of 0.3 mg. nitroglycerine (NG). RESULTS: Z_P was shown to be nearly identical to Z_L at all levels of stenosis. The regression equation for SS is $Z_P = 0.067 + 1.04Z_L$ ($r = 0.97$) and for NG is $Z_P = 0.082 + 1.07Z_L$ ($r = 0.89$) (units: mmHg min ml^{-1}). The phase (hysteresis) of the pressure-flow loops appear to be directly related to the Z_{IN} phase of the first two or three harmonics. CONCLUSIONS: 1) Pressure-flow loops provide a measure of input impedance modulus and phase in the range of the fundamental heart frequency. 2) Z_P provides a measure of large vessel impedance and thus a reliable index of severity of arterial stenosis. (Supported by North Carolina Heart Association Grant 1974-75-A-62, and HL 05392 and HL 00487.)

EFFECTS OF AN ENDOPEROXIDE ANALOG ON THE CANINE RENAL VASCULAR BED. L.P. Feigen*, B.M. Chapnick*, and P.J. Kadowitz* (SPON: R. Lowe). Depts. Physiology and Pharmacology, Tulane Medical School, New Orleans LA 70112

The influence of intra-arterial administration of a stable analog of the prostaglandin endoperoxide PGH_2 on renal blood flow was studied using an electromagnetic flow meter. Resting renal blood flow in these pentobarbital anesthetized dogs averaged 194 ± 20 (SE) ml/min. equivalent to 3.80 ± .27 (SE) ml/min/g kidney weight. Intra renal arterial injection of (15S)-Hydroxy-11α, 9α-(epoxymethano) prosta-5Z, 13E-dienoic acid as a bolus in doses of 0.1, 0.3, and 1.0 µg resulted in a dose related decrease in renal blood flow but had no effect on mean arterial blood pressure. Renal vascular resistance increased 25%, 109% and 274% at the 0.1, 0.3, and 1.0 µg doses respectively. The constrictor response was rapid in onset and of short duration, with t 1/2 for recovery of about 30 seconds. These responses were similar to those elicited by Norepinephrine (NE) in that the same doses of NE caused a 63%, 350% and 556% increase in resistance respectively. In contrast, PGE_2, the predominant natural renal prostaglandin, increased renal blood flow in a dose related manner. Renal vascular resistance decreased 22%, 27%, and 29% at 0.03, 0.1 and 0.3 µg respectively. On the other hand $PGF_{2\alpha}$, the other natural renal prostaglandin, caused only small and inconsistant effects on renal vascular resistance. These data show that the endoperoxide analog is an extremely potent renal vasoconstrictor substance, having about 1/2 the potency of NE. PGE_2 was a renal vasodilator and $PGF_{2\alpha}$ had little effect. Results of this study suggest that prostaglandins and endoperoxide intermediates of renal origin exhibit a wide spectrum of activity on the renal vascular bed.

ULTRAMICROVASCULAR SURGERY. J.M. Fein. Department of Neurosurgery, Albert Einstein College of Medicine, Bronx, New York 10461

Bypass grafts between extracranial and cerebral cortical arteries, approximately 1,000 microns outer diameter (o.d.), may augment cerebral blood flow in brain at risk of cerebral ischemia. Ultramicrovascular surgery has been developed to broaden the potential applications of neurovascular procedures. This has required modification in suture materials and techniques and in the use of ancillary aids to prevent suture line thrombosis. Successful arteriotomy repair has been achieved in 46% of arteries 400-750µ o.d. Patent end to side bypass grafts have been achieved in 36% of dog cortical arteries 400-900µ o.d. Hypertrophy of the graft has been documented in selected instances, but is important if effective augmentation of flow is to be achieved. In 4 ultramicrovascular grafts <900µ o.d. the percentage rate of hypertrophic growth was significantly greater than in 5 grafts >1,000µ o.d. Future attention will be directed at means to stimulate this post-operative change.

TISSUE PERFUSION IN GUINEA PIGS DURING EARLY BURN SHOCK. J.L. Ferguson*, G.F. Merrill*, R.R. Wolfe, H.I Miller, and J.J. Spitzer, Dept. of Physiology, L.S.U. Medical Center, New Orleans, La. 70112.

Experiments were performed on 10 control and 10 burned guinea pigs to determine changes in tissue perfusion 15 and 75 minutes after a 70% body surface area scald. Flow determinations were made using three differently labeled 15μ microspheres. Cardiac output and tissue perfusion were unchanged in the control group. In the burned animals cardiac output (thermal dilution) decreased from 297±13 (pre-burn) to 169±21 and 127±13 ml/min at 15 and 75 minutes post-burn, respectively. Tissue perfusion was altered as seen in the following table:

% Cardiac output/gm of tissue (Mean ± SEM)

TISSUE	PRE-BURN	15' POST-BURN	75' POST-BURN
Brain	0.50±0.07	0.70±0.10	0.86±0.15
Heart	1.90±0.17	3.18±0.75	3.38±0.42
Liver (arterial flow)	0.04±0.01	0.08±0.02	0.19±0.04
Liver (portal flow)	0.65±0.07	0.71±0.10	0.64±0.07
Pancreas	0.77±0.15	0.63±0.14	0.40±0.08
Adrenal	1.29±0.21	1.85±0.28	3.46±0.73
Renal	3.33±0.40	2.44±0.38	3.30±0.45
Skin (burned)	0.22±0.03	0.11±0.02	0.02±0.01
Skin (non-burned)	0.32±0.07	0.25±0.03	0.15±0.02
Adipose tissue	0.36±0.08	0.26±0.06	0.20±0.04

Thus in early burn shock in guinea pigs, blood flow to the vital organs is favored, whereas the pancreas, skin, and adipose tissue receive a reduced portion of the already compromised cardiac output. (Supported in part by NIH Grant HL.07098 and ONR Contract N00014-74A-0054-0003.)

VENTILATORY RESPONSE TO A STEP DECREASE IN VERTEBRAL ARTERY CARBON DIOXIDE TENSION FOLLOWING CAROTID BODY DENERVATION. P.J. Feustel*, D.F. Donnelly*, E.J. Smith*, R.A. Berkman*, M. Taylor*, and R.E. Dutton. Dept. of Physiol., Albany Medical College, Albany, NY.

Slow recovery of ventilation during hypocapnic vertebral artery perfusion was attributed by us to domination of the central chemoreceptors by cerebrospinal fluid P_{CO_2} (Am J Physiol 217:1178, 1969). The present study was undertaken to determine the role of the carotid body in this sustained ventilation, and its implications for a peripheral chemoreceptor contribution to ventilation during CO_2 breathing. In 13 dogs anesthetized with Na pentobarbital, 53 perfusions of hypocapnic blood (P_{CO_2}<11 mmHg) were made into the vertebral arteries. End-tidal P_{CO_2} was maintained at 56 mmHg. Six of these dogs had undergone carotid body denervation 7 days prior to perfusion. Following a 5 min CO_2 breathing period, perfusion of hypocapnic blood was started and maintained for 10 min unless apnea occurred or the perfusate blood supply was depleted. Ventilation, expressed as a ventilation ratio (VR) to the level observed during CO_2 breathing, dropped significantly by 10 sec in both intact and denervated animals. A carotid body contribution to ventilation could not be identified during the first 30 sec of hypocapnic perfusion, but was seen by 40 sec (intact VR=.90±.01 vs denervated VR=.87±.01)($P<.05$), and, thereafter, assumed a greater proportion of ventilation as recovery proceeded. At 40 sec, 87% of the ventilatory response to CO_2 persisted in intact dogs and 82% in denervated dogs. Depressed levels of ventilation (less than 1/2 air breathing control level) were reached during 14 of 33 perfusions in denervated animals, but in only 1 of 20 perfusions in intact animals. Thus, the carotid bodies appear to contribute significantly to the ventilatory output elicited by CO_2 breathing. (Supported by NIH Grant HL-12564)

EFFECTS OF DEXAMETHASONE ON ENDOTOXIN SHOCK, HYPOGLYCEMIA AND IN VIVO & IN VITRO GLUCOSE HYPERCATABOLISM. Dianne P. Figlewicz*, Bernard J. Buchanan and James P. Filkins, (Sponsored by C.N. Peiss) Department of Physiology, Loyola University, Stritch School of Medicine, Maywood, Illinois 60153.

The present study evaluated dexamethasone protection in endotoxin shock in relation to prevention of post-endotoxin alterations in glucose metabolism. Dexamethasone acetate (100 µg ip) reduced lethality in fasted male Holtzman rats from 70% and 80% to 5% and 10% at 4 and 8 mg Salm. enteriditis endotoxin/rat respectively. Dexamethasone (75 µg ip) ameliorated post-endotoxin hypoglycemia in fasted rats administered 5 mg of endotoxin such that while plasma glucose levels fell from 87 to 24 mg/dl in untreated rats, simultaneous administration of dexamethasone augmented plasma glucose levels from 85 to 129 mg/dl. Endotoxic glucose hypercatabolism as reflected in augmented oxidation of U-^{14}C-glucose to $^{14}CO_2$ was diminished to control levels by simultaneous administration of dexamethasone. Epididymal fat pads from endotoxic rats demonstrated enhanced U-C^{14}-glucose oxidation to $^{14}CO_2$; dexamethasone treatment in vivo reduced the glucose hypercatabolism. Dexamethasone added to post-endotoxin fat pads in vitro in concentrations of 100 and 200 µg/ml also significantly depressed the enhanced glucose oxidation. These data suggest that dexamethasone protection in endotoxin shock is associated with the prevention of hypoglycemia and glucose hypercatabolism. (Supported by USPHS Grant HL 08682).

ATP PROTECTION IN ENDOTOXIN SHOCK AND PRESERVATION OF GLUCOSE HOMEOSTASIS. James P. Filkins. Department of Physiology, Loyola Univ. Stritch School of Medicine, Maywood, Illinois 60153.

Exogenous ATP inhibits insulin-stimulated glucose transport by selective membrane phosphorylation (*J. Biol. Chem.* 249: 3170, 1974). Since insulin is intimately involved in both the lethality and altered glucose homeostasis of endotoxicosis (*The Physiologist* 18: 155, 1975), the present study evaluated the ability of ATP to reduce endotoxin shock lethality and to preserve glucose homeostasis. ATP-Mg++ iv (10µM/100gm) increased the LD_{50} for Salm. enteritidis endotoxin in male Holtzman rats (300 ± 10gm) from 1.8 to 6.0 mg/rat. Endotoxin (3mg iv, 5 hrs prior) produced a profound hypoglycemia (12 ± 4 mg/dl, N=10) which was prevented by co-treatment with ATP (78 ± 6mg/dl, N=10). ATP increased glucose tolerance to 400 mg glucose ip such that the glucose half-time was increased from 32.5 min (N=22) in controls to 66.8 min (N=17) with ATP. Treatment with ATP prevented the depression in gluconeogenesis induced by endotoxin as evaluated by the in vivo conversion of ^{14}C-alanine to ^{14}C-glucose. ATP reduced the oxidation of ^{14}C-glucose to $^{14}CO_2$ in vivo and also reduced post-endotoxin glucose hypercatabolism. These data suggest that exogenous ATP alters glucose homeostasis in a fashion compatible with inhibition of insulin action and thereby prevents both lethal endotoxin shock and the accompanying derangements in glucose homeostasis. (Supported by USPHS Grant HL 08682.)

ASZ(DCPB)

INTERACTION BETWEEN GONADOTROPIN AND THYROTROPIN PRODUCTION IN THE WHITE LEGHORN COCKEREL. W.E. FINDLEY* (SPON:C. Lu). Dept. of Zoology, Indiana University, Bloomington, Ind. 47401Δ

In order to examine the biological relationship between the production of gonadotropin (Gn) and that of thyrotropin (TSH), experimental designs which were subject to analyses of variance (ANOVA) were used. The various factors included hypogonadism-induced increases in Gn production due to unilateral or bilateral castration (H), hypothyroidism-induced increases in TSH production due to PTU administration (P), and hyperthyroidism-induced decreases in TSH production due to thyroxine administration (T). When hypothyroidism and hypogonadism were induced simultaneously, there was no interaction between target organ responses after 10 days of treatment. However, when increased TSH production was stimulated several days prior to increased Gn production, the degree of compensatory testicular hypertrophy was elevated (i.e. significant HP interaction). Depending on the conditions of the experiment, this increased hypertrophy was reversed by thyroxine (i.e. significant PT interaction). The thyroidal growth was generally not affected. The release, but not the sysnthesis, of Gn by the pituitary was consistently increased by thyroxine (i.e. significant T main effect). Depending on the conditions of the experiment, significant interactions (i.e. HP, PT, and HPT) were also present in the assays of pituitary Gn content. These results indicate that the production of Gn is subject to modification by the pituitary-thyroidal axis when TSH production is plateaued at an elevated level or is decreasing.

(Partial fulfillment of Ph.D. requirements at Indiana University).

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THE EFFECT OF PROLONGED ETHANOL CONSUMPTION ON SPONTANEOUS AGGRESSION AND WEIGHT OF REPRODUCTIVE ORGANS OF MALE MICE. E. A. Fink* and J. H. Ferguson. Department of Biological Sciences, University of Idaho, Moscow, Idaho 83843.

Indices of aggressive behavior were measured in paired male mice which were given tap water, 5 percent, or 15 percent ethanol as the only source of drinking fluid from 21 days to time of pairing at 35 days of age. The effect of prolonged 15 percent ethanol consumption on the weight of the gonads and accessory reproductive organs was evaluated.

A suppression of spontaneous-aggression was observed in both the 5 percent and 15 percent ethanol-treated groups. A significant reduction ($P < .005$) in the weight of the seminal vesicles, coagulating glands, and prostates was also observed in the 15 percent ethanol-treated mice, while testes weights remained unaffected.

The reduction in spontaneous aggression as well as the weights of accessory reproductive organs in the ethanol-treated groups is possibly the result of decreased testosterone activity or synthesis.

BMES

PACEMAKER-ELECTRODES IMPEDANCE AT PRACTICAL OPERATING POINTS. H. Fischler* and H.P. Schwan. Dept. of Bioengineering, University of Pennsylvania, Philadelphia, PA 19174

It is common practice to characterize metal electrodes in contact with electrolyte by an equivalent series resistance and capacitance. These parameters have been widely studied for biological electrodes at a.c. signals of varying strength and frequency.

But little work has been done on the time domain behavior of electrodes in general, and pacemaker electrodes in particular. Such work is needed to understand and evaluate their performance. The time dependence of the electrode potential resulting from applying a rectangular uni-phasic voltage pulse to the total system comprising electrodes immersed in saline, tissue impedance and generator output impedance, is considered. Analysis of the electrode potential allows computation of the impedance components of the electrodes. These depend on the material and construction of the electrodes and on the operating point set by the output stage of the pacemaker. Applying pulse signals of varying amplitude and durations, conforming with the pacemaker manufacturers' data, the operating conditions of the electrodes are studied and their correlation with the a.c. impedance results is examined. From the electrode potential form, the energy affecting stimulation can be integrated, along with that part which is lost on the electrode-electrolyte interface.

FLOW DEPENDENCE OF VENTILATION DISTRIBUTION AND CHEST WALL MOTION. M.S. Fixley*, C.S. Roussos* and L.A. Engel. Meakins Christie Laboratory, McGill University Clinic, Royal Victoria Hospital, Montreal, Canada.

Six seated subjects inspired 150 ml He boluses from FRC in 3 different ways: (i) with rib cage motion, contracting only the intercostal and accessory muscles (RC); (ii) with abdominal motion (Ab), associated with marked increase in transdiaphragmatic pressure (Pdi); and (iii) spontaneously (Sp). RC inspiration was controlled by avoiding increases in Pdi during inspiration of the first 500 ml. During VC expirations performed at <0.3 lps with a fixed thoraco-abdominal sequence, expired He concentration was measured at the mouth. The changes in slope of phase III of the alveolar plateau (S_{III}) thus reflected changes in topographical distribution of inspired gas. After RC inspirations at 0.3, .75 and 1.5 lps S_{III} was .03 ± .01 (mean ± 1 SE), .07 ± .01, and .09 ± .02%He/l, respectively. After Ab breaths at the same 3 flow rates S_{III} was not significantly different from zero. The Sp breaths produced slopes intermediate between RC and Ab inspirations: 0 ± .01, .02 ± .01 and .05 ± .02%He/l, respectively. Our results suggest that (i) gas distribution at FRC may be substantially altered independently of flow, the RC breaths favoring lung apices whereas Ab breaths distribute preferentially to lung bases. (ii) The flow dependent Sp distribution of inspired gas may be due to an increased contribution of intercostal and accessory muscles at higher flow rates. (Supported by the MRC of Canada and Kansas Lung Association).

EFFECTS OF HYPOPHYSECTOMY AND GROWTH HORMONE ON PROTEIN SYNTHESIS IN PERFUSED SKELETAL MUSCLE. K.E. Flaim*, J.B. Li*, and L.S. Jefferson, Dept. Physiology, Penn. State Univ., Col. of Med., Hershey, PA 17033

The role of growth hormone (GH) in regulating skeletal muscle protein synthesis in 200 gm rats was examined using a modified hemicorpus perfusion technique. Perfusion was achieved in the absence of red blood cells and protein synthesis measurements were made over short time periods (30-60 min). Perfusion flow rate was elevated to ensure adequate tissue oxygenation and 10x normal plasma levels of phenylalanine (Phe) were used to ensure rapid equilibration of external amino acid with intracellular pools. The physiological state of the system was tested by determination of muscle ATP and creatine phosphate and tissue oxygen consumption. Incorporation of labelled Phe, an amino acid not synthesized or catabolized by muscle, was used to determine protein synthesis. In hypophysectomized (Hypox) rats protein synthesis rates and RNA levels in gastrocnemius muscle decreased to 40% and 50% of normal levels respectively. In vivo treatment of Hypox rats with GH (250 µg/day) increased both protein synthesis and RNA. The maximum response compared to normals was reached after 5 days of treatment (protein synthesis = 50%; RNA = 60%). Protein synthesis relative to RNA also decreased in hypophysectomy (75% of normal) and was not completely restored (85% of normal) with GH. These data support the concept that GH control of protein synthesis in skeletal muscle is mediated both by an effect on tissue RNA levels and by an increase in ribosomal activity. However, GH replacement alone does not completely reverse the inhibitory effects of hypophysectomy on protein synthesis. (Supported by Grant #AM 15658 from NIH and by an award from the American Diabetes Association).

EFFECTS OF CONTINUOUS AND INTERMITTENT STATIC EXERCISE ON OXYGEN CONSUMPTION IN ISOLATED CANINE GRACILIS MUSCLE. S.F. FLAIM, S.H. NELLIS*, and R. ZELIS. Dept. of Medicine and Physiology, Penn. State Univ. Sch. Med., Hershey, PA 17033

Eight, isolated auto-perfused canine gracilis muscle preparations were used to compare the metabolic effects of static and intermittent isometric exercise on skeletal muscle. Stimulation voltage was varied by an integrating servo which maintained the gracilis muscle contractile tension, as measured by Statham tension transducer, equal to an external reference signal. Maximum contractile force (MCF) was predetermined for each muscle and static exercise tensions were maintained at 2.5%, 5.0%, 10.0%, or 20.0% of MCF. During periods of intermittent exercise, the muscle was made to respond to a square-wave reference signal at a frequency of 1 cycle per second. Tension alternated between 0 and 5.0%, 10.0%, 20.0% or 40.0% of MCF. All exercise periods were equal to 4 minutes in length. Data from each period of static exercise were paired to those for a period of intermittent exercise having an equal integrated time-tension index (ITTI). Gracilis muscle blood flow and arterial-venous oxygen contents were determined and muscle oxygen consumption ($\dot{V}O_2$) was calculated before and during each exercise period and systemic blood pressure was continuously monitored. Data were normalized in terms of percent change from control. Changes in ITTI corresponded to statistically significant changes in $\dot{V}O_2$ for the 3 lower levels of exercise (max. $p<.05$). No significant difference in $\dot{V}O_2$ was observed between static and intermittent exercise periods with the same ITTI (min. $p>.2$). These data indicate that the levels of oxygen demand which are stimulated in skeletal muscles subjected to equal periods of static and intermittent exercise with equal ITTI are similar. (Supported in part by NHLI grant HL-17853 and a PA Heart Assn. grant.)

CONTINUOUS CHANGES IN HYPOTHALAMIC THERMOSENSITIVITY DURING INDIVIDUAL BOUTS OF HIBERNATION IN MARMOTS (Marmota flaviventris). G. L. Florant and H. C. Heller, Dept. Biology, Stanford Univ., Stanford, CA. 94305.

In this study hypothalamic thermosensitivity of 3 marmots was characterized throughout entire bouts of hibernation. Hypothalamic temperature (T_{hy}) was manipulated with chronically implanted, water-perfused thermodes while rate of oxygen consumption was continuously measured. The threshold T_{hy} for eliciting an increase in metabolic heat production (MHP) was determined by repeated manipulations of T_{hy} at many points during hibernation. During entrance into hibernation lowering T_{hy} induced one of two thermogenic responses: 1) that associated with an increase in the T_{hy} MHP threshold, and 2) that during which T_{hy} threshold continued to decline. Over the range of body temperatures (T_b) from 36°-16° the T_{hy} MHP threshold progressively declined and remained close to T_b. Between 16° and 12°, this threshold fell rapidly to 3°-5° but increased again to 7°-8° as T_b fell below 10°C. Throughout deep hibernation at an ambient temperature of 5°C, T_b plateaued near 7.5°C, but T_{hy} MHP threshold showed a continuous slow decline of .2 to .4° a day, until one day prior to arousal. Proportional regulation of T_b was demonstrable at all times during deep hibernation. The average proportionality constant for the MHP response to hypothalamic cooling during deep hibernation was 0.08 W/Kg°C, in comparison with 1.10 W/Kg°C during euthermia. Within a day before a spontaneous arousal was initiated, T_{hy} MHP threshold began to rise. These results demonstrate that the CNS regulator of T_b is continuously active throughout hibernation, but there are progressive changes in its thermosensitivity. (Supported by N.I.H. Grant NS 10367.)

BENEFICIAL EFFECT OF ARACHIDONIC ACID DURING HEMORRHAGIC SHOCK IN DOGS. John T. Flynn and Allan M. Lefer. Dept. of Physiology, Jefferson Med. College, Thomas Jefferson University, Philadelphia, PA 19107.

Arachidonic acid (AA), the precursor of bisenoic prostaglandins (PGs), was infused (120 μg/kg/min) into the vena cava of dogs subjected to hemorrhagic shock (HS) to assess the effects of stimulation of the prostaglandin synthetase system on the shock state. HS was induced by bleeding to a mean arterial blood pressure (MABP) of 40 mm Hg for 150 min followed by reinfusion of all remaining shed blood. In sham shock dogs receiving AA vehicle (0.1 M Na_2CO_3), there were no significant changes in MABP, superior mesenteric arterial flow (SMAF), renal arterial flow (RAF), PGE_2 or $PGF_{2\alpha}$ concentrations, or in cathepsin D or myocardial depressant factor (MDF) activities during the 250 min experimental period. Untreated HS dogs exhibited dramatic reductions in MABP, SMAF, and RAF during oligemia which were transiently restored following reinfusion, but markedly decreased 100 min after reinfusion. Cathepsin D, MDF, PGE_2 and $PGF_{2\alpha}$ values increased significantly in these dogs. AA given during oligemia did not prevent changes in SMAF or RAF, but maintained MABP at normal values after reinfusion. AA also significantly protected against the plasma accumulation of both cathepsin D and MDF in HS dogs. Circulating $PGF_{2\alpha}$ and PGE_2 values increased rapidly in AA treated dogs and plateaued at 3.6 and 4.8 times control values respectively during oligemia. HS dogs receiving AA and Na-meclofenamate, a PG synthetase inhibitor, were not significantly different from shock dogs receiving vehicle except that the circulating PG concentrations did not increase. Thus, products of the PG synthetase system appear to prevent the plasma accumulation of lysosomal hydrolases and of MDF, and may significantly preserve MABP during HS in the dog. (Supported by NIH Grant No. HL-17745).

EFFECT OF ACID SECRETION ON METABOLITE LEVELS IN GASTRIC MUCOSA.
J. J. Foley*, G. I. Moonsammy*, G. Sachs*, V. D. Wiebelhaus* & H. M. Sarau* (SPON: H. Saunders). Smith Kline & French Labs., Philadelphia, PA 19101 and University of Alabama, Birmingham, Ala. 35294

Metabolite levels were measured in defined parietal cell samples of dog gastric mucosal tissue at various stages of acid secretion to elucidate the primary energy source for maintenance of the secretory process. We have shown that the levels of ATP, ADP and phosphocreatine do not change with onset of or during histamine stimulated acid secretion. The sole change observed in pyridine nucleotide levels was an increase in NADH with secretion. These studies were extended to other metabolites to determine which of the various metabolic pathways are stimulated to account for the increased respiration accompanying acid secretion. Glycogen levels decreased reaching a new lower steady state level with initiation of secretion which is maintained during extended acid secretion suggesting a possible role for initiation but not for sustaining secretion. Glucose, G-6-P and F-6-P increased slightly while FDP increased several fold. Substantial increases occurred for glyceraldehyde-3-phosphate, dihydroxyacetone phosphate, 3-PGA, Pyr and Lac with secretion while the only decrease in the glycolytic pathway was PEP. The data is generally consistent with an increase in glycolysis through activation of phosphofructokinase. Kreb cycle intermediates citrate, isocitrate, α-KG, fumarate and malate all increased with secretion while succinate was unchanged, a metabolic pattern which indicates the activation of succinate dehydrogenase. Glycerol levels decreased while α-glycerol phosphate increased as did acetyl CoA and free CoA with acid secretion. The results are consistent with an increased flux through the Krebs cycle. The data indicate that the energy needed for acid secretion in canine mucosa is supplied by fatty acid oxidation with possible simultaneous increases in the glycolytic flux.

PHASIC CHANGE IN HUMAN CORONARY BLOOD FLOW WITH AORTIC INSUFFICIENCY. J. D. Folts, G. G. Rowe, D. R. Kahn, *G. M. Kroncke, * and W. P. Young. * Depts. of Medicine & Surgery, University of Wisconsin Medical School, Madison, Wisconsin 53706

We have previously shown that acute aortic insufficiency (AI) in chronically instrumented dogs produce a reverse in the normally high ratio of diastolic to systolic (D/S) coronary blood flow. Coronary flow with acute AI becomes high during systole and low during diastole, presumably due to the low diastolic pressures associated with AI. Right coronary blood flow was measured with an electromagnetic flowmeter in seven patients with severe AI and a dominant normal right coronary artery before and after surgical repair of the aortic valve. Before the valve was repaired the RCBF averaged 114 ± 32 ml/min and the D/S flow ratio averaged 0.86 ± 0.15. Mean arterial blood pressure (MABP) averaged 108 ± 18 mm Hg, heart rate 84 ± 19 beats/min, mean diastolic pressure averaged 70 ± 9 mm Hg. After the aortic valve was repaired with an average heart rate of 90 ± 15 and mean blood pressure of 105 ± 16 mm Hg the RCBF had increased to 170 ± 72 ml/min $p < 0.01$ with a D/S ratio of 2.2 ± 0.9 $p < 0.005$. Mean diastolic pressure averaged 84 mm Hg ± 16 after the valve was repaired. In all cases the RCBF increased after the valve was repaired. We postulate that the RCBF increased due to the improved diastolic perfusion pressure, and the change from predominantly systolic coronary flow to greater diastolic flow.

CALORIGENIC POTENTIAL OF RAT BROWN ADIPOSE TISSUE AND MUSCLE RE-EVALUATED FROM BLOOD FLOW MEASUREMENTS WITH TRACER MICROSPHERES. D.O. Foster * (Spon: O. Héroux), Div. Biological Sciences, Natl. Research Council of Canada, Ottawa, Ontario K1A 0R6.

Cardiac output (CO) and the fractional distribution of gamma-labeled, 15μ, tracer microspheres (3M Co.) injected into the left ventricle were used to calculate blood flow to the tissues of barbital-sedated, cold-acclimated (CA) or warm-acclimated (WA) rats at rest and during their maximal calorigenic response to infused noradrenaline (NA). In CA rats total flow to the major masses of brown adipose tissue (BAT; 5.24g/375g rat) increased from 2.4 ml/min (2.6% of CO) at rest to 57 ml/min (33.5% of CO) during infusion of NA. In WA rats flow to BAT (3.06g/400g rat) increased from 0.85 ml/min (1.0% of CO) to 13 ml/min (11.1% of CO). Total flow to skeletal muscle increased in CA rats from 10 ml/min at rest to 14.7 ml/min during infusion and it increased in WA rats from 10.9 ml/min to 14.7 ml/min. A comparison of the fractional distribution of $^{86}Rb^{+}$ to that of simultaneously injected microspheres indicated that previous studies in which blood flow during NA-mediated calorigenesis in CA rats was estimated with $^{86}Rb^{+}$ could have underestimated flow to BAT by as much as 10 times and overestimated flow to muscle by 2-3 times. From the new estimates of flow it may be calculated that BAT might account for about 2/3 of the metabolic response of the CA rat to NA, while muscle could account for no more than 20%.

THE EFFECT OF GAS DENSITY ON THE FREQUENCY RESPONSE OF PRESSURE TRANSDUCERS USED IN RESPIRATORY MEASUREMENTS. G. Francis*, R. Gelfand* and R. Peterson.* (SPON: D. Y. Cooper). Institute for Environmental Medicine, University of Pennsylvania, Phila., Pa. 19174

The effects of gas density on dynamic responses of four pressure transducers commonly used for measurements of ventilation and transpulmonary pressure in environmental extremes were experimentally determined over an air density range of 1.2 to 25.0 g/l. Each transducer was driven with a variable frequency sinusoidal pressure source over a frequency range of 3 to 70 Hz. The pressure reference was a catheter-tip transducer with a natural frequency of 35 KHz (Millar, Inc.). The pressure transducers evaluated were: Statham P23Dd, Medistor P-11, Validyne DP-45 and DP-103. The frequency response of the Statham P23Dd was predominantly a function of the characteristics of the connecting catheter. As gas density increased, the resonant peak of this system became more pronounced and shifted to a slightly higher frequency, illustrating a decrease in damping. The dynamic responses of both the Validyne DP-45 and the Medistor P-11 were found to be lowered by an increase in gas density. These transducers exhibited linear relationships between the resonant frequency and the inverse of the square root of the density. Increasing gas densities had no noticeable effect on the frequency characteristics of the Validyne DP-103. This was attributed to the fact that the DP-103 transducer is a highly damped system which does not resonate. These measurements show that increased gas density does not uniformly affect the frequency response characteristics of pressure transducers. (Supported by NIH grant HL-08899-12 and ONR grant N00014-76-C-0248 .)

ASZ(DCPB)

EVALUATION OF K^+-RICH ELECTROLYTE SOLUTION DURING EXERCISE IN HEAT. K.T.Francis *and R.MacGregor III, Dept. Physical Therapy and Biology University of Alabama in Birmingham, Birmingham, Alabama.

Potassium losses have been shown to be important in development of heat illness. K^+-rich solutions have been suggested as means of replacement of electrolytes lost during exercise in hot climates (Balakian, et. al). Exact replacement values needed to prevent depletion of body fluid K^+ during exercise in heat are unknown. It has been suggested that replacement solutions be twice the K^+ concentration of sweat (Schamadan, et. al). Both males and females of average age and fitness were exercised at 50% max. VO_2 for 2 hours at 31°C. Replacement fluids consisted of H_2O or a K^+-rich electrolyte solution (20 mEq/L-K^+, 20 mEq/L-Na^+). The comparison between subjects receiving H_2O or K^+-rich solution at each sample period (pre-exercise, 1 & 2 hr. during exercise and 1 hr. post exercise) resulted in no significant difference in Hct, Hb, serum protein concentration, serum Na^+, K^+ or Cl^-. The volumes and concentration of sweat electrolytes were unaltered by the use of K^+ rich solution as compared to H_2O replacement. The K^+-rich solution resulted in a doubling of the loss of total urine Na^+ and K^+ as compared to the H_2O replacement. The K^+ replacement therapy resulted in 35% reduction of the total body fluid Na^+ loss and no net loss of body fluid K^+. Therefore these results confirm that a replacement solution of 20 mEq/L of K^+ in a volume sufficient to maintain body water may function as a significant prophylaxis to heat illness. (Supported by U.A.B. Medical Center Faculty Research Grant) References: Balakian,G. and W.Englewood.Action Aid for Athletes. J.Med.Soc. New Jersey 67:517-522,1970. Schamadan,J.L. ,Lt.W.R.Godfrey, and W.D.Snively. Evaluation of Potassium-rich Electrolyte Solutions as Oral Prophylasix for Heat Stress Disease. Indust.Med.Surg., 677-684,Sept.1968.

LIVER FUNCTION IN HYPERTHERMIC RABBITS. H. Frankel, L. DePaola and W. Collier. Dept. of Physiology and Bureau of Biological Research Rutgers University, New Brunswick, N.J. 08903.

The effect of hyperthermia on liver function was studied by following the rate of disappearance of the dye indocyanine green(ICG) from arterial blood as well as ICG appearance in bile. Rabbits were maintained at a body temperature (T_b)of either 37-38°C (normothermic) or 41.5°C (hyperthermic). The $t_{\frac{1}{2}}$ for clearance of ICG from arterial blood was 246 seconds in normothermic and 150 seconds in hyperthermic rabbits given 10 mg/kg. This difference was statistically significant. There was not significant difference in rate of bile flow measured in the normothermic and hyperthermic animals. ICG administration depressed bile flow at both T_b. The percentage of injected dye dose that appeared in bile during the first 30 minutes following injection was significantly less in hyperthermic compared to normothermic rabbits given doses between 1 and 10 mg.kg. The possibility that increased temperature increased transport into the hepatocyte and retarded transfer within the hepatocyte or into bile canaliculi is under investigation. Research is supported in part by the Charles and Johanna Busch Fund and by a donation of ICG from Hynson, Westcott and Dunning).

PLASMA RENIN ACTIVITY AND BLOOD PRESSURE RESPONSE TO RENAL ARTERIAL HYPOTENSION IN DOGS WITH VARYING SODIUM DIETS. J.C.S. Fray, M.D. Johnson*, and A.C. Barger, Department of Physiology, Harvard Medical School, Boston, Mass. 02115.

The plasma renin activity (PRA) and systemic blood pressure responses to renal arterial constriction (RAC) were studied in conscious dogs on low Na (10 meq/day), normal Na (70 meq/day), or high Na (120 meq/day) diets. The animals were adrenalectomized, unilaterally nephrectomized, and chronically catheterized; the catheters were implanted in the aorta, vena cava, and renal artery distal to an externally inflatable constricting cuff through a lateral abdominal incision. Lowering renal arterial pressure to 50 mm Hg for 45 min induced a rapid and substantial increase in PRA and mean arterial pressure (MAP) when the animals were maintained on a low Na diet. Similar RAC caused only a modest rise in PRA and MAP in dogs on a normal Na diet, but did not affect PRA or MAP in dogs on a high Na diet. Calculated open loop gain was highest for the low Na dogs (-1.2) compared to that for normal (-0.7) and high (-0.1) Na dogs. The rise in MAP correlated well with the logarithm of the rise in PRA ($r = 0.7$). Converting enzyme inhibitor (SQ 20,881) at 45 min reversed the elevated MAP observed during RAC in the low and normal Na dogs. Although numerous reports have suggested that animals on low sodium diet have decreased sensitivity to infused angiotensin II, our observations strongly suggest that the renin-angiotensin system becomes quantitatively more effective in the regulation of blood pressure as Na intake is reduced.

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EVIDENCE OF AIRWAY CLOSURE AT POSITIVE TRANSPULMONARY PRESSURES IN EXCISED RAT LUNGS. D.G. Frazer*, P.W. Stengel*, and K.C. Weber, Appalachian Laboratory for Occupational Safety and Health and Dept. of Physiology & Biophysics, WVU Medical Center, Morgantown, WV 26506

Excised rat lungs were ventilated in a temperature-controlled, air-filled plethysmograph. Six different pressure-volume (P_L-V_L) curves were recorded for each lung. Each curve consisted of a 4-cycle sequence in which the minimum pressure $P_{L(min)}$ for cycles 1, 2, and 3 was either +6, +4, +3, +2, 0, or -5 cm H_2O. The lungs were inflated-deflated at a rate of 3.82 cc/min and prior to each sequence the lungs were degassed in a vacuum jar. In cycle 1, lungs were inflated from 0.0 to 30 cm H_2O ($P_{L[max]}$) and deflated to $P_{L(min)}$. During cycles 2 and 3, lungs were inflated-deflated between $P_{L(min)}$ and $P_{L(max)}$. On cycle 4 lungs were inflated to $P_{L(max)}$ and deflated to -5 cm H_2O. The volume of trapped air in the lung after four cycles was measured at -5 cm H_2O (Vm) and divided by the maximum lung volume in cycle 4 ($V_{L[max]}$). $Vm/V_{L(max)}$ is proportional to the amount of bubbles generated in the lungs during inflation (Fed. Proc. 33:1494, 1974). To produce bubbles airways must functionally close so that menisci are formed across the airways; i.e., if airways remain open a foam cannot be generated. Examination of P_L-V_L sequences showed that $Vm/V_{L(max)}$ started to increase, i.e., a foam was generated, as $P_{L(min)}$ was lowered to between +3 and +4 cm H_2O indicating that the airways were beginning to close at these positive transpulmonary pressures. Approximately 1/2 the airways were closed at transpulmonary pressures above +2.0 cm H_2O.

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PREDICTION OF RESPIRATORY SYSTEM INPUT IMPEDANCE FROM 1 - 10,000 Hz BY SELF-CONSISTENT ANALYSIS. J.J. Fredberg and A. Hoenig*, Cambridge Collaborative, Cambridge, MA 02142

For the purposes of learning about pulmonary structure, interpretation of high frequency respiratory system impedance may be facilitated by implementation of a theoretical prediction of input impedance. Owing to the complex nature of the asymmetric branching of airways, current symmetric models fail to account for a variety of observations directly attributable to this branching asymmetry. Special classes of asymmetric structures can be successfully treated by a self-consistent analysis of input impedance. This self-consistent analysis, which assumes that small sub-units can be joined in an appropriate manner to simulate ever-larger branching structures, is also capable of incorporating the dynamic properties of the airways, including gas inertance and compliance; airway wall inertance, compliance, and resistance; viscous and thermal boundary losses of the gas; and a chest impedance. The airway units are composed of flared or uniform cylinders whose admittances add at bifurcations. This analysis has been successfully applied to models of asymmetric branching airways of adult and infant lungs and predicts trends which mirror those found in existing data. Wall properties and asymmetry are both found to be important at low frequencies ($\lesssim$ 1kHz), while it is the asymmetric nature of the structure which predominates at higher frequencies ($\gtrsim$ 3kHz). [Supported by Contract No. N01-HR-6-2901 of NHLI.]

CONTROL OF ALDOSTERONE IN SODIUM-DEPLETION: ROLE OF THE RENIN-ANGIOTENSIN SYSTEM. R.H. Freeman, J.O. Davis, G.A. Stephens*, and B.E. Watkins*. Dept. of Physiology, Univ. of Missouri, School of Medicine, Columbia, Missouri 65201.

Studies were conducted in conscious dogs subjected to either chronic (4-5 days) or acute (3-4 hr) sodium-depletion. Plasma aldosterone (PA), 141±60 and 126±41 ng/100 ml, and plasma renin activity (PRA), 26±2 and 29±4 ng/ml, were markedly elevated in chronically sodium-depleted dogs. Infusion of [Sar^1, Ala^8] angiotensin II for 210 min at 6 $\mu g/kg\ min^{-1}$ decreased PA to 39±8, 23±17, 20±8, and 45±28 ng/100 ml ($p<0.05$ for the first 3 values) after 30, 90, 150 and 210 min, respectively. Sixty min after infusion of the antagonist was stopped, PA returned to 136±56 ng/100 ml. Acute sodium-depletion (50 mg ethacrynic acid, i.v.) increased PA from 5±0.5 and 8±2 ng/100 ml to 16±1, 24±4, 30±2, 31±3 and 27±4 ng/100 ml ($p<0.05$) after 30, 60, 90, 120 and 180 min, respectively; PRA increased approximately 2-fold above control levels of 10±2 ng/ml. In a 2nd series of acutely sodium-depleted dogs, infusion of [Sar^1, Ala^8] angiotensin II for 30 min prior to ethacrynic acid did not significantly change either PRA or PA ($p>0.05$) although PA did tend to rise during analogue infusion; presumably, this slight rise in PA was due to intrinsic agonistic properties of [Sar^1, Ala^8] angiotensin II. PA did not increase further after ethacrynic acid with continued infusion of the antagonist for 90 min (range 10±1 to 13±5 ng/100 ml.) Sixty min after infusion of the antagonist was stopped, PA increased to 40±8 ng/100 ml ($p<0.05$). These data demonstrate that the renin-angiotensin system is the primary regulator of PA during both acute and chronic sodium-depletion.

VENTRICULAR FUNCTION DURING HEAT STRESS. M.A.B. Frey, R.A. Kenney, N.J. Davenport*. Dept. Physiology, Wright State Univ.Sch.of Med., Dayton, OH 45431, and Dept. Physiology, Geo.Wash.Univ.Sch.of Med., Wash., DC 20037

Changes in ventricular function have been studied during heat stress by systolic time interval analysis. Increased heart rate and venous capacitance, decreased arteriolar tone, and increased circulating epinephrine have been previously observed with increased skin (Ts) or core (Tc) temperature in man. In the present studies, 7 subjects, M&F, 22-35 yr, immersed their lower legs in water 42-44°C for 30 min; trunks and upper legs were enclosed in non-permeable plastic to prevent evaporative heat loss. Thus, an immediate increase in Ts would be expected to precede a moderately increased Tc. HR, R-R interval, left ventricular ejection time (LVET), pre-ejection period (PEP), PEP/LVET, and blood pressure were monitored periodically during heating and 15-min recovery. Oral temp. was recorded. The stress induced increased HR from 72 to 97 bpm. R-R and LVET were significantly decreased ($p \leq .05$) by 5 min--PEP was not decreased until 15 min. R-R and LVET were significantly increased by 1 min recovery but did not reach control level by 15 min--PEP, unaltered at 1 min, overshot control by 15. A small rise in SBP was maintained in heating and recovery. Oral temp. increased approx. 1°C, 50% dissipated by 15 min recovery. LVET's during heat stress were shorter than at similar HR's at rest. Regression of LVET on R-R through 30 min heating showed LVET=0.134 R-R + 145. This differs somewhat from the equations for recovery (LVET=0.089 R-R + 178) and the first 15 min heating (LVET=0.102 R-R + 170) and from previously reported (by others) equations for LVET in exercise. Results are consistent with some increase in sympathetic inotropy during mild heat stress and subsequent enhancement, possibly due to developing increase in Tc and/or epinephrine release.

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PULMONARY HEMODYNAMIC CHANGES DURING EXERCISE IN TEENAGERS UTILIZING A REBREATHING TECHNIQUE. M. Friedman*, K. Kovitz*, D. Miller*, and M.A. Sackner. Mount Sinai Medical Center, Miami Beach, Florida 33140

Utilizing a modification of a rebreathing method (Sackner et al.: Am. Rev. Resp. Dis. 111: 157-165, 1975) for estimation of pulmonary capillary blood flow ($\dot{Q}_c$), diffusing capacity (D_L), oxygen consumption ($\dot{V}O_2$), pulmonary tissue plus capillary blood volume (VTPC), and functional residual capacity (FRC), 17 high school male students were studied during exercise while seated on a bicycle ergometer. Measurements were obtained at rest and at increasing power outputs (200,500, 900, and 1200 Kpm/min). The rebreathing gas test mixture consisted of 0.3% $C^{18}O$, 0.5% C_2H_2, 10% He, 21% O_2, and the balance N_2. After 5 min. of exercise at a given power output, the subjects rebreathed into an anesthesia bag filled with 2.5 L of the test mixture for a sampling period of 10 sec. to avoid inaccuracies due to recirculation at higher cardiac outputs. Breathing frequency was maintained at 50/min to enhance gas mixing between the bag and lung during this short sampling period. Duplicate measurements were taken at each level of exercise and averaged. In over 90% of the measurements, the observed reproducibility was + 5% of the mean. All test gases were continuously sampled by means of a mass spectrometer and the analog signals were inputted into a digital computer that analyzed the samples at 21 times per sec. The following equations were derived:

Rebreathing DL_{CO} (ml/min.mmHg) = 24.7 + .01 x $\dot{V}O_2$ (ml/min) r = 0.73

Rebreathing DL_{CO} (ml/min.mmHg) = 17.3 + 1.3 x $\dot{Q}_c$ (L/min) r = 0.81

$\dot{Q}_c$ (L/min) = 6.1 + .008 x $\dot{V}O_2$ (ml/min) r = 0.87

No changes in VTPC and FRC were observed. The non-invasive rebreathing technique for estimation of pulmonary hemodynamic parameters with on-line data processing is a rapid and reproducible method for evaluation of the exercise stress test.

ULTRASTRUCTURE OF GASTRIC SURFACE EPITHELIUM: A COMPARATIVE STUDY. M.H.F. Friedman and Lolly M. Marchant*, (SPON: D.A. DeBias), Dept. of Physiology and Division of Electronmicroscopy, Philadelphia College of Osteopathic Medicine, Philadelphia, Pa., 19131.

The surface epithelium of the gastric mucosa was studied in 12 species of vertebrates by scanning electron microscope (SEM), transmission electron microscope (TEM), and light microscope (LM). In all species except the pigeon the surface epithelial cells (SEC) present a cobblestone appearance due to slight convex surfaces of cells compressed together. Among the species studied to date (from frog to man), all except the pigeon show regular distribution of gastric pits. The foveolae are most numerous in the rat, adjacent pits being separated by 3 to 6 SEC. In the monkey the pit mouths are widest and separated from eachother by 10 to 20 SEC. All SEC show microvilli, either short rounded knobs or elongated rods. The foveolae of the pigeon are situated on the tops of hillocks, each separated from adjacent hillocks by 50 or more SEC. The hillock constitutes an infolding of a ring of individual pits which empty into a central channel. The effects of erosive materials, ulcerogeric agents, and mechanical manipulation on the SEC will also be exhibited.

THE EFFECTS OF TRYPTAMINE ON EVOKED EXCITATORY POST SYNAPTIC POTENTIALS OF MUSCLE FIBERS OF THE LOBSTER WALKING LIMB. R.N. Friedman*, R.P. Shank*, and A.R. Freeman (SPON: R.W. Sevy) Dept. of Physiology, Temple Univ. Sch. of Medicine, Philadelphia, Pennsylvania 19140

5-Hydroxytryptamine (Serotonin, 5HT) has been shown to increase the amount of transmitter released at the crustacean neuromuscular junction upon excitatory nerve stimulation (Dudel, J., Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmak. 1965). We have studied the effects of 5HT analogs on the excitatory post synaptic potentials (EPSPs) recorded intracellularly from single muscle fibers in lobster (Homarus americanus) walking limbs. Our results indicate that tryptamine (1.0 mM), when superfused onto the muscle fibers during excitatory nerve stimulation, markedly depressed the EPSPs. In addition, we observed a potentiation of the EPSPs upon washing the tryptamine treated muscle fibers with an artificial sea water control solution. Tryptamine did not alter the conduction velocity of excitatory or inhibitory axons of the lobster. Preliminary studies show that tryptamine does not produce conductance changes in the muscle fiber and does not depress the excitatory action of glutamate iontophoretically applied to the muscle fiber. These observations indicate that tryptamine diminishes the release of transmitter from the presynaptic terminals. A number of possible mechanisms which may explain the potentiation observed after the wash are currently under investigation. (Supported by NIDA fellowship 05022-01).

ION TRANSPORT BY RABBIT COLON: EFFECTS OF CYCLIC AMP AND CALCIUM IONOPHORE. Raymond A. Frizzell, Dept. of Physiology, Univ. of Pittsburgh School of Medicine, Pittsburgh, Pa. 15261

Previous studies have suggested that (a) the short-circuit current (I_{sc}) across descending rabbit colon is normally determined by the rate of active Na absorption and (b) the active absorption of Cl is mediated by a Na-independent, electrically-neutral, anion exchange process involving HCO_3 secretion. Addition of cyclic AMP (7.5 mM) to the bathing media has no effect on Na absorption, but elicits electrogenic Cl secretion, doubles the I_{sc} and increases tissue conductance 40%. This response to cyclic AMP is precisely mimicked by the Ca ionophore, A23187 (0.1 μg/ml), added to the mucosal solution; however, A23187 has no effect on the cyclic AMP levels of colonic mucosa. The secretory response to Ca ionophore is abolished if external Ca concentration is reduced to 10^{-6}M with EGTA, but an immediate stimulation of secretion is observed when medium Ca is returned to control levels (10^{-3}M). In contrast, the response to cyclic AMP is not affected by reducing external Ca to 10^{-6}M. Addition of cyclic AMP elicits an increase in Ca washout from strips of colonic mucosa preloaded with Ca-45. These results suggest that elevation of intracellular Ca concentration is an effective stimulus for colonic electrolyte secretion and that cyclic AMP may act by releasing Ca from intracellular stores. (Supported by U.S.P.H.S., NIAMDD, #AM18199)

EFFECT OF ENDOTOXIN ON GLUCOSE UPTAKE BY THE ISOLATED FORELIMB OF THE DOG. P. A. Furr*, T. V. Peterson*, J. E. Dale*, L. B. Hinshaw and M. J. Keyl, Dept. of Physiology and Biophysics, Univ. of Oklahoma Health Sciences Center and V. A. Hospital, Oklahoma City, OK 73190.

The hypoglycemia of endotoxin shock has been postulated to be due, in part, to an increased utilization of glucose by peripheral tissues. The glucose uptake by the isolated innervated or denervated forelimb was determined in dogs before and after endotoxin administration. The results indicate that E. coli endotoxin per se does not increase the uptake of glucose by the forelimb. No increase occurred when the blood glucose concentration was normal or below normal. However, when endotoxin hypotension induced a significant hyperglycemia or when blood glucose concentration was elevated by exogenous glucose administration, an apparent increase in glucose uptake occurred. It is proposed that when the arterial blood glucose concentration is elevated, the glucose concentration of the interstitial space in the forelimb equilibrates with the glucose-rich arterial plasma. When the blood glucose concentration decreases, glucose-rich interstitial fluid is returned to the circulation, giving rise to a venous blood glucose concentration which exceeds the arterial blood glucose concentration momentarily. It is concluded that endotoxin does not increase the uptake of glucose by skin and muscle except that it causes a hyperglycemia secondary to an increased sympathoadrenal discharge in the shock state. If the dog is made sufficiently hyperglycemic, an apparent increase in glucose uptake occurs. (Supported in part by ONR #N0014-75-C-0843 and V. A. Hospital, Oklahoma City, Oklahoma).

FILTRATION AND REABSORPTION OF ENDOGENOUS LOW MOLECULAR WEIGHT PROTEINS IN THE RAT KIDNEY. R.G. Galaske* and J.B. Van Liew. Dept. Physiology and Medicine, SUNY and Veterans Administration Hospital, Buffalo, N. Y., 14215.

LMW proteins (MW<Alb.) constitute the major fraction of urinary proteins in the rat although their low concentrations in plasma have hindered an accurate description of the factors involved in their excretion by the kidneys. We have isolated five LMW protein fractions from the urine of male Wistar rats. These have been labelled (I^{131}) and injected intravenously (<2µg) into rats prepared for micropuncture of surface proximal tubules and collection of bladder urine. Rat IgG (Miles Laboratory) was similarly labelled and infused. Fractional fluid reabsorption was simultaneously assessed from inulin values. From specific activity of capsular fluid and plasma the sieving coefficient for each protein was determined and reabsorption was calculated from tubular fluid values. The Table compares mean values of sieving coefficients (S.C.), fractional reabsorption and clearance ratios (C_{LMW}/C_{In} x 100) of LMW proteins, IgG and endogenous albumin.

Fraction	IgG	Albumin	LMW				
MWx10^{-3}	150	69	45	35	23	12	2.5
S.C.	0.0054	.00039	0.50	0.30	0.75	0.42	1.00
Reabsorption (%)	90.6	84.0	92.9	84.1	93.0	96.4	97.0
C/C (%)	0.052	.0065	3.43	4.75	5.43	2.59	3.05

Discrepancies between filterability and molecular size are apparent over the range of proteins tested. Reabsorption of filtered proteins at these plasma levels is virtually complete. Clearance ratios of LMW proteins are particularly uninformative since they incorporate values for both filterability and reabsorption.

ALTERATIONS IN TISSUE NON-PROTEIN SULFHYDRYL COMPOUNDS FOLLOWING IONIZING RADIATION. M.J. Galvin, Jr.*, N.M. Bailey* and S.M. Reichard, Depts. Radiology and Physiology, Medical College of Georgia, Augusta, GA 30902.

The administration of glutathione and other SH compounds is known to increase the survival of animals exposed to lethal amounts of ionizing radiation. However, there is a paucity of information concerning the tissue levels of sulfhydryl compounds during the post irradiation period. It was felt that such knowledge would contribute to a better understanding of the pathophysiological alterations set in motion by this environmental stimulus. Data from these experiments indicate that profound changes occur in the distribution of sulfhydryl compounds in the spleen and kidney of irradiated rats.

Non-protein sulfhydryl (NPSH) compounds were determined in tissues of adult CF-Nelson rats using a modification of the method of Tietze. Rats were sacrificed at various time periods (15 min, 2 hr, 4 hr, 12 hr, 24 hr, 5 days and 21 days) after exposure to 650 R of x-irradiation. Livers, spleens and kidneys were rapidly removed at each time period and tissue levels were analyzed. In the spleen there was a significant increase in NPSH occurring as early as 15 minutes after exposure. In contrast to these changes, NPSH levels in the kidney remained stable for 24 hr, at which time they decreased sharply. In the liver no changes were observed during the post radiation period.

These results suggest that in addition to their pharmacologic role, glutathione and other SH compounds may be important in the physiologic response to radiation. Similar changes were previously observed in rats following exposure to trauma. It is possible that the alterations in the concentration of this body component reflect a common homeostatic adjustment by which the animal responds to harmful stimuli.

PULMONARY RESPONSES IN THE RHESUS MONKEY FOLLOWING INTRAVENOUS (I.V.) BRONCHOPROVOCATIVE CHALLENGE OF HISTAMINE, METHACHOLINE, $PGF_{2\alpha}$ AND CORRELATION WITH IMMUNOLOGICAL HYPERSENSITIVITY. G. Garay*, H. Carter*, M. Okada*, B. Vickery* and R. Weissberg* (SPON: R. Hill). Depts. Physiology and Pharmacology, Syntex Research, Palo Alto, Ca. 94304

A comprehensive investigation of pulmonary function has been undertaken in spontaneously breathing rhesus monkeys studied under inhalation anesthesia. Airflow ($\dot{V}$); tidal volume (V_T); intrapleural pressure were recorded on magnetic tape and analyzed on a breath-to-breath basis using a pulmonary calculator-computer to obtain respiration rate, dynamic compliance (C_{dyn}) and airway resistance (R). Monkeys were characterized by immediate-type hypersensitivity responses to intradermal antihuman IgE. A group of animals was selected containing very, moderately and mildly reactive monkeys. Dose related pulmonary responses to i.v. histamine (H) methacholine (M) and $PGF_{2\alpha}$ were obtained in this group of 17 monkeys by repeated testing over a period of months. The dose range for all compounds was 1.25-50 µg/kg. Pulmonary responses were characterized by decrease in $\dot{V}$, V_T, C_{dyn} and increases in respiration rate and R for all compounds. These responses could be blocked by i.v. bronchodilators such as isoproterenol (5-625 ng/kg) or PGE_2 (0.625-5 µg/kg). Both H and $PGF_{2\alpha}$ elicited changes in pulmonary mechanics that correlated significantly with the immunological status of the monkey, while M responses did not. Findings suggest that the bronchial tree of the allergic monkey is hyper-responsive to broncho-constrictor challenge. Certain features of this primate model resemble human atopic asthma suggesting that it might be useful for evaluating potential therapeutic agents.

PLASMA CORTISOL LEVELS DURING CEREBROVENTRICULAR PERFUSION OF CONSCIOUS CATS WITH ADRENERGIC AND CHOLINERGIC ANTAGONISTS. A. M. Garcy* and S. F. Marotta. Dept. Physiology and Research Resources Center, University of Illinois at the Medical Center, Chicago, IL 60680.

Much emphasis has been placed on the effects of the adrenergic and cholinergic systems in regulating various physiological activities (e.g. circulatory, etc.); however, the contribution of both these neural systems to the basal regulation of the hypothalamo-hypophyseal-adrenocortical (HHA) system is not readily known. The present study was undertaken to determine whether cerebroventricular perfusion with mock cerebrospinal fluid (CSF) containing nicotinic (mecamylamine; MEC), muscarinic (atropine; ATR), alpha (phentolamine; PHE) and beta (propanolol; PRO) blockers would affect the HHA system. Cats were prepared with left lateral ventricular and external jugular cannulae at least 7 days prior to use. Ventricles of non-stressed cats (5-9/grp.) were perfused with CSF for 30 min. (control period) and then for 80 min. with CSF containing adrenergic and/or cholinergic blockers. Jugular blood samples were taken at 30, 60, 90 and 110 (20 min. after IV ACTH) min. and the plasma analyzed for cortisol. These studies showed that perfusion with 1) MEC (0.8µg/min) and/or ATR (0.8µg/min) did not appreciably alter plasma cortisol levels; 2) PHE (1.0µg/min) caused 50-70% elevations in cortisol levels; 3) PRO (0.3µg/min) only caused 20-40% increases in plasma steroids; 4) a combination of PHE and PRO markedly elevated (60-90%) cortisol levels; and 5) four blockers simultaneously raised cortisol levels 45-70%. ACTH approximately doubled cortisol levels. These data suggest that the cholinergics play a minimal role in regulating the basal activity of the cat's HHA system, whereas the adrenergics exhibit a tonic inhibitory action on the hypothalamo-hypophyseal complex. (ONR contract NR 201-020.)

INTERSTITIAL FLUID COMPOSITION AS SAMPLED BY WICK CATHETERS IN SKELETAL MUSCLE. Lawrence P. Garetto* and Alan R. Hargens. Orthopedic Division, University of California and V. A. Hospital, San Diego, Ca. 92161

Interstitial fluid in the anterolateral compartment of the canine hindlimb was acutely sampled using wick catheters and insertion techniques which minimize trauma. The catheter was constructed from 1.0 mm (O.D.) nylon tubing tipped with a filamentous wick of braided Dexon. Introduction of the wick catheter into the muscle was facilitated by prior insertion of a Jelco I.V. Placement Unit. The i.v. unit was inserted just through the compartment fascia after which the sharp trocar was removed. The outer shielding tube was next advanced into the muscle tissue following lines of least resistance away from the fascial insertion point. The wick catheter was then passed through the length of the shielding tube and the latter was withdrawn, leaving only the wick catheter in the muscle. After placement, a slight suction was applied to counteract the normal negative tissue fluid pressure and to expedite sample collection. Only erythrocyte-free samples were analyzed. Total protein was assayed by microbiuret techniques in samples ranging from 5-10 nanoliters and 1-2 microliters as collected over a period of 1-2 hours. Total protein in muscle fluid ranged from 50-60% of that found in plasma. Our values agree with those obtained by Aukland and Johnsen (Acta Physiol. Scand. 91: 354, 1974) employing wholly-exposed nylon wick material in rat skeletal muscle. Thus, our tissue fluid samples have a higher protein concentration than that reported for lymph (30-40% of plasma) collected from dog hindpaw (Taylor, Gibson, Granger, and Guyton, Lymphology 6:192, 1973). (Supported by grant AM-18824 from USPHS.)

RELATION OF 24-h RHYTHMS OF TISSUE FREE FATTY ACIDS AND TRIGLYCERIDES TO THAT OF GLYCOGEN IN THE RAT HEART AND DIAPHRAGM. S.M. Garthwaite* and D.K. Meyer. Dept. of Physiology, Univ. of Missouri, School of Medicine, Columbia, Missouri 65201.

A 24-h rhythm of glycogen content has been described in cardiac muscle and the diaphragm of the white rat but the relationship of these rhythms to levels of other endogenous tissue substrates has not been defined. Glycogen (G), free fatty acids (FFA) and triglycerides (TG) levels were measured in heart and diaphragm of male Wistar rats at 4 h intervals during the day. Weight of stomach contents of the same rats was also determined as a measure of food consumption. The rats (150-300 g) were sampled after 2 weeks of entrainment 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 Circadian rhythm (CR) in heart glycogen was found as in previous studies with a peak at 0600 h and a nadir at 1800 h. Heart FFA and TG levels also showed a CR, but 180° out of phase with the glycogen rhythm. The peaks were at 1800 h and the nadir at 0600 h. Similarly a CR of diaphragmatic glycogen with a peak value preceding the cardiac peak by about 4 h was again demonstrated. However, the diaphragm FFA and TG peak values coincide with the G peak. In the unstressed animal these two muscle types, both active through the 24 h day exhibit different control mechanisms in the metabolism and storage of endogenous substrates. The diaphragm stores and depletes all three substrates in a pattern that in a general fashion corresponds to the feeding pattern of the rat while the myocardium tends to store lipids and deplete glycogen during that time when feeding activity is reduced and to deplete lipids and store glycogen when the feeding activity is maximal.
(Supported by NIH Grant HL 16041)

STUDIES ON THE SELECTIVE RELEASE OF FSH DURING THE EARLY MORNING HOURS OF ESTRUS IN THE RAT. Vernon L. Gay, Dept. of Physiology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261.

In the cyclic female rat both LH and FSH are released during the "critical period" on the afternoon of proestrous but a second phase of FSH secretion occurs during the early morning hours of estrus, including a period of several hours during which serum LH has returned to basal levels (Science 148; 75, 1974). Twenty-four hours prior to the period of expected preovulatory gonadotropin release, adult cyclic female rats were injected (i.v., ether anesthesia) with 1.0cc of an antiserum against estradiol (supplied by Dr. G.D. Niswender). Such treatment blocked the LH "surge", prevented ovulation and prevented both phases of FSH release. In a separate experiment either saline or an ovulatory dose of LH (NIH-LH S18, 12 ug/rat) was injected on the fourth day of the 5-day estrous cycle (24 hrs prior to the anticipated LH "surge"). Rats injected with LH ovulated during the subsequent night and serum FSH increased during the periovulatory period (3 AM) to levels (564 ± 41 ng RP1/ml) typical of that phase in the normal cycle. In such animals serum estradiol decreased 5-fold. In saline injected animals serum FSH remained low (199 ± 15 ng/ml). These data suggest that the positive feedback effects of circulating estradiol are necessary for both phases of FSH release. However, some of these positive feedback effects of estrogen on FSH release can be produced by properly timed injections of LH, suggesting that endocrine changes secondary to LH release and ovulation may be important stimuli for the selective release of FSH during the periovulatory period. (supported by PHS research grant HD 06664).

IDENTIFIED SEROTONERGIC NEURONS MODULATE FEEDING IN THE TERRESTRIAL MOLLUSC, LIMAX MAXIMUS. Alan Gelperin, Department of Biology, Princeton University, Princeton, N. J. 08540.

The metacerebral giant cells (MGCs) are a pair of identified serotonergic neurons located in the cerebral ganglia of Limax maximus and several other gastropod mollusks. The MGCs make synaptic connections with buccal neurons involved in generating the feeding motor program (FMP) which is the rhythmic motor output underlying feeding movements. The effect of MGC activation on FMP expression was assessed by stimulating the MGCs intracellularly while recording from buccal ganglion motor roots. MGC activity at 1/sec, a physiological frequency for this cell in Limax, occasionally produces a few cycles of FMP. Many cycles of FMP can be produced in the absence of MGC activity. The frequency of FMP triggered by lip chemostimulation can be increased by concurrent MGC activation. The synaptic potentials elicited in buccal ganglion cells by the MGCs are small (0.2-2.0 mV), show little facilitation and have half decay times of several seconds. These data suggest that the MGCs act to modulate the intensity of FMP expression.
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APPARENT CONSISTENCY OF TWO DYNAMIC MODELS FOR THE PRESSURE-FLOW RELATION OF THE LEFT VENTRICLE. D. B. Geselowitz, Dept. of Bioengineering, Pennsylvania State University, 328 Hammond Building, University Park, PA 16802

Suga and Sagawa (S-S) have proposed a model of the canine left ventricle which relates instantaneous pressure, P, and volume, V, (Circ. Res. 32:314, 1973; 35:117, 1974). According to their model $P(t) = E(t)\,[(V(t) - V_d)]$ where V_d is an experimental constant and E(t) is an experimentally determined function which depends on the state of the heart, but is invariant for a given contractile state. Elzinga and Westerfrof (E-W) have a proposed model for the cat heart which relates pressure and aortic flow, Q, as follows. $P(t) = H(t) - Z(Q)$ where Z is a linear operator representing the internal impedance of the pump and H(t) is a "hydromotive" pressure source (Circ. Res. 32:178, 1973). We have been able to show that these two disparate models are apparently consistent, at least for mean values, designated by a bar. For the E-W model $\bar{P} = \bar{H} - R\bar{Q}$ where R is 10 mm Hg/ml/sec. H was observed to increase with end diastolic volume, V_{ED}, while the source impedance remained constant. Manipulation of the S-S equation gives approximately $\bar{P} = \bar{E}(V_{ED} - V_d) - \hat{E}\bar{Q}$ where $\hat{E}$ is the area under E(t). This equation is exactly of the form of the (E-W) result with $R = \hat{E}$ and $\bar{H} = \bar{E}(V_{ED} - V_d)$. From the S-S data $E \approx 1$ mm Hg/ml/sec. Since stroke volume is approximately 10 times greater for the dog than for the cat while pressure curves are similar it is reasonable to assume that E is approximately 10 times greater for the cat, thus giving a value for R in agreement with that reported by E-W. The S-S model also predicts the increase of H with end diastolic volume.

ATP-MEDIATED CONTRACTION OF INTESTINAL BRUSH BORDER MICROVILLI. P. E. Giebel* and R. G. Faust. Dept. of Physiol., Univ. of North Carolina, Sch. of Med., Chapel Hill, N. C. 27514.

Partially demembranated brush borders from hamster jejunum were obtained by extraction with 1% (v/v) Triton X-100 in 60mM KCl, 5mM $MgCl_2$, 1mM EGTA, and 1mM dithiothreitol (DTT), pH 7.0. Electron photomicrographs revealed that only portions of the plasma membrane remained on the microvilli and that the core filaments and terminal web region were intact. When incubated for 10 min at 37°C with ^{14}C-D-glucose and ^{3}H-D-mannose in media containing 20mM Tris, 100mM NaCl or 100mM KCl, 10mM $MgCl_2$, and 1mM DTT, pH 7.4, preferential Na^+-stimulated binding of D-glucose to the partially demembranated brush borders occurred. Incubation at 37°C with di-Na ATP (10^{-4}M) in either 10mM $MgCl_2$ and 100mM NaCl or 10mM $MgCl_2$, 10mM $CaCl_2$, and 100mM NaCl (both in 20mM Tris, pH 7.4) caused the demembranated brush borders to contract. Electron photomicrographs revealed that the core filaments were protruding through the terminal web region. This effect did not occur when di-Na ADP was substituted for ATP, or with brush borders which were not demembranated with Triton X-100. Contraction appears to be associated with ATPase activity. It is possible that the contraction of the microvilli in the presence of ATP with mono- and divalent cations, together with Na^+-stimulated preferential binding of D-glucose, could play a role in the transport of actively transported sugars from the microvillar region (after movement across the plasma membrane) into the cytosol of the mucosal cell. Supported in part by NIH Grant AM 07998 and an NIH Fellowship AM 05240 awarded to PEG.

WHOLE BODY UTILIZATION AND RENAL TRANSPORT OF LACTATE DURING INTRAVENOUS INFUSION OF LACTATE IN DOGS. J.M. Ginsburg, D.H. Pashley, and D.K. George. Dept. Physiology, Medical College of Georgia, Augusta, Ga. 30902.

Renal tubular transport of D-Lactate (D) and L-Lactate (L) was measured by standard clearance methods in dogs anesthetized with pentobarbital. Arterial blood pH was controlled by adjustment of ventilation rate and CO_2 content of inspired air. Inulin clearance was used as a measure of GFR and renal plasma flow was measured by the direct Fick method with C^{14} labeled NMN. Plasma concentration was raised by infusion of sodium salts of L or mixtures of D and L in modified Ringer's solution. Whole body lactate utilization (Q) was estimated as the difference between the lactate infusion and renal excretion rates. During infusion of L renal reabsorption of L was 95 to 98 % complete and linearly related to plasma L concentration up to 10 μM/ml. Under these conditions both Q and renal utilization of L were also linearly related to plasma L concentration. At higher L concentrations both renal utilization and fractional reabsorption of L decreased, but Q did not. During infusion of D-L mixtures both Q and renal reabsorption of L were reduced significantly below levels observed during infusion of L alone. Under these conditions, D was reabsorbed at rates similar to that for L but its Q was half that for L. The data demonstrate significant, but unequal, Q rates for both isomers of lactic acid and suggests a competitive inhibition between the isomers for renal transport.

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EFFECTS OF HYPOTHALAMIC MAMILLARY REGION STIMULATION ON SERUM GLUCOSE CONCENTRATIONS IN THE RAT. Erika G. Gisel* and David L. Innes. Department of Physiology and Biophysics, Temple University Health Sciences Center, Philadelphia, Pennsylvania 19140

Studies on plasma glucose levels have suggested that the anterior and lateral hypothalamus, including the ventral medial hypothalamus (VMH), might be involved in central glucose regulation. To test this hypothesis, specific hypothalamic, limbic and thalamic nuclei were stimulated electrically using 36 gauge bipolar nichrome electrodes positioned stereotaxically within the rat brain. Femoral blood pressure was recorded polygraphically and serum glucose concentrations were measured before and after stimulation using a micro sampling technique. Blood samples were removed from the left carotid artery at 5, 10 and 15 min post stimulation. Stimulus parameters ranged from 0.01 to 0.1 mA using a 0.01 to 0.1 msec square wave applied at a rate of 50 Hz for 3 min. Serum glucose was determined by enzymatic estimation with hexokinase. Stimulation of either the right VMH nucleus or the right supramamillary (SUM) nucleus consistantly produced elevations in serum glucose concentrations 20% above pre-stimulation levels which peaked between 5-10 min after the onset of stimulation. This response occurred with both sodium pentobarbital and urethane anesthesia. Elevations in serum glucose concentrations were obtained in all instances following stimulation of either the VMH or SUM nuclei, regardless of the stimulation parameters employed. In contrast, stimulation of the dorsal amygdaloid and thalamic nuclei failed to produce any changes in blood glucose concentrations. These results suggest that at least one other hypothalamic nucleus may be involved in the central regulation of blood glucose.

BLOOD CADMIUM AND THE CONTROL OF BLOOD PRESSURE. Stanley C. Glauser, C.T. Bello* and Elinor M. Glauser. Dept. Pharm. & Med., Temple Univ. School of Medicine, Philadelphia, Pa. 19140

Previous experiments have shown that moderate elevations in blood cadmium (Cd) in animals induces hypertension due to increased cardiac output. Human hypertensive patients at necropsy had elevated liver and kidney cadmium. In this study normotensive patients (N) are compared with mild to moderate hypertensives (H). The N group had a blood pressure (BP) of 117±3.4/77.6±2.0 mmHg with a Cd of 3.4±0.5 ng/ml. H group had a BP of 159.8±4.4/102.5±2.3 mmHg with a Cd of 11.1±1.5 ng/ml. The H values are all significantly different from N values. Persons occupationally exposed to cadmium vapor (E) had a Cd of 6.7±0.8 ng/ml with a BP of 131.8±6.2/86.2±3.2 mmHg. With no family history of hypertension three of the eight persons in the E group were hypertensive. These values in the E group differ significantly from the N group values of zero hypertensives out of ten patients.Untreated hypertensives were divided into 2 groups and treated with either chlorothiazide (T) or guanethidine (G). T group pre therapy had BP of 154.3±7.3/100.3±4-1 mmHg with a Cd of 12.2±3.6 ng/ml. T group post therapy had a BP of 132.0±2.6/85.6±1.8 mmHg and Cd of 3.7±0.8 ng/ml. All the pre-post values differ significantly. G group pre therapy had BP of 174.8±5.6/106.0±3.8 mmHg and Cd of 9.3±1.0 ng/ml. G group post therapy had a BP of 146.5±7.1/96.0±3.6 mmHg and a Cd of 8.9±0.4 ng/ml. The systolic BP was significantly decreased post therapy while there was no change in diastolic BP or Cd. Comparison of post G and T groups showed significantly increased drop in Cd and diastolic BP with no significant change in systolic BP. Thus, elevation in Cd are, associated with elevations in the diastolic BP.

THE PARTIAL CHEMICAL NATURE OF A PANCREATIC CARDIOTOXIC FACTOR. R.D. Goldfarb and P. Weber*. Departments of Physiology and Biochemistry, Albany Medical College, Albany, N.Y. 12208.

The presence of a cardiodepressant factor of pancreatic origin has been reported in the plasma of experimental animals and man in a variety of shock states. Conflicting data concerning the exact chemical nature of this compound have appeared. Its activity is measured in the isolated cat papillary muscle assay system. The incubated pancreatic homogenate was used as a source of this factor, and after protein precipitation, ultrafiltration through 10,000 and 1,000 MW cut-off membranes, dialysis through 250 MW cut-off hollow fiber device and lyophilization, the residue was chromatographed on a Sephadex G-10 column in order to ensure the removal of all salts. The non-retarded material of the Sephadex column contained all the cardiodepressant activity of the filtered, dialyzed pancreatic homogenate and none of the salt content. Ashing of this fraction destroyed the cardiodepressant activity. Nonincubated pancreatic homogenates contained no cardiodepressant activity. To further isolate this factor, the active nonretarded G-10 fraction was applied to a cation exchange column (Aminex A-5) and eluted with a pyridine acetate buffer gradient (pH 2.85-4.85). The material eluted at pH 3.70 contained the cardiodepressant activity indicating the presence of positive charges in the cardiodepressant substance. Two dimensional thin layer chromatography (cellulose) revealed the presence of 5 ninhydrin positive spots in this fraction. Thus, it appears that the cardiodepressant activity in the pancreatic homogenate is associated with a peptide of 250-1000 molecular weight rather than with inorganic salt as suggested by Wagensteen et al. (J. Trauma 13: 181-194, 1973).

TESTICULAR BLOOD FLOW AND TESTOSTERONE SECRETION RATES IN NORMAL AND CRYPTORCHID RATS. W.R. Gomes, N.D. Kien* and R.L. Hamlin, Animal Reproduction Teaching and Research Ctr. and Department of Veterinary Physiology and Pharmacology, The Ohio State University, Columbus, Ohio 43210

Testicular blood flow (TBF) and testosterone secretion rates (TSR) were estimated in 44 mature rats. Twenty rats were made artificially cryptorchid by surgically translocating both testes to the abdominal cavity and 20 rats were sham-operated; 4 rats were used as unoperated controls. At 2, 4, 8, 16 and 32 days after surgery, blood flow and hormone measurements were made in groups of 4 cryptorchid and 4 sham-operated rats. Blood flow was measured by the relative uptake of ^{141}Ce- or ^{85}Sr- labeled microspheres. Testosterone concentrations in testicular venous and femoral arterial blood were measured by radioimmunoassay. TBF rates for 8 testes from unoperated rats were 17.8±6.2 ml/min/100g (0.34±0.08 ml/min/testis). Sham-operated testes averaged 16.9±3.3, 17.3±1.6, 17.0±7.4, 16.5±2.0, and 17.2±1.5 ml/min/100g for 2, 4, 8, 16 and 32 days, whereas TBF in cryptorchid rats was 37.4±14.9, 39.4±7.9, 50.8±13.7, 41.0±9.7, and 55.5±16.1 ml/min/100g, respectively. TBF in ml/min/testis averaged 0.60±0.25, 0.77±0.15, 0.56±0.12, 0.25±0.06 and 0.35±0.10 in cryptorchid rats. TSR were 1.70±0.59 ng/min/g of testis (3.16±0.93 ng/min/testis) for unoperated controls and 1.94±0.73, 1.99±0.46, 1.81±0.55, 1.95±0.36 and 1.61±0.98 ng/min/g for sham-operated controls at 2, 4, 8, 16 and 32 days. Values for cryptorchid rats were 2.71±1.34, 1.75±0.64, 0.80±0.24, 0.32±0.21 and 0.17±0.21 ng/min/g and 4.51±2.64, 2.81±1.32, 0.90±0.76, 0.21±0.22, and 0.11±0.09 ng/min/testis, respectively. Although testosterone concentration in the testicular vein is decreased by cryptorchidism, increased TBF maintains TSR for at least 4 days.

EFFECT OF INDOMETHACIN ON SKELETAL MUSCLE HEMODYNAMICS DURING PROLONGED ELECTRICAL SYMPATHETIC STIMULATION. R.R. Gonzalez, Jr. and E.D. Duke*, Dept. Physiology and Pharmacology, Loma Linda Univ. Sch. of Med. Loma Linda, CA 92354

It is well known that Prostaglandins (PG) can inhibit the effects of catecholamines on vascular smooth muscle. This series of experiments was completed to determine if the escape from sympathetic drive, that resting skeletal muscle exhibits, could result from synthesis and liberation of PG from the skeletal muscle. Mongrel dogs were anesthetized with 30 mg/kg pentobarbital sodium. Hind limb skeletal muscle venous outflow was isolated by tying off the lateral and medial saphenous veins, and by placing a tourniquet around the hock. Flow was measured from the femoral vein by a cannulating type electromagnetic flow sensor. Venous pressure was taken from a port in the flow transducer and arterial pressure from a catheter in the cranial femoral artery. The lumbar sympathetic chain was isolated and cut at the L4 level. The caudal stump was placed on platinum electrodes and stimulated (SS) at approximately 7 volts with 15 stimulations per second having a 2 msec duration. Prior to indomethacin (IND) administration, SS elicited a 75% increase in skeletal muscle vascular resistance for periods up to 20 minutes. Thereafter resistance decreased back towards prestimulation values until resistance was essentially back to control after 22 minutes of SS. After intravenous administration of 1-3 mg/kg IND resistance decreased towards prestimulation values after 30 minutes of SS. After 60 minutes of SS resistance was still only 50% of control. These data suggest that PG may be instrumental in skeletal muscle vascular escape to prolonged SS. (This study was partially funded by the Dept. of Surg., Loma Linda Univ. Sch. of Med. and the Walter E. Macpherson Society.)

DYNAMIC GEOMETRY OF THE LEFT ATRIUM IN THE INTACT DOG.
Douglas A. Gordon*, Ramesh Padiyar*, Irving Lipton* and Anastasios G. Tsakiris. University of Sherbrooke Medical School, Sherbrooke, Québec, Canada.

Multiple determinations of size, shape and diameter lengths of the left atrium during the cardiac cycle were made, under conditions of varied ventricular outflow resistance (controlled by the infusion of angiotensin and acetylcholine), in intact anesthetized dogs in which small radiopaque markers, chronically attached to the mitral annulus and the valve cusps, permitted visualisation of the atrioventricular junction. The measurements were made from left atrial angiograms (120 frames/sec) obtained after injections of contrast medium into the main pulmonary artery. With spontaneous sinus rhythm and normal aortic pressure maximal atrial area at the end of ventricular systole averaged 11.0 $\pm$ 6.4 cm^2 and emptying (area change) early in diastole averaged 43 $\pm$ 3%. When aortic pressure was increased average maximal area increased to 12.9 $\pm$ 3.7 cm^2 and emptying decreased to 25 $\pm$ 3% whereas, when aortic pressure was decreased, maximal and minimal atrial areas were similar to values obtained at control although cardiac output, heart rate and ventricular ejection fraction were considerably increased. Atrial contraction reduced atrial area by 24% during control and conditions of decreased aortic pressure and 18% when aortic pressure was increased, while the shape of the left atrial cavity did not change significantly under any of the conditions studied (average max. transverse diameter * average max. antero-posterior diameter: 1.3 $\pm$ 0.2). These findings suggest that atrial emptying may be near maximal at the resting state and that the atrium may possess only a small systolic reserve volume.

Transient Analysis of Intestinal Lymph Flow and "Secretion." D. N. Granger and A. E. Taylor. (Spon. M. D. Turner) Dept. Physiology, Univ. Miss. Med. Cntr., Jackson MS 39216.

In 15 anesthetized cats, lymph flow and "secretion" rate were determined from isolated autoperfused cat ileal preparations following either 1) constant infusion of Tyrode's solution (2.5 ml/min-Kg), 2) elevation of intestinal venous pressure to 30 mm Hg, or 3) exposure of the gut lumen to cholera toxin (10 gm %). Mean systemic arterial pressure, intestinal venous pressure, hematocrit, and plasma colloid osmotic pressure were monitored. Lymph flow (J_L) and "secretion" rate (J_s) were measured at 15 min intervals. Control mean values ($\pm$S.E.M.) for J_L and J_s in the venous hypertension group were 0.05$\pm$.01 and 0.00 ml/min-100 gm, respectively. Following elevation of venous pressure, J_L increased dramatically reaching a peak value of 1.04$\pm$.06 ml/min-100 gm (20X control) in 5 min, after which time a progressive decrease in J_L occurred. Concomitant to the rapid decrease in J_L was a rapid increase in J_s. At 240 min, J_L returned to its control value while J_s reached a value of 1.23$\pm$.05 ml/min-100 gm. In the plasma dilution group, J_L reached a peak value of 1.50$\pm$.11 ml/min-100 gm (38X control) in 40-60 min followed by a rapid decrease in J_L and concomitant increase in J_s. At 240 min J_L returned to its control value while J_s reached a value of 2.45$\pm$.29 ml/min-100 gm. Following cholera toxin challenge no significant changes in lymph flow were observed until 45 min. A maximum J_L of 0.15$\pm$.02 ml/min-100 gm (75% increase) was measured at 60 min. At 120 min "secretion" began and J_L = 0. A maximum J_s of .99$\pm$.08 ml/min-100 gm was observed at 240 min. This study indicates that the onset of intestinal "secretion" and the decline in lymph flow are highly correlated in the plasma dilution and venous hypertension groups whereas the lymph flow changes observed following cholera toxin challenge are not related to the onset of "secretion." (Supp. HL 15680)

GLUCOCORTICOIDS EFFECT ON BRAIN BIOGENIC AMINES LEVELS. J.N. Gray,* K.F.A. Soliman and C.A. Walker, School of Pharmacy, Florida A & M University, Tallahassee, Florida 32307

The levels of norepinephrine (NE), serotonin (5-hydroxy-tryptamine, 5 HT), dopamine (DA) and 5-hydroxindoleacetic acid (5HIAA) were studied in the cerebral hemisphere, cerebellum, midbrain, caudate nucleus and pons, in relation to the administration of glucocorticoids. Male Sprague Dawley rats were maintained under controlled light (12D:12L) and temperature (23 ± 1°C). The glucocorticoid dexamethasone (9α-fluoro-16α-methylprednisolone) was injected (2.0 mg/kg) and the animals were sacrificed at 1-hour intervals for 4 hours. DEX administration resulted in a significant change in biogenic amines content of the different parts of the brain studied. Dopamine concentration increased at least fourfold in the cerebellum and threefold in the pons by the third hour. In the midbrain, both NE and 5HT increased significantly ($P \leq .01$) by the second hour. Significant increase ($P \leq .01$) was noticed in the cortex NE level by the first hour and DA level by the third hour. In the caudate nucleus, there was no significant ($P \leq .05$) difference in the levels of any of the biogenic amines. The result of this experiment indicates that dexamethasone has a definite effect on the biogenic amine level of the different parts of the brain studied, except the caudate nucleus. The data indicate that glucocorticoids' effect on the body might be mediated by their effect on brain biogenic amine levels.
(Supported by a grant from NASA.)

EFFECT OF TRASYLOL ON PLASMA CONCENTRATIONS, BIOLOGICAL ACTIVITY AND IMMUNOLOGICAL HALF-LIFE OF GROWTH HORMONE IN RATS, R. E. Grindeland and S. Ellis*, NASA-Ames Research Center, Biomedical Research Division, Moffett Field, CA 94035

Plasmin digestion of rat and bovine growth hormone (GH) *in vitro* incurs an 85% loss of complement-fixing activity without loss of growth promoting activity. Thus, the aims of this study were to determine the effects of Trasylol, an inhibitor of plasmin and other trypsin-like proteases, on endogenous plasma GH titers, and biological activity and immunological half life of exogenous GH *in vivo*. Plasma GH levels (radioimmunoassay) of male rats given 100,000 KIU Trasylol/kg were unchanged from those of appropriate controls at 20, 60 and 180 min as were GH titers of fasted rats 45 min after 1 U insulin/kg (20,000 KIU Trasylol/kg). The effect of Trasylol on growth was determined by tibial assay in hypophysectomized rats. Epiphyseal growth of rats given 25 µg rat GH was inhibited 23 ($p<0.02$), 47 ($p<0.001$) and 83% ($p<0.001$), respectively, by 5-, 10- and 20 x 10^4 KIU/kg. Native bovine GH growth responses were inhibited 45% by 100,000 KIU Trasylol/kg and paralleled those of bGH + saline. Growth evoked by porcine, ovine and partially degraded bovine GH was inhibited 55-80% by 200,000 KIU/kg. By contrast the latter dose of Trasylol had no inhibitory effect on growth following injection of human GH, monkey (Rhesus) pituitary extract, plasmin-degraded rat GH or plasma from intact rats. Trasylol more than doubled the half life of native rat GH (5.5 vs 13 min), but did not change the half lives of either human or plasmin-degraded rat GH. These results indicate that dimeric growth hormones must undergo a protease-mediated transformation in order to express their growth activity *in vivo* and confirm that rat GH is secreted in a form modified from that of pituitary GH.

THE ROLE OF SURFACE POTENTIAL IN THE REGULATION OF TRANSEPITHELIAL Na TRANSPORT. S. Grinstein* and D. Erlij Dept. of Physiology, Centro de Investigación IPN México 14, D.F.

There is evidence suggesting that a potential sensitive component localized in the apical membrane of the frog skin participates in transepithelial sodium transport. Such a component should be sensitive not only to externally applied voltages but also to modifications in the surface potential of the apical membrane. To test this prediction we measured the effects of conditions which affect surface potential on the transepithelial sodium transport. Those conditions that increase the screening of negative charge and therefore depolarize the outer membrane are expected to have effects homologous to a depolarization caused by external current. Indeed, when the composition of the outside solution was modified by a) increasing ionic strength, b) adding polyvalent cations (La^{+++}, Co^{++}, Ni^{++}, Cd^{++}) c) lowering pH, an increase in active Na transport was detected. Moreover, the presence of small concentrations of polyvalent cations which screen the surface charge, markedly dampens or even eliminates the effects of pH or ionic strength on Na transport. These findings provide additional support for the existence of a potential sensitive component in the apical membrane of the frog skin, and offer a theoretical framework to explain the effects of numerous cationic agents on transepithelial transport that hitherto remained unexplained.

SPECIFIC TRANSPORT OF PROTONS AND CO_2 BY A HIGH MOLECULAR WEIGHT (3×10^6 daltons) PROTEIN. G. Gros and H. Gros (SPON: Donald Scott). Institut für Physiologie, Universität Regensburg, 8400 Regensburg, W-Germany.

The transport of protons in solutions of Lumbricus terrestris hemoglobin (Hb Lt; mol wt 3.2×10^6) was evaluated from studies of facilitated diffusion of CO_2, which has been shown to be due to equivalent fluxes of protons and bicarbonate. We measured steady state facilitated CO_2 fluxes across thin layers of Hb Lt solutions with an average pCO_2 of 2 - 3 torr and pH of 7.4. The facilitation of CO_2 diffusion in 7, 14, and 26 g% solutions of Hb Lt amounted to 110, 120, and 100 % of free diffusion, respectively. The proton fluxes underlying these facilitated CO_2 fluxes are greater than is expected on the basis of so far described mechanisms of proton transport: (a) free diffusion of H^+ can provide at most 1/1000 of the measured fluxes, and (b) facilitated H^+ transport by translational diffusion of Hb Lt can explain only 1/5 of the measured fluxes or less. This latter figure was obtained using translational diffusion coefficients of Hb Lt which were determined indirectly from measurements of facilitated oxygen diffusion in Hb Lt solutions (facilitated O_2 diffusion was 10 % of free diffusion in 7 and 14 g% solutions of Hb Lt, it was not detectable in 26 g% solutions). It is concluded that a third mechanism of proton transport acts in solutions of Hb Lt in addition to those listed under (a) and (b). Rotational diffusion of the large Hb Lt molecule may lead to a facilitation of proton transfer.

CARDIAC OUTPUT ESTIMATION IN HUMANS FROM RESPIRATORY MEASUREMENTS USING A COMPUTER MODEL OF PULMONARY GAS EXCHANGE

T. Grove*, J. Haywood*, M.D., G. Bekey, University of Southern California, Los Angeles, CA. 90007

Cardiac output, venous O_2 and venous CO_2 contents are estimated in human subjects using on-line measurements of expired O_2 and CO_2 concentrations and respiratory airflow. A mathematical model consisting of a dead space compartment, an alveolar compartment, a venous blood compartment and an arterial blood compartment is simulated on a digital computer. The model is driven by the measured airflow signal. Estimates of the desired parameters are obtained by minimizing a performance criterion based on the differences between measured and predicted expired gas concentrations. Results have been obtained from four catheterized patients using voluntary hyperventilation maneuvers to force the model. Resulting cardiac output estimates are compared with dye dilution or thermal dilution measurements. Dependence of results on various physiological parameters and on certain types of modeling errors due to pathological respiratory dysfunction are examined by means of simulation.

OXYGEN TENSION DEPENDENT MECHANICAL TENSION IN RABBIT AORTA. B. Grubb* and R.F. Coburn (Spon: A. Whereat), Dept. of Physiol., Sch. of Medicine Univ. of Pennsylvania, Philadelphia, Pa., 19174.

We have previously found evidence suggesting that the oxygenase involved in effects of altering organ bath PO_2 ($OBPO_2$) on mechanical tension of in vitro rabbit aorta strips is not cytochrome oxidase. This was based on (a) comparison of oxygen uptake-mechanical tension relationships ($\dot{V}O_2$-MT) during exposure of the strips to Norepinephrine, with graded changes in $OBPO_2$, and with graded [NaCN]; and (b) the finding that mechanical tension was still influenced by $OBPO_2$ after $[CN^-]$ which completely inhibited detectable $\dot{V}O_2$. We have now compared these data with data from experiments where tension was generated with 59 mM K^+. Norepi. (1×10^{-6} g/ml) and 59 mM K^+ resulted in equivalent increases in tension and in $\dot{V}O_2$. With 59 mM K^+ tension, variation of $OBPO_2$ from 300 to $\cong$ xero mm Hg, or variation of [CN] 0.05 to 2 mM, produced the same $\dot{V}O_2$-MT relationship. $\dot{V}O_2$-MT plots with graded $[CN^-]$ were similar in Norepi. tension and 59 mM K^+ tension experiments. But with Norepi. tension, for a given fall in $\dot{V}O_2$ resulting from lowered $OBPO_2$, much greater falls in mechanical tension occurred, than with 59 mM K^+ tension. Conclusions: (1) Since $\dot{V}O_2$ and presumably tissue PO_2 gradients were similar with 59 mM K^+ and with Norepi. tension, the data suggest that oxygen tension dependent mechanical tension is not due simply to changes in aerobic energy production. (2) The blunted effect of altering $OBPO_2$ on mechanical tension during 59 mM K^+ suggests a role of the surface membrane in transduction of oxygenase signals to contractile proteins. (3) The 59 mM K^+ data strengthen the hypothesis based on Norepi. experiments that cytochrome oxidase is not the oxygenase involved in oxygen tension dependent mechanical tension in rabbit aorta. Supported by HL 10331.

CANINE DUODENAL MUCOSAL NEUTRALIZATION OF ACID. N. J. Gurll* and J. W. Harmon* (SPON: R.J.T. Joy). Division of Surgery, Walter Reed Army Institute of Research, Washington, D. C. 20012

While much is known about the contributions of Brunner's gland, biliary and pancreatic secretions to the neutralization of gastric acid in the duodenum, the role of the duodenal mucosa itself has not been completely elucidated. We measured acid loss (ΔH^+) from 10 cm long duodenal Thiry-Vella fistulas (distal to Brunner's glands, bile duct, and pancreatic ducts) in 8 mongrel dogs. ΔH^+ was calculated from the amount of acid required to keep duodenal fluid pH at 2.0 using the pH-stat technique and a recirculating reservoir. Net fluxes for ions and volume were determined from changes in mass over consecutive 30 min study periods: control, after the topical administration of 10^{-4} M acetazolamide to the duodenal mucosa, and after the intravenous injection of $NaHCO_3$ 4 meq/kg. A duodenal-venous CO_2 gradient (ΔCO_2) was determined by simultaneous measurement of duodenal fluid and venous blood pCO_2. Inhibition of carbonic anhydrase with acetazolamide significantly reduced ΔH^+ from 1172 $\pm$ 117 to 993 $\pm$ 104 µeq/30 min ($p<.05$). This was accompanied by a fall in duodenal fluid Na^+ gain from 2394 $\pm$ 250 to 1874 $\pm$ 301 µeq/30 min and a decrease in ΔCO_2 from 7.2 $\pm$ 1.9 to -0.5 $\pm$ 2.1 mm Hg ($p<.05$). Induction of systemic alkalosis reversed these effects so that ΔH^+ increased to 1245 $\pm$ 105 µeq/30 min ($p<.01$), Na^+ gain increased to 2614 $\pm$ 391 µeq/30 min ($p<.01$) and ΔCO_2 increased to 11.1 $\pm$ 2.8 mm Hg ($p<.001$). There were no significant changes in the net gains of Cl^-, K^+, or volume. The responses of the duodenal mucosa to acetazolamide and alkalosis resemble those of other HCO_3^- secreting epithelia. This suggests that at least some of the duodenal mucosal acid loss is due to $NaHCO_3$ neutralization and that carbonic anhydrase is involved.

CHANGES IN EXTRAVASCULAR LUNG WATER CONTENT AFTER CORONARY ARTERY LIGATION IN DOGS. P.A. Gwirtz*, M.H. Gee and J.A. Spath, Jr., Dept. of Physiology, Thomas Jefferson University, Philadelphia, PA 19107.

Following thoracotomy in anesthetized dogs, we placed catheters to record pressures in the left common carotid artery, the pulmonary artery and the left atrium. We ventilated the lungs on 100% O_2 with positive inspiratory pressure at tidal volumes of 15 to 20 ml/kg and positive end-expiratory pressures of 2 to 5 cm H_2O. After 1 hour, we ligated the circumflex artery for 2 hours (5 dogs) or 4 hours (3 dogs). At the conclusion of each experiment, we excised the heart and lungs for measurement of myocardial creatine phosphokinase (CPK) activity in ischemic and non-ischemic left ventricular tissue and for determination of extravascular lung water content. No systematic changes occurred in any of the hemodynamic variables after 2 hours. CPK activity in ischemic cardiac tissue was not significantly different from CPK activity of the non-ischemic myocardium. Furthermore, extravascular lung water as grams per gram dry, blood-free lung (Qwl/dQl) averaged 3.55 ± 0.13 (S.D.) which is a normal value for dog lungs. After 4 hours of coronary artery ligation, mean arterial pressure decreased from an average of 148 to 124 mm Hg; heart rate decreased from 155 to 133 beats/min. Mean pulmonary artery pressure was unchanged, but mean left atrial pressure increased slightly (2 cm H_2O). The CPK activity of ischemic tissue was decreased 21% when compared to non-ischemic left ventricular tissue. The Qwl/dQl of lungs excised after 4 hours averaged 3.91 ± 0.14 which was significantly greater than the extravascular water content of lungs after 2 hours of coronary artery ligation. These results indicate myocardial cell damage occurs after 4 hours of ischemia. In addition, there appears to be an increase in net fluid filtration into the pulmonary interstitium in the absence of a change in pulmonary microvascular pressure.

HYPERINSULINEMIA AND ALTERED GLUCOSE HOMEOSTASIS AFTER RES DEPRESSION.
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The present study investigated the relationship between altered RES function, specifically of the hepatic Kupffer cells, and insulin-glucose regulation. Two models of RES depression were utilized in male Holtzman rats (300±20g): colloidal carbon blockade (CB) and acute lead (Pb) administration. CB 8 hr prior resulted in elevated basal fasting serum insulin (IRI-μU/ml) levels (41.8±6.3, N=6) compared to sham-vehicle injected (18.2±2.8, N=6) and uninjected controls (23.1±2.8, N=6). A 5 min ivGTT (400 mg) 8 hr after CB increased IRI to 115.0±10.5 (N=7) while sham and uninjected control levels were 29.2 ±2.0 (N=6) and 39.6±3.5 (N=5) respectively. Recovery of RES function 18 hr after CB returned IRI (27.9±2.7, N=8) to control levels (27.0± 2.3, N=6) and (26.8±2.6, N=4). Similarly, 4 hr after Pb iv basal IRI (15.2±2.1, N=8) were elevated over control levels (9.4±0.5, N=8). Pb also incremented glucose-stimulated IRI (235.5±17.4, N=8) vs. controls (34.6±4.7, N=8). CB and Pb sensitized rats to insulin-induced hypoglycemic convulsive deaths i.e., 1.0 U of insulin/rat produced 11% lethality in control groups (N=64), 100% lethality after CB (N=24) and 70% lethality after Pb (N=30). CB and Pb also increased glucose tolerance as shown by decreased half times of intravascular disappearance. Gluconeogenesis as measured by an iv alanine load was depressed after RES depression. These data demonstrate a hyperinsulinemia and altered glucose homeostasis with depressed RES function and suggest a novel role for the RES in hepatic modulation of insulin levels. (Supported by USPHS Grant HL 08682).

THE EFFECT OF SLEEP STATE ON INTERCOSTAL MUSCLE ACTIVITY AND RC MOTION.
R. Hagan,* A.C.Bryan, M.H.Bryan,* and G. Gulston*. Research Institute, Hospital for Sick Children, Toronto, Canada.

We have studied 10 infants relating the intercostal and diaphragmatic EMG to rib cage motion in active and quiet sleep. The intercostal and diaphragmatic EMG were recorded using surface electrodes placed in the 2nd intercostal space parasternally and the right 7th interspace in the mid clavicular line. EMG signals were filtered, rectified, and quantitated with a moving time averager. Rib cage and abdominal motion were monitored with separate magnetometer pairs. Sleep state was identified by behavioural criteria electroencephalogram and electro-occulogram. In all infants there was a marked decrease in both tonic and phasic intercostal EMG with no change or an increase in diaphragmatic EMG in active sleep compared to quiet sleep. This was accompanied by paradoxical motion of the rib cage during active sleep. The rate of inward distortion during inspiration appears to be linearly related to the ratio of the intercostal EMG to the diaphragmatic EMG. During active sleep there was marked variability of intercostal EMG activity. The rate of rib cage distortion affected both inspiratory and expiratory time suggesting an intercostal-phrenic reflex. We suggest that the variability of respiratory rate in active sleep is secondary to variability of intercostal muscle activity. Supported MRC Grant No. MA-5609.

MODULATION OF THE DEVELOPMENT OF SPONTANEOUS MAMMARY ADENOCARCINOMA : PREGNANCY ASSOCIATED FACTOR. Anwar A. Hakim. Depts. Physiol. and Surgery. Univ. Ill. Med. Center. Chicago, Illinois.

Serum from mice bearing transplantable spontaneous mammary adenocarcinoma(TSMAdCa) enhanced the growth of the tumor, whereas serum from mice immunized with TSMAdCa-associated glycoprotein retarde the growth of the tumor (Hakim, Surg.Forum, 26,175,1975). The present studies report on a pregnancy-associated factor (RAF). CF1 inbred,brother-sister (18-20g) mice were divided into: Female mice which were inoculated s.c. with: 1. $5x10^5$TSMAdCa cells. When tumors became palpable they were bred. These mice rarely became pregnant(5 out 25).The litters varied between 1 to 4 per mother, and the tumors regressed completely during pregnancy. 2. 0.1 ml of serum from normal mice, at the same time as in (1) the mice were bred. Eight out of ten became pregnant giving litters between 10 to 15 per mother. 3.Mice were first mated.When pregnant, animals were inoculated with the TSMAdCa cells,the animals expired within 48 hrs. 4. Mice were first mated, when pregnant, animals wer inoculated with serum from pregnant mice, animals survived. 5. Mice first treated with serum from pregnant animals, 72 hrs. later, they were inoculated with TSMAdCa cells. None of the animals developed tumor. 6. Mice treated with serum from normal mice, 72 hrs later they were inoculated with TSMAdCa cells. All the nice developed tumors. Male mice were treated with : 7. serum from pregnant mice. When inoculated with TSMAdCa cells, none of the mice developed the tumor, whereas all the male mice treated with serum from normal mice developed tumors. 8. Fetus homogenates were prepared and inoculated, s.c. 72 hrs prior TSMAdCa transfer. Only one out of 25 mice developed tumor. These results indicate a direct effect of pregnancy on the development of the mammary adenocarcinoma. They suggest the presence of a factor in the serum of pregnant animals which inhibits proliferation of the tumor.

CIRCADIAN RHYTHMIC POLYAMINE EXCRETION BY RATS WITH IMMUNOCYTOMA. F. Halberg, C.W. Gehrke*, H. Zinneman*, W.L. Nelson*, L. Cadotte*, A. Rosenberg*, L. Soong*, H. Bazin* and R.A. Good*. Dept. of Lab. Med. & Path., Univ. of Minn., Mpls., Minn. 55455.

Ten ~5 month old male LOU rats were housed in metabolic cages at 24°C and 50% relative humidity in a room lighted daily from 07^{00}–19^{00}. Six had been implanted subcutaneously with an immunocytoma. To prevent contamination of urine with food all rats were removed from the metabolic cages for feeding (with Purina rat chow) between 17^{15} and 18^{15} daily. Water was available at all times. 17 days after tumor implantation urines were collected manually every 4 hours for 24 h. Collection of 4-h urines using an automatic collector continued, on tumor-bearing rats only, for another 3 days. Urines pooled for consecutive 4-h spans yielded 24 pools in 4 days for tumor-bearing rats and 6 pools in 1 day for controls and were analyzed for putrescine, cadaverine, spermidine and spermine according to Gehrke et al. (J. Chromatography 89: 231–238, 1974). Control rats exhibited within-day changes of >300% in excretion of each polyamine during a single day. At all comparable times, excretory rates were lower in controls than in tumor-bearing animals ($P<0.01$). Bioperiodicity in rate of urinary excretion also was observed for all 4 polyamines throughout 4 days in rats with immunocytoma. Polyamine excretion increased prior to the daily meal and reached highest values soon after the onset of darkness. By least squares fitting of a 24-h cosine curve (Halberg et al., Physiol. Teacher 1: 1-11, 1972) statistically significant circadian rhythms were indicated for putrescine, cadaverine and spermine with acrophases at -330° (-301, -358), -305° (-285, -324) and -294° (-255, -333)--as potential markers in tumorous rats with a periodic light chain excretion, documented by more extensive longitudinal samples. Supported by USPHS(5-KO6-GM-1398-1-14), N.C.I. (1RO1-CA-14445-01) and Hoechst Italia, Milano, Italy.

ROLE OF ANGIOTENSIN II IN ALVEOLAR HYPOXIC VASOCONSTRICTION.
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The role of angiotensin II in the pulmonary vasoconstriction induced by alveolar hypoxia was investigated with the competitive inhibitor of angiotensin, saralasin acetate. Unilateral alveolar hypoxia was induced in dogs by ventilation of one lung with 100% N_2 through a double lumened endotracheal cannula while adequate systemic oxygenation was maintained by ventilating the other lung with 100% O_2. Pulmonary perfusion was monitored with xenon^{133} and external detectors. In 8 dogs perfusion to the test lung on room air prior to N_2 ventilation was 49.2% (SEM $\pm$ 3.8) of total lung perfusion. After 7 minutes of nitrogen ventilation, perfusion to that lung was 35.6% (SEM $\pm$ 2.9) of cardiac output ($p < .001$), a reduction of 27.5% (SEM $\pm$ 2.4). After infusion of 6-24 μg/kg/min of saralasin acetate, beginning 2 minutes prior to the alveolar hypoxic challenge and continuing through it, unilateral alveolar hypoxia continued to reduce perfusion to that lung by 28.8% ($p = .6$ from control). In two dogs a higher infusion of 60 μg/kg/min failed to reduce the alveolar hypoxic vasoconstriction and in two dogs a 15 minute infusion of 6 μg/kg of saralasin acetate prior to alveolar hypoxic challenge and continuing through it, still failed to inhibit alveolar hypoxic vasoconstriction. Thus, no role was demonstrated for angiotensin II in acute alveolar hypoxic vasoconstriction of the dog.

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FURTHER TESTS OF THE VALIDITY OF MICROSPHERE TECHNIQUES†. J.R.S. Hales* and W.J. Cliff* (SPON: L.B. Rowell). Ian Clunies Ross Animal Res. Lab., Sydney, and John Curtin School of Medical Res., Canberra, Australia.

Radioactive plastic microspheres (3M Co.) of 15 μm diameter, were injected into the left cardiac ventricle of the conscious rabbit; cinemicrographs of the microcirculation in ear chambers have been taken, & radioactivity was monitored: (1) 10-20s lapsed before spheres entered the field of observation, but this long circulation time is a reflection of either the type of tissue in ear chambers, or of the circulation at this microscopic level, because ear radioactivity reached its peak in 2s. (2) The final location was usually reached within 30s, but up to 50 min could be taken. (3) The total number of spheres visible 1-4h after injection had decreased by 20% within 5-25 days, however, radioactivity monitoring showed that the spheres were moving within the ear & not being lost. (4) Spheres lodged in end-arterioles or capillaries & therefore would provide a measurement most closely resembling 'nutrient' blood flow ($\dot{Q}$). (5) After a sphere had lodged, it usually behaved as a poorly fitting ball-valve, with RBC's squeezing past, or else it completely stopped flow, whereupon in 0-30s collateral flow appeared; thus, the effect of embolization appears to be negligible. (6) Platelets and white cells passed by the microspheres, not adhering at all, however, after 4 mths most spheres were extravascular & these were often partially surrounded by macrophage cytoplasm; the spheres were therefore biologically inert, at least to the extent of not adversely influencing the microcirculation. These observations further validate the use of microspheres for circulatory studies, but with the proviso arising from (1) & (2) above, that care must be taken in assessing fine details of the distribution of $\dot{Q}$ within an organ (as distinct from total $\dot{Q}$).

†A 22 min film is available.

UNCOUPLING OF RENAL BLOOD FLOW (RBF) AND GLOMERULAR FILTRATION RATE (GFR) AUTOREGULATION AFTER RENIN DEPLETION. J.E. Hall* and A.C. Guyton. Univ. Miss. Med. Ctr., Jackson, MS 39216

Autoregulation of RBF and GFR during changes in renal artery pressure (RAP) was examined in dogs fed a "normal" diet (Group 1, n=8) and in renin-depleted dogs (Group 2, n=11). Group 2 received 210 mEq sodium and 80 mEq potassium per day and daily injections of 5 mg deoxycorticosterone acetate (DOCA) for 21-28 days prior to the study. After a 60-90 min control period, RAP was reduced in steps from the control values of 124 ± 4 and 137 ± 3 mm Hg in Groups 1 and 2, respectively, to 100, 85, and 70 mm Hg and RBF and GFR were determined 15-20 mins after each step reduction in RAP. Renal venous plasma renin activity increased progressively as RAP was reduced in Group 1, but was undetectable even after RAP was decreased to 70 mm Hg in Group 2. Average RBF in Groups 1 and 2 was unchanged from the control values of 4.69 ± 0.35 (S.E.) and 4.70 ± 0.37 ml/min per gm kidney wt. as RAP was reduced to 100 or 85 mm Hg, and decreased to 90 ± 3 and 90 ± 6%, respectively, of the control values at a RAP of 70 mm Hg. In Group 1, average GFR was unchanged from the control value of 0.89 ± 0.06 ml/min per g kidney wt. as RAP was reduced to 100 or 85 mm Hg, and decreased to 90 ± 6% of the control value at a RAP of 70 mm Hg. In Group 2, GFR decreased from a control value of 0.79 ± 0.06 ml/min per g kidney wt. to 90 ± 3, 77 ± 5, and 58 ± 6% of the control value as RAP was reduced to 100, 85, and 70 mm Hg, respectively. These data indicate that renin depletion, caused by DOCA and a high salt diet, uncouples autoregulation of RBF and GFR as RAP is reduced. These data also support the hypothesis that the renin-angiotensin system participates in the stabilization of GFR during reductions in RAP, possibly by an efferent arteriolar mechanism. (Supported by NIH grants HL 11678 and HL 05050).

ASZ(DCPB)

NEUROTRANSMITTER REGULATION OF PROLACTIN RELEASE IN VITRO. T.R. Hall*, J.P. Advis*, C. Hodson and J. Meites. Dept. of Physiology, Michigan State Univ., East Lansing, MI 48824.

There are a variety of putative neurotransmitters (PN) found in relatively high concentrations in the mammalian hypothalamus (Ann. Rev. Physiol. 38:153, 1976). Experiments were designed to test the effects of PN on prolactin release from rat pituitaries in vitro. Paired pituitary halves were incubated alone or with the hypothalamus in 2 ml medium 199 (Difco) for periods of up to 6 hr. Acetylcholine (ACh), glycine (GLY), aspartic acid (ASP), histamine (HIS), atropine, pimozide (PIM), pchloroamphetamine (PCA) and pchlorophenylalanine (PCPA) were added to the medium in doses ranging from 1 ng to 10 μg/ml.

At these concentrations, none of the drugs directly affected prolactin release from pituitary halves, but all, with the exception of ASP, altered the hypothalamus-inhibited release of prolactin. PIM, a dopamine blocker, stimulated prolactin release, thereby confirming the dopaminergic inhibition of prolactin. Both PCA and PCPA further inhibited prolactin release, indicating a serotoninergic prolactin stimulatory mechanism. HIS marginally stimulated prolactin release from pituitary halves co-incubated with hypothalami, whereas both ACh and GLY further inhibited release of prolactin. The effects of all these drugs were proportional to the dose of the drug incorporated into the medium. The cholinergic inhibition of prolactin was further examined. Atropine, a cholinergic antagonist, blocked the effects of ACh. Pituitaries and hypothalami were incubated with PIM, PCA or PCPA together with ACh. PIM, but not PCA or PCPA, blocked the effects of ACh, indicating that the cholinergic inhibition of prolactin is mediated through the dopaminergic system.

CORONARY ARTERIAL pH AS A DETERMINANT OF MYOCARDIAL OXYGEN CONSUMPTION. Alden H. Harken,* Monty Woods,* and Ray A. Olsson. Division of Surgery, Walter Reed Army Institute of Research, Washington, D. C. 20012

The purpose of this study was to examine the effects of pHa on myocardial oxygen uptake ($M\dot{V}O_2$). In order to isolate and control the recognized determinants of $M\dot{V}O_2$, a perfused heart preparation was developed which permitted control of heart rate and pressure and flow work. The perfusion system allowed independent regulation of O_2, N_2 and CO_2 gas flows to a membrane lung and total control of coronary blood flow such that myocardial oxygen delivery (CaO_2 x flow) could be held constant ($\pm$ 1%) during 4 hours of perfusion. Blood temperature was maintained at 37.27 $\pm$ 0.07°C. Each heart was paced at a fixed rate and catheter decompression of both ventricles allowed collection of coronary venous blood. Seventeen dogs were studied. $M\dot{V}O_2$ was directly and significantly related to coronary arterial pH in all animals studied ($p<0.001$). The mechanism of altered $M\dot{V}O_2$ was evaluated in an additional eight dogs by relating ventricular contractility (dp/dt) and $M\dot{V}O_2$ to pHa in control, beta-blocked and potassium arrested hearts. Arterial pH did influence ventricular contractility and thus $M\dot{V}O_2$. This effect was mediated only partially by the synergistic effect of catecholamines and pHa. Basal $M\dot{V}O_2$ in the perfused potassium arrested heart was also sensitive to pHa. An increase in pHa of 0.1 will increase $M\dot{V}O_2$ by 10%. Arterial pH influences dp/dt and thus $M\dot{V}O_2$ and this is in part mediated by the synergistic effect of catecholamines. Basal $M\dot{V}O_2$ of the potassium arrested heart also responds to pHa. This study isolates pHa as a determinant of myocardial oxygen uptake and indicates that progressive alkalosis induces increased myocardial oxygen uptake which must be recognized in the treatment of patients with compromised myocardial function and regional areas of ischemia.

ASZ(DCPB)

LABELING NEUTRAL AND PHOSPHOLIPIDS IN THE RAT UTERUS: EFFECT OF ESTROGEN ON UTILIZATION OF PYRUVATE-3-14C. Julie W. Harris. Div. of Biological Sciences, Arkansas State University, State University, Ar. 72467.

The effect of varying periods (1-2Chrs) of in vivo 17β-estradiol treatment on the subsequent in vitro incorporation of pyruvate-3-14C into rat uterine lipids was examined. Throughout these time periods, estrogen accelerated pyruvate-3-14C incorporation into lipid. Further study involved the addition of supplemental sugar substrates to the incubation medium in order to ascertain the labeling pattern of pyruvate-3-14C into the uterine lipids. The addition of either glucose or gluconate to the incubation medium enhanced the incorporation of pyruvate into uterine lipids. Subsequent separation of uterine neutral lipids and phospholipids showed that differential synthesis of specific lipids did not occur after two hours of in vivo estrogen treatment. Separation of neutral lipids into major classes likewise did not show preferential labeling; rather there was a coordinate labeling in all classes. The conclusion was made that estrogen's acceleration of pyruvate incorporation into uterine lipid could be due to a concomitant effect on glucose metabolism.

PROBLEMS WITH THE SPONTANEOUSLY HYPERTENSIVE RAT (SHR) AS A MODEL FOR ESSENTIAL HYPERTENSION. C.J.Hart*, W.M.Manger, M.Hulse*, R.J.Weiss* and S.Dufton*. N.Y.U. Med. Ctr., N.Y. 10016

Certain abnormalities occurring in SHR are not evident in patients with essential hypertension. SHR have markedly elevated red blood cell counts and pronounced elevations of serum thyroid stimulating hormone. Recently we (F.S.Franco and Manger) as well as K.Nakamura found significant elevations of plasma adrenocorticotropic hormone in SHR; plasma corticosterone levels were unchanged. These elevations are not seen in essential hypertensives and suggest caution in assuming hypertensive mechanisms in SHR and man are similar. Furthermore, we have found significant variability in adrenal weights and their catecholamine concentrations among SHR and normotensive Kyoto rats (K) when obtained from different supply sources: New York University(NYU); Taconic(Tac); Cox.

Strain	Source	BP (mmHg)	Adrenal wt. (mg)	Epinephrine (mg/g)	Norepinephrine (mg/g)
K	NYU (5)	135±6	24.51±1.37	0.497±0.030	0.000±0.000
K	Cox (5)	121±4	21.61±0.95	0.241±0.050	0.025±0.004
K	Tac (5)	127±1	25.78±1.15	0.298±0.027	0.016±0.002
SHR	NYU (5)	173±3	17.96±0.93	0.885±0.065	0.020±0.008
SHR	Cox (5)	173±6	22.17±0.50	0.518±0.018	0.011±0.004
SHR	Tac (5)	178±6	22.47±0.78	0.376±0.022	0.021±0.002

Adrenal weights were significantly greater ($p<.001$) in K than in SHR from two sources but similar in rats from a third source. Adrenal epinephrine was greater ($p<.005$) in SHR than in K from three sources; norepinephrine was greater ($p<.02$) in SHR than in K from two sources but greater ($p<.05$) in K than in SHR from one source. Such variability can create problems in comparative studies of adrenal glands in SHR and K. (Partly supported by Inst. Rehab. Med. and Manger Fnd.)

EFFECT OF CELL SIZE ON LIPOLYSIS IN RAT ADIPOCYTES OF DIFFERENT DEPOTS. Arthur D. Hartman* and Dean W. Christ* (SPON: P. L. Hawley). Department of Physiology, Univ. Ill. Med. Ctr., Chicago, Ill. 60612

Lipolytic sensitivity to norepinephrine (NE) of adipocytes from epididymal (Epi), perirenal (Pr), subcutaneous (Sc), and mesenteric (M) adipose tissue depots was determined in rats of different size. The first group averaged 250 g and the second, 400 g. Complete dose-response curves to NE in the first group showed no significant differences in glycerol release per 10^6 cells between Epi, Pr, and M (cell sizes: 11.7 ± 2.6; 15.9 ± 3.8; and 6.4 ± 0.7 µg triglyceride/cell, respectively) whereas Sc showed a significantly reduced release of 1/3 - 1/2 of that in the other depots over the middle portion of the dose-response curve (cell size: 12.3 ± 1.6 µg triglyceride/cell). In the larger rats, cell size in the depots was 2- to 3-fold greater than in small rats except in the Sc depot, which showed no increase. In all depots except Epi, glycerol release per 10^6 cells in response to NE was significantly attenuated. In marked contrast, in the Epi depot, no alteration in the dose-response relationships was observed in spite of a 3-fold cellular enlargement. In the smaller animals, FFA/glycerol ratios were not significantly different between the depots. In the larger rats, these ratios were significantly reduced in the Epi and Pr depots compared to the smaller rats, but not in the Sc and M depots. These data indicate that the lipolytic response to NE is the result of a complex interaction between cell size, age, and anatomical location with no depot accurately reflecting metabolic activity of adipose tissue as a whole. (Supported by PHS AM-17660)

PRIMATE LARYNGEAL MUSCLES. M.H. Hast, Ph.D. and V. Sahgal, M.D.*
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The contraction time of primate laryngeal muscles varies from 14-56 m/sec. The ratio of fiber types differs in various muscles. In this study we present the effect of denervation on the thyroarytenoid and posterior cricoarytenoid muscles. Muscles were removed 1, 2 and 4 weeks after denervation and the tissue was processed for ATPase, DPNH, and electron microscopy. Morphometrics of the cytoplasmic organelles was performed by the methods of both Loud (J.Cell Bio., 1960) and Hally (J.Micro.Sci., 1964). THYROARYTENOID: One week after denervation there was a 20-30% increase in the mean mitochondrial area without significant change in the myofibrillary area. At 2 weeks, the mitochondrial area was unchanged while myofibrillary area showed a 40% decline. At 4 weeks there was 40-50% decrease in the mitochondrial as well as myofibrillary area. At this time splitting of the Z band and disruption of the I band was observed. POSTERIOR CRICOARYTENOID: This slow muscle, one week after denervation, showed a significant decrease in myofibrillary area while the mitochondrial area was normal. Two and four weeks after denervation both myofibrillary and mitochondrial areas decreased by 50-60% and at this time target fibers, myofibrillary disruption and alterations in Z band were observed. Histochemical reactions showed changes only in PCA. After 4 weeks, there was a decrease in the size of Type II fibers and target fibers were observed. These findings indicate that thyroarytenoid of fast muscle shows initial increase in mitochondrial mass and decrease in myofibrillary area while in PCA (slower muscle) there was simultaneous decrease of both mitochondrial and myofibrillary area.

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COMPARISON OF DIAPHRAGM ELECTRICAL ACTIVITY AND OCCLUSION PRESSURE IN CONSCIOUS GOATS. M. Haxhiu*, M.D. Altose*, S.G. Kelsen* and N.S. Cherniack. University of Pennsylvania, Philadelphia, PA 19104

Previous studies have shown that in anesthetized animals, the force produced by the inspiratory muscles contracting isometrically against an occluded airway correlates well with diaphragm electrical activity (EMG). However, cortical or reflex responses to occlusion not present during anesthesia could influence the relationship between diaphragm EMG and occlusion pressure. In the present study, changes in occlusion pressure were compared to diaphragm EMG under conditions of changing respiratory drive in six conscious goats. Drive was increased chemically by exposing the animals in separate trials to progressive hypoxia and hypercapnia produced by rebreathing techniques. Reflex increases in respiratory drive were produced by applying an inspiratory flow resistance (10 cm H_2O/L/sec). Diaphragm EMG was quantified by the moving average technique which allowed electrical activity and occlusion pressure to be compared during single breaths as well as over multiple breaths. Both diaphragm EMG and occlusion pressure increased with hypercapnia and hypoxia. At any given level of P_{CO_2} or P_{O_2}, occlusion pressure and diaphragm EMG tended to be greater in the presence of the inspiratory flow resistance. EMG and occlusion pressure changed proportionally both when measured during a single occluded breath and when peak occlusion pressure was compared to peak electrical activity of preceding unoccluded breaths. The results show that in conscious goats, there is a linear correlation ($r > 0.9$) between occlusion pressure and diaphragm EMG during hypoxia, hypercapnia and flow resistive loading and indicate that in conscious animals, occlusion pressure satisfactorily indicates changing respiratory neuron motor output.

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EFFECT OF THEOPHYLLINE ON THE MOVEMENTS OF SODIUM IN FROG STRIATED MUSCLE. E. T. Hays* and P. Horowicz. Dept. Physiology, University of Rochester, Rochester, New York 14642.

In freshly isolated frog sartorius muscle, sodium efflux is nearly equally divided between glycoside-sensitive and glycoside-insensitive fractions. External potassium activates the glycoside-sensitive fraction, while external sodium affects both the glycoside-sensitive and glycoside-insensitive fractions. 2mM theophylline produces about a 35% stimulation of the efflux of sodium into normal Ringer's containing both sodium and potassium. In the presence of $3X10^{-5}M$ strophanthidin most of the stimulation of sodium efflux response to theophylline appears to be abolished. In sartorius muscles application of strophanthidin and the removal of sodium results in a large reduction of the sodium efflux to 10-15% of its normal value. This remaining sodium loss or the residual sodium efflux is insensitive to the application of 2mM theophylline. When 2mM theophylline is applied to muscles in sodium-free lithium containing Ringer's fluid the per cent stimulation of sodium efflux is not significantly different from the stimulation obtained in sodium containing Ringer's fluid. In addition to its effect on sodium efflux 2mM theophylline causes about a 10% reduction in sodium influx. Thus the findings presented in this report indicate that the major effect of 2mM theophylline is a stimulation of the active transport of sodium out of the cell and that this stimulation of the active sodium transport does not depend on the presence of external sodium.

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A MODEL OF POTASSIUM EFFLUX DURING EXERCISE OF SKELETAL MUSCLE. Y. Hazeyama* and H.V. Sparks. (SPON: J.A. Faulkner) The University of Michigan, Ann Arbor, Michigan 48109.

Potassium is a vasoactive agent and is released from muscle cells during exercise. A simple diffusion model does not predict the time course of K^+ efflux during exercise which decreases as the exercise progresses. We used the concept of a Na^+-K^+ ion pump to account for the decreased efflux of K^+ during exercise. In our model, K^+ and Na^+ are actively as well as passively transported and Cl^- is transported only passively. Passive fluxes are calculated by the Goldman equation. Active fluxes are constrained to balance these passive fluxes at rest. The pump actively exchanges interstitial K^+ for intracellular Na^+ in the ratio of 2 K^+: 3 Na^+. Pump activity may change and is dependent on extracellular [K^+] and intracellular [Na^+]. During exercise interstitial [K^+] and intracellular [Na^+] increase due to action potentials. Hence, the pump activity increases and the uptake of K^+ by the cells increases and the net K^+ efflux decreases. The number of ions crossing the cell membrane is calculated and used to calculate the membrane potential. This potential and the interstitial and intracellular ion concentrations are used to calculate passive fluxes. The simulation was made using the Continuous System Modeling Program (IBM) and a digital computer. The simulated venous [K^+] was compared with data obtained from an isolated skeletal muscle preparation of dog hind limb (Morganroth et al. Am.J.Physiol. 229:38, 1975). The time course of K^+ efflux during 20 minutes of continuous exercise and after the exercise was predicted very well by the model. (Supported by USPHS grant HL-14516.)

SIMULATION OF LUNG TISSUE OXYGEN EXCHANGE USING SILICONE RUBBER CAPILLARIES. F.G. Heineken*, P.K. Predecki* and G.F. Filley. Univ. of Colorado Medical Center, Denver, CO 80220 and Univ. of Denver Research Institute, Denver, CO 80210

Capillaries of 7 and 12.5 μm diameter have been fabricated in silicone rubber in order to simulate lung tissue oxygen exchange conditions. Uniformly sized capillaries are obtained in a film of silicone rubber with a thickness of 75 μm. These capillaries have been perfused with whole blood treated with heparin. Oxygen transport studies have been carried out by perfusing the 12.5 μm diameter capillaries with saline in order to determine how rapidly oxygen will permeate the silicone rubber. Currently available oxygen microelectrodes with tip diameters of 3 to 5 μm have been used to measure continuously the Po_2 in the saline perfusing these silicone rubber capillaries. Analysis of the data obtained with the oxygen microelectrodes indicates that 1. oxygen will permeate the silicone rubber fast enough so that both the 7 and 12.5 μm diameter capillaries will simulate lung tissue oxygen transport and 2. oxygen will therefore reach blood perfusing these capillaries rapidly enough to allow reaction rates of whole blood with oxygen (θ) to be measured. (Supported in part by USPHS Young Investigator Pulmonary Research Grant HL 16195-01A1).

EEG DEPRESSION BY CARBON DIOXIDE ADDED TO OXYGEN AT HIGH PRESSURE. Franklin G. Hempel*, (SPON: H.A. Saltzman). Duke Univeristy Medical Center, Durham, North Carolina 27710.

When oxygen is breathed at 4 atmospheres absolute (4 ata), there is enough oxygen physically dissolved in plasma to accommodate the metabolic needs of the brain, and hemoglobin remains saturated in transit through the tissue. I have investigated the effect of high inspired carbon dioxide tensions on the EEG of the cat *cerveau isolé* preparation at 4 ata where any possible decrease in oxygen supply to the brain resulting from the Bohr shift or pH effect on hemoglobin oxygen affinity can be ruled out. Analysis of the EEG frequency spectrum showed no change on switching from 0.2 ata O_2 to 4 ata O_2. A mixture of 0.06 ata CO_2, 3.94 ata O_2 produced significant ($p < 0.05$) EEG changes with an 8% average reduction in voltage. Ventilation with 0.09 ata CO_2, 3.91 ata O_2 reduced all frequency bands to an average 72% of their control values in air. Drastic EEG depression accompanied inspiration of 0.2 ata CO_2, 3.8 ata O_2. The EEG assumed a low voltage profile, about 32% of its control level, and was typically represented by sporadic bursts superimposed on a quiet baseline. Exaggeration of the delta rhythm (2-4 Hz) seen with 0.2 ata CO_2, 0.8 ata O_2 did not occur here. With 0.6 ata CO_2, 3.4 ata O_2, the brain falls electrically silent. Resumption of oxygen breathing restores the EEG to control values. For any CO_2 tension, reductions in power occurred nearly equally at each of the 5 frequency bands, i.e., no significant differences prevailed among the 5 rhythms analyzed. I conclude that in the *cerveau isolé* cat, hypoxia may influence the EEG with hypercapnia at 1 ata (cerebral PvO_2 found as low as 30 mmHg) when comparisons are made to electrical activity at hyperbaric pressures (cerebral PvO_2 > 600 mmHg in these studies). Therefore, a specific effect of hypercapnia is uniform depression of all EEG frequencies. (Supported by grant HL 07896 from the NHLI)

ROLE OF NEUROMUSCULAR ACTIVITY IN CHONDROGENESIS AND OSTEOGENESIS. Dorothy H. Henneman, Downstate SUNY, Brooklyn, N.Y., D. Drachman, Johns Hopkins Med. Sch., Baltimore, Md., 21205.

Skeletal movement is essential for joint cavity formation, appearance of sesamoid cartilages and intra-articular ligaments, and articular sculptoring. Present studies examined the role of muscular contraction in chondrogenesis and osteogenesis by repeated intravenous injections of botulinum toxin or by a single injection of Coxsackie Virus A_2; both agents produce arthrogryposis (Drachman, et al, Arch Neurol 1976). Meckel's cartilage, dermal mandibular bones, vertebral bodies, long-bone epiphyses and long-bone metadiaphyses in 12-,15-, and 17-day old chick embryos were studied. Marked retardation of long bone early-endochondral osteogenesis occurred after either toxin or virus. Decreased collagen and mineral salts accompanied decreased ^{14}C-proline and ^{45}Ca incorporation in vivo and in vitro. Amino acid analyses of purified collagen and measurement of ^{14}C-hydroxylysine showed increased percentages of glycosylated hydroxylysine but normal percentages of hydroxylated proline and lysine. Increased glycosylation suggests retardation of normal maturation during mineralization. Hexosamine content, also elevated in the diaphyses further suggests failure to shift from chondrogenesis to osteogenesis. In contrast, dermal osteogenesis (jaw) developed normally. Vertebral endochondral development was unaffected. Thus skeletal movement appears to be essential for long-bone endochondral osteogenesis but not for dermal bone development. This may be of significance during fetal growth in general and during later remodeling and repair processes in particular.

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DEVELOPMENTAL CHANGES IN MEMBRANE FLUIDITY OF CULTURED MYOGENIC CELLS. B.A. Herman* and S.M. Fernandez* (SPON: R.D. Berlin). Physiology Department; University of Connecticut Health Center; Farmington, Connecticut 06032.

A novel approach, fluorescence relaxation microscopy, has been employed to study changes in membrane structure and dynamic state which occur during fusion and further development of myogenic cells in vitro. For this purpose primary chick embryo myoblasts, post-fusion multinucleated myotubes and fusion-arrested myoblasts (grown in the presence of EGTA) were labelled at different stages of development with 1-8-anilinonaphthalene sulfonic acid (ANS). Fluidity of the membranes is inferred from measurements of the mean rotational correlation time (ϕ) of the membrane bound ANS and from studies of nanosecond resolved emission spectra. ϕ is calculated with Perrin's equation from values of the static anisotropy (r) and the mean excited state lifetime (τ) of the probe as measured in single living cells or portions thereof. Our results reveal a monotonic decrease in static anisotropy from 1-7 days in the case of "normal" cells, whereas in the fusion arrested cells a steady increase in anisotropy is seen during the same period. In both cases, lifetimes increase during this time resulting in a relatively constant ϕ for the "normal" cells, but in a steadily increasing ϕ for the fusion arrested cells. This suggests a decrease in membrane fluidity in the latter case. A significant feature of this approach is that it combines the nanosecond time resolution with the spatial resolution afforded by the microscope. Thus, we have been able to observe heterogeneity in the dynamic behavior of ANS bound to different regions of a single myotube.

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CEREBRAL BLOOD FLOW AUTOREGULATION IN THE RAT: EVIDENCE FOR BREAKTHROUGH. M.J. Hernandez*, R.W. Brennan* and G.S. Bowman* (SPON: S.H. Nellis). Division of Neurology, Hershey Medical Center, Hershey,PA 17033.

The applicability of the albino rat for the study of cerebral blood flow (CBF) has been demonstrated in recent studies. However, CBF autoregulation (CBFA) to changes in perfusion pressure has not been previously reported in the rat. We have used a modification of the Kety and Schmidt technique employing ^{133}Xenon to measure CBF during induced alterations in mean arterial blood pressure (MABP). In 51 paralyzed adult Sprague Dawley rats passively ventilated with 70% nitrous oxide and 30% oxygen, CBF was derived by analysis of paired serial 20 ul samples of arterial, and of cerebral venous blood from the superior sagittal sinus, during desaturation. At a MABP of 121 ± 19 mm Hg, and a mean arterial pCO_2 of 36.2 ± 2.9 mm Hg, mean CBF was 103 ± 22 ml/min/100 gm of brain. CBF responses to hypercarbia were 4.91 ml/min/100 gm per mm Hg change in arterial pCO_2. CBF was measured during steady state levels of hypo- and hypertension induced by phlebotomy, or by intravenous metaraminol, over the MABP range of 48-205 mm Hg. CBF values were corrected for differences in arterial pCO_2. From a MABP of 80 to 160 mm Hg, CBF remained nearly constant, indicating the presence of CBFA. However, when MABP exceeded 160 mm Hg, CBF became pressure dependent, indicating a "breakthrough" of autoregulation in acute severe hypertension.

THE EFFECT OF pH, KCl, AND ATP ON CALCIUM TRANSPORT BY THE VESICULAR FRACTION OF VASCULAR SMOOTH MUSCLE. M.L. Hess and G.D. Ford. Dept. of Physiology, Medical College of Virginia, Richmond, Va. 23298.

A vesicular fraction capable of actively transporting calcium has been isolated by differential centrifugation from bovine ascending aorta. Calcium uptake (unidirectional calcium transport utilizing oxalate) was maximal at pH 7.0. This pH optimum was very sharp, falling approximately 2%/0.1 pH unit as the medium became more basic and 3%/0.1 pH unit as the medium became more acidic. Varying KCl in the incubation medium from 0 to 120 mM had no significant effect on the velocity of calcium uptake (range 10.0±0.1 to 13.7±0.5 μmoles Ca^{+2}/g-min) but was slightly depressed at 140 mM KCl. This depression was apparently an ionic strength effect since increasing the $MgCl_2$ an appropriate amount produced the same inhibition. 100 mM NaCl could be substituted for KCl without any appreciable effect on calcium uptake. Calcium binding (calcium transport in the absence of oxalate) was found to be maximal (39.64 μmoles Ca^{+2}/g) at 100 mM KCl and be significantly inhibited at concentrations below 80 mM KCl. The cyclic nucleotides GTP, UTP, CTP, and ITP could not be substituted for ATP as the energy source for calcium uptake. In contrast, calcium binding could be partially supported by nucleotides other than ATP in the following order of potency: ATP>CTP>ITP>GTP. At 5 mM $MgCl_2$, calcium uptake was found to be maximal at 5 mM ATP (134 μmoles Ca^{+2}/g) with substrate inhibition seen at 10 mM ATP. A similar spectrum of calcium uptake was found when Mg^{+2} and ATP were varied between 0.01 -10 mM with optimal uptake noted at 5 mM. A Lineweaver-Burke plot of 1/uptake velocity vs. 1/ATP yielded values of K_m (3.59×10^{-3}M) and V_{max} (25 $\frac{\mu moles\ Ca^{+2}}{g,min}$). This data supports the concept that the vesicular fraction is capable of serving as a sink and/or source of coupling calcium in VSM.

Possible Mechanisms of E. coli Endotoxin Action on Lipolysis in Human Fat Cells. I. Hikawyj-Yevich and J.A. Spitzer, Dept. of Physiology, Louisiana State Univ. Medical Center, New Orleans, La. 70112

E. coli endotoxin increases basal, but not norepinephrine (NE)-stimulated lipolysis in human omental adipocytes [Hikawyj, Roberts and Spitzer, Fed. Proc. 34, 465 (1975)]. This effect is not dose dependent (.032-.32 µg/0.5 ml cell suspension). Endotoxin does not influence cyclic adenosine 3',5'-monophosphate (cAMP) concentrations. Further studies were initiated to determine whether endotoxin is altering NE receptors or Ca^{++} fluxes in affecting its action on basal lipolysis. Human omental adipose tissue was obtained from abdominal surgery cases. Aliquots of isolated cells were pretreated with E. coli endotoxin (0.032 µg/0.5 ml cell suspension, Difco) for 10 min at 37°C. After washing, cells were incubated with different agents. Changes in free fatty acid (FFA) and glycerol (G) release were determined after 1 hr of incubation; cAMP levels were monitored after 10 min. of incubation. Propranolol (PR, 10^{-2}mM) had no influence on basal, and depressed NE-stimulated lipolysis as well as cAMP concentrations. Endotoxin did not alter PR actions. Phentolamine (PA, 10^{-2}mM) did not affect basal, and did not consistently enhance NE-stimulated lipolysis, whereas it further increased NE-stimulated cAMP levels. Endotoxin obliterated the PA effect on NE-stimulated cAMP levels. The divalent cation ionophore A23187, (10^{-2}mM) stimulated G, but not FFA release; its effect on G was additive with that of NE. Endotoxin did not influence ionophore actions on lipolysis. These results indicate that endotoxin is not altering the beta receptor, but may be affecting the activity or structure of the alpha receptor. Some of the similarities between the action of endotoxin and the ionophore, suggest that alteration of Ca^{++} fluxes may be--at least partially--responsible for the action of endotoxin on lipolysis. (Supported by ONR Contract #202-501)

HUMAN CARDIORESPIRATORY RESPONSES TO IMPULSES OF WORK DURING CIRCULATORY OCCLUSION. J.R. Hildebrandt and R.K. Winn*. Virginia Mason Research Center, Seattle, WA. 98101.

The ventilatory ($\dot{V}_E$) response to an impulse of work (2200 Kgm/min for 10 sec) superimposed on a background work level of 200 Kgm/min on a bicycle ergometer consists of a rapid component accounting for 16% of the total response and a slow, delayed component accounting for the remainder (J.A.P. 35:58, 1973). When the circulation to the exercising legs is occluded by thigh cuffs inflated to 280-300mm Hg., the rapid component of $\dot{V}_E$ is potentiated whereas the slow, delayed component is reduced to a variable degree. The time of occurrence of the impulse following the onset of occlusion (1 or 2 min) does not affect the response, thus the rapid component is probably not affected by the build-up of metabolites in the limbs but may be related to the relative sense of effort necessary to perform the work. The change in heart rate was depressed during occlusion probably due to the increase in blood pressure. On release of the cuff pressure, heart rate rose within 2-3 seconds in all but 1 subject. Within 10 seconds of cuff release, end tidal P_{CO_2} started to rise, reaching a peak in another 10 seconds. $\dot{V}_E$ started to rise 15 to 20 seconds following cuff release. This delayed rise in $\dot{V}_E$ suggests that the sole ventilatory stimulus in this situation was via known arterial and central chemoreceptors and that increased delivery of CO_2 to the lung does not stimulate ventilation. (Supported by grant HL 13233).

CANINE GASTRIC EMPTYING OF A DIGESTIBLE SOLID (RADIOACTIVE LIVER) SLOWED BY DEXTROSE SOLUTIONS. R.A. Hinder* and K.A.Kelly. Dept. of Surgery and Gastroenterology Unit, Mayo Fdn., Rochester, MN 55901.

^{57}Co cyanocobalamine (20 to 50 μc) was injected intramuscularly into calves and their livers harvested 24 hr later. Fifty-gm portions of the labelled liver diced into 1 cm cubes were fed to each of four fasted dogs together with 400 ml solutions containing ^{3}H PEG and either 1% dextrose (4 tests/dog) or 10% dextrose (4 tests/dog). A solution of 0.9% NaCl with ^{14}C PEG was perfused at 2.4 ml/min through the proximal limb of a chronically implanted, double-lumen duodenal catheter for 4 hr, while 2 ml samples of duodenal content were aspirated every 5 to 10 min from the distal limb at a site 10 cm aborally. The quantities of the markers in the duodenal aspirate were determined, and rates of gastric emptying calculated. Gastric emptying of liver was slow whilst the dextrose solutions were being emptied, and then speeded after they had emptied (Table). Since the 10% dextrose emptied more slowly than the 1% dextrose, the initial period of slow emptying of liver lasted longer when the liver was given with the 10% dextrose. Conclusion: Intragastric dextrose solutions slow gastric emptying of solid liver.

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	Liver, gm emptied† (SE) Hr after meal			Dextrose, % emptied† (SE) Hr after meal		
Meal	½	2	4	½	2	3
Liver and 1% Dextrose	4(1)	30(4)	43(3)	75(4)	99(0)	100(0)
10% Dextrose	1(0)*	6(2)*	26(6)*	26(2)*	76(3)*	97(1)

*Values differ from those above; $P < .05$.
†Means; n = 16.

MECHANISMS OF HYPOGLYCEMIA IN ENDOTOXIN SHOCK: ROLE OF THE BLOOD. L. B. Hinshaw, L. T. Archer*, B. K. Beller*, G. White*, and T. Schroeder*. V.A. Hospital and Univ. Okla. Health Sci. Ctr., Okla. City, Okla. 73104

The cause of death in experimental septic shock is associated with an imbalance between glucose uptake and production. Our recent work has demonstrated an accelerated uptake of glucose in the blood following endotoxin administration, with components of the buffy coat responsible for the increase. The purpose of this study was to determine factors instrumental in increasing glucose utilization by the blood, particularly emphasizing the role of the leukocytes. Heparinized venous dog blood was administered an approximate LD_{100} endotoxin dose (Difco) and incubated in vitro for 4-6 hours. Saline controls were studied similarly. Results show that addition of endotoxin in vitro elicits a significant increase in uptake of glucose, an elevated lactic acid concentration and decreased pH within 1-3 hours. Further, glucose uptake was elevated as a function of an increased number of white blood cells, although the uptake of glucose per white cell was diminished. Pretreating in vivo blood with sublethal injections of endotoxin daily for 4 days yielded blood with marked leukocytosis, but following endotoxin administration in vitro glucose consumed per cell was not usually elevated. Temperature elevation increased glucose uptake after endotoxin (Q_{10}=1.95); however, the Q_{10} of the saline controls was significantly higher (2.5; $p<0.02$), suggesting a depressant action of endotoxin on the metabolism of glucose. A significant number of white cells were destroyed by endotoxin within 3-6 hours of incubation ($p<0.05$), as compared with the controls. These observations suggest the interaction of both stimulating and depressant factors in the rate of glucose disappearance from the blood in endotoxin shock.

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PROSTAGLANDINS: REGULATION OF MYOCARDIAL BLOOD FLOW. Thomas H. Hintze* and Gabor Kaley, New York Medical College, Valhalla, New York.

Numerous reports in the literature involve prostaglandin (PGs) in the regulation of coronary blood flow. A comprehensive study was undertaken to evaluate the effects of inhibition of PG synthesis upon a variety of reactions in the coronary vascular bed of anesthetized, open-chest dogs. In 23 animals an electromagnetic flow probe (EMFP) and hydraulic occluder were placed around either the left anterior descending or circumflex branches of the coronary artery and a needle was inserted distal to the EMFP. Injections into the coronary artery of arachidonic acid (AA), bradykinin, adenosine, angiotensin and PGE_2 were given before and after inhibition of PG synthesis by indomethacin (IND) or meclofenamate (MF). The effect of the inhibitors on reactive hyperemias resulting from 5,10,15 and 20 second occlusions and the dilation resulting from 90 second exposure to 8% O_2 were also examined. In each experiment, inhibition of PG synthesis was ascertained by the elimination of vasodilation to AA. Baseline coronary blood flow was slightly, but significantly, reduced whereas systemic blood pressure was increased by the inhibitors. After administration of IND or MF, peak increase in blood flow due to all vasodilators was reduced but total increment of blood flow was not significantly altered. Similarly, while the peak dilation and volume of reactive hyperemia were decreased, the percent flow debt repaid was unchanged. In addition, total increment of coronary blood flow due to hypoxia-induced vasodilation was unaltered. Vasoconstrictor responses to angiotensin were also not changed in the absence of PG synthesis. These results indicate that while the inhibitors of PG synthesis increase coronary resistance, they do not adversely affect vascular responsiveness. We conclude that PGs play little, if any, role in modulating coronary blood flow. (NHLI Grant #12342 and Westchester Heart Association)

CENTRAL RESPIRATORY CHEMORECEPTORS IN THE TURTLE. B.M. Hitzig*, J.C. Allen* and D.C. Jackson, Div. of Biol. and Med., Brown University, Providence, R.I. 02912

Semi-aquatic turtles (Pseudemys scripta elegans) of either sex, weighing 1-2 Kg had chronic needle catheters stereotactically implanted in the lateral and 4th ventricles of their brains. After recovery mock cerebrospinal fluid (CSF) with normal (30 meq/L) or low (15-22 meq/L) [HCO_3^-] was perfused through the brain ventricles of the unanesthetized animal. Respiratory minute volume and O_2 consumption were measured continuously and, in some animals, arterial blood samples were taken periodically and analyzed for pH and $[CO_2]_T$. Turtles were studied at either 10°C (n=1), 20°C (n=4) or 30°C (n=2) following acclimation at each test temperature. Ventilation was unaffected by perfusion with normal [HCO_3^-] mock CSF and, except at 10°C, resembled previous data on unoperated turtles. Perfusion with low [HCO_3^-] mock CSF resulted in increased ventilation of from 3 to 15 times control values and hyperventilation continued in spite of lowered arterial PCO_2 and [H^+]. The relative response was similar at each temperature. In one animal CSF samples were taken following acclimation to 10°C, 20°C and 30°C. CSF pH decreased with temperature (-0.015 units/°C) while calculated PCO_2 increased (1.2 torr/°C). These changes closely resemble temperature effects previously observed in blood samples from this and other ectothermic species. In conclusion, these data: 1) provide evidence for sensitive central chemoreceptors in the turtle and 2) indicate, in a preliminary way, that CSF pH, like blood pH, is temperature dependent. (Supported by grant HL-16653 from NHLI (to DCJ)

SERUM THYROTROPIN AND TRIIODOTHYRONINE IN MEN DURING ACUTE COLD STRESS. P.F. Hoar*, L.P. Georges*, L.W. Raymond, R.E. Johnsonbaugh* and J. Sode. Naval Med. Res. Inst. and Nat. Naval Med. Center, Bethesda, Md. 20014.

Both acute and chronic cold stress have been found to activate the pituitary-thyroid axis in small mammals. Although chronic cold stress can produce a similar activation in man, the effects of acute cold exposure upon human thyroid function have not been widely investigated. We recently showed that immersion of divers in 25.5°C (78°F) water for one hour results in substantial cold stress with marked shivering, discomfort, reduced skin and rectal temperatures, elevated plasma and urinary catecholamines, and diuresis (Hoar et al., J. Appl. Physiol., in press). Despite this acute cold stress, the 14 men studied showed no changes in serum thyrotropin (TSH) or triiodothyronine concentrations. In an effort to study the effects of subacute cold stress on thyroid function in a similar population, we measured serum TSH levels in 6 divers pressurized to 49.5 atm. abs. for 4 weeks in a hyperbaric chamber filled with helium (99.5%) and oxygen (0.5%). When ambient temperature in the chamber was at the lower limit of the comfort zone (32°C), some subjects complained of chilliness and intermittent shivering at night. Elevations of serum TSH accompanied these responses. Restoration of chamber temperature to a more comfortable level was associated with a return of TSH values to the pre-stress range. It is concluded that acute cold stress in divers does not stimulate thyroid activity, whereas subacute cold exposure in helium at high pressures, increases serum TSH concentrations. (Navy Medical Research and Development Command, Research Task MPN 10.02.6011).

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HEMORRHAGIC SHOCK IN PIGS WITH ON-LINE EEG ANALYSIS. B.C. Hodgkin, E.T. Angelakos, R.A. Bonner*, and C. Munroe*. Biomedical Research Institute, Univ. of Maine, Portland, Maine 04102.

Hypovolumic hemorrhagic shock was produced in young domestic pigs by rapid bleeding to 50 mmHg and maintaining this pressure for one hour. Blood volume measurements indicated an average loss of 49% of original blood volume. Heart rate (HR) increased to 264 ± 30 BPM 39 ± 11 min. from the start of bleed. All blood was reinfused when HR dropped to 100 BPM. In the control group, 33% of the animals recovered while the remainder terminated in irreversible shock with a post-reinfusion median survival time of 98 min. It was observed that the EEG rapidly declined in amplitude, becoming essentially flat 6-9 min. before HR dropped to 100. The EEG was used as a predictor of impending shock and as an indicator of cerebral recovery following reinfusion. A simple index of EEG amplitude and frequency was derived which allows on-line analysis of the EEG. The amplitude window was divided into 5 microvolt steps. Threshold crossings counted over a one min. period produced a distribution reflecting both amplitude and frequency characteristics of the EEG. With impending shock, the absolute value mean threshold, the variance of the distribution and the total number of threshold crossings all decreased. The ratio of the number of zero crossings to the total number of threshold crossings increased, reflecting a concentration of low amplitude EEG activity. Following reinfusion, all survivors responded with an increase in pressure while only one non-survivor so responded but failed to maintain the increased pressure. EEG distributions returned to normal shape in survivors but EEG activity failed to return in the absence of a blood pressure response.

ALTERATIONS IN ORTHOSTATIC RESPONSES RELATED TO SPACE FLIGHT. G. W. Hoffler* and R. L. Johnson* (SPON: W.C. Alexander). NASA Johnson Space Center, Houston, Texas 77058.

Skylab provided the opportunity to study inflight orthostatic tolerance of man which was previously known to be diminished after even relatively short orbital space flights. Lower body negative pressure (LBNP) was chosen as a major inflight medical experiment because at approximately one-fifteenth sea level atmospheric pressure differential it causes cardiovascular responses qualitatively and quantitatively similar to those produced by the upright position in one-gravity and because it is readily applicable in zero-gravity. Cardiodynamic data from this experiment suggest significant contribution from altered fluid compartments. It has been conjectured that mechanisms which maintain intravascular volume under earth conditions would undergo reversal in weightlessness due to a centripetal fluid shift registered as excess vascular volume and inducing reduction by diuresis. That a notable cephalad fluid shift occurs soon upon entering orbit is well documented by Skylab measurements of 10-15% reductions in leg volume with concomitant objective and subjective evidence of head congestion. Though modest weight loss has been a consistent accompaniment of space flight, leg volume decrements are disproportionately larger. Moreover, calf volume change during LBNP and leg blood flow are greatly increased inflight over preflight control values. Multiple resting vectorcardiographic measurements show inflight changes consistent with augmented intracardiac volume and the opposite effect during LBNP. Immediate postflight findings reveal a rapid reversal of most of these conditions and it is tempting to conclude that many, if not all, major alterations associated with space flight are related to the physical and physiological phenomena attributable to adaptation.

SEROTONIN DISTRIBUTION IN THE GASTRIC MUCOSA OF ACUTELY PREPARED POUCH DOGS. F. Hohenleitner and C. Linguiti*. Dept of Physiology & Biophysics, Temple University, Philadelphia, Pa. 19140

Previously we reported (Fed Proc 33:310, 1974) that in fasted dogs there is a gradient in the amount of serotonin (5-HT) obtainable from gastric mucosa ranging from low values in the pylorus to high ones in the corpus. In the pylorus greatest concentrations were found near the antral-corporal margin. In this study these observations are more sharply defined and extended. Six dogs of both sexes were anesthetized with pentobarbital, and prepared with gastric fistulas, which were permitted to drain for 5 hrs. In each dog gastric secretory rate was greatly reduced and juice pH increased to a mean terminal value of 7.2. The mean pH of 11 other stomachs removed from control dogs immediately after anesthesia induction was 3.0. After gastrectomy 5-HT was determined from representative sites in the corpus and in the entire antrum and pyloric canal. 5-HT in both dorsal and ventral proximal corpus and the pyloric canal were significantly different from samples taken from control animals immediately after anesthesia induction. Values are ug 5-HT/g mucosa. Dorsal corpus control = 2.58±0.85. Pouch = 5.73±2.27. Ventral corpus control = 1.96±1.03. Pouch = 6.68±2.95. When mean 5-HT values were compared, no region within the stomach could be determined to be significantly different from any other area. Pyloric canal 5-HT increased from 0.44±0.39 to 4.40±1.75 (n=6/group). In sum, we have demonstrated a substantial increase in mucosal 5-HT in gastric mucosa in both corpus and pyloric canal, eliminating the gastric 5-HT gradient. The coincident changes in pH suggest that the gastric secretory state or the luminal pH may influence mucosal 5-HT concentration.

THE EFFECT OF SARALASIN AND HIGH SALT INTAKE ON RABBITS WITH TWO-KIDNEY GOLDBLATT HYPERTENSION. D.R. Holmes*, J.C. Romero and C.G. Strong, Dept. of Internal Medicine and Physiology, Mayo Clinic and Foundation, Rochester, Minn.

Two-kidney Goldblatt hypertension (2KGH) was produced in 40 New Zealand male rabbits by constriction of the left renal artery with silver clips. Depending on the internal diameter of the clip, varying degrees of hypertension were obtained. Severe 2KGH was characterized by extracellular fluid volume (ECFV) (inulin space) contraction, elevated plasma renin activity (PRA), and a mean blood pressure (BP) $>$ 108 mm.Hg. (N=13). Moderate 2KGH was characterized by normal ECFV, decreased PRA and a mean BP $\sim$ 108 mm.Hg. (N=13). Sham clipping in 11 animals resulted in normal BP, ECFV and PRA. In severe 2KGH there was a significant correlation between severity of BP and elevation of PRA. There was no correlation between BP and PRA in the other two groups. Saralasin infusion caused a significant fall in mean BP in animals with severe 2KGH but no change in animals with moderate 2KGH or in controls. In severe 2KGH there was a significant correlation between the fall in BP and the baseline BP. There was also a significant correlation between the fall in BP and the baseline PRA. A high salt diet partially corrected the ECFV contraction and caused a reduction in mean BP in severe 2KGH but not in the moderate or normotensive groups. After the high salt diet, saralasin caused no further change in BP in severe 2KGH. These results suggest that in severe 2KGH that the high level of BP is maintained by elevated PRA which is in turn maintained by ECFV contraction. Interrupting the cycle by ameliorating the ECFV contraction reduces BP to moderately hypertensive levels and renders it no longer renin angiotensin dependent.

THE SOMA AND AXON OF APLYSIA GIANT NEURON: A COMPARISON WITH SQUID AXON. R. Horn* and J. Miller* (SPON: D. Junge). Dept. Anatomy & Physiology, UCLA, Los Angeles, Calif. 90024

Intracellular recordings were obtained from the soma and axon of the giant neuron (R2) of Aplysia californica. It has been demonstrated previously that the somatic spike of R2 has a mixed Na/Ca dependency while the axon spike is mainly Na dependent. Extracellular 25mM tetraethylammonium bromide (TEA) causes an increase in the somatic spike duration. This effect decreases to an insignificant level within the first 3mm of axon. The action of TEA on both the soma and the proximal axon is reversibly abolished by adding 30mM $CoCl_2$ to both. It is enhanced by adding 30mM $CaCl_2$ to the bath. Both effects suggest that inward current during the TEA-induced plateau is maintained by Ca. The hyperpolarizing I-V relationship of the R2 axon is linear for membrane potentials up to -130mV in contrast with the well-established inward rectification of the soma. The axon fires repetitively only for a limited range of depolarizations (33-47mV). Large stimuli in the axon only produce one spike, in contrast with the soma, which fires repetitively for depolarizations greater than 90mV. With respect to (1) the ionic dependency of the spike, (2) the insensitivity to extracellular TEA, (3) the hyperpolarizing I-V relationship, and (4) the ability to fire repetitively for high levels of constant current, the R2 distal axon is more like squid axon than its own soma.

ACCELERATED DEVELOPMENT OF INTESTINAL AND LIVER HYDROLASES IN SUCKLING RATS OF HYPERTHYROID MOTHERS. C. Horowitz*, J. Jumawan*, O. Koldovsky and H. Lau*. Children's Hospital and Dept. Pediatrics, University of Pennsylvania, Philadelphia, Pa. 19104

Application of L-triiodothyronine (T_3 - 1.25 mg/100 g of body weight, daily) from day 11 to day 15 postnatally to lactating mothers was followed by a significant increase in T_3 levels in their sera (3 x as compared to controls) and milk (4x), as well as in the sera of suckling rats reared by the T_3 treated mothers(2). The activity of jejunal sucrase and maltase was precociously increased (sucrase = Controls: 0.021μmol/mg/prot/60 min ±0.0026 (S.E.M.) exp. :0.46±0. 0.052: maltase = Controls: 2.05±0.12, experimentals: 5.12±0.56). Liver acid β-galactosidase, β-glucuronidase and N-acetyl-β-glucosaminidase were also significantly increased in pups of T_3 treated mothers.

These findings indicate that the milk may function as an endocrinal link between the mother's hormonal and metabolic systems and those of the sucklings. The basis for this hypothesis is the presence of various hormones in normal milk and the higher permeability of the gastrointestinal tract during the suckling period of many mammals including, to some extent, man.

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POST-ISCHEMIC VAGAL STABILIZATION OF THE CANINE VENTRICLE. E.J. Hoskins*, D.V. Iriola and G.K. Weiss. Dept. Physiology, School of Medicine, University of New Mexico, Albuquerque, New Mexico 87131

Recent work has demonstrated that vagus nerve stimulation increases the ventricular fibrillation threshold (VFT) of the ischemic canine ventricle. This project was undertaken to show a direct, vagally mediated, electrical effect giving a mechanism for the increase in VFT. 10 barbiturate-anesthetized adult mongrel dogs were prepared using a left thoracotomy in the fifth interspace. The heart was suspended in a pericardial cradle and a distal branch of the left anterior descending coronary artery (LAD) was dissected free with a removeable silk ligature placed around it. Bipolar surface electrodes were sutured to the surface of the left ventricle (LV) within and without the regions of intended ischemia. The heart was paced from the LV at approx. 180 beats per minute. The LAD was occluded for periods of 3½ minutes with and without supramaximal right vagus nerve stimulation (RVS). Periods of ischemia without RVS caused a depression of both surface bipolar electrogram amplitude (AMP) and upstroke dV/dT. RVS in conjunction with ischemia produced no significant difference in the AMP and dV/dT. However, in the presence of adrenergic blockade with practolol, RVS during ischemia increased both AMP and dV/dT by an average of 20 ± 9 and 27 ± 15% respectively ($\bar{X}$ ± SEM) over ischemia without RVS. This was measured at 30 sec intervals from one min. after the onset of ischemia until cessation of RVS 3 min. later. These results suggest that a post-ischemic RVS-mediated stabilization of the canine LV does exist and is manifest only in the absence of sympathetic neural activity. Therefore, the presence of sympathetic neural activity may actually be detrimental to the electrical stability of the ischemic heart.

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GLUCOLUXUS: A SATIETY MECHANISM IN PIGS. K.A. Houpt and T.R. Houpt, N. Y. S. College of Veterinary Medicine, Cornell University, Ithaca, N.Y. 14853

Isotonic glucose loads given by gavage in doses of 1.0-2.5 g/kg body wt have been shown to depress subsequent intake in suckling pigs (Houpt et al., Fed. Proc. 34:374,1975). To determine the site of action and threshold doses necessary to produce short-term satiety, silicone rubber catheters were implanted in the upper GI tract of female weanling Yorkshire pigs (5-30 kg). It was found in preliminary experiments that ileal infusions of glucose did not depress feed intake, gastric and jejunal infusions did, but duodenal infusions were most effective. Therefore, for this study duodenal catheters were placed in 9 pigs which were fasted for 3 hrs and then infused with 5 ml/kg body wt of either a glucose solution (5-40%) or 0.9% NaCl. Infusions were followed immediately by a 10 min feeding period during which pelleted pig feed was available ad lib. Neither 0.3-0.5 nor 0.6-0.9 g/kg glucose significantly depressed subsequent intake which was 98% and 84% of control intake respectively. Doses of 1.0-1.2 g/kg (49% of control; $p<0.02$); of 1.4-1.6 g/kg (57% of control, $p<0.005$); 1.8 g/kg (38% of control, $p<0.005$); and 2.0 g/kg (45% of control, $p<0.001$) significantly depressed subsequent intake. Intrajugular infusion of glucose sufficient to raise plasma glucose to levels observed after duodenal infusion of 2.0 g/kg glucose did not depress intake (as has been previously demonstrated by Stephens and Baldwin, Physiol. Behav. 12:923,1974). Intestinal glucoluxus appears to produce satiety in pigs when levels $\geq$ 1.0 g/kg glucose are present in the upper small intestine. The mechanism, whether neural or hormonal, of glucoluxic satiety remains to be determined.

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HYPERGLYCEMIC RESPONSES TO CEREBRAL GLUCOPRIVATION: DOG AND GOAT COMPARED. T. R. Houpt and H. E. Hance*, N. Y. S. College of Veterinary Medicine, Cornell University, Ithaca, N. Y. 14853.

If insufficient glucose is available for central nervous system metabolism, the sympathetic nervous system is activated to cause secretion of epinephrine from the adrenal medulla which will augment plasma glucose as hepatic glycogenolysis is accelerated. Such cerebral glucoprivation can be caused by 2-deoxy-D-glucose (2-DG) which competes with glucose intracellularly. The plasma 2-DG concentration which initiates the sympathetic response has the characteristics of a threshold value which is signalled by the abrupt appearance of hyperglycemia. Five goats and 3 dogs were infused with solutions of 2-DG via i. v. catheters so as to slowly raise plasma 2-DG concentration. The 2-DG concentration at which hyperglycemia appeared was the threshold value and was determined in dogs and goats at their normal glucose levels and in goats with plasma glucose elevated by infusion of glucose. In the dogs mean plasma glucose immediately before the hyperglycemic response began was 103 ± 4.1 mg/100 ml ($\pm$SE); mean plasma 2-DG was 18.6 ± 1.29 mg/100 ml; and mean of ratios of 2-DG/glucose at threshold was 0.18 ± 0.01 ($n=14$). In goats comparable values were: 78 ± 4.9 mg/100 ml glucose; 14.4 ± 1.53 mg/100 ml 2-DG; and ratios 0.18 ± 0.02 ($n=16$). In goats with elevated plasma glucose: 123 ± 7.4 mg/100 ml glucose; 23.9 ± 4.55 mg/100 ml 2-DG; and ratios 0.19 ± 0.03 ($n=7$). The similar ratios of 2-DG/glucose for activation of the sympathetic nervous system in both species at difference plasma glucose levels can be interpreted in terms of an intracellular glucoreceptor mechanism separated from plasma glucose by a carrier-type transport system which is normally saturated, and it is suggested that intracellular sensitivity of these glucoreceptors is probably similar in ruminants and carnivores despite their different normal plasma glucose concentrations.

THE EFFECT OF HYPER-AND HYPOSMOTIC SOLUTIONS ON THE ACTION POTENTIAL OF CANINE CARDIAC PURKINJE FIBERS. S.R. Houser* and A.R. Freeman, (SPON: M.J. Oppenheimer). Dept. of Physio., Temple Univ. Sch. of Med. 3420 N. Broad St., Phila., Pa. 19140.

The effect of hyper-and hyposmotic solutions on the action potential of canine cardiac purkinje fibers (PF) was studied in 20 experimental preparations. Basic action potential parameters such as maximum diastolic potential (MDP), action potential duration at 20% repolarized (APD_{20}), and action potential overshoot (OS) were recorded with intracellular electrodes. The perfusing medium was made hyperosmotic by addition of either NaCl or Sucrose and hyposmotic by removal of NaCl. The results of the hyperosmotic studies showed a change in OS with little or no alteration in MDP. With NaCl hyperosmolarity the OS increased, whereas with Sucrose it decreased. It was also discovered that the APD_{20} varied with the osmolarity of the perfusate. When the preparation was perfused with hyposmotic solutions, the APD_{20} decreased. When bathed in hyperosmotic solutions, the APD_{20} increased. A difference was recorded in the amount of change in APD_{20} which depended on the substances used to increase the osmolarity. When sucrose was studied, the APD_{20} increased 10.5%/100 mOsm added to the normal Tyrode. When NaCl was used, the APD_{20} increased 21.65%/100 mOsm of NaCl added. These results are consistent with the generally held idea that an ionic current flowing during a given phase of the cardiac action potential is proportional to the EMF of the ion involved. Changes in the EMF should therefore produce an alteration in the current. The results are also consistent with the idea that a difference in the intracellular ionic strength may effect intracellular gating mechanisms which control phase 2 duration. Additional experiments are under way to investigate this possibility.

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MAMMOTROPIN ASSAY OF PROLACTIN, STH AND TERM PLACENTAS OF CATTLE AND SWINE. W. F. Houska* and R. R. Anderson, Dept. Dairy Science, University of Missouri-Columbia, Columbia, MO. 65201

Abdominal inguinal mammary glands of immature hypophysectomized female rats were injected daily with either prolactin, STH or extracts of term placentas for 5 days as a bioassay of mammotropic activity. Basis of the bioassay was mammary gland growth in response to local injection of mammogenic hormones. Three right mammary glands were injected with saline carrier and left glands with standard hormone or extract. Glands were removed on sixth day and wet weight, dry fat-free weight and DNA weight determined. Only DNA was a satisfactory measure of mammary growth for bioassay purposes. Six rats were replicated at each of 3 standard doses and 3 doses of unknown with an interval of log 2. Fifty-four animals were used in each assay. Index of precision for five assays using DNA data was .28. Based upon 6-point parallel line assay statistics, potencies were determined. Bovine STH had one-fourth the potency of prolactin on a weight basis. One IU of STH equaled 5.7 IU ovine prolactin. A fraction of swine term placenta precipitated at pH 4.5 had a potency of 0.23 IU ovine prolactin standard per mg dry tissue. This is approximately one-hundredth the potency of prolactin standard (25 IU per mg). Cattle term placental cotyledons precipitated at pH 4.5 had a potency of 0.61 IU ovine prolactin. These findings suggest that the placentae of swine and cattle are significant sources of mammotropic hormone during pregnancy.

ROLE OF THE URINARY BLADDER IN OSMOREGULATION IN THE MARINE AGLOMERULAR TELEOST, OPSANUS TAU. Duncan B. Howe* and John Gutknecht. Duke Univ. Marine Lab., Beaufort, N.C. 28516

NaCl and water reabsorption have been demonstrated in the isolated urinary bladder of several teleosts. The object of our study was to determine the nature and function of bladder fluid absorption in vivo in an aglomerular marine teleost, the toadfish. Urine excreted from the kidney and the bladder was collected separately in two groups of fish. The rates of ion and fluid reabsorption by the bladder were determined from the difference between ureteral and bladder flow rates. The bladder reabsorbed 60% of the urine excreted by the kidney or 7.6 $ul \cdot 100\ g^{-1} \cdot hr^{-1}$. Na and Cl reabsorption by the bladder was 1.21 and 1.17 $umoles \cdot 100\ g^{-1} \cdot hr^{-1}$, and the concentration of NaCl in the absorbate was thus about 156 mM. Thus, the absorbate is a NaCl solution isosmotic with plasma. Bladder fluid reabsorption was compared to the rate of absorption of drinking water to determine the importance of the bladder in water balance. In marine teleosts drinking compensates for dehydration due to urinary losses plus osmotic losses across the body surface. By means of ^{125}I-labeled Glofil and a rectal catheter we calculated gut fluid absorption from the difference between the drinking rate and the rectal fluid loss rate. Gut fluid absorption was 32 $ul \cdot 100\ g^{-1} \cdot hr^{-1}$, which was 80% of the drinking rate. Thus, the amount of water conserved by the bladder is equal to about 24% of the fluid absorbed by the gut. In other words, without the bladder the toadfish would have to drink about 24% more seawater, which would require a roughly proportional increase in the amount of salt which would have to be actively absorbed by the gut and then actively excreted across the gills. Thus, fluid reabsorption by the urinary bladder provides a significant decrease in the total metabolic cost of salt transport in the toadfish. (Supported by USPHS Grant HL 12157.)

THE BIOLOGICAL EFFECT OF TOBACCO CIGARETTE SMOKE ON THE HOST DEFENSE SYSTEM OF THE LUNG. G.L. Huber, V. Pochay*, V. Mahajan*, J. Shea* and C. Sornberger*. Dept. of Medicine, Harvard Medical School, Beth Israel Hospital, Boston, Massachusetts 02215.

To evaluate the effects of cigarette smoking on the host defenses of the lung, male CD rats were exposed to fresh whole smoke for 60 consecutive days. Intrapulmonary deposition of smoke and animal exposure levels, quantified with decacholorbiphenyl and other smoke tracers, indicated a daily exposure equivalent to approximately one pack per day in man. Pulmonary alveolar macrophage function in situ was quantified by the inactivation of an aerosolized challenge of Staphylococcus aureus 6 hrs after inoculation. Controls (n=120) inactivated 88.81 ± 0.64% of the staphylococci. Exposure to whole smoke did not impair intrapulmonary antistaphylococcal defenses, with inactivation rates of 89.84 ± 0.97% (n=49) and 89.12 ± 0.46% (n=74) at 30 and 60 days, respectively. Inactivation distribution frequency analysis in controls revealed that 7% of animals had inactivation values greater than 2SD of the mean. With prolonged exposure there was a more symmetric grouping towards the mean with less skewing towards the abnormal. Alveolar macrophages harvested from smoked animals were comparable in viability and in vitro antistaphylococcal activity to controls. These studies indicate that chronic exposure to tobacco smoke does not impair, and in fact may stimulate, the host defenses of the lung, as evaluated by in vivo and in vitro pulmonary alveolar macrophage function.

AMMONIA RESPIRATORY DEAD SPACE IN NORMAL AND MAO-BLOCKED DOGS. R.D. Hunt.*(SPON: M. Jaeger). Dept. Physiology, University of Florida, Gainesville, Florida 32611.

The ammonia content in expired breath of mammals has been observed and measured by direct spectrometric methods, and an equation derived from the Bohr relationship by which ammonia gas respiratory dead space can be determined. A dead space of 17.6± s.e. 1.3% of tidal volume including an apparatus dead space of 21 ml was calculated in 19 determinations for 2 human subjects sample orally. A dead space after subtracting apparatus dead space of up to 10 ml was calculated for 16 determinations in 6 normal tracheotomized dogs intubated to carina. 15 similar determinations in 4 MAO-blocked dogs yielded an average of 44.8 ml for ammonia respiratory dead space. The difference between normal and MAO-blocked dogs is attributed to blockage of ammonia production in airways by metabolism of monamines, probably serotonin and norepinephrine. (MAO = monamine oxidase)

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SYSTOLIC VENTRICULAR ELASTICITY STUDIED VIA FLOW PULSES. W.C. Hunter*, J.S. Janicki*, K.T. Weber*, J. Melbin*, K.B. Campbell*, A. Noordergraaf Dept. Bioengineering, Cardiovascular-Pulmonary Div., and Dept. Animal Biology, University of Pennsylvania, Philadelphia, Pa. 19174

A technique based on impulse-response concepts has been developed to study ventricular elastic properties during systole. In both isolated and in situ canine heart preparations with intact pericardium, a flow pulse (ΔQ) lasting 35-45 msec. was used to withdraw 1-2 ml. from the left ventricle during one beat of an otherwise isovolumic steady-state. Using ECG for time reference, pressure traces from the perturbed beat and the preceding undisturbed beat were superimposed to obtain the time course of the pressure drop (ΔP) produced by ΔQ. Dividing ΔP by the pulse volume provided a measure of elasticity (ΔP/ΔV). The time of applying a flow pulse (Tp) was varied from onset systole (Tp=0) to the time of peak isovolumic pressure (Tp=Tmax) in 20 msec. increments. As Tp varied, the contour of the ΔP/ΔV waveform changed with a consistent pattern. For Tp near 0, ΔP/ΔV rose and then fell nearly in phase with isovolumic pressure. For later pulse times, an initial rapid transient appeared, which grew steadily in magnitude as Tp increased, reaching a peak for Tp near Tmax. The decay following the transient overshoot tended toward the same ΔP/ΔV curve seen when Tp=0 for any pulse within the range Tp=0 to Tp=2/3 Tmax. However, for Tp near Tmax, ΔP/ΔV decayed below this common elastance curve. These observations provide a stringent test for simple mechanical models. A single varying elastance predicts the common curve but not the transient overshoots. Parallel damped and undamped elastance predicts appropriate transients but not the behavior for Tp near Tmax. Thus, this pulse method provides a description of ventricular elasticity which can be related to, but is more complete than the simple models which have been proposed.

MATHEMATICAL MODEL OF PROXIMAL TUBULE SOLUTE AND WATER TRANSPORT. R. E. Huss* and J. L. Stephenson. NHLI, NIH, Bethesda, Md. 20014. D. J. Marsh, USC, Los Angeles, Ca. 90007.

A model of solute and volume transport from tubule to peritubular capillary that includes cellular and shunt pathways has been developed. Fluxes, concentrations, and hydrostatic pressures in cell, lateral intercellular channels, and interstitial space are computed. Driving forces are Starling forces in the tubular and capillary lumens, and osmotic pressure generated by active solute transport into the lateral interspace. Numerical results show that although hydrostatic and osmotic pressures are of the same order of magnitude across the lateral cell membrane, net reabsorption is determined primarily by the rate of active solute transport into the channel and the relative magnitudes of the flow resistances at the two ends of the channel. These results are in agreement with recent experimental evidence that changes in external driving forces moderate the flow, but can account for only a small fraction of total reabsorption. Further results show that the osmolality of the reabsorbate is highly sensitive to the osmolality of the luminal fluid. As reabsorption progreses, luminal fluid and reabsorbate equilibrate at an osmolality that is within a few milliosmoles of isotonicity over a wide range of externally applied Starling forces.

PULMONARY VASCULAR EFFECTS OF ARACHIDONIC ACID IN THE DOG. A. L. Hyman, A.S. Mathe*, E.W.Spannhake*, and P.J. Kadowitz*. Depts. of Pharmacology and Surgery, Tulane Medical School, New Orleans, La. 70112. (Spon: Norman R. Kreisman)

Aracidonic acid (AA), the precursor for prostaglandins (PG) $F_{2\alpha}$ and E_2, was used to study the role of PG's in the lung. Pulmonary vascular effects (PVE's) of the endogenously produced PG's and intermediates were compared to those of exogenous PG's under conditions of controlled blood flow in intact dogs. AA, $F_{2\alpha}$ and E_2 increased pulmonary vascular resistance by actively constricting lobar arteries and veins in a dose-related manner. $F_{2\alpha}$ was 10 times more potent than E_2 and 1000 times more potent than AA. Low yields of E and F-like PG's and metabolites indicated low conversion of AA to PGE_2 and $PGF_{2\alpha}$. PG synthetase (PS) inhibition by indomethacin blocked PVE's of AA, but enhanced PVE's of $F_{2\alpha}$ or E_2. Perfusion with dextran instead of blood greatly enhanced PS activity, since the PVE's of AA were tripled, without changing PVE's of $F_{2\alpha}$ or E_2. Endotoxin enhanced PS activity, since PVE's of AA were increased but not PVE's of $F_{2\alpha}$ or E_2. Hypoxia depressed PS activity but enhanced PVE of $F_{2\alpha}$. This study indicates that AA, $PGF_{2\alpha}$ and PGE_2 constrict pulmonary vessels, but conversion of AA to PG is low; however, production of intermediates may be greater. PS activity can be altered by pathological states, and thus contribute to regulation of the pulmonary circulation.

THE EFFECTS OF THYROID HORMONE ON DIFFERENT TYPES OF SKELETAL MUSCLE
C.D. Ianuzzo and V. Chen* (SPON: H. G. Knuttgen). Depts. of Physical Education and Biology, York University, Toronto, Ontario M3J 1P3, Canada

The purpose of this investigation was to determine the effects of hypo- and hyper-thyroid states on the activities of selected enzymes in skeletal muscles comprised predominately of one of each of the 3 fiber types. The experimental groups consisted of hypo-, eu- and hyper-thyroid Sprague-Dawley albino rats (Hormone Assay, Chicago). The hyperthyroid condition was induced in thyroidectomized (TDX) animals by subcutaneous injections (30 ug/100 g) of Na-3, 3',5-triiodo-L-thyronine(T3) on alternate days. Following 6 weeks of injections the animals were sacrificed and the enzyme activities of alpha-glycerolphosphate dehydrogenase (GPDH), phosphofructokinase (PFK), succinate dehydrogenase (SDH), and beta-hydroxyacyl-CoA dehydrogenase (HADH) were determined on the liver, plantaris (P), soleus (S), peripheral white portion (WG) and axial red portion (RG) of the gastrocnemius m. GPDH activity was significantly less ($p<.05$-$.001$) than normal in the liver and muscles of the TDX group. The GPDH activity was significantly higher in the S, RG, and liver ($p<.01$-$.001$) of the TDX + T3 group. PFK activity tended to be lower in all muscles of the TDX group but was significantly less only in the P and RG. SDH activity was significantly lower ($p<.001$) in muscles of the TDX group with exception of the WG. HADH was significantly lower in the RG of the TDX group and significantly elevated in the S, WG, and RG of the TDX + T3 group. The findings indicate that T3 differentially influences the metabolic character of the different muscle fiber types.

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A NOTE ON BLOOD PRESSURE REGULATION. A. S. Iberall, General Technical Services, Inc., Upper Darby, Pa. 19082.

Recent single nephron pressure measurements (1,2,3) provide a basis for modelling mammalian blood pressure regulation. The story: Central pressure 100 mm Hg; 55 mm drop to afferent glomerular arteriole, due to vascular architecture (50-40 mm expected at 15-20 μm diameters (4)); 45 mm in glomerular capillaries; 10 mm in efferent arteriole and first branch capillaries; 7 mm capillary net pressure; 9 mm Bowman space and proximal tubal pressure; 6 mm distal tubule pressure; 4 mm renal venous pressure. In other circulations, one finds about 24 mm in arteriolar capillaries and 16 mm venular (4). Thus the downstream 10-4 = 6 mm drop in renal capillaries is like other capillary nets (8 ± 4, compared to 6). The critical difference in renal capillaries is the 35 mm drop from capsule to efferent. This has no known nervous control base. Yet it is a functional resistance. The proposal is that which dominates this 35 mm drop controls the central pressure as: 35 mm functional drop + 10 mm architectural capillary drop + 55 mm architectural arterial drop. A Model: Bowman capsule 'squeezes' internal capillaries either mechanically or electrochemically via internal gel-like constituents (e.g., chemical control of a renin-angiotensin-hyaluronic acid-collagen chain originating at juxtaglomerular apparatus). That squeeze controls amount of ultrafiltration into capsule. While other circulations also leak out at their capillaries, they are not as permeable. Thus the very leaky renal capillaries control the extra 35 mm boost (higher in hypertension).

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EFFECT OF AN ANGIOTENSIN II ANTAGONIST ON CARDIAC OUTPUT AND ARTERIAL PRESSURE IN RABBITS WITH PERINEPHRITIS HYPERTENSION. S. Ichikawa*, J.A. Johnson, M.W. Stanton*, C.G. Payne*, and W.F. Keitzer* (SPON: M.L. Zatzman). Research Service, H.S Truman Mem. VA Hospital, and Depts. of Surgery and Physiology, University of Missouri, Columbia, Mo. 65201.

Perinephritis hypertension was produced in 6 rabbits by wrapping one kidney in cellophane and removing the opposite kidney; 5 unoperated rabbits were normotensive controls. Mean arterial pressure (MAP) and cardiac output (CO) were measured before and after 30 min. of infusion of an angiotensin II (A-II) antagonist, 1-sar-8-ala A-II. The MAP of the hypertensive group (HG) averaged 125 ±6 (SEM) mm Hg, which was significantly higher ($P<0.001$) than the MAP of 87 ±2 for the normotensive group (NG). A transient rise in MAP was seen in both groups at about 3 min. of analog infusion; MAP in the NG increased 7 ±1 while the HG increased by 15 ±2. MAP was not altered after 30 min. of analog infusion in either the HG or the NG. In the HG the CO averaged 167 ±12 ml/min. per kg both before and after analog infusion; the CO in the NG was 263 ±27 prior to analog infusion and was unchanged at 261 ±27 after infusion of the A-II antagonist. CO in the HG was significantly ($P<0.01$) less than in the NG both before and after analog infusion. Total peripheral resistance (TPR) in the HG before and after analog infusion averaged 0.79 ±0.08 and 0.77 ±0.08 respectively, while in the NG the TPR were 0.34 ±0.04 and 0.33 ±0.04 during these periods. TPR in the HG was greater ($P<0.005$) than in the NG, but was unaltered in either group by infusion of the A-II analog. Plasma renin activity was 1.7 ±0.4 ng of angiotensin I for the HG and 5.2 ±1.4 for the NG, values which were not significantly different. These results indicate that hypertension induced by perinephritis in rabbits is due solely to vasoconstriction, and suggest that A-II is not involved in maintaining the hypertension.

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NON INVASIVE MEASUREMENT OF THE EFFECT OF INTRAVENOUS ISOPROTERENOL ON LEFT VENTRICULAR DYNAMICS IN INTACT UNANESTHETIZED MAN. N.B. Ingels, Jr., G.T. Daughters,II, M.J. Specter*, J.W. Mason*, E.B. Stinson*, and E.L. Alderman*, Palo Alto Medical Research Foundation and Stanford University School of Medicine, Palo Alto, California 94301.

Both improvement and degradation of left ventricular segmental function have been reported in previous studies of systemically administered inotropic agents. To examine this conflict, left ventricular dynamics were studied by computer-aided fluoroscopic analysis of radiopaque tantalum markers implanted into the left ventricular midwall in 11 patients, before and after isoproterenol infusion (2 mcg/min, I.V.). Significant ($P<.01$) and equivalent reductions in end-diastolic volume (114±9 to 93±7 ml) (mean±SEM) and end-systolic volume (56±7 to 38±5 ml) resulted in constant stroke volume (58±4 to 55±3 ml) such that ejection fraction increased significantly (52±3 to 60±3%) and cardiac output was enhanced significantly (4.8±.3 to 6.4±.4L/min) by the significant increase in heart rate (84±6 to 117±7b/min). Mean extent of fiber shortening increased significantly (20.1±.9 to 22.9±1.0%) as did mean contractile velocity (.77±.06 to 1.26±.06 circ/sec). While the contractile pattern of 49 of the 64 segments (76.6%) studied remained unchanged and 4 (6.3%) showed some improvement, a deleterious effect was noted in 11 (17.2%) segments (in 9 of the 11 patients) similar to that observed in experimental regional ischemia. This resulted in a significant increase in asynergy (15±2 to 32±5%) in the group as a whole. These results suggest that systemically administered isoproterenol has a variable effect on left ventricular segmental dynamics, with the dynamics of most segments relatively unaltered and degradation more frequent than improvement in the remaining segments. The nature of these effects after drug administration suggests myocardial blood flow redistribution in response to inotropic stress as a probable underlying mechanism.

HYPOTHALAMIC AND EXTRAHYPOTHALAMIC SITES CONTROLLING SERUM GLUCOSE IN THE RAT. D.L. Innes, E.G. Gisel* and L.R. Viola*. Department of Physiology and Biophysics, Temple University Health Sciences Center, Philadelphia, Pennsylvania, 19140.

In a previous study it was observed that both the ventral medial hypothalamic (VMH) and supramamillary (SUM) nuclei are involved in the neural control of serum glucose. The present study attempts to evaluate other structures within the rat brain that may also play a role in this central regulation. In the first series of experiments bipolar nichrome electrodes were positioned stereotaxically into discrete nuclei of the diencephalon and rhinencephalon using sodium pentobarbital anesthesia. Stimulus parameters ranged from 0.01 to 0.1 mA with 0.01 to 0.1 msec square waves applied at a rate of 50 Hz for 3 min. Serum glucose concentrations were determined before and after stimulation using enzymatic estimation with hexokinase. Arterial blood was withdrawn from the carotid at 5, 10 and 15 min post stimulation. Our data indicate that VMH or SUM stimulation causes increased serum glucose levels, but that stimulation of the lateral mamillary nucleus or certain ventral amygdaloid nuclei results in decreased levels of serum glucose. Dorsal amygdaloid or thalamic stimulation produced no significant differences in blood sugar. In the second series of experiments multiunit recordings of ongoing hypothalamic neuronal activity were conducted following IP insulin injections. Within minutes there was a decrease in the spontaneous electrical activity of the VMH which at times persisted for over 1 hr. It is hypothesized that extrahypothalamic as well as hypothalamic nuclei can influence serum glucose concentrations and that insulin levels could possibly be the mechanism through which the VMH regulates blood glucose.

ASZ(DCPB)

EFFECTS OF LINEAR ALKYLATE SULPHONATE ON TRITIATED WATER UPTAKE BY ISOLATED PERFUSED GILLS OF RAINBOW TROUT. W.F. Jackson* and P.O. Fromm. Dept. Physiology, Michigan State Univ., E. Lansing, MI 48824

Tritiated water (HTO) uptake by isolated perfused gills of rainbow trout (Salmo gairdneri) was observed after exposure to various concentrations of an anionic detergent LAS (Linear alkylate sulphonate). Perfusate flow (0.5 ml min^{-1}) through the arches and the HTO and osmotic gradients were held constant. During the 65 min. experimental period gills treated with 5, 10, 20, and 100 $mg^{-1}l$ LAS showed an exponential increase in HTO uptake with time, the equilibrium influx values being approximately 15, 50, 95 and 250 percent greater than pre-treatment control levels respectively. The rate constants for the above mentioned experiments ranged from 0.05 to 0.38 min^{-1}. Isolated gills were also perfused with solutions containing either epinephrine (10^{-5}M) or acetylcholine (10^{-8}M). When these arches were exposed to 10 mg l^{-1} LAS results similar to those described above were obtained, although the equilibrium HTO influx levels were less than those seen in arches not treated with vasoactive substances. These results indicate that LAS has a rapid, dose related effect on the HTO uptake of the isolated perfused gill preparation. It appears that the responses seen are more probably due to changes in the permeability characteristics of the gill epithelium invoked by interactions of the detergent with components of these biological membranes rather than to alterations in the pattern of perfusion flow through the gills. (Supported by NIH training grant #HL 05873.)

VENTILATORY RESPONSE TO INHALED CO_2 IN INFANT MACACA NEMESTRINA. J.P. Jacky* (Spon: J. Hildebrandt). Dept. Physiology & Biophysics, University of Washington, Seattle, Wash. 98195

CO_2 responses were observed in premature and full term infant pigtail macacques. Subjects were tested on the first day of life and at intervals until ten weeks old. Subjects were studied late at night and spent most of the experiment asleep. Sleep state was classified as "active" (REM) or "quiet" (non-REM) based on observations of gross activity, eye movements, and regularity of respiration. Sleep state is undisturbed if inhaled CO_2 does not exceed 4%. Younger infants show no response below 2%. This threshold decreases, and CO_2 gain increases, as infants mature. Resting ventilation and CO_2 gain are elevated in REM sleep. It appears that weight is a better predictor of performance than either gestational or postnatal age. In younger infants, neurogenic factors are the most important influences on respiration unless alveolar CO_2 is extremely elevated. It seems unlikely, therefore, that abnormal CO_2 sensitivity is responsible for the periodic breathing or apnea seen in some infants.
(Supported by grants HDO-8633 from NICHD and GM 00260 and RR-05432-14 from NIH.)

AGGREGATION PHEROMONE FROM THE EGG-MASS OF APLYSIA. B. Jahan-Parwar, Worcester Foundation for Experimental Biology, Shrewsubyr, MA 01545.

In an aquarium containing a group of mature Aplysia, if one in the group starts laying eggs, or if a separately kept egg-laying Aplysia is introduced into the aquarium, it usually attracts the others and elicits a characteristic chain mating and/or egg laying in these hermaphroditic animals. These behaviors can also be triggered if an Aplysia egg-mass alone is transferred into the aquarium. In an experiment involving three Aplysia willcoxi, an egg-mass obtained from a fourth separately kept animal was placed in one corner of the 50 gal. aquarium for 17 days and S's positions were recorded every morning before and during 30 minutes following presentation of food (sea weed) to the opposite corner of the aquarium. Before presentation of food, S's were consistently (97%) found near the egg-mass, frequently coupulating and/or laying eggs. Food placed in the opposite corner of the aquarium attracted S's in most (80%) trials except when laying eggs. Similar shuttle-response between egg-mass and food was also obtianed from a group of 5 Aplysia californica: 70 trials, 83% egg-response, 83% food response. These results confirm previous data on distant-chemoreception in Aplysia and suggest further: a) presence of an aggregation pheromone in the egg-mass of Aplysia; b) a dominant position of the egg-laying behavior over the feeding behavior which in turn appears to dominate mating behavior.

(Supported by grant NS 11452 from NICDS).

BODY TEMPERATURE AND THE VENTILATORY RESPONSE TO CO_2 DURING ACUTE AND CHRONIC HYPERCAPNIA. D. B. Jennings, Dept. of Physiology, Queen's University, Kingston, Ontario, Canada.

We have previously reported that changes in ventilation in conscious dogs exposed to 5% CO_2 in air over 14 days were not clearly related to changes in acid-base balance (Physiologist 17:255, 1974). It is documented by many workers that body temperature falls during acute hypercapnia and returns to normal during acclimation to CO_2. Since changes in body temperature are known to affect the ventilatory response to carbon dioxide, we have carried out studies of the ventilatory response to CO_2 in relation to rectal temperature in 7 conscious resting dogs during control and at 2 days and at 13-17 days of exposure to 5% CO_2 in air.

During the control ventilatory response curves to carbon dioxide, there was an average fall in the rectal temperature of about 0.8°C. At 2 days of hypercapnia and at 13-17 days of hypercapnia there were no consistent deviations of ventilation relative to $PaCO_2$ or pha from the control studies. However, both at 2 days and 13-17 days of breathing 5% CO_2 in air, rectal temperature had returned to air control levels in the dogs. Thus, during the ventilatory response curves obtained in chronically hypercapnic dogs, body temperature was higher at every level of inspired carbon dioxide in comparison to breathing the same gas mixture at control. These observations would support the possibility that a higher body temperature during chronic hypercapnia may potentiate the ventilatory response to carbon dioxide and explain, at least in part, the lack of shift of the ventilatory response curve to the right in chronically hypercapnic resting conscious dogs. (Supported by grants from the Medical Research Council of Canada and the Ontario Thoracic Society).

DISTRIBUTION OF BICARBONATE BETWEEN BLOOD AND CEREBROSPINAL FLUID IN THE NEONATAL RAT IN METABOLIC ACIDOSIS AND ALKALOSIS. C.E. Johanson*, D.M. Woodbury*, and C.D. Withrow*. (SPON: J.W. Woodbury) Department of Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, Ut. 84132.

The nature of the blood-cerebrospinal fluid barrier to HCO_3 in the neonatal rat was investigated by analyzing changes in concentrations of total CO_2 in CSF in response to acutely-induced systemic metabolic acid-base distortions. One-wk-old rats were injected ip with a solution containing either $NaHCO_3$, NaCl (control) or NH_4Cl. In metabolic alkalosis of 2 hr duration, the concentration of HCO_3 in CSF H_2O becomes nearly equal to the elevated concentration (i.e., to 40 mEq/L) in plasma H_2O. However, in metabolic acidosis (2 hr), the CSF system of the neonatal rat is somewhat protected against a substantial fall (i.e., to 15 mEq/L) in plasma HCO_3, the reduction in CSF HCO_3 being about one half the fall in plasma HCO_3. The observed changes in the concentration of HCO_3 in neonatal CSF in response to acid (or alkali) loading are considerably greater than those found in adult rats. The results suggest that the permeability of the blood-CSF barrier to HCO_3 is greater in the neonate than in the adult and/or that carrier-mediated system(s) for translocating HCO_3 (or hydrogen ion) between CSF and blood are operating at a lower capacity in the neonatal rat than in the adult of this species. Thus, the neonatal rat may prove to be a useful model in the study of the nature of CSF pH regulation. (Supported by Program-Project Grant No. NS-04553.)

EFFECT OF AN ANGIOTENSIN II ANTAGONIST ON CARDIAC OUTPUT AND ARTERIAL PRESSURE IN Na-DEPLETED RENAL HYPERTENSIVE RABBITS. J.A. Johnson, D.H. Stubbs*, M.W. Stanton*, C.G. Payne*, S. Ichikawa*, and W.F. Keitzer*. Research Service, H.S Truman Mem. VA Hospital, and Depts. of Surgery and Physiology, University of Missouri, Columbia, Mo. 65201.

Experiments were performed to determine if hypertension would persist in rabbits during decreased extracellular fluid volume and angiotensin II (A-II) antagonism. Four groups of 9 rabbits each were studied. Group 1 was normotensive, normal Na rabbits. Group 2 rabbits were normotensive and Na depleted. Group 3 rabbits were normal Na but had renal artery stenosis and hypertension. Rabbits in group 4 were hypertensive and Na depleted. Rabbits in groups 2 and 4 were infused with the A-II antagonist 1-sar-8-ala A-II; the arterial pressure (AP) and cardiac output (CO) were determined before and after analog infusion. AP in group 1 rabbits averaged 82 ±7 (SD) mm Hg; CO was 190 ±32 ml/min per kg, and total peripheral resistance (TPR) was .43 ±.07. In Na-depleted normotensive rabbits (group 2) AP was unchanged at 86 ±7 but the CO decreased to 154 ±40 ($P<.05$) and TPR increased to .56 ±.14 ($P<.05$). Analog infusion decreased AP to 72 ±12 ($P<.01$) and TPR to .44 ±.15 ($P<.05$) but CO was unchanged at 163 ±80. Hypertensive normal Na rabbits had an increased AP of 118 ±18 and TPR of .67 ±.13 ($P<.01$); CO was unchanged at 176 ±25. In Na-depleted hypertensive rabbits AP was 115 ±19; CO was less at 153 ±19 ($P<.05$) and TPR was .75 ±.14. A-II analog infusion decreased AP to 100 ±20 and TPR to .56 ±.13 ($P<.01$) while CO increased ($P<.05$) to 180 ±37. The hypertensive Na-depleted rabbits with A-II antagonist had significantly ($P<.05$) higher AP and TPR than the normotensive, normal Na rabbits. These results indicate that in rabbits with renal artery stenosis and hypertension the increased AP and TPR do not depend solely on increased fluid volume or A-II.

RED CELL MASS CHANGES RESULTING FROM SPACEFLIGHT. Philip C. Johnson*, Stephen L. Kimzey*, and Theda B. Driscoll*, Department of Medicine, Baylor College of Medicine, Houston, Texas 77030 and NASA/Johnson Space Center, Houston, Texas 77058. (Spon:O.E. Reynolds)

Measurement of crewmember's circulating red cell mass (RBCM) and plasma volume (PV) have been performed before and after spaceflight using ^{51}Cr red cells and ^{125}I human serum albumin.

Flight	N	Days Duration	Atmospheric pO_2	% Decrease RBCM	% Decrease PV
Apollo 14-17	12	10 - 14	258	11±1.3*	4.4±1.7*
Skylab II	3	28	180	14.3	8.4
Skylab III	3	59	180	12.2	13.1
Skylab IV	3	84	180	6.8	15.9

* Mean ± SE

These studies indicate that spaceflight should be added to the factors known to decrease RBCM and plasma volume. PV showed a progressive decline with mission duration while RBCM did not. It has been theorized that these changes are a result of muscular inactivity plus a hyperoxic effect during the Apollo flights. Bedrest studies designed to test the effect inactivity has on RBCM has shown $\%\Delta RBCM = 0.24X + 1$ where X equals days of bedrest to 35 days. Flight induced RBCM changes are significantly greater than the bedrest induced changes which suggests a factor(s) in addition to inactivity as the cause of the red cell mass decreases.

CATION PERMEABILITY AND INTERNAL pH OF ISOLATED CHROMAFFIN VESICLES. R.G. Johnson* and A. Scarpa, Dept. Biochemistry and Biophysics, University of Pennsylvania, Philadelphia, Pennsylvania 19174

The passive ion permeability, regulation of volume, and the internal pH of isolated bovine chromaffin granules were studied by radiochemical, potentiometric, and spectrophotometric techniques. The granules behave as perfect osmometers between 340 and 1000 mosM in choline chloride, NaCl, and KCl as measured by changes in absorbance at 430 nm or from intravesicular water measurements using $^{3}H_2O$ and ^{14}C-polydextran. By suspending chromaffin granules in iso-osmotic media of various metal ions and selectively increasing the permeability to either the cation or ion by intrinsically permeable ions or specific ionophores, it is possible to determine the permeability to the counterion by turdidity and potentiometric measurements. These measurements indicate that the chromaffin granule membrane is impermeable to all of the cations tested (Na^+, K^+, H^+, Ca^{++}, and Mg^{++}). Measurement of the extra-intravesicular distribution of ^{14}C-methylamine in a choline chloride medium indicates that a significant ΔpH exists across the membrane with the intravesicular space over one pH unit more acidic than the surrounding medium. Similar ΔpH values were obtained in sucrose, NaCl, and KCl media. The pH gradient can be enhanced in the presence of nigericin or collapsed in the presence of nigericin and K^+ or A23187 and Ca^{++}. Addition of A23187 causes an accumulation of calcium against an apparent concentration gradient with calcium uptake exceeding 50 nmoles/mg of protein. Measurement of catecholamine release under conditions where intravesicular calcium accumulation is maximal indicates that catecholamine release does not occur. These results offer a basis for understanding the ion permeability and regulation of catecholamine uptake, storage, and release in isolated bovine chromaffin vesicles.
(Supported by grants GM-02046 from NIGMS and 18708 from NIH)

STUDIES OF ATHEROSCLEROSIS: AMINO ACID COMPOSITION CHANGES ON AGING IN HUMAN AORTIC INTIMA. W.T.M. Johnson*, Lincoln Univ., Pa. 19352 and O. Horwitz, Univ. Pa., Pa. Hosp., Phila., Pa. 19107

The purpose of this study was to determine changes in protein composition or structure of the arterial intima with aging and atherosclerosis. Our first approach was to determine amino acid compositions of 14 lesion-free aortic intimal specimens, aged 21 to 71 years. Causes of death were trauma in the younger group and coronary heart disease (CHD) and cancer in the older group. Many striking changes in amino acid composition were found. For comparative purposes, compositional changes were assumed to be linear with age and the data were calculated as least squares equations. In moles/1000 residues, Glycine (GLY) was 210. at birth and increased at a rate of .170 moles per year or GLY = 210. + .170 x AGE. ALA (alanine), HYP (hydroxyproline), and VAL (valine) show relatively large changes with age. ALA = 151. - .666 x AGE; HYP = 17. + .536 x AGE; and VAL = 58. - .510 x AGE. PRO (proline) = 102. + .262 x AGE. Mol ratio changes are relatively small for GLY/HYP : GLY/HYP = 8.9 - .067 x AGE, and relatively large for HYP/PRO: HYP/PRO = .20 + .004 x AGE. There is considerable scatter in some of the data that may indicate dependence on variables other than age. Results suggest that the lesion-free areas of aortic intima undergo significant changes in protein composition/structure with aging and /or disease. It seems very unlikely that such changes would not play a role in the pathogenesis of atherosclerosis. This work was supported by MBS Grant R 08002, DRR, NIH, and the Foundation for Vascular-Hypertension Research, Philadelphia, Pa. 19107

ROLE OF ALDOSTERONE IN HYPER-OSMOTIC SALINE INDUCED INCREASES IN UREA PRODUCTION IN THE FROG, Rana pipiens pipiens. J.W. Johnston* and A.M. Jungreis (SPON: H. G. Welch). Department of Zoology, University of Tennessee, Knoxville, TN 37916

The leopard frog, R. pipiens pipiens increases its rate of urea production in response to mild dehydration in air [Jungreis, Comp. Biochem. Physiol. 47A, 39 (1974)] and hyper-osmotic (0.15 M) NaCl [Jungreis, J. Exp. Zool. 178, 403 (1971)]. This increase is seasonal and occurs after 6 hours of stress in naturally active Spring-Summer (SS) versus dormant Fall-Winter (FW) stages of the life cycle. SS frogs have a reduced capacity to synthesize and store glycogen relative to FW animals. Therefore, the increase in urea production was thought to be a by-product of an enhanced rate of gluconeogenesis from amino acids that was needed to maintain serum glucose. When the role of glucocorticoids in the enhanced rate of urea production was studied [Jungreis et al., Comp. Biochem. Physiol. 34, 683 (1970)], corticosterone levels declined following salt loading in SS frogs, whereas FW levels remained unchanged. Since aldosterone (aldo) is also a potent glucocorticoid, its role in rea production was studied. In response to dehydration in 0.15 M NaCl, werum aldo declined slightly in FW and drastically in SS frogs. Yet exogenously administered aldo induced an increase in urea production in SS versus FW frogs. Following salt loading or aldo administration, livers were incubated in modified Krebs Bicarbonate Buffer and urea synthesis measured. Regardless of treatment, ^{14}C-Bicarbonate was incorporated into urea at virtually constant rates in FW and SS frogs. Thus, no increase in capacity to synthesize urea had occurred. While aldo could induce an increase in urea production in SS frogs, its role in the observed increase in vivo is unclear. Supported by Biomedical Sciences Support Grant #07088.

COMPARISON OF SA NODAL AND SUBSIDIARY ATRIAL PACEMAKER FUNCTION IN THE DOG. Stephen Jones, E. Hardie*, D. Euler*, and W. C. Randall. Dept. of Physiology, Loyola Univ. Medical Center, Maywood, IL. 60153.

In the absence of the SA node, subsidiary atrial pacemakers, exclusive of the junctional region, can be demonstrated in the unanesthetized dog. A 3-4 cm section of the Sulcus Terminalis (including the SA node) was excised from the right atrium via a right thoracotomy in dogs under pentobarbital anesthesia. After recovery of days or weeks, ECG records indicated the return of a P-wave. Animals either developed a stable P-wave and rhythm or demonstrated variations between junctional and P-wave rhythms. Dogs developing P-waves and stable rhythm were studied further to characterize the subsidiary pacemakers. Maximal rates of non-nodal pacemakers achieved with exercise and beta adrenergic stimulation (isoproterenol iv) were compared with maximal SA nodal rates in the same animal preoperatively. Maximal subsidiary pacemaker rates were equal to or less than those prior to SA node removal. Maximal SA nodal and subsidiary atrial heart rates in response to right stellate stimulation under anesthesia were less than unanesthetized, maximal isoproterenol heart rates but comparable to maximal exercise heart rates. Subsidiary pacemaker location was studied by mapping the area of earliest electrical activation with stationary bipolar plunge electrodes and an exploring suction electrode. P-wave morphologies were compared with earliest epicardial activation which included areas of the inferior vena cava and inferior right atrium. Subsidiary atrial pacemakers in the absence of the SA node are under sympathetic control in the conscious animal but may not always be capable of the same maximal response as the SA node. (Supported by USPHS Grant HL 08682.)

INTRACELLULAR RECORDINGS OF ANTIDROMICALLY IDENTIFIED FACIAL MOTONEURONS AND UNIDENTIFIED BRAIN STEM INTERNEURONS OF AWAKE, BLINK CONDITIONED CATS. S. E. Jordan*, J. Jordan*, G. Brozek* and C. D. Woody. Neuroscience Program and Depts. of Anatomy and Psychiatry, UCLA Medical Center, Los Angeles, Ca. 90024.

Techniques were developed for intracellular recording and stimulation of facial motoneurons and brain stem interneurons in awake cats. Four of 7 animals were conditioned to blink by pairing click-CS with glabella tap-US. 26 facial motoneurons with transmembrane potentials of 57 ± 29 mV were identified by antidromic stimulation of the facial nerve at the angle of the jaw. Antidromic action potentials (AP) followed stimulation rates of over 250 per sec with constant latencies, averaging 1.0 ± 0.6 msec for the population studied. In cells with AP's greater than or equal to 44 mV, input resistance, measured by differential spike height method and by IV plots, was 5.1 ± 4.7 MΩ and 10.9 ± 8.5 MΩ, respectively. Cells with smaller AP's had resistance values in the same range. Threshold-latency curves determined by intracellular application of linearly rising currents showed that facial motoneurons accommodate slightly or not at all. With rectangular depolarizing current pulses (20 msec at 100 Hz), less current was required to discharge motoneurons in conditioned cats (3.0 ± 1.6 nA) than in naive cats (4.0 ± 1.7 nA, $p < .05$ Mann-Whitney). In conditioned animals, facial motoneurons that projected to eyeblink musculature required less current for discharge (1.6 ± 0.8 nA, $p < .05$) than did other motoneurons studied. Unspecific differences in thresholds to intracellular current injection as a function of conditioning were not noted in 271 cells recorded from the region of the superior olivary nucleus and the reticular formation. These cells frequently showed rapid accommodation to intracellularly injected ramp currents. (Supp. by USPHS HD-05958, HD-04612)

INCREASED ROLE OF ALPHA-ADRENOCEPTORS IN ISCHEMIC MYOCARDIAL ZONES. A. Juhasz-Nagy* and D. M. Aviado. Dept. Pharmacology, Univ. of Pa., Philadelphia, PA 19174.

The sympathetic responses of the mammalian heart muscle and coronary bed are known to possess predominantly β-adrenergic character, i.e. On the other hand, the collaterals penetrating the acutely ischemic cardiac regions were previously found to have an increased α-adrenergic sensitivity. In this investigation the effect of acute local cardiac ischemia on the quality of adrenoceptors mediating inotropic responses has been studied in open-chest dogs anesthetized with pentobarbital sodium. Inotropism of the left ventricle was measured with Walton strain gauge arches. Occlusion of a major coronary branch (1/2-1 hour prior to the testing) decreased considerably, but did not abolish the control active tension in the respective area. Moreover, epinephrine (0.2 - 0.8 μg/kg i.v.) and stellate stimulation elicited a nearly identical percent increase of contractile force in the normal and ischemic regions as well. The contractility increase of the normal area was practically unaffected by phentolamine (0.5 mg/kg), while this α-antagonist significantly reduced the responses of ischemic area to pharmacological and neural adrenergic stimuli. Thus, the persistence of contractile behavior in acutely ischemic myocardium seems to be related to the increased role of an α-adrenergic component.

INSENSITIVITY OF DEVELOPING INSECT TISSUES TO OUABAIN: THE ROLES OF POTASSIUM AND SODIUM-POTASSIUM ADENOSINETRIPHOSPHATASES. A.M. Jungreis and G.L. Vaughan*, Dept. Zoology, U. of Tennessee, Knoxville, TN 37916

Lepidoptera are reported to have epithelia which are insensitive to cardiac glycosides such as ouabain. These same epithelia are found to actively transport K^+ in the virtual absence of Na^+. Since K^+ blocks ouabain binding, it was thought that the insensitivity of these epithelia to ouabain was an artifact caused by the presence of high K^+ in the incubation media. Therefore, ouabain binding to larval and adult midgut of the Cecropia silkworm, Hyalophora cecropia, the tobacco hornworm, Manduca sexta, and the monarch butterfly, Danaus plexippus was determined in the presence of high Na^+ and low K^+. Midgut epithelia failed to bind ouabain on either inner or outer membrane surfaces and lacked Na^+-K^+ ATPases. Neuronal tissues from the same species did bind ouabain and had Na^+-K^+ ATPases. Whereas H. cecropia and M. sexta Na^+-K^+ ATPases had $K_{i-50\%}$ toward ouabain of 5-10 μM, that in D. plexippus was 5 mM, three orders of magnitude less sensitive. When administered in vivo, 5 mM ouabain failed to disrupt development in M. sexta, despite the observation that in vitro, this concentration completely inhibited neuronal Na^+-K^+ ATPases. The effect of K^+ concentration on Na^+-K^+ ATPases was therefore studied. K^+ at a concentration of 25 mM completely reverses ouabain inhibition. We conclude that the insensitivity of midgut epithelia toward ouabain results from the absence of Na^+-K^+ ATPases, while insensitivity of neuronal tissues in vivo results both from K^+ interference with ouabain binding to this enzyme, and in monarch to a low affinity toward ouabain. Supported by NSF Grant PCM 75-23456 and Biomedical Sciences Support Grant #07088.

A NEUROANATOMICAL SEARCH FOR CELL BODIES OF EFFERENTS TO THE CAROTID BODY, ORIGINATING IN THE BRAIN STEM OF THE CAT. M. Kalia and R.O. Davies. Dept. of Physiol. and Biophys., Hahnemann Med. College, Phila., PA 19102, and Dept. of Animal Biology, School of Veterinary Medicine, Univ. of Pennsylvania, Phila., PA 19174.

There is considerable controversy between the observations of DeCastro (1928), confirmed by Hess and Zapata (1972), and the studies of Biscoe and Sampson (1962) and McDonald and Mitchell (1975) regarding the presumed efferents to the carotid body originating in the brain stem. Recent studies on the vagus, De Vito et al (1974) and Kalia (1975), have demonstrated the use of horseradish peroxidase (HRP) as an effective method for labelling efferent cell bodies in the medulla. We have used this technique to demonstrate the brain stem location of possible glossopharyngeal efferents in the carotid sinus nerve (CSN). In 5 cats the left CSN was dissected out in the neck and crystals of HRP were applied to the cut central end over a period of 2-4 hours. After 24 hours the animals were perfused with 0.5% paraformaldehyde and 2.5% glutaraldehyde in 0.1 M PO_4 buffer pH 7.2, and the brain, petrosal and nodose ganglia were removed and processed for demonstration of HRP labelled cells. In all 5 cats, no labelling in the medulla was found following the CSN exposure to HRP. In 2 cats, HRP was also applied to contralateral vagus as a control. In all 5 experiments intense labelling of afferent cell bodies in the ipsilateral petrosal ganglion was seen. In 1 experiment, in which HRP solution 33% was injected into the nucleus of the solitary tract (NTS) of one side, the ipsilateral petrosal ganglion showed marked labelling with HRP, demonstrating that the NTS is the site of termination of first order afferents from the petrosal ganglion. We have however not been able to demonstrate efferent cell bodies in the brain stem with axons in the CSN. (Supported by RCDA HL 00103 and grant HL 17800 from NHLI.)

RECEPTOR MECHANISMS OF THE ACTIVE PEPTIDE FRAGMENTS OF GASTRIN AND CHOLECYSTOKININ (CCK). D. L. Kaminski and M. J. Ruwart* Saint Louis University, St. Louis, Missouri, USA.

Previous studies demonstrated that the interactions of the peptide hormones gastrin, CCK and secretin in the stomach were not evident in the biliary system (J Surg Res 17:26, 1974). This study evaluates the hormone-receptor interactions of the active peptide fragments of gastrin and CCK in the biliary system and the stomach. In dogs with chronic biliary and gastric fistulas,receiving a continuous infusion of intravenous bile salts, bile volume, bile composition and gastric hydrogen ion output were measured. The common tetra and pentapeptide fragments of CCK and gastrin in doses of 2, 4 and 8 μgm-kg-hr increased gastric hydrogen ion output in a dose related manner but did not alter bile output. Similar results were produced by the administration of the 6, 7 and 8 amino acid fragments of CCK without sulfation of tyrosine in position seven. Administration of the hepta and octapeptide fragments of CCK with sulfation of tyrosine in position seven, in doses of 0.25, 0.5, 1 and 2 μgm-kg-hr produced dose related increases in hepatic bile flow and gastric hydrogen ion output. When the non-sulfated octapeptide (4 μgm-kg-hr) was administered with sulfated peptide it did not inhibit the choleresis produced by the sulfated peptide. Dose response analysis demonstrated that the D_{50} values for stimulation of gastric hydrogen ion output of both the sulfated and non-sulfated peptides were not significantly different from the affinity of the common tetrapeptide (0.64 μgm-kg-hr) while the CMR values or efficacies were significantly different. The ability to combine with the receptor is the result of the c-terminal tetrapeptide while the effect is produced by the subsequent amino acid sequence. (Supported by USPHS Am 17084)

ACUTE CORONARY OCCLUSION AND CARDIAC AFFERENT NERVE ACTIVITY. J.P. Kampine*, Z. Bosnjak*, E.J. Zuperku*, and R.L. Coon. (SPON: W.J. Stekiel). The Med. Col. of Wisc. and Wood VA Ctr., Milw. Wisc. 53226

Segmental left coronary artery occlusion (CAO) produced a decrease in segmental myocardial contractile force (MCF) and an increase in segmental myocardial length (ML) in the area of the myocardium supplied by the occluded artery. Segmental CAO was studied in six dogs anesthetized with sodium thiopental 15-20 mg/kg and halothane in O_2 (0.5-1.0% inspired concentration). Left ventricular pressure (LVP), ECG, MCF, ML, and sympathetic afferent nerve activity were measured before and after snare occlusion of the left anterior descending (LAD) and left circumflex (LC) coronary arteries (15, 20, 60 and 90 sec. occlusions). Sympathetic afferent nerve activity was recorded in single fiber preparations dissected from slips of left upper thoracic white rami communicantes. Only nerve activity recorded from left ventricular receptors was selected for study. Location of the receptors was confirmed by probing the epicardial and endocardial surfaces of the beating and arrested heart. Acute CAO was associated with a significant increase in afferent nerve activity ($P<.05$). The increase in nerve activity coincided with changes in segmental ML even in the absence of changes in LVP. (Supported in part by the Wisconsin Heart Association and NIH Grant Hl 16511-01A2).

RETICULOENDOTHELIAL DYSFUNCTION DURING DISSEMINATED INTRAVASCULAR COAGULATION: RELEVANCE TO POST-SHOCK MICROEMBOLIZATION. John E. Kaplan* and Thomas M. Saba (SPON: P. Gudewicz). Department of Physiology, Albany Medical College, Albany, New York 12208.

Reticuloendothelial (RE) function has been related to both the clearance of coagulation products as well as survival from traumatic shock, and intravascular coagulation (IC) occurs during shock. The present study evaluated RE phagocytosis during IC in order to ascertain the importance of IC on RE stability. IC was initiated by the injection (IP) of bovine thrombin (500 U/100gm) into male rats (200-300g). RE function was evaluated by the vascular clearance of ^{131}I-test colloid and hepatic Kupffer cell phagocytosis by in vitro bioassay. Hepatic sinusoidal blood flow was evaluated by the fractional clearance rate technique. Thrombin injection resulted in a transient ($\frac{1}{2}$-2 hr) but significant ($p<.05$) RE depression with the phagocytic index (K) being reduced from 0.031±0.002 to 0.018±0.003 at 1 hr post-IC. There was no decrement in K after injection of saline (K=0.034±0.003) or heat-inactivated thrombin (K=0.033±0.003). RE depression was primarily due to a 37% decrease ($p<.001$) in hepatic colloid clearance and associated with increments in lung (82%) and marrow (100%) colloid localization with no splenic alterations. While IC resulted in decreased hepatic blood flow at $\frac{1}{2}$ and 2 hr, sinusoidal flow was normal during maximum RE impairment (1 hr). The in vivo clearance depression was not reflected as a Kupffer cellular deficit when evaluated in a heparin supplemented in vitro system. The results indicate a transient but profound RE dysfunction during IC, the mechanism of which remains to be elucidated. These data may have significance to the microembolization of fibrin and damaged platelets in association with RE depression during shock (GM-21447,T32-GM07033).

EFFECT OF ERYTHROPOIETIN ON THE ANEMIA OF RENAL ALLOGRAFT REJECTION. S.M. Kaplan, C.E. Sloane*, R.N. Taub, M. Haimov*, S.J. Piliero, A.S. Gordon, and L. Burrows*, Depts. Physiology and Histology, NYU Dent. College, Dept. Biol., N.Y. Univ., and Dept. Surgery, Mt. Sinai Hosp., N.Y., N.Y.

Erythropoietin (Ep), a glycoprotein hormone, is generally acknowledged to be the prime regulator of erythropoiesis in higher organisms. It is now well documented that the kidney is the major site of production of the hormone in the intact adult animal. Various studies have proposed that a decreased production of the hormone is the major underlying factor in the etiology of the anemia associated with renal failure. The present studies were designed to determine whether the anemia of renal allograft rejection in rats might be attributable to a decreased activity of the hormone and/or a decreased production. Kidney allografting was performed by microsurgical techniques involving grafting of LBNF-1 kidneys into Lewis rats. Rat serum was assayed for Ep content in the exhypoxic polycythemic mouse. Prior to assay, the serum was dialyzed against deionized water for 48 h at 5° C. Each assay mouse received 1.0 ml of rat serum. Results indicated elevated levels of circulating Ep despite severe impairment of renal function due to the rejection process. To test the possibility that although serum Ep was elevated in these animals activity of the hormone might be impaired, rats anemic from rejection of renal allografts were injected with 10 International Reference Preparation Units of Ep for 5 days. Examination of hematological parameters revealed no significant enhancement of erythropoiesis during or following Ep administration. These data suggest that while the rejecting kidney is capable of producing Ep, there is an impairment of the marrow response to the hormone in animals as a consequence of the rejection process.

A STANDARDIZED MODEL FOR ASSESSMENT OF EARLY INTERVENTIONS DESIGNED TO PROTECT ISCHEMIC MYOCARDIUM. Ronald P. Karlsberg*, Burton E. Sobel and Robert Roberts. Washington University School of Medicine, St. Louis, Missouri 63110

Evaluation of interventions to protect ischemic myocardium has been difficult, in part because of variation in infarct size among animals. Methods based on curve fitting plasma enzyme values entail considerable delay for data acquisition prior to the intervention. In this study we developed a standardized model of infarction in the dog with infarct size estimated from myocardial creatine phosphokinase (CPK) depletion normalized for left ventricular weight. We have previously shown that regional CPK depletion correlates with infarction estimated histologically. Myocardial infarction was produced in 20 conscious dogs by constriction of an exteriorized snare previously placed around the left anterior descending coronary artery 1 cm distal to the first medial branch, and the animals were sacrificed 24 hours later. CPK activity (IU/g) in 16,000 g fractions of extracts from normal myocardium multiplied by left ventricular weight were used to calculate the initial CPK content of the ventricle prior to infarction (CPKn). The difference between CPKn and total measured left ventricular CPK represented CPK depleted (CPKd). CPKd ranged from 13,000 to 71,000 IU, CPKn from 110,000 to 280,000 and left ventricular weight from 58 to 134 g. When infarct size was calculated from CPKd corrected for ventricular weight, mean infarct size was 25% of the left ventricle with a standard error of only 2%. Use of this model avoids problems encountered with morphological estimates of infarct size due to histological heterogeneity and delays required with curve fitting plasma enzyme values. The model permits detection of 22% salvage of myocardium resulting from interventions initiated before or any time after coronary occlusion, in 20 treated compared to 20 control dogs.

ASZ(DCPB)

EFFECTS OF MERCURIC CHLORIDE ON CHINESE HAMSTER OVARY CELLS IN VITRO. M. R. Kasschau and R. E. Meyn.* School of Sciences and Technologies, University of Houston at Clear Lake City, Houston, Texas, 77058 and Department of Physics, University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute, Houston, Texas, 77025

A great many studies have been performed concerning the effects of various pollutants on the physiological functions of whole animals. In contrast, our interest was in elucidating some of the effects of a partucular pollutant mercuric chloride at the cellular level. Chinese hamster ovary (CHO) cells in Vitro were treated with $HgCl_2$ at various stages in the cell cycle and the effects of this chemical on cell survival, DNA replication and cell division time were observed. The early G_1 treated cells were found to be most sensitive showing a significant reduction in the rate of DNA synthesis which correlated with a long division delay and a low level of cell survival when compared to the resistant late S-G_2 phase cells. Cells treated in early S while less sensitive than the G_1 stage cells were relatively more sensitive than the late S-G_2 treated cells. The ability of CHO cells to recovery from chronic treatments of $HgCl_2$ were observed. DNA replication and cell division delays were analyzed while cells were grown in the presence of $HgCl_2$ and analyses were continued following the removal of the mercury solution. Cellular recovery as observed by these techniques was rapid and complete for all remaining viable cells.

(Supported in part by NIH grant CA04484.)

PHOSPHOCREATINE (PC) SPLITTING BY STRETCHED FROG MUSCLE. C. Kean* E. Homsher, V. Sarian-Garibian* and J. Zemplenyi*, Department of Physiology, U.C.L.A., Los Angeles, California 90024.

If frog semitendinosus muscle is stretched to a sarcomere length of 3.65 μm, A and I filament overlap and active force development are abolished, and energy production is reduced to 0.3 of maximum. This energy is called the activation heat. Energy production and PC hydrolysis measurements in stretched and unstretched muscle allow comparison of the energy balance in the absence and presence of actin-myosin interaction, and by inference the balance for the crossbridges. Paired Rana pipiens semitendinosus muscles at 0°C were stretched to a sarcomere length of 3.6 μm. One of the pair was tetanized for 5 sec and both were then frozen. Differences in content of free and total creatine (C_F and C_T), phosphate (Pi) and adenine nucleotides were measured. Heat production was measured in other muscles, which were analyzed for C_T.

Heat production	0.63 ± 0.024 mJ/μmol C_T (n = 15)
$(\Delta C_F + \Delta Pi)/2$	9.5 ± 1.5 nmol/μmol C_T (n = 36)
There was no net ATP splitting.	

Using the value ΔH_{PC} = -34 kJ/mol (Woledge (1972) Cold Spr. Harb. Symp. 37: 629), we calculate the energy explained by the above PC splitting to be 0.32 mJ/μmol C_T, or only half of that observed. Comparison of this explained enthalpy fraction with the value of 0.74 (Homsher et al. (1975) J. Gen. Physiol. 65: 1) for frog muscle in isometric contraction at optimum length, suggests that crossbridges may have an explained enthalpy fraction close to unity, or that the unexplained fraction may derive from the activation or relaxation mechanisms of the muscle. (Supported by USPHS grant # HL 11351 and AHA-GLAA grant # 525.)

INTERACTION OF PHLORETIN-2' -(2-DEOXY-D-GLUCOSIDE) WITH RENAL SUGAR TRANSPORT SYSTEMS. D.J. Keljo* and A. Kleinzeller (SPON:D.E. Goldman). Dept. of Physiology, University of Pennsylvania, Philadelphia, Pa. 19174.

Phloretin-free phloretin-2'(2-deoxy-D-glucoside) [2-dGP] was studied as a possible inhibitor of sugar transport. Binding of ^{3}H-phlorizin and ^{3}H-2-dGP to a partially purified rabbit renal brush border membrane preparation (Relative enrichment: trehalase 8.6, Na/K ATPase 2.0 and succinic dehydrogenase 0.1) was studied in 111mM NaCl, 8.9mM Tris HCl (pH 7.6), 4.4mM EDTA, and 2.0mM trace ^{14}C-labelled mannitol at room temperature, separating bound from free by centrifugation. 200μM 2-dGP had no effect on the phlorizin high-affinity binding site. No high-affinity binding site was seen for 2-dGP. Scatchard plots of ^{3}H-2-dGP binding were linear, and at 0.02μM and 8μM concentrations of the compound, 200mM D-glucose, 2-deoxy-D-glucose or 2-deoxy-D-galactose had no detectable effect on binding. In renal cortex slice experiments, relative to 0.5mM phlorizin or phloretin, 0.48mM 2-dGP was intermediate in potency as an inhibitor of 2-deoxyglucose and 2-deoxygalactose transport and less effective than either with respect to α-methyl-D-glucoside transport. The inhibitory potency of 2-dGP correlates best with its lipid solubility, suggesting that the hydroxyl on carbon 2 is of prime importance for interaction with the sodium-dependent glucose carrier, and that a free C-1 hydroxyl may play a similar role in the sodium-independent transport system. (Supported by a grant from the Prudential Insurance Company of America through the Insurance Medical Scientist Scholarship Fund and N.I.H. grant AM12619. Tritiation of precursors synthesized by R.F. Sullivan and purifications by Smith Kline chemists were courtesy of Smith Kline Corporation.)

EFFECT OF CO_2 AND pH ON ISOLATED HEART AND SKELETAL MUSCLE.
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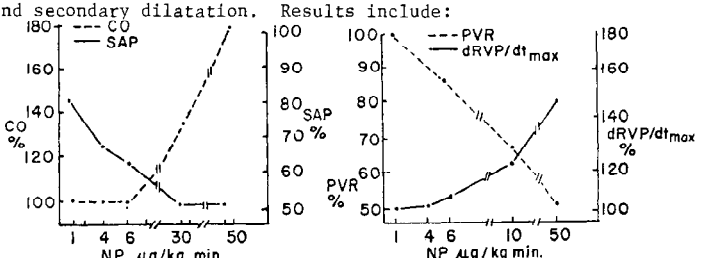
Our previous experiments on the isometric tetanic tension of rat and dog skeletal muscle (in vitro and in vivo) showed that keeping PCO_2 constant and lowering pH did not significantly decrease the tension developed by the muscles. However, keeping pH constant and increasing PCO_2 caused a significant decrease in muscle tension. Thus, it appeared that changes in intracellular pH (pH_i) rather then extracellular pH (pH_e) were responsible for these differences. Raising bicarbonate concentrations (HCO_3^-) raised the tension only slightly.

In the present study changes in isometric left ventricular tension (ΔP_{LV}) were investigated in isolated blood perfused dog hearts. When these hearts were exposed to increases in PCO_2 from 36 to 74 mmHg producing changes in pH from 7.38 to 7.13 ΔP_{LV} decreases averaged 41%. HCO_3^- increased from 18 to 23 meq/L (+26%). When exposed to metabloic acidosis pH range from 7.37 to 7.19 PCO_2 ranged 36 to 40 mmHg ΔP_{LV} decreases averaged 44%. HCO_3^- decreased from 19 to 15 meq/L (-25%). The infusion of HCO_3^- to restore pH to normal values reversed the changes in P_{LV}. This reversal was less complete in metabolic then in respiratory acidosis. Our results indicate that both cardiac and skeletal muscle respond similarly to increased CO_2 tensions. But during metabolic acidosis the effect of increasing extracellular (H^+) concentrations while not significant in skeletal muscle is highly significant in cardiac muscle. These data suggest that in cardiac muscle in contrast to skeletal muscle equlibration across the membrane of HCO_3^- and/or hydrogen iron (H^+) is appreciably faster then in skeletal muscle.
(Supported By: HL 10342 and ES 00454).

EFFECT OF NITROPRUSSIDE ON THE RIGHT SIDE OF CANINE HEART. N. D. Kien* and R. L. Hamlin. Dept. Veterinary Physiology and Pharmacology, Ohio State University, Columbus, Ohio 43210

This study was designed to establish the effect of graded doses of sodium nitroprusside (NP) on parameters of the right side of the heart. Eight mongrel dogs, anesthetized with acepromazine and sodium pentobarbital, were given doses of NP (1,4,6,30,50uG/kg min). Cardiac output (CO) pulmonary trunk (PTP) and systemic arterial (SAP) pressures and dRVP/dtmax were measured. Pulmonary (PVR) and systemic vascular (SVR) resistances were calculated. Heart rate , CO, and RV contractility increased gradually with increments in NP, while SAP and SVR decreased. There was no change in PTP, therefore PVR decreased. Orthogonal lead ECG's showed ST-T alterations in leads aVF and V3. These changes may have been related directly to NP or simply a heart rate response. It is impossible from this study to conclude whether NP caused a decrease in PVR by direct vasodilatation of that bed or merely as a response to the increase in CO and secondary dilatation. Results include:



(Supported in part by grant HL-16563 from NHLI)

EFFECTS OF THEOPHYLLINE AND INDOMETHACIN ON HYPOXIC AND HYPERCAPNIC DILATION IN THE FORELIMB OF THE ANESTHETIZED DOG. R.H. Kienitz,* J.M. Dabney, F.J. Haddy, and J.B. Scott. Dept. Physiology, Michigan State University, East Lansing, Michigan 48824

The vasodilation seen in most vascular beds exposed to hypoxemia or hypercapnia may be mediated via a direct action on vascular smooth muscle or indirectly via release of vasoactive chemicals. Adenosine, AMP, and prostaglandins are possible candidates as mediators of the indirect response. We tested this possibility by quantitating the vascular response of the isolated, innervated forelimb to local hypoxemia and hypercapnia before and during local infusions of theophylline (2.74 mg/min) and indomethacin (1.72 mg/min). At this rate, theophylline blocked the responses to 25 µg bolus injections of adenosine and AMP, and other studies have demonstrated that, at the dosage given, indomethacin inhibits the synthesis of prostaglandins. Local changes in blood gases were achieved by pumping blood through an extracorporeal lung circuit established between a femoral artery and the brachial artery. Results are given below:

	Hypoxia				Hypercapnia			
	ΔPp	A	IS		ΔPp	A	IS	
Control	-36	526	0.48	n = 11	-28	425	0.47	n = 6
Theophylline	-29	437	0.42		-18*	365	0.55	
Control	-25	368	0.30	n = 6	-21	398	0.56	n = 6
Indomethacin	-39	612*	0.28		-53*	902*	1.14*	

Pp = perfusion pressure, mmHg; A = area of response, mm^2; IS = initial slope of response, mmHg/sec. *P<0.05 compared to control.

The larger responses after indomethacin are probably related to the fact that the agent elevated forelimb resistance. These results fail to provide evidence that adenosine, AMP or prostaglandins play an important role in hypoxic or hypercapnic dilation in the dog forelimb.

EFFECTS OF LUNG VOLUME AND ESOPHAGEAL ELECTRODE POSITION UPON THE DIAPHRAGMATIC ELECTROMYOGRAM RECORDED FROM THE ESOPHAGUS. M. J. Kim*, W. S. Druz*, J. Danon* and J. T. Sharp. V.A. Hospital, Hines, Ill. and Departments of Physiology and Medicine and College of Nursing, University of Illinois, Chicago

In 13 dogs the rectified and integrated electromyogram (EMG) of the diaphragm was recorded from multiple sites in the stomach and esophagus via a catheter electrode and compared to the EMG simultaneously recorded directly from three diaphragmatic sites via bipolar wire electrodes. Studies were done both supine and prone and results were similar in the two positions. In all dogs comparisons were made at lung volumes varying from FRC to 1600 ml above F.R.C. with trachea occluded, the object of the study being to assess the effects of changing lung volume and of changing esophageal electrode site upon the magnitude of the diaphragmatic EMG signal. Both cervical phrenic nerves were stimulated tetanically (frequency 120 CPS) at supra maximal voltages. Neither directly recorded EMG's nor signals recorded via the esophageal electrode varied significantly as a function of lung volume. The EMG recorded from the esophageal electrode reflected the EMG recorded from lateral and anterior portions of the diaphragm as closely as that recorded from the crura. However, large variations in the diaphragmatic EMG record from the esophagus occurred when the recording site was altered, with the maximal signal being recorded 4 cm. below the level of the cardiac sphincter. At the level of the cardia the EMG was attenuated by about 30% below maximal. Electrode positions varied from 8 cm. above the cardia to 7 cm. below.

(Supported in part from USPHS grant HL-08789.)

THE APPLICATION OF SYSTEMS ANALYSIS AND MATHEMATICAL MODELS TO THE STUDY OF ERYTHROPOIESIS DURING SPACE FLIGHT. S. L. Kimzey*, J. I. Leonard*, and P. C. Johnson* (SPON: G.G. Armstrong). Metabolic & Biochemistry Branch, NASA Johnson Space Center, General Electric Company, and Baylor College of Medicine, Houston, Texas 77058.

Exposure of man to the weightless environment of space flight causes a modification to the normal rate of erythropoiesis resulting in a significant reduction in the circulating red cell mass. The decreases in red cell mass average -10±1% for the 9-13 day Apollo flights and varied from -7 to -19% for the longer duration (28-84 day) Skylab flights. Concomitant with the change in red cell mass during the Skylab missions were a reduciton in plasma volume (-9 to -16%), an increase in hemoglobin concentration, an increase in serum phosphate levels, and a morphological change in the shape of the circulating erythrocytes. All of these factors can influence the balance between red cell production and destruction and, thereby, alter the circulating red cell mass. A mathematical model of erythropoiesis has been defined to systematically investigate these relationships. Computer simulations of the erythropoiesis model have been conducted using data relative to plasma and red cell volume, hemoglobin concentration, tissue pO_2 and changes in hemoglobin-oxygen affinity. These were collected during space flight, bedrest studies, and/or exposure to hypoxic stress. The model can predict the changes in erythropoiesis and the resultant change in red cell mass which are consistent with the observed results. Comparison of the model's response with data from the Skylab missions suggest that several complex mechanisms are responsible for the reduced red cell mass.

BMES

DEAD SPACE MEASUREMENT IN LUNGS WITH UNEQUAL DISTRIBUTION OF VOLUMES: THEORY. Neal B. Kindig and David R. Hazlett, Pulmonary Function Laboratory, Fitzsimons Army Medical Center, Denver, Colo. 80240.

Dead space can be measured during a sequence of two breaths of equal tidal volume, V_T. The first inspired breath contains inert gas, F_I. The second inspired breath contains no inert gas. The first and second expired breaths are collected separately, F_{E1} and F_{E2}. The total anatomic dead space is $V_D = V_T(F_{E1} - F_{E2})/F_I$. The lung model consists of a shared dead space, two parallel dead spaces of unequal volume, and two alveolar compartments of unequal volume and ventilation. Perfect mixing exists in the alveolar compartments while plug flow exists in the dead spaces. Perfect axial mixing exists in the dead spaces. The method should be valid for multiple parallel compartments with unequal volume distribution if all of the dead spaces are ventilated. No assumptions about volume distribution are required in contrast with Fowler's washout method or the single breath nitrogen method. The error in the estimate of dead space is approximately proportional to the square of the alveolar dilution ratio, $[(V_T - V_D)/(V_A + V_T)]^2$. It increases with increasing tidal volume and inequality of volume distribution. The method can be used for studies of mixing of inert gases with different diffusing coefficients and for providing dead space values in studies of pulmonary diffusing capacity. The experiment requires a pulmonary function valve which will connect the mouthpiece to one of four different ports under automatic control of the breathing pattern. Some preliminary experimental results are reported.

CALCIUM EFFLUX FROM SKELETAL MUSCLE IN THE ABSENCE OF EXTRACELLULAR CALCIUM. Albert C. Kirby, Department of Physiology, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106.

Several groups of workers, including our own (J. Physiol. 253: 37-52, 1975) have reported extra efflux of $^{45}Ca^{++}$ from skeletal muscle during electrical, potassium or caffeine stimulation. Frog ELD IV muscles were equilibrated with $^{45}Ca^{++}$ solution for 15-18 hours, then washed in radioisotope-free Ringer for 2 hours. Ca^{++}-free Ringer containing 2 mM Mg^{++} was introduced at this time. Upon introduction of Mg^{++}-Ringer, resting efflux of $^{45}Ca^{++}$ initially decreased then returned to normal values in 4-5 minutes. Re-introduction of Ca^{++}-Ringer after 30 minutes was followed by an increase in resting efflux which returned to normal in 4-5 minutes. Upon electrical stimulation in Mg^{++}-Ringer muscle contractile activity was equivalent to control but no extra efflux of $^{45}Ca^{++}$ occurred. Caffeine (2-5 mM) contractures in Mg^{++}-Ringer were equivalent to control and extra efflux of $^{45}Ca^{++}$ occurred. These observations suggest at least two and possibly three different mechanisms of $^{45}Ca^{++}$ efflux in skeletal muscle. Resting efflux is not dependent on extracellular calcium whereas extra efflux upon electrical stimulation appears to be an exchange diffusion process requiring the presence of extracellular calcium. Resting efflux may be across the surface membrane whereas the stimulated efflux is probably via the T-tubules and terminal cisternae.

(Supported by NIH Grant NS-10196)

SKELETAL MUSCLE PO_2 CHANGES DURING REACTIVE HYPEREMIA. R. E. Klabunde and P. C. Johnson. Physiology Dept., University of Arizona College of Medicine, Tucson, Arizona 85724.

Changes in tissue pO_2 are thought to be directly or indirectly involved in local blood flow regulation. The present study was undertaken to examine the hypothesis that changes in tissue pO_2 directly regulate reactive hyperemia blood flow in skeletal muscle. Tissue pO_2 was continuously monitored using the Whalen-type oxygen microelectrode while simultaneously recording capillary red cell velocity in the anterior latissimus dorsi (ALD) muscle of the chicken. The muscles were bathed with a standing solution. Tissues exhibiting reactive hyperemia had a mean control pO_2 of 36±4 (SE) mmHg and a control capillary red cell velocity of 0.76±.08. During a one minute period of total blood flow occlusion, pO_2 fell to within 10% of zero in 12.3±1.4 seconds. Following occlusion release, pO_2 returned to its control value in 12.6±1.5 seconds. In addition, 75% of the pO_2 recordings showed an overshoot in pO_2 above control levels with a time-to-peak of 32±2.4 seconds (time from occlusion release to peak pO_2 overshoot) and a peak-to-control pO_2 ratio of 1.47±.06. Capillary reactive hyperemia velocity had a time-to-peak of 7.7±1.7 seconds and a peak-to-control velocity ratio of 2.25±.16. The recovery of reactive hyperemia to the postocclusion control velocity usually preceded the pO_2 overshoot recovery. These data demonstrate that the onset of tissue hypoxia is very rapid in the ALD following blood flow deprivation and that tissue pO_2 returns to control or transiently overshoots at a time when reactive hyperemia flow is near maximum. This latter finding is inconsistent with the hypothesis that tissue pO_2 directly regulates blood flow during reactive hyperemia. (Supported by AHA-Arizona Affiliate Research Fellowship and by NIH grants HL 15884, HL 17421, and HL 15390)

VARIATIONS IN BLOOD FLOW DURING LAPAROSCOPY. S.Kleinhaus*, R.J. Sammartano* and S.J. Boley, Dept. Surgery, Montefiore Hospital & Medical Center-Albert Einstein College of Medicine, Bronx,N.Y. 10467.

Laparoscopy with intraperitoneal insufflation of CO^2 is a useful modality for the evaluation of ischemic bowel. To investigate the possible deleterious effects of elevated intraperitoneal pressure (IP) on blood flow to normal and partially compromised bowel the following experiments were performed. In five dogs superior mesenteric blood flow (SMBF), carotid blood flow (CBF), femoral blood flow (FBF), blood pressure (BP) and central venous pressure (CVP) were recorded at IP of 10,20,30 and 40 mmHg. In five other dogs the SMBF was reduced to 50% of normal by partial occlusion prior to the performance of identical experiments. Increasing IP in 10mm increments from 10-40 mmHg in the first group produced stepwise reductions in the SMBF, CBF and FBF from 18-49%, from 9-31% and from 36-75% respectively. BP and CVP were increased from 0-11% and from 24-55% respectively. In the second group, increases in the IP as above produced further stepwise reductions in SMBF, CBF and FBF by 10-28%, 12-42% and 40-68% respectively, and increases in BP and CVP from 3-11% and 33-39% respectively. These results seem to indicate that the changes in the parameters measured are a result of direct pressure on the aorta, superior mesenteric artery and inferior vena cava. We conclude that laparoscopy can be performed without undue risk even in patients with vascular compromise if done rapidly and care is taken to utilize the lower ranges of IP.

EFFECT OF EXPIRATORY ELASTIC AND RESISTIVE LOADING ON THE DURATION OF EXPIRATION. Raymond C. Koehler* and Beverly Bishop. Dept. Physiology, State Univ. of N.Y. at Buffalo, Buffalo, N.Y. 14214.

To examine how the respiratory center processes pulmonary afferent information during expiration for determining its duration, T_e, elastic and resistive loads were presented during single expirations, thereby altering the volume-time profiles. Cats were anesthetized with Dial-urethan, tracheotomized and placed in a full-body box for recording lung volume above FRC. The airway was connected to a two-way valve through which the expiratory line was randomly linked to 1 of 4 resistive or 6 elastic loads after a normal inspiration. As the cat expired into an elastic load (a bottle), tracheal pressure gradually increased and airflow decreased faster so that lung volume reached a plateau above FRC by middle to late expiration. When the prolongation of T_e beyond control, ΔT_e, was plotted as a function of the volume above FRC at the end of expiration, ΔV, the curve was concave towards the ΔT_e axis for elastic loads, i.e., a greater ΔV resulted in a greater gain in the response. This concavity may be explained by assuming that T_e is a function of the time-integral of vagal feedback since an increase in ΔV results in a greater than proportional increase in the integral of the volume-time profile. Resistive loading, which did not produce a volume plateau, resulted in a greater ΔT_e than elastic loading for the same ΔV. This difference further supports an integration mechanism since the integral of the volume-time profile for resistive loads was greater at the same end-expiratory volume. Inspiring 5.9% CO_2 resulted in both larger inspired volume, ΔV and ΔT_e for a particular load. However, the ΔT_e vs. ΔV curve for hypercapnic loading was a continuous extension of the normocapnic curve, indicating that CO_2, per sé, does not directly potentiate the prolongation of T_e. (Supported by USAF F41609-75-C-0003 and NIH 5T01GM0034116.)

HOW DECREASED BLOOD FLOW DERANGES METABOLISM IN CARDIAC ISCHEMIA: A HYPOTHESIS. Michael C. Kohn* and David Garfinkel, Moore School of Electrical Engineering, University of Pennsylvania, Philadelphia, Pa. 19174

A recently completed model of purine metabolism in perfused rat heart accounts quantitatively for the known depletion of adenine nucleotides in ischemia (submitted to Am. J. Physiol.). To account for the behavior in ischemia, it was necessary to lower the rate constant for diffusion of purines between the interstitial fluid and the perfusate to adjust for lower coronary flow rate. This is interpreted to indicate that the increased residence time of perfusate in capillaries permits local equilibration between these two compartments where normally there are gradients between them and a high rate of washout. We propose that a similar phenomenon should occur for O_2, CO_2, glucose, pyruvate, and lactate, while the tissue may be making a normal biochemical response to the resulting reduced rates of substrate delivery and waste product removal. At low coronary flow rates, glucose, O_2, and pyruvate equilibrate so interstitial level and cellular uptake are lowered; conversely CO_2 and lactate accumulate in the interstitium and consequently in the cells. This accounts for lowered tissue glucose and pH and high tissue lactate in ischemia and is supported by data on changes in cardiac lymph composition in ischemia. O_2 depletion and CO_2 acidosis will then eventually lead to depletion of glycogen and high energy phosphates and will ultimately destroy viability.

(Supported by NIH grant HL 15622.)

ABOLITION OF CEREBRAL VASODILATION DUE TO HYPOTENSION AND ARTERIAL HYPOXIA BY INCREASED LOCAL SUPPLY OF OXYGEN. H.A. Kontos, E.P. Wei*, A.J. Raper, W.I. Rosenblum and J.L. Patterson, Jr. Departments of Medicine and Pathology, Medical College of Virginia, Richmond, Va. 23298

Anesthetized cats were equipped with a cranial window for observation of the pial microcirculation. Cerebral arterioles dilated from $57 \pm 3\mu$ to $86 \pm 5.7\mu$ in response to hypotension. Arterial hypoxia induced by breathing 7% O_2 also produced dilation ($49 \pm 2.1\mu$ to $67 \pm 3.8\mu$). Both types of dilation were abolished by perfusion of the space under the window with fluorocarbon (FC-80) equilibrated with 100% O_2. Dilations were not affected by FC-80 equilibrated with 100% N_2. Artificial CSF equilibrated with 94% O_2 was only partially effective in reversing these dilations. FC-80 carries 48 ml O_2/100 ml and in addition increases O_2 diffusivity twofold, thereby markedly increasing the local supply of O_2 to vessels and brain under the window. The effect of local O_2 on the vessels themselves seems modest, since FC-80 equilibrated with 100% O_2 constricts resting vessels by only 10% and CSF equilibrated with 94% O_2 has an even smaller effect. Our data are compatible with the hypothesis that hypotension and hypoxia produce dilation by a common mechanism, local brain hypoxia, which is counteracted by increasing O_2 supply to the brain via the use of oxygenated fluorocarbon. The data make it unnecessary to postulate that reflex mechanisms, initiated at a distant site, are responsible for the dilation seen in either arterial hypoxia or hypotension.

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BMES

METHODOLOGICAL ASPECTS OF MUSCLE SURFACE pH MEASUREMENTS. Gerald J. Kost* (SPON: A. Fronek). Dept. of AMES-Bioengineering, University of California, San Diego, La Jolla, CA 92093.

In anesthetized rabbits surface pH (SpH) probes were positioned so as to selectively record the SpH of the medial gastrocnemius (MG) and soleus (S) muscles. MG & S surface temperatures, arterial pH (ApH), femoral venous pH (VpH), and blood pressure were also recorded. SpH system calibration drift (0.00 ± 0.03 s.d., range: -0.07 to 0.05, 7.38 pH buffer test) at the end of experiments (6-8 hrs.) was negligible. Calibration slope adjustments (7.38 and 6.84 pH buffers) did not change. Small temperature fluctuations observed did not require compensation. Reproducible data resulted when the pressure of the SpH probe against the muscle surface was minimized, fascia and skin were closed independently around the probe shaft, and minor bleeding was not allowed to contaminate the measuring site. Data from experiments indicated that the relationship: ApH > VpH > MG SpH ~ S SpH holds during control conditions. ApH, VpH, MG SpH, and S SpH were, respectively: 7.47 ± 0.06 s.d., 7.45 ± 0.06, 7.44 ± 0.04, 7.42 ± 0.05 -- initial; 7.49 ± 0.04, 7.47 ± 0.04, 7.40 ± 0.04, 7.40 ± 0.05 -- end of 1 hour control; and 7.50 ± 0.04, 7.45 ± 0.06, 7.41 ± 0.06, 7.41 ± 0.05 -- end of experimental period. During control periods, a slight probe movement would result in SpH elevation, then a rapid return to the former range. In conclusion, during control periods SpH is approximately equal for different muscle types. ApH, VpH, and SpH are consistently and reproducibly related. (Supported by Grants PHS HL07089 & HLI2690-07A1.)

MODULATION OF SYMPATHETIC CARDIOVASCULAR REFLEXES BY CAROTID SINUS BARORECEPTORS AND OTHER VAGALLY MEDIATED MECHANISMS IN THE CANINE. D.R. Kostreva*, E.J. Zuperku*, G.L. Hess*, R.L. Coon, and J.P. Kampine* (SPON: H.M. Klitgaard) Med. Col. of Wisc. and Wood VA Ctr., Milw. Wisc. 53226

Excitatory cardiovascular responses to electrical stimulation of the upper thoracic sympathetic afferent nerves were observed in seven halothane - anesthetized mongrel dogs. The central end of the transected ventral limb of the left ansa subclavia was stimulated before and after several types of denervation. The supramaximal stimulus parameters were found to be 20 Hz, a pulse duration of 1 msec, and a current strength of 3 ma. Significant increases in right and left ventricular maximum systolic pressures, systolic and diastolic systemic blood pressures, and aortic flow were observed. The carotid sinuses were denervated bilaterally and stimulation of the ansa was repeated. Complete denervation was verified by the absence of heart rate and blood pressure responses to simultaneous bilateral carotid sinus compression. The cardiovascular responses to stimulation were greater in magnitude than those observed prior to denervation. The marked increase in sympathetic efferent responses to afferent stimulation after carotid sinus denervation seems to indicate that these baroreceptors do have an attenuating effect on upper thoracic sympathetic reflexes. Cardiovascular responses to stimulation of the ventral ansa after bilateral cervical vagotomy were siginificantly less than the responses observed after carotid sinus denervation prior to vagotomy. However, the responses after vagotomy were statistically identical to responses obtained while stimulating the ventral ansa when the carotid sinuses and vagi remained intact. This introduces the possibility of the existence of vagally mediated mechanisms, other than the carotid baroreceptors, that may modify spinal reflexes. (Supported in part by the Wisconsin Heart Association and NIH Grant HL 16511-01A2)

THE EFFECT OF OXYGEN AT HIGH PRESSURE ON PYRUVATE DEHYDROGENASE (PDH) ACTIVITY IN CORTICAL BRAIN SLICES. G.B. Kovachich* and Niels Haugaard*, Institute for Environmental Medicine & Dept. of Pharmacology, University of Pennsylvania Medical Center, Philadelphia, Pa. 19174 (Spon: C. P. Bianchi)

Recent experiments in our laboratory showed that in cortical brain slices PDH activity is increased by exposure to a medium containing increased levels of potassium chloride as determined by subsequent enzyme assay of the crude homogenate (Pharmacologist, 1976). Maximal effect of 30% increase in activity was observed at 75 mM KCl. The dependency of the potassium effect on both calcium and sodium ions in the medium suggests that the activation of this mitochondrial enzyme is indirect, mediated probably through changes occurring in the cell membrane. The effect of 100% oxygen was studied on this system in the 1 to 5 atm range. It was found that PDH is susceptible to a dose-dependent inhibition by oxygen. The activation of PDH by potassium was reversed within 20 min at 5 atm O_2. Under the same conditions, in the presence of normal Krebs-Ringer medium, the inhibitory effect of O_2 was only slight. Exposure to helium at increased pressure in the presence of 1 atm O_2 had no effect. The mechanism of the oxygen-related depression of PDH activity is currently under study. When sodium was omitted from the high potassium medium, oxygen inhibition was not observed. The requirement for sodium in the high potassium medium suggests that the effect of oxygen is not a direct one but is related to changes in the activity of the sodium pump. (Supported by grants NIH HL-08899-11 and Office of Naval Research N00014-76-C-0248.)

EFFECT OF PRESSURE PULSATIONS ON TIME MEAN FLOW RATE. C.K.Krishnakumar* Allen A. Rovick and Zalman Lavan*. Dept. Physiology, Rush Medical Coll. Chicago, Ill. 60612

Recent studies have reconfirmed observations that pulsatile arterial pressure (PP) produces a time average blood flow ($\bar{Q}$) that is different from the flow (Q) caused by non-pulsatile pressure (P) perfusion at the same mean pressure gradient. This study evaluates possible hydrodynamic contributions to such a flow difference by comparing Q and $\bar{Q}$ in rigid glass tubes perfused with water and dog's blood. Using water, Q exceeds $\bar{Q}$ in a long tube (length (L) to diameter (D) ratio = 110.5), in which entrance effects are small. The magnitude of this flow difference is only slightly and not systematically affected by pulse frequency (varied between 1 and 4 Hz), but increases with increasing pulse amplitude (varied between 20 and 80% of input P, peak-to-peak). The flow decrement results from early transition to turbulence. It appears first at Reynolds number (Re) near but below the P transition value, increases to a peak value at Re$\sim$2100 and declines as the P turbulence intermittancy increases. In a shorter tube (L/D=30.5), where entrance effects are significant, the water flow-reducing action of PP is smaller. Blood flow reductions caused by PP in this tube are slightly larger than water, appear at lower Re and occupy a narrower Re range. In a tube of L/D=20, the blood flow-reducing action of PP is nearly absent. Since blood vessels have L/D of 20 or less, the arterial pulse probably cannot produce a significant increase in hydraulic impedance in them by early induction of turbulence or by increasing turbulence intermittancy value or intensity.
(Supported by Chicago Heart Association)

AN ALTITUDE INDUCED RESPIRATORY OSCILLATOR - OCCURRENCES AND GENERAL DESCRIPTION. R. Kronauer†, P. Brusil†, P. Gulesian, Jr.†, and T. Waggener†
(SPON: J. Whittenberger). Harvard School of Public Health; Div. Eng'g & App. Physics. Harvard University, Cambridge, MA 02138.

Magnetometers were used to monitor the respiration of 16 supine subjects for up to 45 mins. at near sea level and then at various stages of acclimatization to an altitude of 10,000 ft. Gross breath shape was defined by the parameters: inspiratory duration, T_i, expiratory duration T_e, total breath duration, T_t, inspired volume, Vi, expired vol., V_e, and ventilation $\dot{V}_e$. A "comb-filter" computer program permitted dynamic breath pattern analysis and revealed that the chronological sequences of these variables often display large, sustained, simultaneously occurring oscillations. The period of these oscillations is 23 sec (S.D. $\pm$3); the average amplitudes (expressed as percent deviations about the mean) are typically 12% for T_t, 15% for V_e, and 29% for $\dot{V}_e$. The amplitude of $\dot{V}_e$ oscillations was observed to be as large as $\pm$75% of the mean $\dot{V}_e$ level. In these large $\dot{V}_e$ oscillations, the breath-to-breath changes in V_e and T_t oscillate out-of-phase, i.e., the maximum of V_e corresponds to a minimum of T_t, so that the $\dot{V}_e$ oscillations are reinforced and thus more significant than either the V_e or T_t component. The oscillatory changes in T_t are accounted for primarily by changes in T_e, while T_i changes paradoxically. While only 25% of the subjects display such reinforcing oscillations, the frequency regime of these reinforcing oscillations is remarkably consistent from subject to subject. These oscillations are exhibited only at altitude (most prominently after acclimatization) and are not a function of acid-base balance. Generally, these oscillations appear in bursts of about 8 cycle duration, but occasionally they are sustained for durations up to 12 mins. (Supported by NIH Grant 1 RO1 HL 16325-01A1 and Fellowship 1F22 HL 01254-01.)

SECRETION OF HUMAN PLASMA OXYTOCIN. P. Kumaresan, A. Vasicka*, G. S. Han*, and Malathi Kumaresan*. Dept. of OBS-GYN, Coney Island Hospital., Brooklyn, N. Y. 11235.

Plasma oxytocin (OT) has been measured by radioimmunoassay throughout pregnancy in weekly intervals, labor and delivery and in another study during saline and prostaglandin ($PGF_{2\alpha}$) in midtrimester. In 8 clinically healthy normal patients during early stage of pregnancy the level of plasma OT markedly fluctuated, then a regular steady pattern of increase of OT began at around 28-32 weeks until near term. However, the level dropped one or two weeks before true labor started. This kind of pattern was noticed consistently in all patients. There was marked difference in plasma OT levels in individual patients: from 25 μU/ml to 150 μU/ml at 20 weeks of gestation. However, generally a good producer of OT remained a good producer throughout pregnancy. In general during labor OT was found less than that during the surge of OT at near term. The pulsating pattern of OT was found during labor. Four patients showed slightly more prominent surge of OT at delivery than at 40 weeks of gestation. Saline and $PGF_{2\alpha}$ treated groups first surge of OT was found between 2-8 hours after abortifacient instillation. The highest OT levels found in plasma were associated with the shortest duration of the abortion time in both groups. Conclusions: Oxytocin secretion is not peculiar only to the second stage of labor; indeed it is present in maternal blood throughout pregnancy and labor. It is secreted in spurts; it increases toward term; declines before labor starts and shows no consistent increase during labor. (Sup.by USPHS HD04984)

REGULATION OF MEMBRANE FLUIDITY IN CHICK EMBRYO HEART DURING DEVELOPMENT. H. Kutchai, M. Martin*, and D. Dunning*, Dept. of Physiology, University of Virginia, Charlottesville, Va. 22901

We have previously reported that marked decreases in the fluidity of the plasma membrane of chick embryo heart occur during embryonic development and during post-hatching development. We have also reported that the degree of unsaturation of plasma membrane fatty acids increases during development and hypothesized that the increase in membrane fluidity is partly due to the increased unsaturation. An inconsistency remained in that between 10 and 20 days of embryonic life there is no significant change in membrane fluidity even though the degree of membrane fatty acid unsaturation increases significantly during this period. More recently we have determined the cholesterol/phospholipid molar ratio (C/P) of plasma membrane enriched fractions of chick embryo heart at 5-6, 10, and 20 days of embryonic life (hatching occurs at 21 days) and in adult heart. The pattern of changes of C/P during development is strikingly parallel to changes in membrane microviscosity as measured by the depolarization of fluorescence of diphenylhexatriene. Taken together, the changes in C/P and fatty acid saturation that occur during development can qualitatively explain the changes of membrane viscosity that occur. The changes in lipid composition that occur are not confined to the plasma membrane: both whole heart homogenate and the fraction enriched in mitochondria and endoplasmic reticulum show similar developmental changes in C/P and fatty acid composition. The developmental changes in fatty acid composition are neither unique to chick heart nor universal among developing chick organs: liver and skeletal muscle show similar decreases in fatty acid saturation, but brain fatty acids increase in saturation with development. The metabolic mechanisms by which membrane lipid composition is altered are obscure.

IDENTIFICATION OF FOOD CHEMICALS RESPONSIBLE FOR POSTPRANDIAL INTESTINAL HYPEREMIA IN DOGS. P. Kvietys*, S.P. Sit*, R. Pittman,*J.M. Dabney and C.C. Chou. Dept. of Physiol. Mich. State Univ. E. Lansing, MI 48824

Presence of digested food in the jejunal lumen increases local blood flow (Am. J. Physiol. 230:589, 1976). To identify which products of food digestion are responsible for the hyperemia, we studied the vascular effects of luminal placement of isotonic solutions of the following chemicals: 1) glucose, 2) a mixture of 8 essential L-amino acids (8EAA), 3) a mixture of 8 non-essential L-amino acids (8NEAA), 4) 8EAA plus 8NEAA (16AA), 5) a mixture of oleic acid, monoolein, and taurocholic acid, (FA), 6) glucose (194mM)+16AA(126mM)+FA(7mM)(G-AA-FA). While measuring venous outflows from two adjacent in situ jejunal segments, one of the above solutions was placed in one while normal saline in the other segment. Before and after this test period, both segments contained normal saline. Venous outflows (ml/min-100gm) of the two segments during the three periods were:

Contents		Segment A			Segment B		
in Test	N	NaCl	Test	NaCl	NaCl	NaCl	NaCl
Glucose	(9)	72.9	77.5*	71.0*	69.6	68.7	69.2
8EAA	(8)	51.3	54.0	50.8	51.8	51.3	51.4
8NEAA	(11)	49.6	55.9*	48.8*	45.3	44.7	44.1
16AA	(10)	49.2	55.1*	50.1*	55.7	54.8	54.5
FA	(9)	63.2	74.0*	60.3*	63.7	61.4	60.7
G-AA	(6)	57.0	66.0*	55.0*	59.0	58.0	55.0
G-AA-FA	(7)	69.5	74.8*	65.6*	68.7	66.0	66.1

*Significantly different from preceding value, $p<0.05$. The study indicates that except for essential amino acids, all the digestive products of carbohydrates, protein and fat tested play a role in the jejunal hyperemia occurring during digestion.(Supported by USPHS Grant#HL15231)

EPITHELIAL LINING AND ORGANIZATION OF THE HAMSTER RENAL PELVIS. Eric R. Lacy* and Bodil Schmidt-Nielsen. MDIBL, Salsbury Cove, Me. 04672.

The mammalian renal pelvis plays a physiological role in facilitating exchange of solutes between urine and renal parenchyma. This study investigates the areas of renal tissue exposed to urine and the type of pelvic epithelium covering these areas. The hamster pelvis was studied using latex casts, gross dissection, vascular injections,clearing techniques, histology and electron microscopy. Cortical, outer (OM) and inner (IM) medullary tissue face the urinary space. OM tissue forms 8 scallop-shaped projections, peripelvic columns (PPC), from the cortex into the urinary space. Adjacent PPC are separated by interlobar arteries and veins. The lateral periphery of each PPC is a free flap, the operculum, which increases the surface area of OM exposed to the urinary space. Opercula from adjacent PPC fuse over the interlobar vessels near the base of the papilla forming a blind tunnel, the fornix. This extension of the urinary space is lined by a simple layer of squamous epithelial cells covering the cortex and a simple layer of cuboidal epithelial cells covering the OM tissue. The ureter joins the cortical parenchyma at the hilus and is characterized by a transitional epithelium covering smooth muscle, adipose and connective tissue. These tissues continue to the level of the PPC where they terminate as a free flap, the primary septum (PS). A blind pocket, the secondary pouch (SP), is present between the PS and the renal parenchyma (RM). The lining of the pelvis changes from a typical transitional epithelium near the hilus to a layer of 1-2 irregularly shaped cuboidal cells covering the PS. In the bottom of the SP, the epithelium becomes abruptly thinner, changing to low cuboidal cells which continue over the PPC (OM). Possibilities for solute and water exchange appear to be present between urine and medullary tissue and between urine and cortical tissue. (Supported by NIH Grant AM 15972).

PERIPHERAL AND CENTRAL EFFECTS OF ACETAZOLAMIDE IN THE CONTROL OF VENTILATION. S. Lahiri, R.G. DeLaney* and A.P. Fishman. (With the technical assistance of A. Mokashi). Cardiovasc.-Pulm. Div., Depts. of Med. and Physiol., Univ. of Pennsylvania, Phila., Pa. 19104

Carbonic anhydrase inhibitor, acetazolamide, is frequently used by sojourners at high altitude for the enhancement of ventilatory acclimatization. It is well documented that ventilation is stimulated, alveolar P_{O_2} raised and P_{CO_2} lowered by the treatment with acetazolamide which is thought to provide a protection against hypoxia. It is not known if the stimulation originates both at the peripheral and central chemoreceptors. We studied the question by recording carotid chemoreceptor activity and ventilation simultaneously in six anesthetized cats. Steady state responses of ventilation and carotid chemoreceptors to changes in end-tidal P_{CO_2} and P_{O_2} as well as arterial blood gases and H^+ were measured before and after acetazolamide treatment (50 mg. kg^{-1} intravenously). It was found that ventilation at a given Pet_{CO_2} was higher after acetazolamide but the slope of $\dot{V}_I$-Pet_{CO_2} response line was not increased. However, the activity and response of carotid chemoreceptors to changes in Pet_{CO_2} diminished considerably. Acetazolamide decreased both carotid chemoreceptor and ventilatory response to hypoxia. These results show that while the central mechanism is stimulated by acetazolamide, the oxygen sensing mechanism is blunted. This blunting is presumably due to a diminished P_{O_2}-P_{CO_2}-H^+ interaction at the peripheral chemoreceptors. If the two responses are mediated at the receptor site through H^+ the results indicate that the $[H^+]$ is manipulated differently at the two sites. (Supported in part by grant HL-08805 from NHLI).

ETHANOL EFFECTS ON STEADY-STATE OXIDATIVE METABOLISM OF CAT AND RAT CEREBRAL CORTEX. Joseph C. LaManna,* B. Wyatt Younts jr.* and Myron Rosenthal. Duke University Medical School, Durham, N.C. 27710.

Although there are well-known behavioral effects of ethanol consumption, efforts at determining the biochemical basis for the neurochemical and electrophysiological alterations produced by this drug have met with difficulty. In this study, we report the effects of ethanol on "resting" energy metabolism of intact cerebral cortex of cats and rats. Changes in the redox level of intramitochondrial NADH were recorded by microfluorometry (450 nm - 366 nm). Redox changes in cytochrome $\underline{a},\underline{a}_3$ were monitored by dual wavelength reflection spectrophotometry (605 nm - 590 nm). These non-invasive optical techniques allowed direct electrical stimulation of the area under observation and recording of ECoG, evoked potentials and shifts in steady potential in the unanesthetized (cerveau isolé) preparations. Low ethanol doses (below 1g/kg) were accompanied by increased levels of reduced NAD and cytochrome $\underline{a},\underline{a}_3$, an effect similar to that produced by phenobarbital and chlorpromazine. This ethanol action appears due to a decrease in tissue activity common to central depressants. Higher ethanol doses (1-2g/kg) were also accompanied by an increased level of reduced cytochrome $\underline{a},\underline{a}_3$ but a decreased level of reduced NAD. Acetaldehyde at all effective doses produced similar changes in NAD and cytochrome $\underline{a},\underline{a}_3$ reduction levels as the higher ethanol doses. The oxidation of NAD at high ethanol doses and at all doses of acetaldehyde appears to be a unique effect of these drugs and to be due to acetaldehyde formation following acute ethanol injection. (These studies were supported by PHS grant NS-10384 and a grant from the North Carolina Alcoholism Research Authority).

ASZ(DCPB)

A SUSPENDED FOLLICULAR CELL SYSTEM FOR THE STUDY OF IN VITRO GONADOTROPIN ACTION ON THE TURTLE (CHRYSEMYS PICTA) OVARY. Valentine Lance and Ian P. Callard, Department of Biology, Boston University, Boston, MA 02215. Supported by NSF Grant # BMS75-18910 to I.P.C.

Suspended ovarian cell systems are extremely sensitive and thus valuable for studies where hormone supplies are limited. We have attempted to adapt such a system for the study of gonadotropin action in the turtle. The technique used for the preparation of ovarian follicular cells was that described by Sayers, Swallow and Giordano (Endocrinology, 88, 1063,1971). After trypsinization, cells were harvested by centrifugation at 100 x G and viability determined by the dye exclusion test. Ovarian cells were diluted in Krebs Ringer bicarbonate medium with bovine serum albumen (0.5%) to give circa 200,000 cells/0.9 ml. and aliquoted into individual vials for incubation at 32°C for 3 hours in a Dubnoff metabolic incubator. Gonadotropins (NIH-LH-S18, ovine; NIH-FSH-S9; ovine) were diluted to give 100 pg, 1 ng, 10 ng, 100 ng, 1 ug, and 10 ug/0.1 ml buffer and 0.1 ml added to each vial. Each point on the curve was run in triplicate and at the end of the incubation period the vials were frozen until extracted for progesterone (P) and testosterone (T) analysis by RIA. FSH stimulated P production from 150 pg/ml to 1000 pg/ml over the full dose range, whereas LH caused only a 2-fold increase. An increase in T production from 10 pg/ml to 4000 pg/ml was elicited by FSH, but only a slight increase was detected at the maximum LH dose. Similar results were obtained in both fall and spring animals. Thus, in contrast to in vitro studies of radioisotopic incorporation where LH stimulated progesterone synthesis and FSH did not, (Callard et al.,Gen.Comp.Endocrinol. 28,2-9,1976),FSH appears to be the more potent hormone when assayed by the stimulation of steroid synthesis from endogenous precursor in isolated cells.

METABOLIC PERFORMANCE AND GASTROINTESTINAL FUNCTION IN THE MAGNESIUM-DEFICIENT RAT. W.E. Landin*, F.M. Kendall, and M.F. Tansy, Dept. of Physiol. and Biophys., Temple Univ. Hlth. Sci. Ctr., Philadelphia, Pennsylvania 19140

With few exceptions, most of the existing literature concerning the effects of chronic magnesium deficiency in the rat considers the gastrointestinal system only in terms of magnesium absorption, excretion, and conservation. The purpose of this study was to determine whether it could be inferred that the gastrointestinal motor functions of rats which had been maintained on a magnesium-deficient diet were different than similar functions in populations of control animals. Seventy-seven adult, male Sprague Dawley rats were used in these studies. Both control and experimental groups were maintained on a normal ad lib. laboratory diet for 30 days, after which the experimental rats were switched to a commercially available ad lib. diet containing a magnesium concentration of 16.2 ppm for a period of 30 days. Ten rats were used to determine the acetylcholine responsiveness of duodenal muscle strips in vitro. In all cases it was concluded that the strips from the deficient rats were hyper-responsive to a fixed dose of acetylcholine. Forty-six rats were used to determine average intestinal transit rate by the method of Macht. It was concluded that average intestinal transit rate was significantly increased in the case of 30-day deficient rats. A final series employed 21 rats who were housed in individual metabolic cages. After five days on the deficient diet the average daily fecal pellet counts and fecal weights were significantly reduced. It is concluded that a state of chronic magnesium deficiency is associated with altered gastrointestinal motor function in the adult, male rat.

ASZ(DCPB)

TEMPERATURE EFFECTS ON OSMOTIC PERMEABILITY OF FROG SKIN. Y.T. Lau and R.H. Parsons (SPON: W. Auclair). Dept. Biology, Rensselaer Polytechnic Institute, Troy, N.Y. 12181

Rana pipiens were acclimated in tap water at 5°C or 15°C for 36-48 hours before use. Osmotic water permeability (Lp) of frog skin in vivo was measured by tying the cloaca and weighing at 1 hr. intervals. Lp was 0.12±0.03(8) and 0.30±0.02(7) $gm \cdot 100cm^{-2} \cdot hr^{-1} \cdot 200mOsm^{-1}$ at 5°C and 15°C respectively. After an acute temperature (T) change of 10°C, between 5° and 15°C, the in vivo response can be divided into two stages. The first stage (first hr. interval after T change) is seen only in vivo and may involve a physiological mechanism at the whole animal level. The second stage (the rest of the experimental period) is seen both in vivo and in vitro, giving a Q_{10} for the 5° and 15°C acclimated animals of 4.25±1.29(8) and 2.65±0.27(7) respectively. An acute T decrease causes a significant decrease in the plasma osmotic concentration from 203±2(13) mOsm to 196±2(21) mOsm within one hour. Since the first stage response after transferring frogs to cold is an increase of Lp instead of the expected decrease, the dilution of plasma within one hr. suggests that the primary effect of T change is possibly on an osmoregulatory mechanism which then changes the skin Lp. (Supported by grant GB-40816 from NSF.)

AN INTEGRATED APPROACH TO THE INTERPRETATION OF BIOCHEMICAL DATA OBTAINED IN MANNED SPACE FLIGHT OPERATIONS. C. S. Leach, P. C. Rambaut* J. I. Leonard*, Metabolic & Biochemistry Branch, Food & Nutrition Branch, NASA/Lyndon B. Johnson Space Center & General Electric Company, Houston, Texas 77058.

In conjunction with the three manned flights of the Skylab program over 1000 man-days of metabolic balance data were accumulated. These data included accurate records of the intake of about forty individual nutrients and urinary and fecal output data on a much larger number of metabolically significant elements and compounds. In addition to these input/output data, analyses were also performed on the plasma level of a series of metabolites and upon the size of various intra- and extracellular compartments. Interpretation of this quantity of data by conventional means represented a task of overwhelming magnitude. A system was, therefore, employed which depended upon data base management systems coupled with statistical analysis and automated simulation models to illustrate consistencies and inconsistencies in the observations. Through the use of this integrated systems approach, three major findings have emerged. (1) Losses of water are primarily a result of decreases in fluid intake rather than increases in urine volume or evaporative losses. (2) Losses in electrolytes are almost entirely attributable to increases in urinary output. The losses in sweat actually diminished but not to an extent sufficient to compensate for the renal losses. (3) Although gross energy consumed in the form of food inflight did not differ significantly from preflight, accompanying losses in adipose tissue suggest that caloric requirements may have been greater in space than on the ground.

ROLE OF METABOLIC ACIDOSIS IN THE PULMONARY HEMODYNAMIC RESPONSE TO HEMORRHAGE AND SHOCK. O.H. LeBlanc* and A.B. Malik (SPON: R.W. Lawton) Department of Physiology, Albany Medical College, Albany, N.Y. 12208

We studied the role of metabolic acidosis in mediating the pulmonary hemodynamic adjustments to hemorrhagic hypotension (He) (arterial pressure of 40 mmHg) and circulatory shock (Sh) defined as decrease in pressure following infusion of shed blood. The response in anesthetized dogs developing acidosis was compared with the response in dogs in which pH was continuously monitored and controlled between 7.32 and 7.35 by HCO_3^- infusion. In dogs developing acidosis (Ac), pulmonary arterial pressure (Pa) did not change during He and increased above control during Sh. In non-acidotic, pH controlled dogs (NAc), Pa decreased during He and returned to control during Sh. Left atrial pressure changes in both groups were similar. Pulmonary blood flow decreased to similar levels in both groups during He, and returned to control in NAc but not in Ac during Sh. Pulmonary vascular resistance increased more ($p<0.01$) in Ac than in NAc during He, and returned to control in NAc but remained elevated in Ac. The distribution in pulmonary perfusion measured with labelled microspheres was not different from the control pattern in Ac during He; however, in NAc, the upper lung regions were poorly perfused during He. Upper lung hypoperfusion in NAc was consistent with decreased Pa during He, and was associated with a large increase in alveolar dead space. During Sh, the distribution of pulmonary perfusion in both groups was not different from the control pattern. Therefore, metabolic acidosis resulting from hemorrhage-induced systemic hypotension maintains the Pa and regional pulmonary perfusion due to the pulmonary vasoconstriction induced by increase in the H^+ concentration. (Supported by HL-17355).

CAPILLARY PERMEABILITY AND FLUID TRANSPORT OF A VASCULAR-PERFUSED INTESTINE. J.S. Lee, Dept. Physiology, University of Minnesota, Minneapolis, Mn. 55455

A 15-cm segment of rat jejunum was perfused through its vascular system with Ringer solution containing 3% bovine serum albumin. Arterial pressure was 20-25 mmHg and venous pressure was 0. Capillary permeability was measured by the rate of serosal flow (S), which was the fluid leaked out from the serosal surface and mesentery. Net fluid transport (J_V) across the intestinal mucosa was the algebraic sum of V-A difference (venous outflow - arterial inflow) + lymph flow (L) + S. A positive J_V indicates net fluid absorption and a negative value indicates fluid secretion into the lumen. Luminal fluid was Ringer solution plus 0.5% glucose. When the intraluminal distention pressure (DP) was 3 mmHg, S was nearly 0 and mean J_V was +27 µl/cm·hr in the early 20 min period of vascular perfusion, but S increased with time and J_V became negative 40 to 60 min later. When DP was 10 mmHg, S increased to 94 µl/cm·hr and J_V was -93 µl/cm·hr even in the early 20 min period, indicating a remarkable increase of capillary permeability and fluid secretion. With DP of 10 mmHg, diphenhydramine (antihistamine) in the perfusate reduced S to 0, and J_V became positive or slightly negative. The hypermotility of the perfused segments was also inhibited by antihistamines. When compound 48/80 was present in the perfusate, the perfused segments behaved similarly to those at high DP with increased capillary permeability and fluid secretion. Based upon these findings and other evidences it is concluded that the release of endogenous histamine is involved in the increase of capillary permeability and fluid secretion by the action of 48/80 and elevation of DP. (Supported by PHS grant AM18085.)

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EFFECT OF PROTEIN LEAKAGE ON THE STEADY-STATE FLUID MOVEMENT BETWEEN THE TISSUE AND VASCULAR COMPARTMENTS, J.S. Lee, Div. Biomed. Eng., Univ. of Virginia, Charlottesville, VA. 22901

Let us model the exchange of solute (the protein) and the fluid in an organ as one across two well mixed compartments, the tissue and vascular one. The latter with a constant colloidal osmotic pressure (COP) is the only fluid and protein source of the tissue. The hydrostatic pressure between these two compartments (ΔP) and that of COP ($\Delta \Pi$) are the two pressures responsible to the fluid flux Jf and protein flux Jp. The condition of homeostasis requires that $Jf \geq 0$ and $Jp = Jf \cdot Ct$ where Ct is the protein concentration in the tissue. For zero fluid and protein accumulation in the tissue, these two fluxes are removed by the lymphatic system. If the endothelium between the two compartments is impermeable to protein, only two steady-state conditions exist: 1) $Jf = 0$ which requires an exact balance of the responsible pressures or 2) $Jf > 0$ and $Ct = 0$. On the other hand , if the endothelium leaks protein, this condition $Jp = Jf \cdot Ct$ can be used to determine the value of Jp, Jf and Ct as a function of the pressure difference ΔP. If the matrix formed by the partial differentiation of the fluxes with respect to the pressure differences is positive definite, one can show that the steady-state filtration is a monotonic increasing function of ΔP. The use of the Kedem-Katchalsky equation, the linear version of the above general relations, shows that the higher the protein permeability, the larger the steady-state fluid flux. In summary, this model study suggests a positive difference in hydrostatic pressure will always cause filtration from blood to tissue if the endothelium leaks protein. (Supported in part by HL 16812)

ACTIONS OF SOMATOSTATIN (SRIF) AND SECRETIN (S) ON STIMULATED OR SPONTANEOUS MYOELECTRICAL ACTIVITIES OF GASTRIC ANTRUM AND DUODENUM.
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In 4 fasting dogs with gastric fistula and platinum electrodes implanted in the antrum and duodenum, effects of SRIF or S on spontaneous myoelectrical activity or activities stimulated by motilin (M), CCK-octapeptide (CCK-OP) and pentagastrin (P) were studied (2 expts/dog). In phase I, i.v. administration of M or CCK-OP or P in doses of 0.125, 0.25, 0.5, 1.0 ug/kg/hr resulted in a significant increase in mean % incidence of spikes in both antrum and duodenum. % spikes over slow wave by M, CCK-OP and P at rate of 1.0 ug/kg/hr were 78.7, 66.8 and 58.7% in antrum, 64.8, 42.1 and 34.7% in duodenum, indicating M is the most potent stimulant of the myoelectrical activities. Intravenous infusion of SRIF or S at 1.0 ug or unit/kg/hr produced a marked inhibition of M, CCK-OP or P (1.0 ug/kg/hr) stimulated myoelectrical activities. The inhibitory effect of SRIF was more profound than that of S. Secretin, 1.0 unit/kg/hr, inhibited phasic activity when it was given in phase I by delaying appearance of phase II, but there was no significant inhibition when it was given in phase III in fasting dogs. SRIF, however, inhibited spontaneous phasic activity in either phase I or phase III. These studies indicate that 1) motilin is the most potent stimulant on the antral and duodenal myoelectrical activities, 2) SRIF and secretin inhibit effects of motilin, CCK-OP and pentagastrin, 3) secretin delays spontaneous phasic electrical activity, but 4) SRIF inhibits the phasic electrical activity by blocking the propagation from phase I to phase II or spike activity in phase III.

ON THE SURFACTANT FILM TRANSFERRED FROM THE LUNG WASH.
L.P. Lee* and J.S. Lee. Div. of Biomed. Eng., Univ. of Virginia, Charlottesville, VA. 22901.

The objective of this study is aimed to investigate the physical properties of surfactant coated on a solid. Because of the highly negative interstitial fluid pressure in the lung, it is probable that any fluid pocket situated in between the surfactant film and the epithelium will be absorbed by the interstitial space. As a result the lining of the surfactant film *in situ* may have different properties from that formed at the top of the lung wash, a film on fluid. To obtain the film on a solid, a modified Langmuir-Blodgett technique was employed to transfer the surfactant film lying at the air-liquid interface of lung wash onto a hydrophilic solid plate. It was found that more surface active materials are obtained by the transferred technique from film in the condensed state than that at the expanded state. Lipid components in the transferred film are comparable qualitatively to those in the surface active material isolated by density gradient centrifugation. A comparison study on the weight ratio of phospholipids to protein of the lung wash, transferred film and surface active material isolated by centrifugation suggests that this transfer procedure is able to isolate more effectively the surface active material and to reduce contamination from the fluid below the interface of the lung wash. The droplets of some nonvolatile and inert fluids were placed on the transferred film to measure their contact angle. It was found that the computed adhesion tension is higher when the surface tension of the lung wash set for film transferring is higher.
(Supported in part by HL 17108 and HL 16812).

RELATIONSHIPS OF PROSTAGLANDINS $F_{2\alpha}$ AND E_2 TO DIGITAL CLUBBING IN CYSTIC FIBROSIS PATIENTS. R.J. Lemen*, A.J. Gates*, W.W. Waring*, P.D. Kadowitz*, A.A. Mathe*, and A.L. Hyman. Dept. of Pediatrics, Physiology, and Pharmacology, Tulane University, New Orleans, LA 70112

Digital clubbing, a common manifestation of pulmonary diseases, may be related to the release or failure of deactivation of vasoactive substances in the lung. Nine patients (ages 5.6 to 26.2 years) with digital clubbing associated with cystic fibrosis were prospectively matched by diagnosis, sex, and approximate age to 9 patients without digital clubbing. We studied the relationships of digital clubbing and disease severity to plasma levels of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and prostaglandin E_2 (PGE_2). The severity of index finger clubbing was determined from the clubbing index (the ratio of distal phalangeal depth to distal interphalangeal depth). Disease severity was determined by the clinical score (Kulczycki and Schwachman) and tests of pulmonary function. Plasma $PGF_{2\alpha}$ and PGE_2 levels were determined by radioimmunoassay. The mean PGE_2 level was significantly ($p<0.05$) increased in patients with digital clubbing (1.8±0.32 SE ng/ml) over that of patients without digital clubbing (0.87±0.20 SE ng/ml). The mean $PGF_{2\alpha}$ level was not significantly different in patients with digital clubbing (0.68±0.07 SE ng/ml) from that in patients without digital clubbing (0.48±0.05 SE ng/ml). Patients with digital clubbing had more severe disease than those without digital clubbing as judged by significantly ($p<.05$) lower clinical scores and vital capacity in the former. These studies suggest that the degree of digital clubbing may be related to the severity of pulmonary disease and to the amount of plasma PGE_2.

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NON INVASIVE EVALUATION OF LEFT VENTRICULAR FUNCTION IN TRAINED MALE AND FEMALE CYCLISTS. David Lemon*, Herman Falsetti, Carl Gisolfi, Judy Cohen* and Brian Claxton*. Cardiovascular Center, Depts. of Internal Medicine and Physiology, University of Iowa, Iowa City, Iowa 52242.

Fourteen male and four female competitive bicycle racers were evaluated utilizing echocardiography, phonocardiography, pulmonary function testing and maximum VO_2 as determined by bicycle ergometry in an effort to define parameters that distinguished this group from the "normal" population. Physical exam was remarkable for resting bradycardia (56±9.3 beats/min) and elevated systolic blood pressure with 6/18 having systolic blood pressure > 140 mmHg. Pulmonary function tests showed above average diffusing capacities (109% of normal). Maximum VO_2 was characteristic of highly trained athletes (62.0±6.9 ml/kg-min) with the observed valves correlating well with competitive performances. Echocardiography showed large stroke volumes (97.5 and ±17ml), normal posterior wall thickness (1.07±.04cm) and normal ejection fraction (71.4±6.33%). Velocity of circumferential fiber (VCF) was below most published normal values (1.16±.13 circumferences/sec). We attribute the low VCF to the large end-diastolic volumes and slow heart rates.

In summary, our findings in bicycle racers are similar to those found in endurance athletes and are characterized by resting bradycardia, improved diffusing capacity, highly developed aerobic capacity, enlarged left ventricle and increased left ventricular muscle mass.

VENTILATORY RESPONSE TO EXERCISE OF DENERVATED EXTREMITIES: OBSERVATIONS IN PERIPHERAL CHEMODENERVATED DOGS. Sanford Levine* (intr. by A. P. Fishman). Cardiovascular-Pulmonary Division, Dept. of Medicine, University of Pennsylvania and VA Hospital, Philadelphia, Pa., 19104.

Previous workers have demonstrated that muscular exercise of denervated extremities elicits increases in ventilation ($\dot{V}E$). In order to clarify the role of peripheral arterial chemoreceptors in mediating this increase in $\dot{V}E$, we completely transected the spinal cord of anesthetized dogs at the second lumbar level (L-2); subsequently, these animals underwent denervation of the carotid and aortic chemoreceptors. Completeness of chemodenervation was tested by rapid intravenous injection of cyanide; no increase in $\dot{V}E$ was observed. Muscular exercise of the denervated hind limbs was then induced by electrical stimulation. Coincident with muscular contraction of the hind limbs, oxygen consumption ($\dot{V}O_2$) increased 172 $\pm$ 33% and $\dot{V}E$ increased 155 $\pm$ 20%; arterial PCO_2 and arterial oxygen saturation remained constant but arterial [H+] increased 4.6 $\pm$ 1.3 nmol/liter. In order to discern the effect of increases in art. [H+] on $\dot{V}E$ in this preparation, isocapnic increases in arterial [H+] were produced in a subsequent group of chemodenervated L-2 spinal transected animals by lactic acid infusion. In these experiments, arterial [H+] increased 10.4 $\pm$ 1.5 nmol/liter; however, the increase in $\dot{V}E$ was limited to 40 $\pm$ 10%. It is concluded that muscular exercise stimulates ventilation by humoral agents other than $PaCO_2$, art. [H+] and arterial oxygen saturation. These unspecified humoral agents act on receptors other than the carotid and aortic chemoreceptors.

EFFECT OF UNILATERAL BRAINSTEM LESIONS ON CEREBRAL BLOOD FLOW (CBF) RESPONSE TO CARBON DIOXIDE IN DOGS. Janice H. Levitt* and C.E. Rapela. (Spon:A. Brodish) Dept. Physiol. and Pharmacol. Bowman Gray Sch. of Med., Winston-Salem, NC 27103.

Previous work by others implicates the CNS in cerebrovascular control. To examine the role of blood pressure changes concommitant with interventions used to study CNS control, cerebral perfusion pressure (CPP)-CBF relationships were studied before and after CNS lesions. CPP changes were obtained by graded compression of the common carotids (CC) with vertebral (V) arteries occluded. The mean between the CC pressure distal to the compression and the (V) wedged pressure was taken as CPP. CBF was recorded by the supratentorial venous outflow method. Pressure-flow (CPP-CBF) curves obtained before and after unilateral midbrain tegmental (UMT) lesions, either during normocapnia ($PaCO_2$=33.8$\pm$0.4mmHg) or hypercapnia ($PaCO_2$=78.5$\pm$5.5mmHg) did not show significant differences. Hypercapnia increased CBF to 268% (pre-) and 257% (post-lesion) of normocapnic values. The CO_2 Index $\left(\frac{\text{CBF (Hypercap-Normocap) ml/min}}{PaCO_2 \text{ (Hypercap-Normocap) mmHg}}\right)$ calculated from CPP-CBF curves at 90mmHg was 0.84 before and 0.65 after the lesions. These results indicate that UMT lesions have no significant effect on the cerebrovascular response to increased $PaCO_2$ within 60 min. of lesion production, but do not rule out the possibility of detecting effects after bilateral lesions. Supported by: NS 11953, HL 5392 and HL 0487.

THEORETICAL ANALYSIS OF LEFT VENTRICULAR FUNCTION. Lucien M. Levy* and Willard M. Daggett (SPON: Laurence R. Young). Harvard Medical School, Massachusetts General Hospital, Boston, Mass. 02114

This study examines the dependence of left ventricular function on cardiac muscle mechanics. Tension (T) versus length (L) relations of isometric or afterloaded contractions can be described by linear expressions of the form $T = c\,L'$ where the force parameter c defines the slope and depends on contractile state, and L' is the muscle length minus its intercept. Relating myocardial wall tension to ventricular segment length and volume at end systole gives stroke volume SV as a function of the corresponding c, end diastolic volume EDV and afterload AL ($SV \simeq EDV' - AL/c$). The steady state relation of SV to AL, heart rate HR and systemic resistance R_S yields new expressions for SV ($SV \simeq EDV'/(1 + R_S HR/c)$). Stroke volume can then be defined by a Starling curve obtained by varying EDV at constant c, HR, and R_S . Since SV was also obtained by varying EDV at constant c and AL, it can thus be defined by the intersection of these two Starling curves. For the Ejection Fraction, the effects of EDV and c balance either those of AL ($EF \simeq c\,EDV'/AL$) or those of HR and R_S ($EF \simeq c/(R_S HR + c)$). Also, EDV is proportional to AL and inversely related to HR, R_S and c ($EDV' \simeq AL\,c/(R_S HR + c)$). This analysis describes the separate contributions of myocardial contractile properties and of cardiovascular parameters to ventricular performance. (Supported by Canadian Medical Research Council.)

EFFECT OF GAS SOLUBILITY ON THE MEASUREMENT OF PULMONARY TISSUE VOLUME. Benjamin M. Lewis, Wayne State Univ. Sch. of Med. Detroit, MI 48201

Overland, Ozanne and Severinghaus (Physiologist 18: 341, 1975) have proposed that pulmonary tissue volume be determined by measuring the concentrations of two soluble gases either after breath holding followed by partial and then full expiration or at two points during rebreathing. I have used this principle to measure tissue volume by rebreathing, taking discrete samples from the rebreathing bag at the end of expiration using 2 different gas pairs: N_2O and C_2H_2 and C_2H_2 and CH_3OCH_3 (DME). The first 2, while differing in solubility by a factor of 2, gave highly variable results because the equation used for calculation is a ratio of differences and changes in concentration beyond the accuracy of analysis (gas chromatography) can markedly affect the value obtained. The 2nd pair differ in solubility by a factor of 10 and the values for tissue volume are little affected by random analytical error. The enormous solubility of DME, however, makes poorly perfused alveoli a large alveolar dead space which delays the onset of exponential decrease in DME concentration to a narrow time period before recirculation distorts concentration changes.

RECOVERY OF DISTRIBUTIONS OF VENTILATION AND PERFUSION AS A FUNCTION OF SPECIFIC VENTILATION. S. M. Lewis, F. M. Longo,* and P. D. Wagner. Department of Medicine, University of California San Diego, La Jolla, California 92093.

Sampling of the washout curve of a poorly soluble gas in the expired air provides data for estimation of the distribution of ventilation ($\dot{V}A$) as a function of ventilation per unit volume ($\dot{V}A/V_O$). If the arterial blood is sampled simultaneously, an estimate of perfusion ($\dot{Q}$) as a function of $\dot{V}A/V_O$ may be obtained in the same manner. Seven anesthetized, ventilated dogs were equilibrated with a mixture of 10% argon, 1% methane, 21% O_2, balance N_2 for 10 min and then rapidly switched to air. The washout of argon ($\lambda = 0.03$) was followed in the expired gas by a mass spectrometer. A series of 12 blood samples were drawn at a fixed point in the respiratory cycle during the first 30 breaths and analyzed for methane ($\lambda = 0.04$) by gas chromatography. Distributions of $\dot{V}A(\dot{V}A/V_O)$ and $\dot{Q}(\dot{V}A/V_O)$ were calculated from the gas and blood data (Fed. Proc. 35: 454, 1976). Prior to the washout the steady state $\dot{V}A/\dot{Q}$ distribution was estimated using a multiple inert gas elimination method. In normal healthy dogs (those showing a narrow distribution of $\dot{V}A/\dot{Q}$) the washout curves of blood and end-tidal gas were similar. Dogs having a wider steady-state distribution of $\dot{V}A/\dot{Q}$ (either spontaneously or as a result of bronchial occlusion) exhibited markedly higher tracer concentrations in the blood than the end-tidal gas at any point in time and the recovered distributions showed considerable perfusion to areas of low $\dot{V}A/V_O$. This technique offers a means of interrelating information about volume, ventilation and perfusion in functional lung units.

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CENTRAL INVOLVEMENT OF ENDOGENOUS OPIATE-LIKE SUBSTANCES DURING NOXIOUS STIMULUS. L. Leybin*, V. Havlicek, M. Rezek*, C. Pinsky*, and F.S. LaBella*. Depts. of Physiology and of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, Manitoba, R3E OW3.

The moderate-temperature hotplate test provides a sustained mildly noxious environment and permits quantification of resultant behavioral responses and their modification by drugs (Pinsky, C. et al., Life Sciences, 16, 1785-1786, 1975). Rats implanted with cannulas in right lateral ventricle were tested on a 44.5°C hotplate for 10 min after intraventricular infusion (10ul/65 sec), with saline or with the endogenous opioid (Hughes, J. et al., Nature, 258, 577-579, 1975) methionine-enkephalin (ME) at 100ug/10ul saline. (Beckman Bioproducts, California.) There was a significantly ($p<0.01$) greater number of hindpaw licks, evaluated over the last 7 min of a 10-min test, in ME-infused rats than in saline controls (+47% and +41% respectively in 2 tests, crossover design). The first 3 min of observation did not show differences between hindpaw licks nor between total licks (hind and forepaw). Latency to first hindpaw lick was significantly shorter ($p<0.05$) in ME-infused rats. All rats infused with ME, but none infused with saline, exhibited signs of opiate narcotic withdrawal (wet dog shakes, rearing, sniffing, restless exploring activity and increased defecation), beginning at 1-3 min after the start of infusion. We interpret these results as indicating that a sustained mildly noxious stimulus promotes the release of an endogenous opiate-like substance, probably other than ME, which can be displaced from its stereospecific receptor site by exogenous ME.

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ROLE OF SODIUM IN STROPHANTHIDIN TOXICITY IN CARDIAC PURKINJE FIBERS. C. I. Lin* and M. Vassalle. Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203

Canine Purkinje fibers were perfused in vitro and transmembrane potentials recorded by means of a microelectrode technique. The fibers (either driven at a constant rate or spontaneously firing) were exposed to strophanthidin 10^{-6}M until spontaneous fast discharge occurred. The following results were obtained. When 52% NaCl in the Tyrode solution was substituted by choline chloride or sucrose, the onset of digitalis toxicity was delayed in both driven and spontaneous preparations. When the NaCl was increased by 20% (and the solution was hypertonic) the time to toxicity was decreased. The mechanism of strophanthidin toxicity in high and low Na solution may not be identical in that in the former solution oscillatory potentials at the plateau level were more frequent and in the latter oscillations appeared in the potential of diastolic depolarization. In solutions (with normal sodium content) made hypertonic by adding sucrose, the time to toxicity was also shortened. When strophanthidin was tested first in a sucrose-hypertonic solution and then in a NaCl-hypertonic solution, toxicity developed sooner in the latter solution. Increasing the tonicity of a low Na solution above normal (by adding choline or sucrose) accelerated the onset of toxicity. The onset of toxicity in isotonic low sodium solution was accelerated by decreasing the $[Ca]_o$ by half. In a solution where all Na was substituted by TEA and Ca, spontaneously firing Purkinje fibers were not intoxicated by strophanthidin; toxicity did appear on returning the preparation to a normal Tyrode solution. It is concluded that both the extracellular and intracellular concentrations of sodium may be important for the onset of strophanthidin toxicity, and no toxicity occurs when all sodium is substituted by other ions. Supported by grant HL17451 from N.I.H.

EFFECTS OF BRAIN MONOAMINE DEPLETION ON THE THERMOREGULATORY RESPONSES OF RABBITS TO DIFFERENT AMBIENT TEMPERATURES. M. T. Lin* and J. T. Stitt. J. B. Pierce Fdn. Lab., Yale Univ. Sch. of Medicine, New Haven, Ct. 06519.

The monoamines norepinephrine (N.E.) and 5-hydroxytryptamine (5-HT) are putative neurotransmitters in the thermoregulatory pathways of the C.N.S. If so, then their depletion by intraventricular administration of 6-hydroxydopamine (6-OHDA) and by 5, 7-dihydroxytryptamine (5, 7-DHT) respectively should markedly impair thermoregulation. We undertook to study the thermoregulatory responses of groups of N.E. depleted or 5-HT depleted rabbits to ambient temperatures (T_a) of 2°, 12°, 22° and 32°C, and to compare these responses to those of untreated animals. Metabolic rate (M), conductance (k), respiratory evaporative heat loss (E_{res}), skin and rectal temperatures were measured continuously in a partitional calorimeter when the animals were in thermal balance at each T_a. Both groups of treated animals maintained their body temperatures within normal limits at all levels of T_a. Animals treated with 5, 7-DHT had significantly higher M at T_a = 2°, 12° and 22°C and had consistently higher values of k and E_{res} than did control animals. Animals treated with 6-OHDA showed marked decreases in M at all levels of T_a, indeed resting M was significantly reduced. E_{res} and k in these rabbits were also consistently lower than for control animals. It is concluded that while brain levels of N.E. and 5-HT alter, in an apparently reciprocal fashion, the thermoregulatory responses of the rabbit, both are not necessary for the maintenance of a normal internal body temperature. (Supported by NIH Grant #NS-04655).

COORDINATED ACTIVITY OF TWO SYNERGISTIC CRAYFISH CLAW MOTOR NEURONS: UNCOUPLING DEPENDS ON DACTYLOPODITE POSITION. B.G. Lindsey* and G.L. Gerstein, Dept. of Physiology, Univ. of Penna., Phila., Pa. 19174

A previous study (Wiens & Gerstein, J. Neurophysiol. 38:909) using statistical methods provided evidence for connections between proprioceptors of the propodite-dactylopodite (PD) organ of the crayfish claw and both the slow closer exciter (CE) and opener inhibitor (OI) motor neurons, synergists innervating respectively the closer and opener claw muscles. A high probability of coincident spike activity in CE and OI was also demonstrated. We now report intracellular monitoring of CE has revealed: 1) unitary monosynaptic excitatory postsynaptic potentials produced by tonically active PD neurons (constant latency, follow 1:1); 2) subthreshold events corresponding to OI spikes, an observation consistent with a direct OI to CE connection or possibly a shared input. Coordinated tonic activity of OI and CE is related to the position of the dactylopodite. Cross-correlation of OI and CE spike trains reveals a high probability of coincident activity when the dactylopodite is held at some positions; at other positions OI activity is present while CE activity may be absent or uncorrelated with OI activity. Temporal stability of these relationships can be demonstrated; repeated samples taken at a given dactylopodite position yield similar results. Cross-correlation analysis also shows that tonic PD neurons may excite both OI and CE at some positions; at other positions the PD-OI interaction persists while CE activity is absent. The results suggest: 1) that the effectiveness of excitation to OI and CE differs, depending on dactylopodite position (various mechanisms are possible), and/or 2) that there is a position dependent active inhibition of CE that prohibits it from firing in response to some but not all inputs.
(NIH 1 F22 NS00220-01 and NS05606)

EXPERIMENTAL CONFIRMATION OF THE THEORY OF LONG RANGE ORDERING OF WATER MOLECULES IN POLARIZED MULTILAYERS BY THE EXTENDED NHCO SITES OF THE EXTENDED PROTEIN BACKBONE AND THE FUNTIONAL CAPABILITY OF THIS WATER TO EXCLUDE SODIUM AND OTHER SOLUTES. G.N. Ling, C.L. Walton*, and J. Bersinger*, Department of Molecular Biology, Pennsylvania Hospital 8th and Spruce Streets, Philadelphia, Pennsylvania 19107

According to the association-induction hypothesis, long range order of water molecules in the state of polarized multilayers may be achieved under the following conditions: (1) The NP-NP system, in which a checkerboard of positively and negatively charged sites on juxtaposed plain surfaces facing each other as in the case of water held between two polished glass surfaces. (2) The NP-NP-NP system in which parallel arrays of chains of alternatingly positive and negative sites polarize and orient deep layers of water among these chains. The theory predicts that in all living cells an NP-NP-NP system exists in the form of extended polypeptide chains whose positively charged NH and negatively charged CO groups are the seats of long range ordering of the bulk of cell water. Studies of experimental models fulfilling the theoretical requirements confirm the anticipated exclusion for Na^+, sugar and amino acids and shrinkage of molar volume and other properties of water in this state of polarized multilayers, etc.

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ACTION OF TETRODOTOXIN ON THE UPSTROKE OF THE SINUS NODE ACTION POTENTIAL. S. L. Lipsius* and M. Vassalle (Spon: G. Lange). Dept. of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203.

Action potentials (AP) of the isolated sinus node of the guinea pig were recorded by means of a microelectrode technique. The upstroke of action potentials showing a fast component (FC) and a slow component (SC) were studied in the absence and in the presence of tetrodotoxin (TTX). Administration of TTX resulted in the gradual disappearance of the FC so that the upstroke was due solely to the SC. The amplitude of the AP was unchanged and the rate of discharge decreased slightly. The rate of rise of the upstroke was markedly reduced. In the absence of TTX, acetylcholine (ACh) increased the "take-off" potential and this resulted in an increase in the amplitude of the FC. At the same time, the SC became progressively smaller. In the presence of TTX, ACh again increased the take-off potential but this did not result in a FC; the only effect was a progressive decrease of the SC. An extra stimulus applied early in diastole results in a larger FC in the absence of TTX and in a SC which is even slower in the presence of TTX. Also, in the presence of TTX the cycle length following the extra stimulus is considerably longer. Driving at a fast rate results in a progressive decrease in the potential value attained by the SC; in the presence of TTX, the preparation does not respond to fast drive as the reactivation of the channel may be too slow. These and other experiments suggest that the FC is due to an influx of Na and is dependent on the take-off potential; in contrast, the SC is due to the activation of a slow channel, is little influenced by the take-off potential but has a more pronounced time-dependence than the FC. Finally, the two components are interchangeable in producing the upstroke of some sinus node cells. Supported by grants HL05037 & HL17451 from N.I.H.

PULMONARY DYSFUNCTION IN RHESUS MONKEYS DURING STAPHYLOCOCCAL B ENTEROTOXEMIA. C. T. Liu, R. D. DeLauter,* and M. J. Griffin.* USA Med. Res. Inst. of Infectious Diseases, Fort Detrick, Md. 21701

A single intravenous (i.v.) injection of staphylococcal enterotoxin B (SEB) at doses of 0.05 to 1 mg/kg produces death within 10 to 20 hr. The exact cause of death is not well understood. Since other investigators have observed pulmonary edema in B enterotoxemic rhesus monkeys, it was our purpose to study pulmonary functions and arterial blood gas tensions, as well as water content and electrolyte concentrations in the lungs of anesthetized normal and SEB-challenged rhesus monkeys. In the period from 6 to 11 hr following SEB injection, the physiological dead space and respiratory quotient increased, while pulmonary resistance, functional residual capacity, CO_2 output, and O_2 consumption decreased. By 11.5 hr after SEB challenge, total lung water content increased as shown by simultaneous accumulations of extracellular Na^+ and water. Conversely, the intracellular lung water and Na^+ decreased. Further, the surface tension of the lung extract increased, suggesting that pulmonary surfactant contents were reduced, and the lungs might have also collapsed slightly in SEB-inoculated monkeys. Although acidemia developed gradually, severe hypoxia, hypercapnia, and decreased dynamic pulmonary compliance were not observed until shortly before death. Positive-pressure breathing (2 to 3 cm H_2O) prevented death or prolonged the survival time after i.v. SEB. These results provide evidence to support the assumption that pulmonary dysfunction and terminal pulmonary edema contribute to death during SEB enterotoxemia in monkeys.

MYOCARDIAL FATTY ACID AND LACTATE METABOLISM IN ALLOXAN-DIABETIC DOGS. Maw-Shung Liu and John J. Spitzer, Dept. of Physiology, Louisiana State University Med. Ctr., New Orleans, La. 70112.

We studied the alteration of palmitate oxidation and incorporation into tissue lipids, as well as lactate oxidation, by heart homogenate prepared from alloxan-diabetic dogs. Heart homogenate was prepared in calcium-free Krebs-phosphate buffer four days after the intravenous injection of 80 mg/kg alloxan monohydrate. The rates of palmitate oxidation and incorporation into tissue phospholipid (PL) and triglyceride (TG) were studied simultaneously by incubating heart homogenate with albumin-bound 1-^{14}C-palmitate in the presence of various cofactors for 30 min at 37°C. Metabolic $^{14}CO_2$ was collected by filter paper soaked in KOH; lipids were extracted by chloroform-methanol (2:1) and separated by thin-layer chromatography. In another group of experiments heart homogenate was incubated with U-^{14}C-lactate and NAD for 20 min. Alloxan administration increased plasma glucose and FFA levels approximately five-fold. The rate of palmitate oxidation was not significantly altered while lactate oxidation was decreased by 53% ($p<0.001$). Incorporation of palmitate into PL and TG was enchanced by about 50%. These findings suggest that alloxan-induced diabetes alters myocardial substrate utilization by decreasing lactate oxidation and enhancing fatty acid incorporation into tissue lipids.
(Supported by NIH Grant HL #16850).

PLASMA OPSONIC AND LYSOSOMAL ENZYME ACTIVITIES DURING THE COMPENSATORY PHASE OF HEMORRHAGIC SHOCK IN RATS. D.J. Loegering and F.K. Carr*. Department of Physiology, Albany Medical College, Albany, N.Y. 12208

Previous studies from this laboratory have shown that depletion of a humoral opsonic factor (alpha-2-glycoprotein) was associated with depressed reticuloendothelial system (RES) clearance capacity during the decompensatory phase of hemorrhagic shock. We have also shown a correlation between elevated lysosomal enzyme levels and post-shock RES failure. The present study evaluated the time course of plasma opsonic activity and plasma lysosomal enzyme changes during the compensatory phase of hemorrhagic shock. Rats (250-300g) anesthetized with sodium pentobarbital (30 mg/kg) were hemorrhaged within 10 min to 40 mmHg arterial blood pressure and maintained at this pressure for 0, 30, 60 min and initial decompensation (mean time of 90 min and identified by 5% uptake of the maximum shed blood volume). Plasma opsonic activity, determined by liver slice bioassay, decreased from a control level of 17.2±1.0 %ID/100 mg to 7.0±1.2 at 0 time (10 min after the start of hemorrhage) and remained near this value at 30 min, 60 min and 5% uptake. This decrease in opsonic activity was associated with a decrease in hematocrit. However, 15 min following reinfusion of the shed blood at 30 min and 5% uptake, opsonic activity remained depressed while the hematocrit returned to control levels. Plasma cathepsin activity was unchanged after 30 and 60 min of hypotension but increased 4-fold at 5% uptake. These data show a disturbance in the humoral control of RES function which begins during the early compensatory phase and is followed by an increase in plasma lysosomal enzyme levels during the late compensatory phase of hemorrhagic shock.
(USPHS,HL-18051 and T32-GM07033).

O_2 STORES AND VENTILATION IN RESPONSE TO LOWER BODY NEGATIVE PRESSURE. J.A. Loeppky* and U.C. Luft. Dept. of Physiology, Lovelace Foundation, Albuquerque, NM 87108

Tilt table studies have demonstrated marked transient changes in blood O_2 stores (O_2B), ventilation (V_I) and gas exchange with posture. (J. Appl. Physiol. 39(1):47-53, 1975). Similar breath-by-breath measurements of pulmonary capillary O_2 transfer and V_I with a box-balloon spirometer and mass spectrometer were made on 3 subjects before, during and after 10 min of lower body negative pressure (LBNP) at -20, -40 and -60 Torr with arterial samples at -60 Torr. Deficits of O_2B resulted during LBNP and repayment of O_2B during recovery was related to LBNP stress. Concurrent calf volume measurements with Hg strain gauge decreased towards baseline well before the peak rise in pulmonary capillary O_2 transfer upon release of LBNP, signifying that O_2B changes were related to blood volume shifts. Return of O_2-depleted pooled blood to the central circulation during the first min of recovery caused significant stress-related hyperpnea which peaked near 30 sec and returned to near baseline after the first min. Three compartment lung model analyses indicated an increase in the ventilated and unperfused lung fraction from 0.09 (control) to 0.17 (8th min at -60 Torr) with the effective compartment decreasing from 0.83 to 0.77. It appears that the 30% increase in ventilation equivalent was primarily the result of less effective lung perfusion during LBNP. (Supported by NASA Contract, NAS 9-14920)

NATRIURETIC EFFECT OF ANGIOTENSIN II BLOCKADE AT THE KIDNEY. T.E. Lohmeier, A.W. Cowley, Jr., N.C. Trippodo, and A.C. Guyton. (Spon.: W.A. Neely). Dept. Physiology & Biophysics. Univ. Miss. Med. Cntr., Jackson, MS 39216

To determine whether endogenous angiotensin II (A-II) *per se* has a direct effect on the kidney to promote sodium (Na) retention, the A-II antagonist 1-sarcosine-8-alanine A-II was infused directly into the renal artery (0.2 $\mu g/Kg\ min^{-1}$) of conscious adrenalectomized dogs at various states of Na balance. Na balance was manipulated daily by varying the amount of mineralocorticoid administered and/or the Na intake. In contrast to the Na replete state, infusion of 1-sarcosine-8-alanine A-II into Na depleted dogs was associated with increases in urinary Na excretion (125-216% of control) as long as arterial pressure remained constant or decreased only minimally. The natriuresis during A-II blockade was more pronounced on days of increased Na deficit. Urine flow, urinary potassium excretion, glomerular filtration rate, and renal plasma flow also increased while filtration fraction decreased during A-II blockade, and by one hour after infusion of the A-II antagonist all measured functions returned toward control levels. The data indicate that endogenous levels of A-II have a direct renal effect to promote Na retention. (Supported by NIH grant HL 05184).

LIVER RETICULOENDOTHELIAL INDEPENDENCE FROM ESTROGEN MODULATION IN THE RAT J.R. Lorenzen*, J.A. Holt*, and T.M. Saba (SPON: G. Kanter). Depts of Physiol and Obstet & Gynecol, Albany Medical College, Albany, NY 12208

Hormonal regulation of hepatic reticuloendothelial (RE) function, particularly by natural and synthetic estrogens, is well documented in mice, but has been seldom examined in other species. Work from this laboratory has indicated a definite interval of hepatic Kupffer cell hyperactivity during the neonatal period of the rat, especially at 14 days, which appears to correlate with a rise in serum estradiol over the same time period (Döhler and Wuttke, Endocrinol 97:898, 1975). The present experiments were to determine if the raised estrogen levels could account for the RE hyperactivity as has been shown to occur in the adult mouse. Orchidectomy was performed in 7 day old male rats to remove the gonadal source of estrogens. At 14 days of age orchidectomized rats showed no change in RE function (phagocytic index (K)=0.063± 0.006) from sham controls (K=0.071±0.010). Radioimmunoassayable estrogen in the castrated rats was 1.01±0.17 ng/ml serum, and 1.18±0.29 in sham controls. Adult male rats injected intramuscularly with 100µg estradiol-benzoate/kg twice daily for 3-4 days produced no discernable increase in RE function over sesame oil carrier injected controls. K as determined by clearance of carbon was 0.021±0.002 in estrogen-treated rats vs 0.017±0.002 in shams; K as determined by the clearance of gelatinized RE test lipid emulsion was 0.026±0.003 after estrogen treatment and 0.026±0.004 in shams. The results indicate that estrogen under these conditions does not have an hepatic RE stimulatory influence in the rat as has been reported for the mouse, therefore estrogen may not be the cause of neonatal liver Kupffer cell hyperactivity at 14 days in the rat. Furthermore, phagocytic activity of the RES appears to be independent of gonadal influence in the young male rat. (CA-16011, NO1-HD-4-2825 Ford Fnd 680-0990).

ENTRAINMENT OF RESPIRATORY FREQUENCY TO STEPPING RATE DURING WALKING. S. Loring†, P. Gulesian†, M. Goldman, and J. Mead. Dept. of Physiology, Harvard School of Public Health.

Breathing frequency (f) during exercise is nearly proportional to total ventilation, and hence to metabolic rate (Hey et al., Resp. Physiol. 1:193, 1966). But f is also influenced by rhythmic activity such as walking, and breathing may become entrained to stepping rate (Milic-Emili & Cajani, Boll. Soc. Ital. Biol. Sper. 33:825, 1957). In order to study the importance of stepping rate in the control of f during steady-state exercise, we varied metabolic rate and stepping rate independently in 10 naive subjects walking on a treadmill. Only four of the subjects showed entrainment of respiration to stepping rhythm (generally at the higher metabolic rates). When entrained subjects walking at 7.2 km/hr increased their estimated metabolic rate 72% as the treadmill was inclined to 10°, stepping rate and f remained nearly constant. Moreover, even subjects who were not entrained showed changes in f, independent of metabolic rate, which were apparently related to stepping rate. For example, when subjects changed from walking at 3.2 km/hr at 10° inclination to 7.2 km/hr at 0°, metabolic rate increased only slightly, but f increased markedly. Similarly, in subjects walking at 3.2 km/hr at 0° and then 10°, stepping rate was nearly constant and f increased less than predicted from the increase in estimated metabolic rate.

We conclude that stepping rate influences breathing frequency with or without entrainment of breathing to stepping rhythm. In studies of the dependence of f on metabolic rate, exercise may have unforeseen effects on f, independent of metabolic rate. (Supported by Grant HL 14580-03S1 HEP).

VOLTAGE-CURRENT RELATIONSHIPS AND VOLTAGE OSCILLATIONS IN Cl-FREE WASHED RAT MUSCLES. H. Lorković, Depts. of Neurology and Physiology and Biophysics, College of Medicine, Iowa City, Iowa, 52240.

Thin sheets of fibers from gastrocnemius muscles of rats were washed in Tris propionate solutions containing 0.6 to 60 mM K. The voltage-current relationship was measured by the two microelectrode technique. The VC relationship has a high dV/dC region, sometimes including a "forbidden" voltage zone, and voltage hysteresis. The mid-point of this zone is about 60 mV positive to E_K. The voltage span of the region is reduced when $[K]_o$ is between 2 and 20 mM, presumably because of an interference with delayed rectification. Voltage hysteresis is particularly strong when Tris is partially replaced by Na at low $[K]_o$. High frequency, low amplitude voltage oscillations are produced by gradually changing the membrane voltage from about -40 mV toward more negative values. The frequency decreases (from about 2/s to less than 5/min), and the amplitude increases (up to 30 mV) with repolarization. Low amplitude oscillations are sinusoidal, high amplitude oscillations resemble pacemaker potentials in other tissues. The results are discussed in terms of an interaction between depolarizing K inactivation and g_{Na} activation, possibly in a channel not involved in spike production.

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EFFECTS OF DIPHENYLHYDANTOIN ON THE LYMPHORETICULAR SYSTEM IN RATS. J.R. Lott and C. K. Gordon*, Dept. Biological Sciences, North Texas State University, Denton, Texas, 76203.

Diphenylhydantoin (DPH) in a carrier solution at pH 12 was injected i.p. into rats daily for periods of 30 and 60 days. Two dosages of DPH were used, 5 mg/100 Gm and 10 mg/100 Gm weight. Overt clinical symptoms, leucocyte changes, and histological changes in the cervical lymph nodes, thymus and spleen were measured. Clinically, the injected animals showed lymph gland hypertrophy, weight loss, splenomegaly, cachexia, and fluid retention, particularly during the later stages. A moderate leucocytosis, eosinophilia, lymphocytopenia, neutrophilia, and monocytosis was observed in all of the injected animals. Histologically the tissues studied displayed marked hyperplasia of the reticuloendothelial cells, fibrosis, prominent eosinophil and neutrophils, focalized necrosis, and some giant cells. Most of the foregoing changes resembled closely those observed in lymphosarcomas. Some of these changes were observed in the carrier-injected animals but were more pronounced in the DPH-carrier injected rats. The results indicate that although DPH may not be directly carcinogenic, it may suppress the immune mechanisms in some animals thereby leaving them more susceptible to carcinogenic antigens or other agents.

ASZ(DCPB)

SEASONAL VARIATION IN RESISTANCE TO COLD STRESS IN STARLINGS (STURNUS VULGARIS) AND COMMON GRACKLES (QUISCULUS QUISCULA). Sheldon Lustick, Department of Zoology, The Ohio State University, Columbus, Ohio 43210

Summer- and winter-acclimatized birds were cold stressed by destroying the insulating quality of the feathers by wetting at ambient temperatures ranging from 5 to 40C. Both species studied showed an increased resistance to cold stress during the winter. Winter-acclimatized starlings and grackles were significantly heavier than their summer counterparts. Although the cooling rate (°C/min) in the grackle was lower during the winter, its peak metabolic rate cc O_2 $g^{-1}hr^{-1}$ was not significantly higher than in the summer grackles. Winter-acclimatized starlings demonstrated a remarkable ability to increase their resistance to cold stress, the cooling rates being significantly lower and the peak metabolic rate (cc O_2 $g^{-1}hr^{-1}$) being significantly higher than in summer birds. In winter-acclimatized starlings, at an ambient temperature of 5C, survival of the test period was greatly increased above that of summer birds whereas, in grackles, it was not. Some possible mechanism of acclimatization will be discussed.

ASZ(DCPB)

THE METABOLIC RESPONSE OF HAMSTERS, MESOCRICETUS AURATUS, TO LOW OXYGEN CONDITIONS AND HIGH AMBIENT TEMPERATURES. L. M. Lutton and Judith Feagin, Biology Department, Allegheny College, Meadville, Penn. 16335

The oxygen consumption of golden hamsters was measured to see if there would be a decrease in their metabolic rates under hypoxic conditions from their normoxic values, as occurs in thermal neutral and below thermal neutral ambient temperatures, T_a. Six experimental conditions were tested with three levels of ambient oxygen (21% O_2/ 79% N_2, 10% O_2/ 90% N_2, and 7% O_2/ 93% N_2) each at two T_a's (28°C - thermal neutral, and 35°C). Body temperatures were measured at the end of each 1.5 h test. While a significant decrease in oxygen consumption occurred from tests in 21% O_2 to those in 7% O_2 at 28°C, 1.15 ± 0.14 ml O_2/ g/ h and 0.85 ± 0.13 ml O_2/ g/ h, respectively, no such decrease was noted at 35°C, 1.15 ± 0.19 ml O_2/ g/ h and 1.18 ± 0.11 ml O_2/ g/ h, respectively. Metabolic values in 10% O_2 fell between the 21% and 7% O_2 values at both 28°C and 35°C. These values represent the minimal oxygen consumption values during the test periods, but average oxygen consumption values showed the same relationships. Body temperatures did not show a significant drop at either T_a, but they were significantly higher at 35°C than those at 28°C for all levels of oxygen. Apparently, the hamsters' greater hypoxic tolerance at high ambient temperatures relative to the white rat, as reported elsewhere, is not due to a greater ability to decrease oxygen consumption under these conditions. Their hypoxic tolerance can most likely be explained simply by lower basal metabolic rates in normoxia and/or greater anaerobic capacities than those of white rats. (Supported by funds from Allegheny College.)

TWO POINT DISCRIMINATION CODES FOR ELECTROCUTANEOUS SENSORY SUBSTITUTION. J. Lyman, M. Solomonow, A. Freedy*, Biotechnology Laboratory, UCLA School of Engineering and Applied Science, University of California, Los Angeles, California 90024

The feasibility of frequency modulated two point discrimination as a design concept for electrocutaneous sensory substitution display has been studied. Three stimulation techniques were tested on human subjects: spatial stimulus, temporal stimulus, and frequency on frequency stimulus. The frequency on frequency technique uses one electrode at constant frequency with variable frequency for the second electrode. Data showed that the frequency on frequency technique is superior over the temporal and spatial techniques. In addition, some of the characteristic behavior of cutaneous sensation is discussed relating two point discrimination with frequency, left and right body locus, as well as several body locations, sensory hysterisis, and dermatonic variations. Implications of the results for clinical applications are reviewed.
(Supported by Veterans Administration Grant V 101-(134)P-330)

AUTONOMIC RESPONSES TO CHANGES IN PREOPTIC AND AMBIENT TEMPERATURE IN SAIMIRI SCIUREUS. W. C. Lynch* (SPON: R. O. Rawson), J.B.Pierce Fndn. and Yale Univ.,New Haven, CT 06519.

Studies of thermoregulation in the dog, cat and rabbit have indicated that the temperatures of the medial preoptic hypothalamus (preoptic) and environment (skin) interact to determine autonomic thermoregulatory responses. Models describing this interaction have taken various forms. By displacing preoptic (T_{po}) and skin ($\bar{T}_{sk}$) temperatures while measuring metabolic heat production (M), Stitt, Hardy and Stolwijk (1974) found that preoptic thermosensitivity ($\Delta M/\Delta T_{po}$) was a linear function of $\bar{T}_{sk}$ within the range 29 to 40°C. The present studies sought to extend these findings to the squirrel monkey who is less well insulated by fur than species previously studied. The level of M, as calculated from oxygen consumption, was recorded in 4 monkeys during 15 min T_{po} displacements ranging from 33 to 43°C. Each displacement was made while ambient temperature was held at a constant value between 10 and 39°C. We found, as expected, that preoptic thermosensitivity increased with reductions in $\bar{T}_{sk}$ from 39 to 29°C. However, contrary to expectation, at values of $\bar{T}_{sk}$ from 29 to 22°C, thermosensitivity decreased, approaching zero. The discrepancy between our findings and those reported by others seems to depend on the range of $\bar{T}_{sk}$ examined; in heavily furred species, $\bar{T}_{sk}$ below 29°C has seldom been reported. The present data suggest the need for a modification of models of thermoregulation concerned with the interaction of thermal inputs from brainstem and skin. (Supported by USPHS Grant NS-11517.)

OXYGEN TENSION IN THE OVIDUCT OF THE RHESUS MONKEY (MACACA MULATTA). Dieter H.A. Maas,* Bayard T. Storey*, and Luigi Mastroianni, Jr., Dept. of Obstetrics and Gynecology, University of Pennsylvania School of Medicine, Philadelphia, PA 19174.

The oxygen tension in the oviduct lumen of adult female rhesus monkeys was measured by means of miniaturized, flexible oxygen electrodes between day 5 and 22 of the menstrual cycle. In the follicular phase, the value was < 10 Torr, which is the limit of accurate detection by the electrode. At the time of ovulation to about 5-7 days thereafter, the oxygen tension in the tube on the side of ovulation increased in about 2 min. after insertion of the oxygen probe from the low level up to 60 to 80 Torr. In the contralateral oviduct, the oxygen tension remained at < 10 Torr. In the late secretory phase, the measured value in both oviducts was again < 10 Torr and remained at that level after probe insertion. These findings suggest that, in the absence of ovulation, the blood-oxygen supply of the oviduct provides nearly the exact oxygen requirement of oxygen tissue with no excess oxygen available for the tubal fluid. At and shortly after ovulation, the presence of a probe stimulates, by an unknown mechanism, an increase in an environment sufficiently well oxygenated for gamete survival, fertilization, and subsequent further development of the embryo. We suggest that the ovum entering the oviduct provides a similar stimulus with a similar result by the same, unknown mechanism. (Supported by HD-06274 from NICHD. D.H.A.M. is a Fellow of the Deutsche Forschungsgemeinschaft).

TICRYNAFEN: A DIURETIC AND URICOSURIC AGENT. Alfred R. Maass*, Robert Erickson*, Ina Snow*, Frank Brennan*, Roy Weedon* and Gerald Hutchings*. (SPON: P. T. Ridley). Smith Kline & French Laboratories, Philadelphia, Pa. 19101

Ticrynafen [2,3-dichloro-4-(2-thienylcarbonyl)phenoxyacetic acid] is an effective diuretic and uricosuric agent. Orally, in the water loaded dog, it caused a significant saluresis at doses of 12.5 mg/kg and above. A significant potassium loss was not obtained until 40 mg/kg was administered. In the phosphate-mannitol infused dog, ticrynafen caused a significant natriuresis at 0.5 mg/kg i.v. and a significant kaliuresis at 2.5 mg/kg. At 15 mg/kg i.v., approximately 11% of the filtered sodium load was excreted in the acidotic dog and 22% in the alkalotic dog. In the hydrated dog, ticrynafen reduced free water clearance while in the hydropenic dog increased the solute free water of reabsorption to the same extent as hydrochlorothiazide. These data indicate that ticrynafen probably acts in the cortical diluting segment of the distal tubule and may not be limited in its natriuretic activity as are the thiazides. Ticrynafen however, also differs from the thiazides in causing a significant uricosuria. In the mongrel, ticrynafen causes a uricosuria not seen in the dalmatian dog. In comparison with literature data, ticrynafen differs in mechanism of action from other uricosuric agents.

BINDING CHARACTERISTICS OF AMILORIDE IN FROG SKIN AS DETERMINED BY SCATCHARD ANALYSIS. D. D. Macchia* and S. I. Helman. Dept. of Physiology and Biophysics, University of Illinois, Urbana, IL 61801

The binding characteristics of amiloride at the outer surface of isolated frog skin were studied by determining the inhibition of the short-circuit current (I_{sc} = net sodium transport) as a function of amiloride concentration (10^{-8} to 10^{-5} M). When the data were plotted according to Scatchard analysis (ordinate = % inhibition/[amiloride], abscissa = % inhibition), at least two pools of receptors were indicated. Each pool could be characterized by an apparent affinity constant, K_a, and the fractional sodium current, % I_{sc}, carried by each pool. For skins of R. pipiens berliendieri the values of K_a were estimated to be 2.2×10^6 and 1.9×10^7 M^{-1} and the corresponding values of % I_{sc} were 83.5 and 16.5 %. When similar studies were done with skins of R. temporaria the values of K_a were higher, 6.2×10^6 and 7×10^7 M^{-1} with corresponding values of I_{sc} of 87.6 and 12.4 %.

It has been suggested that active sodium transport may proceed via independent parallel transport pathways, an idea supported with studies of the kinetics of sodium tracer buildup and studies of the I-V relationships. The above data are also consistent with this view and can be interpreted to mean that sodium entry occurs by way of two independent sodium transport pools via receptors with differing binding affinities for amiloride. Accordingly, sodium transport through the high affinity, low capacity pathway will be inhibited preferentially at the lowest concentration of amiloride. The low affinity pool could account for approximately 85% of the I_{sc} and the high affinity pool for approximately 15% of the I_{sc}. (Supported by USPHS AM 16663.)

EFFECTS OF GLUCAGON ON CANINE ILEAL Na AND H_2O FLUXES AND REGIONAL BLOOD FLOW. D. Mailman and S. MacFerran*, Biology Dept., University of Houston, Houston, TX 77004.

IV glucagon decreases gut absorption in the dog and is also a vasodilator. Starling forces are known to affect gut transport and therefore, the possibility that glucagon can influence gut transport through a cardiovascular effect was investigated. Net and unidirectional Na and H_2O fluxes from the lumen of ileal segments perfused with saline containing ^3H_2O and ^{22}Na were determined. Total (TBF) and absorptive site (ASBF) blood flows were calculated from the appropriate clearances of ^3H_2O. Glucagon (0.05 or 0.5 µg/kg·min) was infused either directly (DIG) into the mesenteric artery of the perfused gut segment (N=7) or indirectly (IIG) into the mesenteric artery of an adjacent non-perfused segment (N=6). DIG (0.05 µg/kg·min) had no effect on net Na or H_2O fluxes but significantly increased secretory and absorptive Na fluxes by 0.23 (±0.10) and 0.28 (±0.05) µeq/gm·min and H_2O fluxes by 3.13 (±0.77) and 2.93 (±0.86) µl/gm·min, respectively. DIG did not affect TBF but increased ASBF by 11.9 (±4.9) µl/gm·min, decreased arterial pressure 10 (±4) and mesenteric venous pressure 1.4 (±0.5) mm Hg. IIG decreased net Na flux by 0.39 (±0.07) µeq/gm·min and net H_2O flux by 2.66 (±0.75) µl/gm·min and, in general, had effects on the other parameters opposite to those of DIG. The larger dose of glucagon had qualitatively similar but quantitatively greater effects for both DIG and IIG. Calculated capillary pressure was linearly related to the unidirectional Na and H_2O fluxes, but the relationship was different for DIG and IIG. Neither directly infused histamine, nor IV insulin nor IV glucose mimicked the effects of glucagon. It was concluded that glucagon affects gut transport, in part, through a cardiovascular effect and a consequent alteration in Starling forces. (Supported by ONR N00014)

NEUROGENIC PULMONARY VASOCONSTRICTION AND EDEMA. A.B. Malik. Department of Physiology, Albany Medical College, Albany, N.Y. 12208.

The pulmonary vascular response to intracranial (ICP) hypertension was studied in 26 anesthetized controlled ventilated dogs in which ICP was elevated to 20 mm Hg below the mean arterial pressure for a 20 min period. Arterial pressure initially increased during elevation in ICP and returned to control by the end of 20 min. Pulmonary vascular resistance (PVR) increased from control value of 2.7±0.30 to 8.3±0.51 mm Hg/l/min at the end of 20 min increase in ICP. Increase in PVR was associated with marked increase ($p<0.001$) in pulmonary arterial pressure from 14.4±1.3 to 35.4±4.0 mm Hg, small increase in left atrial pressure from 5.4±1.2 to 7.9±1.9 mm Hg, and no significant change in pulmonary blood flow. The increase in PVR induced by elevated ICP was associated with increases in lung water, physiologic shunt ($\dot{Q}_s/\dot{Q}_t$) alveolar dead space (V_D), and with hypoxemia (from control PaO_2 of 90.0±3.6 mm Hg to 55.6±4.8 mm Hg during elevated ICP). Pretreatment with propranolol (1.5mg/kg) attenuated the increase in PVR during elevation in ICP; the smaller increase in PVR was associated with a marked increase in left atrial pressure and a smaller increase in pulmonary perfusion pressure. Propranolol treated animals also developed increases in lung water, $\dot{Q}_s/\dot{Q}_t$, V_D, and hypoxemia. In contrast, pretreatment with phenoxybenzamine (1.5mg/kg) abolished the increases in pulmonary perfusion pressure and PVR induced by ICP elevation as well as the increases in lung water, $\dot{Q}_s/\dot{Q}_t$, V_D and hypoxemia. Therefore, a sustained elevation in ICP at a level below the mean arterial pressure in the intact dog results in pulmonary vasoconstriction mediated by α-adrenergic mechanisms. The data suggest that the neurogenic pulmonary vasoconstriction results in the increase in lung water and in hypoxemia. (Supported by HL-17355).

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ACTH RELEASE MEDIATED BY STIMULATION OF PARAVENTRICULAR NUCLEUS(PVN). J.W. Maran, D.E. Carlson*, and D.S. Gann. Dept. Biomed. Engineering, The Johns Hopkins University Sch. of Medicine, Baltimore, Md. 21205

Vasopressin has been shown to facilitate the release of both CRH and ACTH. Recent findings indicate that neurons in the central PVN project directly to capillary loops in the median eminence. To study the possible relation of this pathway to the control of ACTH, we have stimulated the paraventricular region electrically (200 μA, 0.2 msec, 100/sec, 20 sec) and have measured ACTH (RIA). Ten cats were anesthetized with chlorolose-urethane, immobilized with gallamine and respired artificially; body temperature was controlled between 37-38 °C. Blood samples for measurement of ACTH were drawn with simultaneous infusion of isoncotic dextran at 0.5 min prior to, and 1.5, 3.5 and 6.5 min after stimulation. Stimulation sites were mapped into anatomical areas facilitatory or inhibitory to release of ACTH and were analyzed by repeated measures analysis of variance. At 13 sites in a facilitatory region coincident with PVN, mean ACTH values were 310 ± 34 pg/ml prior to, and 410 ± 33, 434 ± 65 and 420 ± 41 pg/ml after stimulation($P<0.01$). An inhibitory region which included posterodorsal PVN, and an area posterior to PVN and anterodorsal to the ventromedial nucleus was found. At 13 sites in this inhibitory region, mean ACTH values were 484 ± 45 pg/ml prior to, and 356 ± 30, 424 ± 37 and 392 ± 27 pg/ml after stimulation($P<0.01$). The region anterior to PVN showed no consistent effect on ACTH. These data suggest that the paraventricular nucleus through the release of vasopressin may be physiologically important in the control of ACTH.

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COMPARATIVE ULTRASTRUCTURE OF ESOPHAGEAL SURFACE EPITHELIUM. Lolly M. Marchant* and M. H. F. Friedman, Dept. of Physiology & Division of Electronmicroscopy, Philadelphia College of Osteopathic Medicine, Philadelphia, Pa., 19131.

A comparative study of the ultrastructure of the esophageal mucosa, especially surface epithelial cells (SEC), was carried out in 12 species of vertebrates. The scanning electron microscope (SEM), transmission electron microscope (TEM), and light microscope (LM) were used. The exhibit presents details by photo-micrographs, charts, tables and text. Depending on the nature of the diet, three types of SEC were found. In the frog all cells from pharynx to stomach exhibited micro-villi and cilia. TEM revealed the cilia to have typical 9 couplets of tubules ranged around a central couplet and extending thru most of the cilia length (up to 7μ). In the turtle similar ciliated SEC were distributed in patches among squamous cells. In the monkey the epithelium is thrown into folds and furrows. SEM shows few microvilli on SEC but numerous microridges (0.2μ dian) sweeping across cell in parallel lines (1.0 apart) and sometimes branching. Microridges of adjoining SEC do not run in same direction. Microridges are lost when upper layer of SEC becomes cornified, fragmented, and desquamated, to be replaced from below by newer squamous SEC with typical microridges. In the dog the SEC microridges are arranged irregularly. In the rat and pigeon, animals ingesting coarse foods, the SEC show numerous short microridges, very irregularly arranged and frequently seen as loops.

MEASUREMENTS OF REGIONAL SPINAL CORD BLOOD FLOW. M.L. Marcus, D.D. Heistad, J.C. Ehrhardt* and F.M. Abboud. Depts. of Medicine and Radiology, Cardiovascular Center, Univ. of Iowa, Iowa City, IA 52242

Previous studies of regional spinal cord blood flow have been limited by methodology. We have used 15μ microspheres labeled with 5 different isotopes to measure blood flow in the spinal cord of sheep and lambs. Five interventions have been examined: 1) increase in systemic pressure from 75±8 (mean ± SE) mmHg to 134±8 mmHg to study regional autoregulation; 2) hypercapnia (pCO_2=56±2 mmHg); 3) hypocapnia (pCO_2=23±2 mmHg); 4) hypoxia (pO_2=32±4 mmHg); and 5) activation of neurons in the lumbar spinal cord by unilateral electrical stimulation of the femoral and sciatic nerves (4 voltz, 5Hz). Under control conditions, grey and white matter flows in the lumbar spinal cord were 125±29 and 25±6 ml/min x 100g, respectively. Hypercapnia and hypoxia markedly increased flow, hypertension did not alter flow, and hypocapnia decreased flow to grey and white matter in the lumbar spinal cord. Similar responses occurred in the cervical spinal cord. Only hypercapnia significantly altered the grey/white ratio from 5.2±0.6 under control conditions to 3.3±0.3 during hypercapnia ($p<.05$). In contrast the grey/white ratio in the brain increased from 2.0±0.3 under control conditions to 2.7±0.3 during hypercapnia. Stimulation of the femoral and sciatic nerves caused a 25% increase in flow to the grey matter on the stimulated side; contralateral grey and white matter flows and ipsilateral white matter flows were unchanged. Conclusions: These data suggest that the regulation of regional spinal cord blood flow generally parallels that of the cerebrum although preliminary data suggests that the response to hypercapnia may be quantitatively different.

EFFECT OF CHOLESTEROL-CONTENT ALTERATION AND STEROID SUBSTITUTION ON THE VARIOUS ATPase ACTIVITIES OF HUMAN ERYTHROCYTES. Stanley J. Masiak and Irma Pirtle*Dept. of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook. N. Y. 11794

Lecithin or lecithin/cholesterol (3/2, W/W) sols were used to decrease or increase human erythrocyte membrane cholesterol content, respectively. These alterations caused an inhibition of the $(Na^+ + K^+)$-dependent and the Ca^{2+}-dependent ATPase activity, dependent upon the membrane cholesterol content. The Mg^{2+}-dependent ATPase was unaffected by the alterations. The apparent K_m value for Na^+ for the $(Na^+ + K^+)$-dependent ATPase increases from 3.2 ± 0.2 to 7.1 ± 0.4 mM in the presence of excess cholesterol in the membrane and decreases to 1.3 ± 0.1 mM with cholesterol depletion. The apparent K_m values for K^+ or Mg-ATP are unchanged by cholesterol alteration. The energy of activation for the $(Na^+ + K^+)$-dependent ATPase was greater for both cholesterol-depleted and cholesterol-enhanced than untreated erythrocytes. The energy of activation of the Mg^{2+}-dependent ATPase remained unchanged. Lecithin/steroid (3/2, W/W) sols were used to incorporate a variety of steroids into the erythrocyte membrane. Several steroids (7-dehydrocholesterol, ergosterol, β-estradiol and 17α- ethynyl estradiol) prevent or retard cholesterol depletion and the subsequent inhibition of the ATPase activities. Stigmasterol, dihydrocholesterol, 6-ketocholesterol, 7-ketocholesterol, androstendiol and androstandione do not prevent cholesterol-depletion or ATPase inhibition. The amount of steroid incorporation into the membrane does not correlate with these effects. A saturated-C_8H_{17} side chain at C-17 enhances steroid incorporation, but does not prevent cholesterol depletion, while conjugated double bonds in the A or B steroid ring and a 3 β-hydroxy group appear to be necessary to prevent cholesterol depletion. (Supported by grant AM16821 from NIH).

CHANGES IN CENTRAL NERVOUS SYSTEM ACTIVITY DURING THE ESTROUS CYCLE OF THE RAT. J.F.Masken, R.J. Morgan*, and W.W. Walker*, Dept. Physiology & Biophysics, Colorado State University, Fort Collins, Colorado 80523.

In a preliminary effort to relate central nervous system activity to the estrous cycle, six cycling adult female Sprague-Dawley rats were each chronically implanted with electrodes in the arcuate-median eminence (ARC-ME), the pre-optic area (POA), and amygdala (AMY). Electrical activity from these three areas was recorded simultaneously for 10 mins. of each half-hour from 9:00 A.M. through 4:10 P.M. on each day of the estrous 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 areas that changed during the estrous cycle. After 4 or 5 days of recording the rats were killed and electrode placement was histologically verified. Crosscorrelograms for three combinations, AMY-POA, AMY-ARC, and POA-ARC, were computed and plotted on microfilm. Delay times between the AMY-POA varied significantly ($P<0.05$) throughout the estrous cycle. The direction of signal flow was from the POA to the AMY on the days of estrus and diestrus-1, i.e., the signal appears first in the POA and then travels to the AMY. On diestrus-2 and the afternoon of proestrus the predominant signal flow is from AMY to the POA. The possible significance of this to the estrous cycle is discussed.

(This work was supported in part by the State of Colorado Experiment Station grant #1672-15-094.)

SODIUM AND BICARBONATE REABSORPTION BY ISOLATED PERFUSED RAT KIDNEY. David L. Maude, Maureen Garvey*, Bruce Gilbert* and Grace Kao-Lo*, Dept. of Physiology, N.Y. Medical College, Valhalla, New York 10595.

Rat kidneys were perfused with iso-natric bicarbonate saline solutions of pH 7.4, 5mM glucose and 2.5 U/liter insulin. The following data were obtained (means of 5 kidneys studied for 5 five-minute clearance periods).

Perfusate (HCO_3)mM/l	GFR $mlmin^{-1}gm^{-1}$	Na Reabs microEq per ml GFR	HCO_3 Reabs microEq per ml gFR	Cl ($Na\text{-}HCO_3$) Reabs microEq/ml GFR
3	.48 ± .04	61 ± 2	2.5 ± 0.1	59
8	.48 ± .03	77 ± 2	6.6 ± 0.2	71
24	.65 ± .07	88 ± 3	20.2 ± 0.4	68
44	.47 ± .06	95 ± 6	28 ± 3	67
88	.47 ± .03	67 ± 5	36 ± 4	41

Bicarbonate reabsorption rises with increasing filtered load, but approaches saturation. Sodium reabsorption parallels HCO_3 when (HCO_3) is 8-44 mM, while Cl reabsorption remains constant. The fall in Cl reabsorption at 88 mM HCO_3^- may reflect un-saturation of a NaCl transport system. (Supported in part by a grant from the Westchester Heart Association).

DEADSPACE BREATHING AS A SCREENING TEST FOR EARLY LUNG DAMAGE. J.L. Mauderly, W.C. Nenno*, G.A. Morrison*, and F.F. Hahn*. Inhalation Toxicology Research Institute, Lovelace Foundation, Albuquerque, New Mexico 87115.

The respiratory pattern while breathing through added external deadspace was compared with variables measured during treadmill exercise to investigate deadspace breathing as a screening test for early lung dysfunction resulting from radiation pneumonitis in dogs. Breathing pattern (f, V_T, $\dot{V}_E$), $P_{I\bar{C}O_2}$, and $P_{E\bar{T}CO_2}$ were measured as 100 ml increments of 2.2 cm I.D. tubing were added to the unsedated dogs' masks. Breathing pattern and ventilatory equivalent for O_2 ($\dot{V}_E/\dot{V}_{O_2}$) were measured after dogs ran for 10 min at 5 mph on a 10% grade. Dogs were also evaluated clinically, radiographically, and by pulmonary function tests at rest before and after inhaling ^{144}Ce in fused aluminosilicate particles. By 4 months after inhalation of ^{144}Ce, there were increases in f and $\dot{V}_E$ during deadspace breathing and in $\dot{V}_E$ and $\dot{V}_E/\dot{V}_{O_2}$ during running. There was a slight drop in CO diffusing capacity at rest but no other functional, clinical, or radiographic changes. One-third of the dogs were sacrificed at 4 months. ^{144}Ce exposed dogs had scattered foci of inflammation in their lungs and controls were normal. Deadspace testing detected early, subclinical lung alterations with a sensitivity and at a time similar to exercise stress testing and deserves further investigation as a screening procedure. (Research performed under U.S. Energy Research and Development Administration Contract E(29-2)-1013.)

DIETARY IODINE AND HEPARIN EFFECTS ON TRIIODOTHYRONINE CONCENTRATION OF CHICKENS. J. D. May, USDA-ARS, South Central Poultry Research Laboratory, Mississippi State, MS 39762

Broiler chickens were reared in environmental chambers with controlled humidity, temperature and lighting, and were fed diets either iodine deficient or supplemented with KI to be adequate in iodine. Blood samples obtained by heart puncture were either processed for serum or clotting was prevented with crystalline heparin. Triiodothyronine (T_3) concentration was determined with a double antibody radioimmunoassay kit. After four weeks, T_3 concentration was the same for chicks fed iodine-deficient and adequate diets, although plasma iodine concentration was significantly greater for chicks on the iodine-adequate diet. Previous reports of failure to observe thyroid enlargement in chickens on low-iodine diets may be explained by failure to reduce thyroid hormone concentration. Chickens have been shown to have high levels of circulating inorganic iodine and low levels of thyroid hormones. Plasma and serum T_3 concentrations were not significantly different. The results suggest that plasma gives as valid results as serum for T_3 assay and the chicken normally has large quantities of circulating iodine that are not rapidly depleted during periods on low-iodine diets. Previous conflicting reports in the literature may be partly due to goitrogenic material commonly present in poultry diets.

NEUROTRANSMITTER AND CYCLIC NUCLEOTIDE MODULATION OF FROG CARDIAC CONTRACTILITY. D. A. McAfee, B. Siegel*, and G. Whiting*. Department of Physiology and Biophysics, Univ. of Miami School of Medicine, Miami, Florida, 33152.

We have confirmed previous reports that epinephrine augments the twitch tension developed by frog ventricular muscle in vitro, and that epinephrine paradoxically decreases the contracture tension developed under depolarization with high extracellular concentrations of K^+. We have tested the hypothesis that catecholamine-induced depression of contracture tension is mediated by cyclic AMP and that cholinergic antagonism of catecholamine action is mediated by cyclic GMP. One approach was to monitor the twitch and contracture tension generated by ventricular strips incubated in an oxygenated organ bath (24°C) and exposed to pharmacologic agents. The other was to measure cyclic nucleotide levels in quadrisected ventricles following exposure to these agents. Results expressed as % of untreated tissue.

	contracture	cAMP	cGMP
epinephrine (10 μM, 5')	69%	528%	104%
carbachol (1μM, 7')	114%	56%	128%
carbachol + epinephrine	116%	161%	102%

The effects of epinephrine were augmented by phosphodiesterase inhibitors and antagonized by a β-blocker. The effects of carbachol were antagonized by atropine (20μM). Exogenous cyclic AMP mimicked the effect of epinephrine while cyclic GMP mimicked the effect of carbachol. Our data are consistent with the hypothesis that the actions of the above agonists are mediated by cyclic nucleotides. (Supported by the Florida Heart Assoc. and USPHS grant NS 11552).

EFFECT OF TAURINE ON HEART CALCIUM IN NORMAL AND CARDIOMYOPATHIC HAMSTERS. M.J. McBroom and J.D. Welty. Dept. Physiology & Pharmacology, The Univ. of South Dakota School of Medicine, Vermillion, SD 57069.

Calcium accumulation has been implicated in the development of cardiomyopathic lesions in BIO 14.6 hamsters. Taurine, a normal constituent of the mammalian heart, has been shown to exert a modulating influence upon calcium levels in the heart under various forms of stress. Heart calcium was determined by atomic absorption spectrophotometry in normal (N), random bred Syrian golden hamsters and their cardiomyopathic (CMP), BIO 14.6, counterparts at 30 days of age and at 50-60 days, the latter age group corresponding to the onset of lesions in the CMP animals. Two groups of 50-60-day-old animals from each strain were studied: Group I - no treatment; Group II - treated with taurine (0.1 M) in drinking water *ad libitum* during the four-week period prior to sacrifice. The values obtained are shown in the table. Numbers of observations are in parentheses.

Heart Calcium (mEq/kg dry tissue ± S.E.M.)

Strain	30 days	50-60 days	
		Group I	Group II
N	14.19 ± 4.13 (5)	18.55 ± 2.72 (6)	8.42 ± 0.72 (3)
CMP	15.97 ± 2.03 (6)	176.25 ± 59.62 (8)	38.55 ± 13.80 (3)

The data indicate that the massive accumulation of calcium (11 x the 30-day value) in the hearts of untreated (Group I) CMP hamsters was markedly reduced by the taurine treatment (Group II). Normal hamsters (N) showed no differences in heart calcium levels among any of the groups studied. These findings support the hypothesis that taurine is capable of modulating abnormal calcium dynamics in cardiac tissue. (Supported by NIH Grant HL 09234 and Ralph W. Parson's Trust Fund.)

ALDOSTERONE RESPONSE TO LONG-TERM INFUSION OF DES-1-ASP ANGIOTENSIN II IN INTACT CONSCIOUS DOGS. Robert E. McCaa. Department of Physiology and Biophysics, University of Mississippi School of Medicine, Jackson, Mississippi 39216

The aldosterone response to chronic infusion of angiotensin II(A-II) and its heptapeptide metabolite, des-1-asp angiotensin II (A-III), was studied in intact conscious dogs to determine whether either of the two peptides can maintain plasma aldosterone concentration at the level of those observed in dogs during sodium deprivation (36.0 ng%). Plasma aldosterone concentration (PAC), plasma cortisol concentration (PCC), and plasma renin activity (PRA) were determined by radioimmunoassay. In 8 dogs maintained on A-II infusion (15.0 ng/kg min^{-1}), PAC increased from 8.1 ± 2.3 to 51.7 ± 7.9 ng% within one hour, returned to near control levels by 24 hours, and averaged 12.6 ± 3.1 ng% during the next 10 days of A-II infusion. During long-term A-II infusion, PCC remained at control levels, arterial pressure increased 45 ± 5 mm Hg above control levels, and PRA was undetectable by radioimmunoassay. In 8 dogs maintained on long-term A-III infusion (30.0 ng/kg min^{-1}), PAC increased from 7.8 ± 2.3 to 37.8 ± 6.9 ng% within one hour and averaged 24.3± 4.5 ng% during the next 24 hours. During long-term infusion of A-III, PAC averaged 13.4 ± 3.6 ng%, PCC and arterial pressure remained at control levels, and PRA decreased from 2.4 ± 0.8 to 0.6 ± 0.3 ng/ml/hr. These data demonstrate that A-II infusion at rates that markedly increase arterial pressure results in slight increases in PAC; A-III infusion at large rates results in slight increases in PAC without an increase in arterial pressure. However, long-term infusion of both A-II and A-III failed to maintain PAC in intact conscious dogs at levels observed during sodium deprivation. Supported by NIH grant HL-09921.

EFFERENT NEURAL COMPONENTS OF VIBRATION INDUCED CARDIOVASCULAR RESPONSES IN DOGS. E.P. McCutcheon, C.F., Knapp, F. Wibel, and A. Bhattacharya, NASA, Ames Research Center and Wenner Gren Research Laboratories, University of Kentucky, Lexington, KY 40506

Previous studies indicated that neurally mediated responses may account for 75% of the changes in mean aortic flow (MAF) in dogs subjected to whole body vibration. To evaluate and quantify the relative contributions of efferent neural mechanisms, tests were conducted in 10 chronically instrumented dogs both awake and tranquilized (mean weight 18.7 kg), restrained vertically and exposed to $\pm$ Gz vibration. The protocol included graded increases of acceleration amplitude ranging from $\pm$ 0.25 to 1.5 G in $\pm$ 0.25 G steps at frequencies of 3 and 12 Hz for a period of 5 min. This sequence was repeated after production of beta-sympathetic and parasympathetic blockade (propranolol 3 mgm/kg and atropine 0.1 mgm/kg, respectively). Control responses at 3 Hz included increased heart rate (HR), MAF, peripheral conductance (PC), as a function of increasing peak net force/body weight, PNF/BW (or G level). After blockade with either drug, HR response was reduced markedly; at PNF levels twice BW, and HR response decreased 68%. MAF response was also markedly damped (-45% at PNF/BW = 2); stroke volume (SV) increased with propranolol blockade only. The similar but reduced alterations at 12 Hz were less affected by blockade. These results indicate neural mediation through parasympathetic and beta-sympathetic efferent pathways is a major component of the cardiovascular (CV) response to vibration, similar to those occurring with exercise. The residual CV responses suggest an additional component of non-neurogenic, locally mediated effects.

SIMULTANEOUS ANALYSIS OF MYOCARDIAL AND TOTAL BODY INTEGRAL EXTRACTION RATIOS OF RUBIDIUM-86. P.F. McDonagh*, A.F. Salel*, E.A. Rhode* and D.T. Mason, Dept. Internal Medicine, School of Medicine, UC Davis, California 95616

Radiorubidium (Rb) has been employed for regional flow measurement, especially myocardial, because rapid tissue uptake causes a Rb distribution which is closely proportional to organ flow. This has led investigators to conclude that the integral extraction ratio of Rb by the myocardium (ERm) is equal to the integral total body extraction (ERtb), where integral extractions are defined as:

$$ERi = [\int_0^t Ca(t)dt - \int_0^t Cvi(t)dt]/\int_0^t Ca(t)dt$$

Ca(t) = arterial conc., Cvi(t) = mixed venous conc. for organ i Other workers feel that this conclusion (ERm=ERtb) is not fully justified. In order to assess this question, allowing continuous, independent measurement of mixed coronary venous and total body venous Rb concentrations following bolus injection, a right heart bypass preparation was employed. ERm and ERtb were simultaneously measured in 29 trials following 1 mC injections in 6 dogs. Representative mean values of blood pressure (121/86), cardiac output (Qco=2.13 l/min), coronary fraction of cardiac output (6.5%) and coronary flow per g myocardium (Qm=0.89 ml/min g^{-1}) demonstrated preparation integrity. ERm showed strongest correlations with Qm (r=-0.69) and a stroke work index (peak systolic pressure x stroke volume/body weight)(r=-0.72). ERtb was poorly correlated with Qco/body weight (r=-0.37). A paired t test showed that ERm (0.558+0.014) was significantly different than ERtb (0.699+0.012)(P<.01). Thus, it is unwise to infer from the rapid extraction of Rb that ERm=ERtb and care should be exercised when using this isotope to quantitate coronary flow.

EFFECTS OF pH AND OUABAIN ON HUMAN RBC GHOST (Na^++K^+)-ATPase AT VARIOUS TEMPERATURES. Alicia McDonough* and Suk Ki Hong. Depts. of Physiology, SUNY at Buffalo, N.Y. 14214 and Univ. of Hawaii, Honolulu, Hi 96822.

In order to characterize the effect of temperature on (Na^++K^+)-ATPase activity of human erythrocyte ghosts we first determined the optimal pH for enzyme activity at various temperatures and next examined the effect of ouabain, a specific inhibitor of (Na^++K^+)-ATPase, using two assay methods at various temperatures. The optimal pH for (Na^++K^+)-ATPase activity decreased from 7.55 at 32°C to 7.45 at 37° and 7.35 at 42°. However, the ratio of (OH^-) to (H^+) of the medium for maximal enzyme activity remained at 22 regardless of temperature. Two methods were used to study the ouabain effect at different temperatures. In both cases, $(OH^-)/(H^+)$ was kept at 22. If the enzyme and 10^{-7}M ouabain were preincubated with Mg^{++}, Na^+, and K^+ and the (Na^++K^+)-ATPase reaction was initiated with ATP, no significant inhibition of the Na^+-and K^+-dependent activity was seen. However when the enzyme was preincubated with 10^{-7}M ouabain, ATP, Mg^{++} and Na^+ and the (Na^++K^+)-ATPase reaction was initiated with K^+, inhibition of Na^++K^+-dependent activity was maximal (100% inhibition at 30° and 34°C, and 83% inhibition at 37°C). This second method provides optimal conditions for ouabain binding to the enzyme. These data suggest that the (Na^++K^+)-ATPase system is in its most active state if the (OH^-)/(H^+) ratio of the medium is fixed at 22, regardless of temperature. At this ratio, ouabain is an effective inhibitor both at 30°C and 37°C, provided that the proper assay method is used.
(Supported in part by Grant NIHL-14414-04.)

RELATIVE CONTRIBUTIONS OF HYPOCARBIA AND HYPERPNEA AS MECHANISMS IN POST-EXERCISE ASTHMA. E.R. McFadden, Jr., D.R. Stearns*, R.H. Ingram, Jr. and David E. Leith. Department of Medicine, Peter Bent Brigham Hospital and Harvard Medical School, and Department of Physiology, Harvard School of Public Health, Boston, Mass. 02115

The purpose of this investigation was to assess the relative contributions of hyperpnea and hypocapnia in the induction of post-exercise asthma. To achieve these ends, eight young asthmatics were exercised on a treadmill while minute ventilation ($\dot{V}_E$) and end tidal CO_2 (Pet_{CO_2}) tension were continuously recorded. The subjects were then restudied using a partial rebreathing technique that allowed separation of minute and alveolar ventilations so that independent evaluations could be made of the relative effects of bulk airflow on pulmonary mechanics as well as a systematic study of hypocapnia in a dose-response fashion. Specific conductance, lung volumes and spirometric variables were measured before and after each experiment. Sustained hyperpnea with $\dot{V}_E$ identical to those recorded during exercise was totally without effect on lung function when the mean Pet_{CO_2} was isocapnic, or lowered to approximately 30 mmHg. Reduction in Pet_{CO_2} to 21.3±0.9 mmHg resulted in significant changes in mechanics; however, in every variable measured, exercise produced much greater alterations and did so at Pet_{CO_2} values significantly higher than those shown to have an effect on airways. Consequently neither high $\dot{V}_E$ *per se*, nor hypocapnia can be considered as the mechanisms underlying exercise induced asthma.
(Supported by grants HL00013, HL17873, HL17382, and HL14580 from NHLI.)

ELECTROPHYSIOLOGY OF CULTURED VASCULAR SMOOTH MUSCLE. Michael J. McLean*and Nick Sperelakis (SPON: R.A. Murphy). Dept. of Physiology, University of Virginia, Charlottesville, Va. 22903

Single cells were trypsin-dispersed from blood vessels (great vessels near the heart and mesenteric vessels) of 10-20 day chick embryos, and induced to reaggregate into small spheres (0.1 to 0.5 mm in diameter) either by gyration or by plating on cellophane. Many reaggregates contracted spontaneously or in response to electrical stimulation during culture periods of up to 6 weeks. When reaggregates were allowed to adhere to glass substrate, cells emigrated and formed monolayers which continued to contract. Thick and thin myofilaments (mean diameters of 146 A and 65 A, respectively) were observable in a large fraction of the cells studied in electron micrographs. Vascular smooth muscle (VSM) cells were identified in the reaggregates by recording resting potentials of -40 to -60 mV, and by action potential generation. The action potentials were preceded by pacemaker potentials, had slow rates of rise (<20 V/sec), and were insensitive to tetrodotoxin (TTX). Thus, the action potentials depend on an inward slow current. Reaggregates of atrial cells, produced at the same time for comparison, had larger resting potentials (up to -80 mV), less automaticity, fast rates of rise (mean of about 85 V/sec), and complete TTX sensitivity, thus indicating dependence on fast Na^+ channels. These findings indicate that identifiable VSM cells can be successfully maintained in primary culture for several weeks, and these cells retain electrical and contractile properties similar to those of smooth muscle cells in intact adult blood vessels. This preparation provides a convienient system for electrophysiological and pharmacological studies of VSM cells. (Supported by NIH grant HL-18711.)

PHASED RETROPERFUSION TREATMENT OF MYOCARDIAL ISCHEMIA. S. Meerbaum, J. Farcot*, T.W. Lang*, K. Hashimoto*, J. Osher*, E. Corday* Cedars-Sinai Medical Center, Los Angeles, Calif. 90048

To overcome difficulties encountered in past applications of coronary venous retroperfusion (RTP) treatment of myocardial ischemia, the current study evolved a new RTP catheter and phased regional RTP system which provided unidirectional augmented RTP in diastole, facilitates coronary venous drainage in systole, and appears applicable in the clinical setting. Experiments were performed in open chest dogs with occlusion (O) of the proximal LAD. RTP was instituted after 1 hr O, and the effects of RTP were measured over a period of 2 hours during maintained O. The effects of RTP were compared with an equivalent untreated control series. Measurements included: myocardial force and epicardial ECG-ST in the ischemic (I) and border (B) regions, ischemic zone lactate and potassium balances, pressure within the anterior interventricular vein (AIV). Relative to 1 hr O, 2 hrs RTP caused a mean 66% and 27% rise in I and B zones force respectively and a 66% and 81% reduction in ECG-ST. Lactate extraction in the I region improved from -74.3 to +13.9%, potassium balance from -.36 to -.05 mEq/L. I zone AIV pressure during RTP was less than 30 mm Hg. LAD flow from distal to the occlusion rose 12% and pO_2 decreased 39%. The latter may be an indication that RTP effectively supplied oxygen to the acutely ischemic myocardium. We conclude that regional unidirectional diastolic RTP is a useful method of treating acutely ischemic myocardium.

MEDIUM-RANGE VISCOELASTICITY OF MESOTUBARIUM SMOOTH MUSCLE.
R.A. Meiss. Depts. of Obstetrics/Gynecology & Physiology, Indiana University Medical Center, Indianapolis, Indiana 46202

Isolated strips of isometrically-contracting rabbit mesotubarium smooth muscle were rapidly stretched at constant velocity by up to 20% of their initial length over a portion of the ascending limb of the length-tension curve. Oscilloscope plots of tension versus length, made continuously during the stretches, showed an initial steep rise in force followed by a rather abrupt yielding; thereafter force rose linearly with continued stretch. Releases from the same initial forces produced an exponential decline in force. The initial slope in both curves was directly dependent on the isometric force; the slope of the linear portion was only weakly dependent on initial force. Increasing the stretch rate during the linear portion produced a parallel upward displacement in the length-tension plot; decreases in rate produced a similar downward shift. The magnitude of the slope was independent of stretch rate over a wide range of values. Subsequent to the stretch the muscle underwent stress-relaxation; following this the isometric tension was inappropriately high for the new length. The dynamic stiffness of the stretch-potentiated muscle, as measured by the tension response to a small sinusoidal length perturbation, was inappropriately low for the new isometric tension. These data appear consistent with a model in which some cross-bridges break when subjected to an external force, behave as a viscous drag during prolonged stretch, and subsequently reform at the new length in a more highly-strained configuration.
(Supported by the Department of Obstetrics and Gynecology, IUMC.)

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INTERACTION OF VASCULAR COMPLIANCE WITH ALTERING VASCULAR TAPER.
J. Melbin* and R. Gopalakrishnan* (SPON: S. Takashima). Sch. Vet. Med.; Dept. Bioeng., Univ. of Penna., Phila., Penna. 19174

The pulmonary trunk is oval in cross section and capable of undergoing large deformations. Elastic constants and initial dimensions contribute to cross section deformation which is more pronounced with greater eccentricity. Inextensible deformation, more important at low transmural loads and extensible deformation, more important at higher loads, contribute to dynamic compliance. Distortion towards a circular cross section reduces eccentricity related compliance. Axial taper also affects vascular wall compliance and the nature of flow. In systemic and pulmonary arteries, geometric and elastic taper exist toward the periphery. With pulmonary arteries, eccentricity also appears. An appropriate taper in a distorting vessel imposes an upper limit to axial velocity without compromising the compliance contribution to axial flow, thus minimizing kinetic work without restricting flow. Also, if taper is uniform about the perimeter, the taper reduces as the cross section enlarges with distortion. Thus, as the rate of cross section increase diminishes, the velocity restraint imposed by taper also diminishes. However, measurements indicate that in the pulmonary trunk, taper on the major axis is greater than that on the minor axis. A consequence of different tapers is an alteration of eccentricity with distance. It can be shown theoretically that, where unequal taper exists on the axes, vascular distortion during inextensible deformation results in an increasing taper on the minor axis while the taper on the major axis decreases. Initially, the taper effect preferentially increases upstream compliance. However, the disparate variation of taper, on the axes, with distortion, appears to shift high compliance downstream to correlate temporally with pulse or fluid propagation.

MAXIMUM EXPIRATORY FLOW CHANGES WITH TRACHEAL LONGITUDINAL TENSION IN MAN. C.G. Melissinos† and J. Mead. Dept. of Physiology, Harvard School of Public Health, Boston, MA 02115.

Studying the causes of variability in Maximum Expiratory Flow ($\dot{V}max$) we noticed consistent $\dot{V}max$ changes in young subjects at high lung volumes with neck hyperextension. Maximum Expiratory Flow Volume (MEFV) curves had consistently higher flows at high lung volumes in 11 of the 15 subjects during hyperextension. At 70% of the vital capacity (VC), 7 subjects had increases of $\dot{V}max$ of more than 10%; three of these subjects had changes at volumes below 50% of the VC. Significant changes in the configuration of the MEFV curve were apparent in 7 of the subjects, all of which had a typical "plateau-knee" configuration of the MEFV curve (see Fig. 1). Neck hyperextension resulted in either obliteration of the knee resulting in a smooth curve without abrupt slope changes, or in transposition of the knee to higher lung volumes. Isovolume pressure flow curves done in 3 subjects in the region of flow changes, showed clear effort independency for both postures, but critical pleural pressure was higher during neck hyperextension. We concluded that tracheal longitudinal tension induced by neck hyperextension, results in decreased tracheal collapsibility under dynamic conditions. Our data are in agreement with previous studies on the localization of the flow limiting mechanism in normal subjects, and are consistent with predictions of the tube wave speed theory regarding the influence of the longitudinal tension on the choke point.

Reg. posture ——
Hyperext. ---

Fig. 1

(Supported by grant HL 14580 USPHS)

SATURATION KINETICS FOR STEADY STATE PULMONARY CO TRANSFER. *C. Mendoza *H. Peavy, B. Burns and G. Gurtner. The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205.

We have previously reported that diffusing capacity of the lung for carbon monoxide (DLCO) measured by rebreathing or single breath techniques in dogs decreased as PCO increased (Fed. Proc. 34:416, 1975, Prog. Resp. Res. 8:166-175, 1975). These results are consistent with the presence of a specific carrier for CO and O_2 similar to the placental O_2 carrier, which we believe to exist on the basis of previously described experiments (J. of Appl. Physiol. 39:728-734, 1975). The magnitude of the rebreathing and single breath DLCO is dependent on two factors: the rate constant for CO disappearence from the lung and the volume of distribution of CO in the lung. Both of these changes as the PCO changes as would be expected with the presence a CO carrier. The direction of the changes, although strongly suggestive of gas to blood facilitated transport might possible be explained by absorbtion of CO by a noncarrier, CO binding molecule in the lung tissue. In order to test the alternative hypotheses, we measured steady state DLCO in anesthetized paralyzed, artifically ventilated dogs at different CO concentrations. The steady state DLCO is a measure of true gas to blood CO transfer and is not affected by tissue absorbtion of CO. The results show that DLCO measured at an alveolar CO concentration of 200 ppm is approximately 1.5 times DLCO measured at 850 ppm. The relative change in steady state DLCO is almost identical with the relative change in rebreathing and single breath DLCO, indicating that the previously observed changes in DLCO are due to facilitated transport of CO from gas to blood. Drugs which interact with cytochrome P-450 reduced the changes in DLCO with changes in CO concentrations.

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GLUCOSE AND LACTATE KINETICS IN THE GUINEA PIG FOLLOWING E.COLI ENDOTOXIN ADMINISTRATION. G.F. Merrill* and J.J. Spitzer, Dept. Physiology, LSU Medical Center, New Orleans, La. 70112

Overnight-fasted, conscious, guinea pigs weighing 425-475 g were used to study the effects of E. coli endotoxin (0.1 mg i.v.) on metabolic and hemodynamic variables. Indwelling catheters were implanted for the simultaneous infusion of Na L(+) U-^{14}C-lactate and 6-^{3}H-glucose and for sampling arterial blood. Control samples were obtained at 90, 105 and 120 min following the beginning of infusion which lasted throughout the experiment. Plasma concentration (mg/dl), and the rates (mg/kg/min) of appearance (R_a), disappearance (R_d), and metabolic clearance (MCR, ml/kg/min) of glucose and lactate were determined before and after endotoxin administration. During control conditions R_a, R_d, and MCR of glucose remained stable at 10.0, 9.9 and 8.1 respectively. Following endotoxin all three rates were consistently elevated; e.g. at 180 min. the three values were, R_a= 14.6, R_d= 14.8 and MCR= 10.3. Following endotoxin, blood glucose levels were normal or elevated, while lactate concentration was markedly increased. Lactate kinetics changed similarly to glucose, e.g., R_a and R_d rose from controls of 8.4 and 8.2 to 12.5 and 12.3 at 180 minutes postendotoxin. The value of glucose derived from lactate increased from a control of 20 to 52 per cent after endotoxin. Total body oxygen consumption decreased following endotoxin from a control of 24.7 to 16.3 ml/min/kg. Cardiac output (thermal dilution) was little affected. Thus, during endotoxic shock the rates of peripheral utilization and hepatic output of glucose were maintained or increased, and a greater fraction of the newly formed glucose was derived from lactate than under control conditions. (Supported by NIH Grants GM 07029 and HL 16850.)

SHORT CIRCUIT CURRENT AND SOLUTE TRANSFER BY THE INTESTINE OF ASCARIS SUUM. J.M. Merz* and C.G. Beames. Dept. of Physiological Sciences, Oklahoma State University, Stillwater, OK 74074

The intestine of the parasitic roundworm Ascaris suum is essentially a straight tube. Its wall consists of a single layer of cells supported on their basal side by a thick basement membrane (basal lamella). When isolated ribbons of the intestine are positioned as a membrane separating two compartments of a modified Ussing chamber, an electrical potential (10-30 mV), pseudocoelomic negative with respect to the luminal surface, rapidly develops. The short circuit current (SCC) that is required to zero the potential is approximately 30 μA. The potential does not develop at low temperature (20C), and it is inhibited by NaF or iodoacetic acid. Addition of glucose to the luminal side of the intestine is followed by a rapid decrease in the SCC, which is suggestive of a saturable carrier mechanism. Certain other sugars produce similar responses in the SCC. The transmural fluxes of Na^+ and Cl^- indicate that neither ion is responsible solely for the SCC. Our failure to quantitate the flux of Na^+ to the SCC may be due to the fact that some other ion(s) is responsible for the observed current. Alternatively, it may be due to a relatively large error that is introduced by a Na^+ diffusional component (shunt pathway) across the tissue. Unidirectional flux measurements indicate that Na^+ is the major current conducting ion into the shunt pathway and that the uptake of Na^+ is quantitatively equivalent to glucose uptake. (Supported by NIH Grant AI 12783)

THIOURACIL FEEDING AND ADRENAL AXIS MATURATION IN THE MOUSE. Lee A. Meserve. Dept. Biological Sciences, Bowling Green State University, Bowling Green, OH. 43403

The influence of thiouracil-induced hypothyroidism on the adrenal release of corticosterone was studied in 15 day old Balb/c mice. Female mice were isolated and fed pulverized laboratory chow with or without 0.25% thiouracil throughout pregnancy and lactation. Litters were reduced to 4 pups on postnatal day 3. At 15 days of age young mice were removed from the nest and either immediately decapitated, exposed to ether fumes and decapitated 15 min later, administered exogenous adrenocorticotropic hormone (ACTH) and decapitated 15 min later, or injected with physiological saline and decapitated 15 min later. Blood was collected in heparinized tubes and plasma samples were extracted. Plasma corticosterone content was estimated by a micro adaptation of the sulfuric acid fluorescence method. Euthyroid mice evidenced responses previously reported for young mice and rats, with ether stress, exogenous ACTH, and saline injection evoking a significant ($P \leq 0.05$) rise in plasma corticosterone. Thiouracil neither altered basal corticosterone concentration nor prevented the response to exogenous ACTH. However, plasma corticosterone response to ether stress or saline injection was prevented by inducing hypothyroidism. It can be concluded that the hypothyroidism-induced alteration of adrenal axis maturation previously described in rats also occurs in mice.

(Supported by a Bowling Green State University Faculty Research Committee Grant).

THE EFFECT OF ETHIONINE ON ENZYME CYCLING RELATED TO FEEDING IN RATS. R. C. Messner* & R. R. Nielson, Department of Zoology, Miami University, Oxford, Ohio 45056

Changes in enzyme activity related to feeding have been demonstrated for several hepatic enzymes, including succinic dehydrogenase, in rats that are placed on a feeding regime. This regime allows for 5 hours of feeding in every 24 hour period with the 5 hour feeding occurring at the same time each day. Periodic assays during the 24 hour regime indicates minimal and maximal succinic dehydrogenase activity at 6 and 21 hours respectively following feeding. At 21 hours the animal is into the next feeding period. Changes in lighting patterns and changes in the time of day of the feeding period have not altered the enzyme cycling. Since enzyme activity can be regulated via activation as well as in increase in total enzyme, the protein inhibitor ethionine was administered in an attempt to determine which mechanism was responsible. One mg/grm DL-thionine administered at the end of a feeding period suppressed the enzyme activity beyond the 6 hour low to a considerably lower activity at 18 hours after feeding, with a dramatic rebound approaching normal activity levels at 21 hours. Repeated doses every 6 hours were able to suppress activity for the entire 24 hour period of fasting and feeding. These results suggest the alterations in enzyme activity is due to variations in the amount of enzyme present. Another interesting effect of thionine injections was noted. Stomach content data indicates very little emptying following feeding.

ALBUMIN CLEARANCE FROM ALVEOLI OF DOGS: RATE AND ROUTE.
E.C. Meyer and R. Ottaviano*. Dept. Surgery, Fitzgerald Mercy Hospital, Darby, Pa. 19023

In anesthetized, ventilated dogs with cannulated right lymphatic ducts (RLD) and thoracic ducts, we instilled 2±0.2 ml iso-osmolar 1% ^{125}I-albumin (125-RISA) solution into alveoli. The instillate was monitored by two opposing 2" external detectors placed at right angles to the plane of bronchial drainage. The detectors had 19-holed focusing collimators with a resolution at focus characterized by a 50% decrease in count rate for a 5 mm lateral (trans-bronchial) shift of the instillate. We separated blood and lymph absorption of 125-RISA by injecting ^{131}I-albumin intravenously for compartmental analysis. In 5 hr. experiments, the 125-RISA decay measured by detector and lung homogenate analyses were identical, indicating no airway clearance of the instillate. Removal of 125-RISA from the lung occurred at a mean rate constant of 3.7×10^{-4} min^{-1}, from the interstitium at 1.6×10^{-3} min^{-1}, and assuming unidirectional transport, from alveoli at 4.8×10^{-4} min^{-1}. The estimated permeability coefficient of alveolar epithelium for albumin was 7.2×10^{-9} cm/sec. Blood absorption averaged 6.4 times lymph absorption. Fractional lymph absorption in individual animals correlated positively with plasma/RLD lymph steady state albumin concentration ratios as predicted by the Renkin equation. We conclude that albumin clearance from alveoli occurs by transport through epithelium into the interstitium. Clearance from the interstitium is predominantly by transcapillary permeation.
(Supported by grant HL 13596 from NHLI).

AN IN VIVO METHOD FOR VISCOELASTICITY OF RESPIRATORY MUCUS.
E.D. Michaelson, S.M. Serafini, H. Watson and S. Zarzecki, Division of Pulmonary Diseases, Mount Sinai Medical Center, Miami Beach, Fla. 33140.

A method has been developed to measure both viscous and elastic properties of respiratory mucus in vivo. A two capillary viscometer, similar to that developed by Philippoff et al. (Biorheology 7:55-67,1970), was constructed by connecting in series a precision bore stainless steel capillary (internal radius (r) = .029 cm x length (L) = .5 or 1.0 cm) with a polyethylene tube (r = .07 cm x L = 1.0 cm). This device, connected to one end of an air filled Tygon catheter (r =.025 cm x L = 100 cm) can be passed through the channel of a fiberoptic bronchoscope. Using a Harvard syringe withdrawal pump connected in parallel to a pressure transducer, a sample is drawn through the viscometer under direct vision at a constant flow rate ($\dot{Q}$), and a record of pressure (P_t) vs time (t) is obtained. Knowing r of the small bore capillary allows calculation of shear rate($\dot{\gamma}$). P_t levels off at a maximum (P_f) which is measured or predicted from an iterative fit of $P_t = P_f(1-e^{-t/RC})$. P_f is determined by viscosity (η) and is used to obtain shear stress (τ); $\eta = \tau/\dot{\gamma}$. The time constant RC (analagous to relaxation time) allows calculation of the total compliance (C_T). The compliance of the catheter-transducer system (C_g) is obtained from P_t vs t with the capillary occluded. Compliance of the sample is $C_T - C_g$. Measurements have been made on Newtonian oils (300 to 70,000 centipoise), viscoelastic polymers and in the airways of anesthetized dogs. The rheological properties of respiratory mucous have, for the first time, been determined in vivo. Other advantages of this method include small sample size (0.01 ml), wide range of constant $\dot{\gamma}$ (varying $\dot{Q}$ or r), and the ability to measure yield stress and estimate surface tension.
(Supported by NHLI HL-17816 and General Research Support PHS FR-05622).

ANALYSIS OF COUPLED FLOWS THROUGH A NONLINEAR COMPLEX MEMBRANE SYSTEM USING NONLINEAR NETWORK METHODS: RECTIFICATION AND CATASTROPHES IN A SERIES MEMBRANE. D.C. Mikulecky. Dept. of Physiology, Medical College of Virginia, Richmond, VA. 23298.

A linear network thermodynamic method for analyzing coupled flows in complex membrane systems such as epithelial membranes in the gut and/or kidney tubule is extended into the nonlinear domain using methods from nonlinear network analysis. Characteristics are plotted for single elements and for series-parallel combinations of the nonlinear elements. Rectification in a series membrane system is studied and the methods of Kedem and Katchalsky (Trans. Faraday Soc. 59:1941 (1963)) and Patlak et al. (J. Theoret. Biol. 5:426-442 (1963)) are compared from the standpoint of nonlinear network theory. It is shown that Patlak's approach is much more compatible with the global analysis of nonlinear network theory. When the flow of volume and solute in a series membrane system is coupled with certain types of chemical reactions or electrokinetic effects, multiple stationary states, oscillations and catastrophes can occur.

VALIDITY OF THE EXPONENTIAL PEELINC TECHNIQUE AS APPLIED TO VENTILATORY TRANSIENTS. H.T. Milhorn, Jr. Univ. of MS Med. Ctr., Jackson, MS 39216

The "exponential peeling" technique has been applied to minute ventilation and tidal volume transients occurring after the abrupt removal of 7, 6 and 5 per cent CO_2 in inspired air in 8 human subjects. These transients, in many cases, were found to be composed of three exponential components, each contributing to the total ventilatory response and each having individual time responses. Gelfand and Lambertsen (J. Appl. Physiol., 35:903-913, 1973) have attributed these components to the peripheral chemoreceptors as a group and to two central chemoreceptors. The finding of two components of about equal magnitude and considered to be of central origin prompted Lambertsen to postulate a dual receptor theory. According to this theory, two distinct sets of central chemoreceptor cells are thought to exist, each contributing about 50 per cent of the central ventilatory drive. Statistical analyses of the contribution of the three components over the range of CO_2 values used in the present study have shown that, although the values for each at the different stimulus levels are not significantly different, the great subject-to-subject variation in the data precludes a firm conclusion about the constancy of the contribution of each component to the total ventilation drive. Because of this and a number of other considerations it is concluded that exponential peeling of respiratory transients following abrupt removal of CO_2 inhalation is not a satisfactory way to approach the problem of the numbers, relative contributions and time responses of the various receptor groups comprising the respiratory controller.

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BMES

DEVELOPMENT AND EVALUATION OF A MODEL OF THE RESPIRATORY CONTROLLER. H.T. Milhorn, Jr. Dept. of Physiology and Biophysics, Univ. of Mississippi Medical Center, Jackson, Mississippi 39216

During the past 25 years numerous models of respiratory control have appeared in the literature. With few exceptions, experimental validation of these models has been scanty or totally lacking, thus rendering the hypothyses on which the models are based inconclusive. In recent years the controlled system (plant) has been developed to a fair degree of complexity and the concept of using a model of this portion of the system to evaluate various hypotheses about the nature of the respiratory controller has evolved. Of primary importance to this approach has been the paucity of good experimental data for the development and evaluation of a controller model. Several recent experimental studies from our laboratory have reduced the magnitude of this problem. From the steady-state data of these studies and from steady-state data from the literature, we have developed a model of the respiratory controller. In the model, two receptor groups are assumed to exist, the peripheral chemoreceptor and a central chemoreceptor. The peripheral chemoreceptor is considered to be an oxygen sensor whose output is modified in a greater-than-additive manner by the local hydrogen ion concentration. The central chemoreceptor is assumed to monitor the hydrogen ion concentration at a point beneath the surface of the medulla on a P_{CO_2} gradient between cerebrospinal fluid P_{CO_2} and deep brain tissue P_{CO_2}. The outputs of the two sensor groups are assumed to be summed by the respiratory center. In addition, a significant input from the reticular activating system is assumed to be present during wakefulness. The output of the respiratory center is considered to have an inherent 6 second time constant. The dynamic responses of the model to several stimuli are very good when compared to experimental data. (Supported in part by HE 11678.)

ASZ(DCPB)

DELAYED RENAL VASOCONSTRICTION DURING ACUTE HYPOXEMIA IN FETAL SHEEP IN UTERO. Ronald W. Millard, Hank Baig*, Massimo Pagani*, and Stephen F. Vatner. Dept. Cardiology, Childrens Hospital Medical Center, Boston, Mass. 02115 and New Engl. Reg. Primate Res. Ctr., Southboro, Mass. 01772

Sustained hypoxemia (HPX) in fetal sheep has been demonstrated to result in significant reduction of peripheral blood flows. The cardiovascular response to acute fetal HPX was examined to determine the dynamic and temporal participation of renal (R), mesenteric (M) and iliac (I) vascular beds. Fetal sheep were instrumented with catheters in the abdominal aorta and vena cava to obtain blood samples and pressures. Blood flows (BF) were measured by doppler and electromagnetic transducers on the M, R, and I arteries and by the radioisotope-labelled microsphere technique. Several days after surgery fetal HPX was induced by allowing the conscious ewe to breath 7-10% oxygen. At control, fetal heart rate (HR) was 175±8 beats/min; arterial pressure (AP), 44±2 mmHg; P_aO_2, 21.5±1.3 torr; P_aCO_2, 32.0±2.7 torr; and pH_a, 7.37±0.01. The fetal vascular response to HPX demonstrated two phases. First, at 5 minutes of HPX, when fetal P_aO_2 was 13.7±1.0 torr, RBF had not changed significantly from a control level of 2.5±0.3 ml/min/gm, but M and I BF had fallen sharply by 35±13% and 74±8% from their respective control values. HR decreased to 135±7 beats/min while AP and pH_a were unchanged. After 20 minutes of HPX all three blood flows were significantly below control levels. At this time P_aO_2 was 11±1 torr, HR was 129±4 beats/min and AP had risen significantly to 53.5±3 mmHg.

Thus, while blood flows to gut and skeletal muscle are decreased markedly throughout the fetal hypoxic period, renal blood flow is initially maintained with significant reduction occurring only after sustained hypoxemia.

ENDOCRINE RESPONSES TO ACUTE COLD IN GOATS. F. L. Miller*, P. Illner*, D. D. Williams*, P. Marques*, S. L. Davis*, W. L. Green*, J. W. Kendall, and C. C. Gale. Depts. of Physiol. & Biophys. & Med., Reg. Prim. Res. Ctr., Univ. of Wash., Seattle, Wash.; Dept. of Anim. Indus., Univ. of Idaho, Moscow, Id.; and Dept. of Med. Univ. of Ore., Portland, Ore.

Endocrine responses to acute cold were studied in 4 female goats kept in metabolism stalls. Ruminal cooling by intubation with 4 liters of ice water caused a prompt fall in rectal temperature (T_r) of 1.8° C (nadir at 40 min). Goats shivered, vasoconstricted (ear pinna) , and restored T_r within 180 min. In jugular blood drawn percutaneously, norepinephrine rose 110% in 20 min and fell to basal by 60 min. ACTH rose 200% within 10 min and fell by 60 min. TSH increased 40% at 40 min and fell by 80 min. T3 rose 66% by 60-80 min and declined by 200 min. T4 rose 13% by 140 min and fell to basal within 8 hours. Values for T3 and T4 were corrected for changes in serum total proteins. To compare endocrine responses to ruminal cooling with rostral hypothalamic cooling, water-perfused thermodes were implanted stereotaxically in the preoptic anterior hypothalamus (POAH) of 2 goats. In 6 experiments, local POAH cooling for 2 hours led to shivering, vasoconstriction, and 1.5° C rise in T_r within 1 hour. T3 rose 61% within 80 min, and T4 increased 42% within 160 min. Cessation of POAH cooling led to prompt cutaneous vasodilatation and panting, with decline in T_r over 1 hour. T3 and T4 declined slowly and were above basal 2 hours after stop of POAH cooling. These data indicate the multiple endocrine responses to total body (ruminal) cooling, and suggest that thermoreceptors in the POAH mediate the thyroidal response to core hypothermia. Presumably hypothalamic TRH stimulated pituitary TSH release. However, serum prolactin was not elevated by ruminal cooling.

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IONIC PERMEABILITIES IN PHASIC AND TONIC VASCULAR SMOOTH MUSCLE. Louis Miller* and Allan W. Jones. Dept. Physiology, University of Missouri, Columbia, MO. 65201.

Membrane permeability to ions was studied in rabbit vascular smooth muscle using radioisotopic techniques and comparisons were made between phasic (portal vein, PV) and tonic (main pulmonary artery, MPA) vessels. Na turnover was significantly faster in the PV (0.2207 ±0.0065 min^{-1}, N=5) than in the MPA (0.0946±0.0053 min^{-1}, N=5). Cellular concentrations of Na averaged 25 mM in PV and 13 mM in MPA. Steady-state permeability to Na (P_{Na}) was estimated to be $0.5x10^{-8}$ cm/sec in PV and $0.2x10^{-8}$ cm/sec in MPA. Relative ionic permeabilities P_K:P_{Na}:P_{Cl} are 1:.1:1.2 in PV and 1:.09:.9 in MPA. Predicted membrane potentials using these values in the Goldman equation are-31 mV (PV) and-33 mV (MPA), while experimental values reported by Somlyo and Somlyo (Microvasc. Res. 1:354, 1969) are-40 mV and-60 mV, respectively. The effects of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) on K and Cl fluxes were also studied. NE, 10^{-5} gm/ml, increased K efflux 316±20% (N=7) from PV and 635±40% (N=7) from MPA. Accounting for changes in the electrical driving forces due to depolarization, P_K increased 186±32% in PV and 257±22% in MPA. NE also increased Cl efflux 97±18% (N=6) from PV and 276±17% (N=6) from MPA and corrected P_{Cl} increased 163±24% in PV and 371±20% in MPA. Supramaximal doses of 5-HT increased K efflux with P_K increasing 102±14% (N=6) in PV and 315±53% (N=6) in MPA. 5-HT also increased Cl efflux with P_{Cl} increasing 57±2% (N=2) in PV and 303±138% (N=2) in MPA. The correlation between increased P_K and P_{Cl} is approximately 0.9. These results add support to the concept that depolarizing agents operate to alter cell membrane potential by increasing membrane permeability to both K and Cl. (Supported by grant HL 15852 and Amer. Heart Assn.)

ASZ(DCPB)

PROSTAGLANDIN F_2 ALPHA-INDUCED ALTERATION OF LUTEAL ULTRASTRUCTURE OF PREGNANT MICE. M.M. Miller* and A.J. Rotermund. Dept. of Biology, Loyola University, Chicago, Ill. 60626.

Exogenous administration of prostaglandin F2α initiates a dramatic series of functional alterations within the mammalian corpus luteum. These changes culminate in luteolysis and the termination of pregnancy. The present study examines ultrastructural changes which parallel this functional decline, and explores potential mechanisms for interference with steroidogenesis. Ovaries from control and prostaglandin F2α-treated ICR-CD1 mice were examined by light and electron microscopy. Eighteen mice were equally divided into experimental and control groups. Animals were injected subcutaneously with either 200 µg of PGF2α or vehicle alone on day 4, days 4 and 5, or days 4, 5, and 6 of pregnancy. Thus each animal received a cumulative dose of either 200, 400, or 600 µg of prostaglandin. On the last day of dosage, the ovaries were prepared for light and electron microscopic examination. Results indicated that PGF2α causes cell injury of luteinizing cells at the ultrastructural level. Alterations were seen 60 minutes after initial injections. Cellular damage was progressive, becoming most definitive after administration of 600 µg of prostaglandin. The corpus luteum at this stage was characterized by marked swelling of mitochondria, dilation of the cisternae of granular and agranular reticula, detachment of ribosomes, alteration of the Golgi apparatus, and the appearance of autophagic vacuoles and secondary lysosomes. Lipid droplets also appeared to increase. These observations correlate with the vasoconstrictor mechanism of prostaglandin-induced luteolysis. (The PGF2α was donated by Dr. Pike, Upjohn Company.)

ASZ(DCPB)

EFFECT OF VASOPRESSIN ON MUCOSAL SURFACE MORPHOLOGY OF THE TOAD URINARY BLADDER. J.W. Mills* and L.E. Malick, Lab. Renal Biophysics, Mass. Gen. Hosp., Boston, Ma. 02114 and Eppley Inst., Univ. of Nebraska Med. Ctr., Omaha, Ne., 68105.

Previous investigations with the scanning electron microscope (SEM) of the vasopressin induced changes in the mucosal cell surface of the granular (G) cell in the toad urinary bladder have produced some discrepancies (Davis et al., J. Cell Biol. 61:544; Spinelli et al., J. Membrane Biol. 23:139, 1975). We reexamined the effect of vasopressin on the morphology of the G cell under different conditions of Na and water flux, employing various preparative techniques for SEM. During any particular physiological state the appearance of the mucosal surface of the G cell is never uniform throughout the epithelium. However, certain structural configurations appear with high enough frequency to be considered significant. In the absence of an osmotic gradient the microvilli of the G cell appear as interconnected ridges of various length and this organization is unaltered by the addition of vasopressin. When vasopressin is added in the presence of an osmotic gradient, the ridges of microvilli become less apparent and in some cells the microvilli appear as individual extensions of the mucosal cell surface. Complete inhibition of Na transport by ouabain (10^{-2}M) prior to the addition of vasopressin does not prevent the hormone related changes in the microvilli of the G cell. Ouabain itself does not effect the morphology of the G cell nor does complete inhibition of Na transport by amiloride (10^{-3}M), which acts on the mucosal surface to prevent Na entry into the epithelium. These results provide further support for the hypothesis that the G cell is the site of the hydro-osmotic response to vasopressin (DiBona et al., J. Membrane Biol. 1: 79, 1969). (Supported by Grant HE 06664, AM 17372 and Contract No. 1-CP 33278, NIH).

EFFECTS OF A HIGH FAT DIET ON THYROID HORMONE AND PROLACTIN LEVELS IN THE MONKEY. J.E. Milmore*and P. Hill*, Division of Nutrition, American Health Foundation, Valhalla, New York 10595(Spon: P-C Chan)

Adult ovariectomized rhesus monkeys were fed either laboratory chow (calories:fat 12.4%, protein 17.5%, carbohydrate 70%) or a liquid high-fat diet (calories:fat 35%, protein 18%, carbohydrate 47%). Total caloric intake and body weight gain were similar in both groups. Thyroid hormone levels and free thyroxine index declined in animals fed the high-fat diet, whereas there was no consistent effect on prolactin levels. Serum levels of prolactin declined after ovariectomy in monkeys fed both diets, and three days of estrogen treatment did not restore normal prolactin levels. These data indicate that high fat intake depresses thyroid function in the ovariectomized monkey but does not affect prolactin secretion. The latter is stimulated by ovarian hormones, but estradiol itself is not responsible for this effect.

(Supported by grant CA-012376 from NCI)

EFFECTS OF TEMPERATURE AND OUABAIN ON THE FROG'S MUSCLE SPINDLE. M. Mirolli and H. Cohen*, Medical Sciences Program, Indiana University, Bloomington, Indiana 47401

Spindles isolated from the extensor long. Dig. IV were kept in a chamber under continuously flowing saline while their spike discharge was monitored; the spindles were either slack or stretched. Both the temperature and the composition of the saline could be rapidly changed. In the slack spindle the static spike frequency increased during exposure to cold (7-2°C). By contrast in the stretched spindle the static frequency decreased in the cold. These effects were reversible. 10^{-4}M ouabain, at room temperature, induced a transient increase in the firing frequency in both slack and stretched spindles, but the effect was more dramatic in the slack spindles which could fire at a rate comparable to that observed in the maximally stretched ones. (Supported by grant AFOSR #72-2383 from the Air Force).

GLUCOPRIVIC FEEDING AND HYPERGLYCEMIA INDUCED BY 3-OXYMETHYL-D-GLUCOSE IN THE RAT. Richard R. Miselis* (Spon: A.N. Epstein). Animal Biology, School of Veterinary Medicine, Univ. of Penn., Phila., Pa. 19174

Twenty one male, Sprague Dawley rats (350-450g b.wt.) were prepared with chronic intravenous catheters and tested on separate days in their home cages for feeding responses and hyperglycemia to acute infusions of 3-oxymethyl-D-glucose (3OMG), a glucose analogue which causes glucoprivation. The rats were on ad libitum food and water except during blood collection for hyperglycemia. Infusions of 3OMG were made remotely in freely moving rats during the day between 1.5 and 3 hours after the last spontaneous meal. Food intake was measured for a 1.5 hour period following the infusion. There was no dose-response relationship for the feeding response as there was for hyperglycemia. The threshold for feeding (app. 400mg/Kg) was above that for hyperglycemia (app. 200mg/Kg). A second group of rats was adrenal demedullated and had the adrenal cortical tissue transplanted to beneath the kidney capsule. After 2-6 weeks of recovery this group of rats underwent the above study. Near elimination of the hyperglycemic response did not affect the amount of food eaten to glucoprivation. It slightly increased the probablity of a feeding response to 3OMG at lower doses. Glucoprivation triggers the ingestion of a meal of a fairly fixed size which is unrelated to the degree of glucoprivation. This is reminiscent of the lack of correlation between the size of a spontaneous meal and the length of the preceding intermeal interval.

This work was done in the laboratory of S. Nicoladis of the College de France and was supported by a grant from the CNRS of France.

FREQUENCY DEPENDENCE OF PRESSURE-VOLUME (P-V) HYSTERESIS AND DYNAMIC COMPLIANCE IN ISOLATED DOG LOBES. W. Mitzner, *J. Grotberg, *S. Davis, Departments of Environmental Medicine and Mechanics and Materials Sci., The Johns Hopkins University, Baltimore, Maryland 21205.

Following exsanguination we removed either the left or right lower lobe from 15 dogs, degassed them, and then connected the bronchus to a pump arrangement which allowed accurate control of the air volume in the lung. Alveolar pressure was estimated by a retrograde catheter placed in a 2-3 mm airway. A constant volume history was obtained by 3 or 4 cycles of slow air inflation (0.15 cycles/min) between 0 and 30 cm H_2O (V_{30}) until at least 2 P-V loops were nearly superimposed. On the subsequent deflation the lung was held at about 50% V_{30}, and a pump was started which generated small tidal volume cycles (approx. 7% V_{30}) at frequencies from 0.1 to 50 per min. P-V loops were recorded at several frequencies within this range. The lobes all showed a monotonic decrease in dynamic compliance with increasing frequency. Ten of the 15 lobes exhibited a local maximum in a work per cycle (hysteresis area) versus frequency plot. The monotonic decrease in dynamic compliance with increasing frequency has been previously reported in excised and intact lobes, but, the hysteresis maximum has not been demonstrated before. These findings for dynamic compliance and hysteresis area are consistent with recent theoretical predicitons concerning the dynamic behavior of surfactant films (L. Horn, S. Davis, J. Collid. Interface Sci. 51:459, 1975) as well as previous experimental work with lung extracts on a Wilhelmy balance (R. Bienkowski, M. Skolnick, J. Colloid Interface Sci. 39:323, 1972). Our results thus suggest that the dynamic as well as quasi-static properties of the lung are governed primarily by the air-liquid interface.

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DEVELOPMENT OF A CONSTANT FLOW EXPIRATION METHOD FOR MEASURING THE PULMONARY DIFFUSING CAPACITY. M. Mochizuki* and T. Ono* (SPON: R. E. Forster). Yamagata Uni., School of Med., Yamagata, 990-23, Japan.

From O_2 and CO_2 concentrations in expired air recorded during a constant flow expiration, we evaluated various parameters such as O_2 uptake and pulmonary blood flow simultaneously, using theoretical equations derived in regard to a simple lung model. A similar method was applied to the measurement of diffusing capacity (D_{Lco}). After inhaling CO test gas as deeply as possible, alveolar gas was exhaled at a constant flow rate of 100 ml/sec. 5 to 10 seconds after the onset of expiration the expired gas was sampled automatically at two time points whose interval was constantly set at 5 seconds, and then, analyzed for CO and H_2 concentrations by using a gas chromatograph. The initial alveolar gas volume was estimated from the inspired gas volume and the H_2 dilution ratio. The D_{Lco} was calculated from the following equation:

$$D_L = (1-P_2/P_1)(V_A - c \cdot t_1 - 2.5 \cdot c)/2.5(P_B - 47)(1 + P_2/P_1), \quad (1)$$

where V_A is the initial alveolar gas volume, c, the expired flow rate and P_1 and P_2 are the P_{Aco} at time=t_1 and t_1+5, respectively. The D_L in Eq.(1) is a function of t_1, P_2/P_1 and V_A, and independent of the initial value of P_{Aco}. The D_{Lco} values were measured in 5 normal subjects by using both the present and breath holding methods. The D_{Lco} measured by this method significantly decreased as the alveolar gas volume was reduced ($D_L = 8.5 \cdot V_A - 0.29$); the correlation coefficient was 0.82. The D_{Lco} values obtained by the breath holding technique were about 20 % smaller than the above values, when compared at the same alveolar gas volume, suggesting an increasing effect of convection of alveolar gas on the D_{Lco} value. (Supported by grant No.911304, from the Education Ministry, Japan)

BMES

AN AUTOMATED ADMISSIONS SYSTEM ON A LARGE SCALE INTEGRATED HOSPITAL COMPUTER. L. R. Monsees, C. W. Johnson*, D. G. McQuarrie*, and R. Harris*, Veterans Administration Hospital, Minneapolis, MN 55417

Since its implementation in 1973 until January 1976, the Admissions Data Medical Information Needs (ADMIN) system has processed 42,000 patients. In 1975, a total of 45,374 admission transactions were logged. The ADMIN system was developed on an existing hospital computer (CDC 3300) which already had over 200 certified medical programs on it. The hardware system includes interactive C.R.T. terminals using an asynchronous serial (RS232C) input-output communications system. Patient information is entered via a reversed video question-answer format in an interactive mode. In addition to entering and updating patient information, the terminals may be used to locate a patient or look up a patient record or history, or to find the number of empty or occupied beds in any ward.

The program (ADMIN) features:

- Automated entry of admitted patient.
- Automated change of ward as patient is moved.
- Establishes and changes ward and bed control
- Maintains patient days of care by month and year.
- Establishes gains and losses waiting list.
- Accounts for patients on pass.
- Entry of narrative remarks.
- Checks for operator errors.

This system has been operational since its installation with all users being well satisfied. It has reduced the time required for initial input information, update, and patient lookup by approximately 30%.

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN CONGESTIVE HEART FAILURE PRODUCED BY CONSTRICTION OF THE SUPRA-RENAL AORTA OF RABBITS.
Brian J. Morris*, James O. Davis, Marvin L. Zatzman and Gary M. Williams*. (Sponsored by W.S. Platner). Dept. of Physiology, University of Missouri, Columbia, MO 65201.

Severe constriction of the supra-renal abdominal aorta of 3 kg New Zealand white rabbits to 3.7±0.2 mm^2 and maintenance of a daily sodium intake of 10 mEq by infusion of 0.9% sodium chloride resulted in a progressive increase in central ear arterial pressure to 106±3 SEM mm Hg (control = 79±1). This was accompanied by a progressive and significant increase in left ventricular end-diastolic pressure to 22±2 mm Hg (control = 3±1), plasma renin activity to 21±5 ng angiotensin·h^{-1}/ml (control = 5±1), plasma aldosterone concentration to 99±23 pg/ml (control = 14±4) and plasma sodium concentration to 142±1 mEq/l (control = 136±1). Urinary excretion of sodium decreased to 3.9±0.7 mEq/day and marked fluid retention occurred. These changes were accompanied by a decrease in hematocrit to 24±2% (control = 40±1), the formation of 36±9 ml of fluid in the thoracic cavity, 33±9 ml of ascites, pulmonary congestion and edema, hepatic congestion and enlargement and hypertrophy of both the left and right ventricles. All animals died of ventricular failure at a time that was partly related to the degree of aortic constriction and that ranged from 2-12 days. The model established is chronic, highly reproducible, easy to produce, inexpensive, and resembles the clinical syndrome of right and left congestive heart failure in man. The studies provide evidence for an important role of the renin-angiotensin-aldosterone system in the fluid retention that leads to pulmonary and systemic venous congestion after supra-renal aortic constriction.

IMMUNOHISTOCHEMICAL EVIDENCE FOR INTRAGRANULAR MATURATION OF NEUROSECRETORY PRODUCT.
J.F.Morris*, P.C.Goldsmith* and M. Rorvik* (SPON: W.F. Ganong). Dept. Physiology, Univ. California, San Francisco, Ca. 94143.

In the hypothalamic magnocellular neurosecretory (NS) neurons the hormones oxytocin and vasopressin and their related neurophysins are thought to be produced as a result of enzymatic cleavage of a precursor protein. Ultrastructural immunohistochemical localization of neurophysin has been used to determine the intraneuronal site at which neurophysin first becomes immunologically recognizable.

Immunocytochemical localization of neurophysin was performed on thin sections of unosmicated tissue from the paraventricular nucleus of rats using the unlabelled antibody peroxidase-antiperoxidase technique. The antiserum (RbANP-2c) was raised to human estrogen-stimulated neurophysin (by Dr. A. Robinson) and recognizes both oxytocin- and vasopressin-neurophysin in the rat and other species.

In the perikarya of the NS cells both the endoplasmic reticulum and the Golgi apparatus were unstained. Most Golgi-related NS granules were either unreactive or weakly reactive. Other granules in the perikarya reacted strongly and virtually all granules within the NS processes were heavily stained.

These results imply that biochemical maturation of NS material is able to proceed after its packaging within NS granules and before the granules have entered the NS processes. Neurophysins possess large regions of their molecules in common across species and some of this relatively constant region is thought to be exposed. The results therefore further suggest that the relatively constant regions in the precursor protein are inaccessible to antibody and that maturation may also involve a major conformational change in the protein.
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WALL STRESS AND MECHANICAL PROPERTIES IN CANINE HINDLIMB VEINS AFTER CHRONIC PRESSURE ELEVATION. T.W. Morris* and M.L. Swain* (SPON: G.M. Fischer). University of Pennsylvania, Philadelphia, Pa.

The purpose of this study was to determine if chronic elevations in venous pressure could bring about changes in vein wall composition and properties. The right femoral veins of 10 mongrel dogs were ligated for 60 (6 dogs) or 30 (4 dogs) days. The diameter-pressure relationships and connective tissue compositions of the right and left femoral and lateral saphenous veins were then determined. The results of the 30 and 60 day experiments are not significantly different and will be considered as one group. Right hindlimb venous pressures were higher than left by 5.6 $\pm$ .8 mmHg. After $NaNO_2$ perfusion the diameters of the right lateral saphenous veins were less than the left by 10 $\pm$ 3, 8 $\pm$ 2, 5 $\pm$2, and 3 $\pm$2% at pressures of 5, 10, 20, and 40 mmHg respectively. Similarly the diameters of the right femoral veins were 8 $\pm$ 4, 7 $\pm$ 3, 6 $\pm$ 2, and 4 $\pm$ 2% smaller than the left. The mass per unit length of the right veins were greater than the left by 6 $\pm$ 8% for the lateral saphenous and 23$\pm$6% for the femoral. The differences in diameter and mass resulted in substantial differences in wall stress. Right femoral vein wall stress was less than that for the left by 35, 33, 31, and 29 % at pressures of 5, 10, 20, and 40 mmHg. Similarly stress differences were 19, 20, 15, and 13% for the lateral saphenous veins. The relative amount of connective tissue was smaller in the right veins which indicated an increase in smooth muscle. The ability of the right and left veins to constrict during NE perfusion was not significantly different. The changes observed are consistent with the hypothesis that pressure elevation results in an increase in the non-contractile components of smooth muscle and a decrease in resting length. (Supported by AHA, Pa. Affiliates and USPHS Grant HE - 07762.)

HYPOGASTRIC NERVE EFFERENT DISCHARGES DURING BLADDER CONTRACTIONS. J.F.B. Morrison*, Verity E. Hick* and K. Floyd* (SPON: I.F.G. Hampton). Dept. Physiology, The University, Leeds LS2 9JT, U.K.

De Groat and Lalley (1972) showed that some hypogastric efferent neurones discharge during bladder contractions, and that these responses could be abolished by pelvic nerve section. This procedure, however, prevents spontaneous bladder contractions and the associated discharges of hypogastric afferents (Floyd, Hick and Morrison, 1976). The role of hypogastric afferents in producing reflex hypogastric efferent discharges during bladder distensions and contractions has been studied in chloralose anaesthetised cats paralysed with gallamine and with an L6 cord transection. Discharges were recorded from single hypogastric efferent neurones during bladder distension and during bladder contractions induced by sacral cord stimulation. The discharge rates of most of the units increased during both procedures. In some units the responses were maintained, while others produced only transient changes. Essentially similar results were obtained after denervation of the colon and pelvic organs. These reflex effects were elicited by intravesical pressures similar to those found in the micturition reflex, and by changes in bladder volume within the physiological range. It is concluded that hypogastric nerve afferents associated with the bladder may be involved in the vesico-sympathetic reflexes described by De Groat and Lalley (1972).

De Groat, W.C. & Lalley, P.M. (1972). J. Physiol. 226 289-309.
Floyd, K., Hick, Verity E. & Morrison, J.F.B. (1976). J. Physiol. (in press).

RED CELL MASS MEASUREMENT: EVALUATION OF CURRENT TECHNIQUES

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Measurement of RBC mass with Cr^{51} is inaccurate, partly because of a variable degree of sequestration or lysis of freshly traumatized, "tagged" cells. We evaluated the reproducibility of measurement with freshly "tagged" homologous (I), autologous (II), or "Hot Dog" (III) RBC's. The latter is drawn into heparin from a donor whose stable, circulating RBC's are extremely radioactive following labeling 48 hours prior with 20 millicuries of Cr^{51}. Fragile cells are lysed and extraneous Cr^{51} cleared by the kidneys. Freshly "chromated" cells are prepared in the usual fashion with .2 mc Cr^{51} immediately prior to use, washed 3X with saline. Each injectate contained 10 microcuries Cr^{51}. The subjects were 7 splenectomized mongrels. In random fashion with each type of cell sequentially, initial RBC mass was measured. This was measured triply again after hemorrhage of 100 ml RBC's, and again after reinfusion of shed blood. A total of 9 determinations were made within 3 hours for each dog. For each cell type, variability increased with increasing background radioactivity. "Hot Dog"(III) donor cells yielded the best reproducibility, with 0-40% error, averaging 12%. Freshly "tagged" autologous cells (II) gave 1.4-63.6% error, averaging 14.8%. Least reliable was the freshly "tagged" homologous cells (I), which gave an error of 2.1-204%, averaging 38.6% error. The "Hot Dog" technique proved to be the most practical. It was simple, inexpensive, and reproducible, with errors within 4% for up to four consecutive RBC mass determinations. Accuracy rapidly deteriorated thereafter.

FUNCTIONAL DEVELOPMENT OF LUNG MECHANICS IN INFANTS AND CHILDREN.

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Postnatal lung development continues in humans during the first decade of life but information on functional development below 5 years has been scarce. We studied pulmonary mechanics in otherwise healthy infants and children under general anesthesia for elective surgery. FRC was measured on left lateral position with helium dilution; TLC = FRC + IC (at Pao: +40 cm H_2O). Static pressure-volume curves and compliance of the lung (C_L) and Thorax (C_W) were measured with an esophageal balloon during stepwise deflations of the lung from TLC. Maximum expiratory flow volume curve (MEFVC) was obtained during forced deflation of the lung (for up to 3 seconds) from TLC to RV by connecting the endotracheal tube to a negative pressure source (-20 to -50 cm H_2O) via a pneumotachograph. Flow and volume (integration of flow) signals were fed into X-Y storage oscillograph and resulting MEFVC was photographed. Results from 56 subjects (2 days to 17 years old) studied with permission showed that both specific C_L and C_W at FRC were significantly elevated in infants and decreased with increasing age, TLC or height (Ht). C_W (%IC/cm H_2O) = 14.1 - 0.054 x Ht ($p < .005$); C_L = 9.5 - 0.025 x Ht ($p < .02$). Maximum expiratory flow rate (Vmax) at low lung volumes, on MEFVC was relatively high in infants and decreased with increasing age and Ht. Vmax at 25%FVC (FVC/sec)= 1.11 - 0.0035 x Ht ($p < .001$). Specific conductance of upstream segment (J.A.P. 22:95, 1967) was high in infants and decreased with age. Thus, contrary to current concept small airway resistance appears disproportionately low in infants and increases with growth.

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EFFECT OF PARATHYROID HORMONE ON RENAL ACCUMULATION OF LEAD. D. R. Mouw, J. G. Wagner, K. Kalitis, A. J. Vander and G. H. Mayor. Dept. of Physiology, University of Michigan Medical School, Ann Arbor, Michigan.

The effect of parathyroid hormone (PTH) on renal accumulation of lead was evaluated in two experiments (A&B) on mature rats. In A, unanesthetized rats were given a single dose of lead (40 mg) per os; thereafter, animals were given 100 units of PTH-extract (Lilly) over the next 41 hours, at which time the animals were sacrificed. A control group of animals received only the PTH vehicle. In B, PTH (Bovine 1-34, Beckman) was administered i.v. to pentobarbital-anesthetized rats as a prime (1.33 μg) and constant infusion (42 ng/min) over a 3 hour period while a control group received only the saline vehicle; lead, 7.8 μg/min, was administered to all animals over the last two hours of PTH or vehicle infusion, and the animals were then sacrificed. PTH caused significant elevations in kidney lead in both experiments: from 5.4 to 8.2 μg/g and from 14.7 to 19.0 μg/g in A&B, respectively. In A, total body lead was elevated by PTH, suggesting an effect of PTH on gastrointestinal (GI) absorption of lead. However, in B (lead given i.v.), the GI mechanism could be ruled out, and the effect was found to be selective for kidney since PTH produced no change in liver, red cell, or plasma lead. We conclude that PTH, by an unknown mechanism, causes increased renal accumulation of lead. (Supported by grant 1 ROl ES01141 from NIEH).

REGIONAL LEFT VENTRICULAR PERFUSION IN NORMAL AND HYPERTROPHIED HEARTS AT REST AND WITH PACING. T.M. Mueller*, M.L. Marcus, R.E. Kerber and F.M. Abboud. Cardiovascular Center and Dept. of Internal Medicine, University of Iowa, Iowa City, IA 52242

Several studies have shown that pressure induced left ventricular (LV) hypertrophy is associated with an approximate 20% decrease in capillary density. To determine the physiological effects of this change we measured regional myocardial blood flow with radioactive microspheres in 7 normal (LV=3.9±SEM 0.5 g/Kg/body wt.) and 12 hypertensive dogs (LV=6.0±0.27 g/Kg/body wt.) at rest and during pacing in the awake state. Hypertension was induced by renal artery stenosis and unilateral nephrectomy. The animals were studied 6 weeks after operation. Mean blood pressure in normal dogs was 99±5 mmHg at rest and 101±3 mmHg with pacing; corresponding values in hypertensive dogs were 130±7* mmHg and 155±8* mmHg. Heart rates were 97±6 for normals and 72±5 for hypertensive at rest, and 197±9 and 209±9 respectively, when paced.

	LV perfusion ml/min x 100g		Coronary Vasc. Resistance		Endocardial Flow / Epicardial Flow	
	C	P	C	P	C	P
Normal	95±9	231±69	.97±.12	.61±17	1.31±.07	1.24±.07
Hypertrophy	100±13	171±13	1.61±.14*	.94±.06*	1.37±.07	1.19±.07

C=control; P=pacing; *significant difference from normal ($p<.05$)

We conclude: 1) Coronary vascular resistance in the hypertrophied ventricles is elevated over normal at rest and with pacing; 2) Regional myocardial perfusion is normal in hypertrophied ventricles at rest and with pacing; 3) Myocardial flow per gram is normal in the hypertrophied ventricles.

METAL-FILM THERMOPILES FOR MYOTHERMIC MEASUREMENTS. L.A. Mulieri, G. Luhr*, J. Trefry* and N.R. Alpert. Dept. Physiology & Biophysics, Univ. of Vermont, Burlington, VT 05401.

We have developed a method of fabricating Hill-Downing type, planar, thermopiles by vacuum deposition techniques. The present model was designed for rabbit papillary muscles as small as 1 mg mass but it also has been used on bundles of frog muscle fibers (20-30). Vaporized bismuth and antimony metals are deposited through a mask to produce thermocouples arranged in a ladder configuration on 5 μm thick mica sheets. Measuring and reference junctions are formed where the two metals overlap at the mid-line and edges, respectively, of the 5 mm long thermopile element. A tap at the 14th junction allows muscles as short as 3.5 mm to be used. A second mica sheet is sealed over the completed element for electrical insulation (> 50MΩ) giving a total thermopile thickness of 20-25 μm. Temperature sensitivity is 1.6 - 2.1 mV/°C for 20 junctions (94 μV/ °C/junction) at 22°C. Measured equivalent thermal capacity and heat loss coefficients of the sensing area (1 mm x 5 mm) are 0.28 mcal/°C and 0.31 mcal/°C/sec, respectively, in room air. Electrical resistance, peak-to-peak noise, risetime, and bandwidth are 180Ω, 0.075μV, 6 msec, DC-60 Hz, respectively, when connected to a Kipp, A80 galvanometer. A 1 mg papillary muscle on the thermopile develops 5-9 g/mm^2 tension and a peak, uncorrected, temperature rise of 0.7-0.9 m°C in a single twitch at 23°C. Cool-off after artificial heating is exactly exponential (τ = 4.9-5.5 sec). Delay between onset of tension and temperature change is about 50 msec with not more than 20 msec caused by thermal conduction delay outside the muscle. (Supported by Vermont Heart Grant Ag-91, American Heart Grant No. 75-822 and NIH Grant No. R01 17592-01.)

THE ROLE OF K^+ IN THE CONTROL OF CORONARY VASCULAR RESISTANCE. P.A. Murray* and H.V. Sparks (SPON: J.W. Bean). The University of Michigan, Ann Arbor, Michigan 48109.

If K^+ participates in the control of the coronary circulation, changes in interstitial K^+ concentration ($ISF[K^+]$) must precede changes in coronary vascular resistance (CVR). We tested this by comparing the time courses of the changes in coronary sinus K^+ concentration ($CS[K^+]$) and the changes in CVR (adjusted to include the delay and dispersive effects of vascular transit between tissue and coronary sinus = CVR*) produced by (1) step increases in heart rate (↑HR) and (2) stopping coronary blood flow (SF) for 15 seconds. The left coronary artery of anesthetized, closed-chest dogs was perfused with blood at constant flow. ↑HR by 60-110 bpm increased myocardial O_2 consumption by 2.19 ± 0.36 $ml \cdot min^{-1} \cdot 100\ g^{-1}$ ($\bar{x}$ ± SEM) and decreased CVR by 0.51 ± 0.12 PRU_{100}. An ↑$CS[K^+]$ (0.53 ± 0.07 mEq/L) was observed in 9 of 9 dogs. This was maintained throughout the 2.5 minute period of ↑HR in 4 dogs, while in the remaining 5 dogs $CS[K^+]$ returned to control levels during the ↑HR period. SF also resulted in an ↑of $CS[K^+]$ (0.55 ± 0.09 mEq/L) in 6 of 6 dogs. The time required for CVR* and $CS[K^+]$ to reach 50% (t_{50}) of their new steady state levels following an ↑HR was 32.4 ± 2.2 sec and 26.3 ± 1.4 sec, respectively ($p < .01$; pair t). t_{90} for the return to control levels of CVR* and $CS[K^+]$ from their peak changes following SF was 122.0 ± 19.5 sec and 97.2 ± 3.9 sec ($p < .075$). We conclude that (1) changes in $ISF[K^+]$ are fast enough to account for initial changes in CVR produced by ↑HR, (2) it is unlikely that K^+ is responsible for the steady state changes in CVR produced by ↑HR, because in 5 of 9 dogs studied, $CS[K^+]$ returned to control levels during the period of ↑HR, (3) the time course of the changes in $CS[K^+]$ after SF are compatible with the participation of K^+ in the vascular response produced by SF. (Supported by USPHS grant (HL-16760).

NA TRANSPORT PROPERTIES OF THE APICAL BORDER OF THE FROG SKIN EPITHELIUM. W. Nagel* (SPON: J. E. Zehr).
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According to Koefoed-Johnson & Ussing, the apical border of the frog skin is thought to behave like a Na selective electrode resulting in a positive potential step in inward direction. Previous microelectrode measurements which were in agreement with this hypothesis, however,turned out to be primarily due to injury of the punctured cells (Nagel 1975, Pflüg.Arch.355,R70). Thus, the response of the intracellular PD to variations of the apical Na (1-110 mM) was reinvestigated using improved micropuncture technique. In the open circuit state, the PD across the apical border (ref: outer sol.) was -94 mV at 1 mM Na and became less negative with incresing Na (34±1 mV/decade). The PD across the basolateral border (ref: corial sol.) increased from -118 mV at 1 mM Na with a slope of 6±1 mV/dec. The transepith. PD had the usual electrode like behavior (28±1 mV/dec). Under short circuit conditions, the intracellular PD of -113 mV at 1 mM Na was depolarized with increasing Na; the slope was 31±1 mV/dec. No difference in response was observed between skins incubated in Cl- or SO_4-Ringer. The results suggest that Na electrode like potentials are of minor importance for the properties of the apical border of the frog skin. Variation of conductance related to the outer Na and concentration dependent influx of Na into the cell explain the observed behavior of the potentials if the conductance of paracellular shunt pathways and of the apical border are of similar magnitude. (supported by Deutsche Forschungsgemeinschaft Na 27/9)

RATE OF IN VIVO GROWTH OF CULTURED AND AUTOGRAFTED HUMAN SKIN. P. Nathan, E.C. Robb*, B.G. MacMillan*, E.J. Law*, H.J. Igel* and A.E. Freeman*. Shriners Burns Inst. and Univ. of Cinti. Medical Center, Cinti., OH and Akron Children's Hospital, Akron, OH.

In the present work 9mm^2 pieces of human skin were cultured on irradiated, non-viable pigskin for 7 to 33 days. The cultured skin of three donors was returned to denuded areas of their own burn wound, graft epidermis to wound dermis, when the burned sites were ready for autografts. The pigskin base served to hold the grafts in place. Grafts were photographed at each wound dressing and the projected visible area of each graft was measured. The photography and measurements were performed under uniform conditions to permit comparisons of the changes of the visible graft size with time. In the first patient a piece of skin was autografted after 7 days in culture. The projected and measured area increased from 0.2 to 0.6cm^2 between the 10th and 28th post-application day (P.A.D.). On the 37th P.A.D. it was 14cm^2 and on the 42nd P.A.D. it was 16.8cm^2. Another graft of cultured skin on this patient showed a similar pattern but the slow growth phase was 20 days and the accelerated growth was evident on the 22nd P.A.D. Accelerated growth continued through the 35th P.A.D. In a second patient the same phasic type growth was observed but the grafts were arranged to be dermis to dermis. Three grafts were followed and the slow phase varied from 10 to 19 days. In the third patient the culture was maintained for 33 days before grafting and its slow phase was only 13 days. The accelerated phase continued through the 32nd P.A.D. This preliminary study indicates that cultured and autografted human skin grows in three phases: a slow phase which may continue for 1½ to 4 weeks, and an accelerated phase which progresses in two stages and may continue for longer than 3 weeks.

EVALUATION OF THE SINGLE NEPHRON GLOMERULAR FILTRATION COEFFICIENT IN THE DOG. L.G. Navar and P.D. Bell*, Dept. of Physiology and Biophysics, Univ. of Alabama Medical Center, Birmingham, Al. 35294

Previous micropuncture experiments in the dog have indicated that interruption of distal nephron volume delivery by oil blockade in the proximal tubule may lead to overestimation of nephron filtration rate (SNGFR) and glomerular pressure. To minimize effects of interrupted distal delivery on feedback regulation of glomerular function, experiments were conducted on 12 dogs in which renal arterial pressure was reduced to the lower limit of the blood flow autoregulatory range. At an arterial pressure of 86±3 (SD) mm Hg, renal blood flow was 3.6±.7 ml/min per g, slightly reduced below control (13%) and GFR averaged .66±.1 ml/min per g, not significantly reduced from control. Filtration fraction calculated on the basis of efferent arteriolar blood hematocrit was .35±.09, which was not significantly different from the whole kidney filtration fraction of .34±.05. Proximal tubule pressure was 20±3 mm Hg, and peritubular capillary pressure was 12±3.5 mm Hg. Stop-flow pressure averaged 38±3 mm Hg and plasma colloid osmotic pressure was 14±2 mm Hg, yielding a value of 52±4 mm Hg for estimated glomerular pressure at reduced arterial pressure. SNGFR based on proximal tubule fluid collections averaged 56±9 nl/min. These values were incorporated into a mathematical model of glomerular dynamics to determine the filtration coefficient (K_f) and the effective filtration pressure (EFP). Average K_f was 4.6±.9 nl/min per mm Hg, and mean EFP was 12±2 mm Hg. Estimated EFP at the efferent end of the glomerular capillaries was 7.9±3 mm Hg, indicating that filtration occurs throughout the length of the glomerular capillaries in superficial nephrons of the dog. (Supported by grants from NIH and Am. Heart.)

RED CELL VELOCITIES IN THE MESENTERIC MICROVESSELS OF STREPTOZOTOCIN-DIABETIC RATS. Karl M. Nelson* and G. P. Pollock. Department of Physiology, Loyola University Medical Center, Maywood, Illinois 60153.

Red cell velocity was measured in the mesenteric microvessels (arterioles, capillaries and venules) of streptozotocin-diabetic rats and compared with the red cell velocity measured in age-matched controls. The measurements were made with a dual-slit photometric system in a vascular loop which consisted of a terminal arteriole, capillaries, and small collecting venules. In non-diabetic animals, the red cell velocities in these vessels were 0.60 ± 0.10, 0.45 ± 0.08 and 0.34 ± 0.07 mm/sec (mean ± SEM), respectively. After one week of diabetes, there was no significant difference in the red cell velocities measured in comparably sized vessels (0.68 ± 0.07, 0.24 ± 0.03 and 0.30 ± 0.04 mm/sec, respectively). There was significant hyperemia after four weeks of diabetes. The red cells velocities were 1.22 ± 0.15, 0.59 ± 0.13 and 0.70 ± 0.08 mm/sec, respectively. No significant differences were observed in MAP or vessel caliber. It is suggested that viscosity changes are responsible for the hyperemia seen after four weeks of diabetes. (Supported by USPHS Grant HL 08682).

ALVEOLAR EPITHELIAL PERMEABILITY IN ALLOXAN PULMONARY EDEMA. R.M. Nelson,* E.A. Egan* and B. McIntyre* (SPON: D.V. Eitzman), Dept. of Pediatrics, University of Florida, Gainesville, FL 32610.

Alveolar epithelial solute permeability and net volume flux in the alveolar space was studied in 8 dogs with acute pulmonary edema induced by alloxan (5,6 dioxyuracil). Volume flux was measured by change in Blue Dextran (molecular radius$\sim$150Å) concentration in an alveolar saline solution infused into part of one lung which had been isolated with a balloon-tipped airway catheter. Solute permeability was determined by measuring the rate of movement of ^{125}I-albumin (molecular radius 35Å) and ^{57}Co-cyanocobalamin (molecular radius 5.3 Å) out of the alveolar saline, and the movement of ^{131}I-albumin into alveolar saline. During edema, volume in the isolated segment increased to 270±33% of initial values. ^{131}I-albumin moved into the alveolar space so that it averaged 80% of plasma levels. ^{125}I-albumin diffused out of the alveolar saline (rate constant -0.021±0.010 min^{-1}) and into the blood, levels reaching 10% of alveolar saline levels. ^{57}Co-cyanocobalamin diffused out of alveolar saline at 10 times the rate of ^{125}I-albumin (rate constant -0.208±0.049 min^{-1}). Alloxan edema induces marked changes in epithelial permeability to protein, and allows diffusional exchange across the alveolar epithelium during edema. Epithelial permeability in alloxan edema is different from that previously described by us in hemodynamic edema in which there is bulk transfer of interstitial fluid into the alveolar space without diffusional exchange of protein across the epithelium.

MAGNITUDE OF THE LEFT VENTRICULAR INTRAMYOCARDIAL PRESSURE (IMP) GRADIENT IN THE CANINE HEART. D. Nematzadeh*, P.A. Kot, J.C. Rose and H.K. Huang*. Dept. Physiology and Biophysics, Georgetown Univ. Med. Ctr., Washington, D.C. 20007

An intramyocardial pressure (IMP) gradient exists across the free wall of the left ventricle (LV) during systole. The magnitude of this gradient varies depending upon the technique used. In this study, a direct measurement was made of IMP gradients in 12 open-chest anesthetized dogs. LVP and IMP were simultaneously recorded by inserting 19 gage needles directly into the LV cavity and to various depths of the LV free wall. Mean values of systolic IMP at subepicardium (0% depth), 25%, 50%, 75%, and subendocardium (100% depth) were 6, 42, 80, 117 and 154 mm. Hg respectively, while the average systolic LVP was 132 mm. Hg. Linear regression analysis was employed to examine systolic IMP/LVP as a function of wall depth. Systolic IMP increased in a linear fashion. The slope was 1·1 and systolic IMP increased from 5% of systolic LVP in the subepicardium to 115% of systolic LVP in the subendocardium. A reverse IMP gradient occurred in late diastole ranging from 5 mm. Hg in the subendocardial region to average values of 20 mm. Hg in the subepicardium. The gradient of IMP indicates the inhomogeneity of myocardial mechanics. High levels of systolic IMP in the subendocardial region explain the sharp drop in instantaneous left coronary artery blood flow (CBF) in early systole. Reversal of IMP gradient in diastole facilitates a selective decrease in resistance of the subendocardial vessels during diastole, compensating for systolic hypoperfusion of this region. Rigorous quantitative analyses are required for an understanding of the mechanical factors regulating CBF on a beat-to-beat basis.

EFFECT OF PEEP AND RAPID RESPIRATORY RATES ON PULMONARY CHANGES IN SHOCK. J.F. Neville, Jr.*, J. Askanazi*, T. Kazui*, S.D. Wax*, W.R. Webb and P. Kane*, Dept. of Surgery, SUNY Upstate Medical Center, Syracuse, N.Y. 13210

This study evaluated the effectiveness of prophylactic PEEP, rapid respiratory rate (RRR) and high tidal volume (HTV) in prevention of congestive atelectasis. Measurements of pulmonary hemodynamics, mechanics, gas exchange, functional residual capacity (FRC), pathology and cine microscopy were performed in 44 anesthetized dogs subjected to hemorrhagic hypotension for two hours. Randomly, the animals were assigned to receive normal ventilation, PEEP (5 cm water), RRR (32/minute), or HTV (20 ml/kg) prior to, during and following hypotension. CO_2 was added as needed to maintain normocapnia. The control animals and the HTV group showed the characteristic changes of congestive atelectasis (capillary congestion and stasis, interstitial edema, periarterial hemorrhage, and alveolar edema and hemorrhage). These microscopic and cine microscopic changes were prevented by both PEEP and RRR and correlated with decreased physiologic shunting (PEEP 10 percent; RRR 13 percent; HTV 22 percent; $P < .01$) in the post shock phase. PEEP increased FRC by 40 percent (PEEP $< .02$) and reduced the pulmonary artery - small pulmonary vein gradient, suggesting a direct effect upon the capillary bed. RRR did not alter FRC but minimized the small pulmonary vein - LA gradient. This effect upon the pulmonary venules theoretically could be mediated by stimulating lymphatic flow. Thus, these two modalities, PEEP and RRR, are both found beneficial, but appear to work by widely differing mechanisms.

THE EXTRACELLULAR NATURE OF THE FLUID IN THE SARCOPLASMIC RETICULUM OF FROG SARTORIUS MUSCLE. Margaret C. Neville, University of Colorado Medical Center, Denver, CO 80220

The efflux of radioactive sucrose, Na, Cl, glucose, xylose, 3-O-methylglucose, glycine, cycloleucine and leucine from frog sartorius muscles was studied at 0°C. All efflux curves could be resolved into three components, which are shown to represent flux from the extracellular space, the sarcoplasmic reticulum (SR) and the sarcoplasm. For all solutes the SR fraction occupied between 6.4 and 8.7% of the tissue when incubation and efflux were carried out in isotonic solution. The distribution space for this fraction increased in solutions made hypertonic by addition of sucrose. The rate of efflux of a particular solute from the SR was linearly related to its diffusion coefficient. The results of these experiments lead to the conclusions that the water of the SR of frog sartorius muscle comprises about 10% of the tissue water and is equally accessible to all small molecular weight components of the bathing medium. The Cl concentration indicates that the electrical potential difference between the SR and the extracellular space amounts to no more than 6 mV. The passage of molecules through the SR-t-tubule junction appears to be a non-specific process akin to diffusion.

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PULSATILE PRESSURE-FLOW RELATIONS IN THE MAIN PULMONARY ARTERY OF MAN
Wilmer W. Nichols and C. Richard Conti*, University of Florida, Gainesville, Florida

Phasic blood flow and pressure were recorded in the main pulmonary artery of 12 patients (pts) using an electromagnetic catheter tip velocity transducer. Seven patients had normal (NOR) pulmonary arterial pressures and flows, and five had pulmonary hypertension (PHT). The nature of the load on the right ventricle was estimated from the hydraulic impedance calculated from the Fourier series of pressure and flow. The spectrum of the input impedance versus frequency was similar to that previously reported for the dog, with the modulus decreasing from relatively high values at zero frequency to a minimum between 3 and 5 Hz. Characteristic impedance (average of moduli above 2 Hz) was lower in the NOR subjects than in those with PHT. (Averages, 24 dyne sec cm^{-5} in the normals vs. 87 dyne sec cm^{-5} in the hypertensives). Average right ventricular power, the integral of instantaneous flow times pressure in the NOR pts was 239 milliwatts (mw), of which 161 mw was associated with mean pressure and flow and 78 mw with pulsations around these means. These power components were elevated in the patients with PHT (averages, total power 534 mw; steady component 403 mw, pulsatile component 131 mw). Kinetic energy accounted for approximately 6% of the total input power in each group.

CONCLUSION: Hydraulic power dissipated by pulsations in the pulmonary bed was higher in the hypertensive than in the normal cases, because of the greater stiffness of the pulmonary arteries as reflected by the elevated characteristic impedance. The elasticity of the pulmonary arterial tree, therefore, appears to be as important as the state of the arterioles and capillaries in determining the power required for phasic pulmonary blood flow.

DETERMINATION OF MIXED VENOUS BLOOD GAS TENSIONS IN THE CHICKEN. T.E. Nightingale* and J. C. Richardi* (SPON: H.Y.C. WONG). USDA Poultry Res. Lab., Georgetown, DE 19947.

Paired right atrial and pulmonary arterial blood gas tensions and pH were examined to determine if right atrial PO_2, PCO_2 and pH values could be considered to be reliable "mixed venous" values in the chicken. Eight adult male White Leghorn chickens were anesthetized with Equithesin (2.5 ml/kg, I.M.). The thoracic cavity was opened, air sacs broken, and unidirectional ventilation begun with 4 L/min of warmed, humidified gas containing varied O_2, N_2 and CO_2 concentrations to produce a range of arterial and, consequently, venous blood gas tensions. Paired 1 ml blood samples were taken from catheters placed in the right atrium (RA) and in the pulmonary artery (PA), and analyzed immediately for PO_2, PCO_2 and pH on an IL blood gas system at 40° C. Over the range of 7.5 to 88 mm Hg PCO_2, regression analysis of PA on RA data indicated a linear relationship ($Y = -1.32 + 0.964X$), with RA values lower by an average of 2.77 $\pm$ 0.33 mm Hg ($P<0.001$). PA blood pH was also linearly related to RA values ($Y = 0.271 + 0.972X$), with PA values higher by 0.062 $\pm$ 0.005 units ($P<0.001$). Over the range of 22 to 79 mm Hg, paired PA and RA PO_2 values differed by -0.66 $\pm$ 0.35 mm Hg (not significant), although the calculated regression slope was significantly different from unity ($Y = -4.94 + 1.123X$). Over the range of 25 to 69.9 mm Hg PO_2, the percentage difference between paired samples was $\pm$ 7% maximum, with $\pm$ 1% difference over the range of 40 to 49.9 mm Hg. These results indicate that RA values for PCO_2 and pH can be corrected by the use of the derived regression equations, and that within the usual physiological range, RA PO_2 values can be used as mixed venous values.

EXTRA-PANCREATIC EFFECTS OF TOLBUTAMIDE IN EVISCERATED RATS. D. Nompleggi,* R. Byrne,* J.C. Penhos and E.R. Ramey. Dept. of Physiology & Biophysics, Georgetown University School of Medicine, Washington, D.C. 20007.

We studied the effect of tolbutamide on the glucose tolerance of sham operated and three eviscerated rat preparations: 1) with functioning liver and kidneys, 2) with only functioning liver, and 3) with only functioning kidneys. All rats were injected i.v. with either glucose alone (125 mg/100 g B.W.) or glucose plus tolbutamide (10 mg/100 g B.W.). Blood glucose levels were measured at 0 hr., 30 min., 1, 2 and 3 hrs. Unlike the improved glucose tolerance observed in sham operated rats treated with tolbutamide, the eviscerated rats with functioning liver and kidneys showed an impaired glucose tolerance at all time intervals when tolbutamide was given (311 ± 13 vs. 409 ± 24 mg/dl; 296 ± 13 vs. 411 ± 17; 278 ± 15 vs. 380 ± 13; 275 ± 17 vs. 384 ± 16). When only the kidneys were in situ, tolbutamide appeared to have no effect on glucose tolerance. When only the liver was functioning the tolbutamide effect was observed only during the first 30 min. of glucose tolerance testing. These data suggest that in the absence of the pancreas, tolbutamide may alter glucose metabolism at the liver and kidney level. The liver effect is more critical as regards blood glucose, but the presence of the kidney is required for the full expression of this extra-pancreatic effect of tolbutamide.

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BMES

TRANSIENT ANALYSIS OF MULTICOMPONENT TRANSPORT IN BRAIN. Randal E. Null* and Daniel D. Reneau. Louisiana Tech University, Ruston, La. 71270

A mathematical model describing the multicomponent transport and reaction in brain has been developed to analyze the transient behavior of the physiological milieu of brain, under adverse conditions such as stroke and arterial hypoxia. The model formulation is based on a compartmentalized capillary-tissue cylinder and conservation of mass. The metabolic reaction systems of glycolysis, Krebs cycle, and oxidative phosphorylation were reduced to a simplified scheme of overall reactions to examine the kinetic-transport interractions. An integral control mechanism was included to simulate autoregulatory responses to tissue hypoxia. Simulation studies included stroke, hypoxia, hyperoxia, hypotensive shock, anemia, and a state of increased energy demand. The model results indicate that flow control plays an important role in maintaining adequate tissue oxygen levels when arterial hypoxia, dilution anemia or hypotensive shock is imposed on the system. The model predicts that acid levels are more severe with minor flow than those under total stroke. During the increased energy demand oxygen was observed to rise in all locations due to rate limited oxygen consumption. Although all the responses are unique to the model formulation, available experimental data tend to validate the dynamic behavior exhibited by the simulations. The mathematical model provides a basis for theoretical-experimental comparison and the natural extension is its use for experimentation design.

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PLASMA ALDOSTERONE IN PRIMATE HEMORRHAGIC SHOCK. J.T. O'BRIAN*, C.L. CZERWINSKI*, L.P. GEORGES*, J. SODE*, J.R. FLETCHER*, AND C.M. HERMAN, National Naval Medical Center and Naval Medical Research Institute, Bethesda, Maryland 20014

Plasma renin activity (PRA), aldosterone (A) and cortisol (F) responses to acute arterial hemorrhage were evaluated in 5 adult male baboons who were sedated with ketamine. Before hemorrhage, PRA was normal while A and F were elevated suggesting that the animals were already stressed. There was no significant correlation between basal PRA and A. Withdrawal of 9.42 ± 1.95 ml/kg of blood from a femoral artery over a 10-20 minute period resulted in a mean arterial pressure (MAP) of 60 mm Hg, a doubling of A, but no change in PRA. Maintenance of MAP at 60 mm Hg for 1 hour by subsequent small additional hemorrhages resulted in a marked increase in PRA, a further elevation in A, and a significant positive correlation between PRA and A. Further hemorrhage to MAP of 45 mm Hg resulted in no additional increase in PRA or A. Complete resuscitation with donor baboon blood resulted in prompt normalization of MAP and PRA, while A did not return to baseline until 1 hour after resuscitation. Plasma F values remained elevated throughout the experiment and in the post-resuscitation period.

We conclude that the initial rise in plasma A during acute hemorrhagic shock is mediated by a mechanism other than renin release. The elevated F suggests that ACTH may be this mechanism. ACTH may be important in the early and late aldosterone responses to acute arterial hemorrhage.

BMES

ASSESSMENT OF LYMPHEDEMA BY XERORADIOGRAPHY. T.F.O'Donnell Jr., L. Kalisher, J.K.Raines, and R.C.Darling. Vascular Laboratory, Mass. General Hospital, Boston, Mass. 02114

Methods for objectively assessing the degree of lymphedema are limited by lack of precision and reproducibility, which prevent an accurate comparison of various treatment programs. To test the value of xeroradiography in the evaluation of lymphedema, 12 patients with secondary lymphedema of the upper extremity following radical mastectomy were studied. The degree of lymphedema (the difference in dimensions between the abnormal and normal limb, Δ) was calculated for arm circumference (ΔC)and volume (ΔV) and correlated with xeroradiographic measurements of skin thickness (X-Skin) and subcutaneous tissue thickness (X-Sub) by regression analysis. The degree of subcutaneous fibrosis (SF^{O}) was also assessed by xeroradiography.

Results Mean ± SEM	ΔC (cm)	ΔV (cc's)	X-Skin (mm)	X-Sub (mm)	SF^{O}
Normal	+0.50	± 100	1±.5	7±3	None → Severe-3
Lymphedema N=12	7.73±1.1	1125±191	4±.06	16.4±2	2

Secondary lymphedema is associated with a two fold increase in X-Sub and an even greater four-fold increase in X-Skin. ΔC correlated with X-Skin ($P<.01$) but not with X-Sub or total tissue width. ΔV did not relate to any of the parameters measured and was subject to individual variation. SF^{O} varied in the 12 patients, being greatest in those with long-standing disease. Although X-Skin, X-Sub and SF^{O} may not correlate individually with clinical assessment and with ΔC or ΔV, xeroradiography provides objective measurements of lymphedema. This method may assist in the selection for and evaluation of therapy.

DISTRIBUTION OF ^{3}H-METHYLPREDNISOLONE (^{3}H-MP) DURING ACUTE MYOCARDIAL ISCHEMIA IN CATS. M.L. Ogletree*, M. Okuda* and A.M. Lefer. Dept. of Physiology, Jefferson Med. College, TJU, Philadelphia, PA 19107.

^{3}H-MP uptake and metabolism was studied in pentobarbital anesthetized cats subjected to myocardial ischemia (MI) or sham MI. Immediately after MI or sham MI, MP (30 mg/kg) + ^{3}H-MP (100 μCi/kg) was infused via the jugular vein. Sixty or 120 min later, a final blood sample was drawn, and the heart and other tissues were excised. Aliquots of plasma samples were isotopically counted. Circulating half-time (t/2) of ^{3}H-MP was 50 min after 1 hr and 90 min at 2 hrs. There was no significant difference in t/2 between MI and sham MI animals at either time. Tissue samples were weighed, homogenized and counted. Final tissue/plasma ratios were determined for each tissue and were as follows: liver, 6.32; kidney, 3.99; pancreas, 3.08; normal myocardium, 2.16; lung, 1.98; ischemic myocardium, 1.40; aorta, 1.35; skin, 1.03; skeletal muscle, 0.72; and fat, 0.36. At two hours, pancreas, lung, myocardium, aorta, skeletal muscle, skin, and fat were unchanged, whereas kidney exhibited an increased and liver a decreased glucocorticoid uptake. Tissue and plasma samples and ^{3}H-MP standard (Std.) were extracted with methylene chloride and chromatographed on silica gel thin-layer chromatography (TLC) plates. TLC revealed one distinct radioactive peak for Std (Rf = 0.52). Tissue and plasma samples showed two radioactive peaks, one at Rf = 0.52 and a second peak at Rf = 0.37. This second peak was pronounced in liver samples, where it was 50 to 70% of the total, and probably represents a MP metabolite. The metabolite peak was about 30-40% of the total in plasma but only about 10% of the total in myocardium. These data indicate that ischemic myocardial tissue takes up considerable quantities of glucocorticoid during the first two hours. Moreover, most of the steroid appears to remain in the myocardium in its native form.

CHANGES IN LUNG FLUID AND PROTEIN BALANCE IN SHEEP AFTER MICROEMBOLISM. K. Ohkuda*, K. Nakahara* and N.C. Staub, Cardiovasc. Res. Inst. and Dept. Physiology, Univ. California, San Francisco, S.F., CA 94143.

We developed a steady-state model of pulmonary microembolism (uneven pulmonary arterial obstruction) with which to study the time course of transvascular fluid and protein exchange. In sheep (bw 44kg) maintained on Halothane-50% O_2 and positive pressure ventilation, we made a right thoracotomy and cannulated the caudal mediastinal lymph node efferent duct and measured lung lymph flow($\dot{Q}$lym)and its protein composition. We measured pressures in pulmonary artery (Ppa) and left atrium (Pla), and thermodilution cardiac output ($\dot{Q}$b). We calculated pulmonary vascular resistance (PVR). We used three different kinds of microemboli: siliconized glass beads (d=200 $\pm$ 15μm)(N=4); mineral oil droplets (d=200 $\pm$ 30μm(N=4) and intravenous thrombin-induced fibrin with tranexamic acid to prevent fibrinolysis (N=2). There were two control sheep. Each experiment lasted 6-8hr; 2 hr baseline, embolization over 1-2hr; postembolization until at 1-2hr steady-state occurred. The responses were not significantly different among the various emboli. Average data $\pm$ 1 S.D. are: baseline $\dot{Q}$lym = 6.3 $\pm$ 1.0 ml/hr; Ppa = 27.9 $\pm$ 1.8 cmH_2O; Pla = 16.9 $\pm$ 1 cmH_2O; $\dot{Q}$b = 4.0 $\pm$ .64 l/min. In the steady state after emboli, $\dot{Q}$lym = 16.7 $\pm$ 2.6 ml/hr. PVR averaged 3 times baseline due mainly to increased Ppa. Pla and $\dot{Q}$b did not change significantly. Lymph/plasma protein ratios remained at baseline period levels. Terminally we removed the lung. Extravascular lung water of the 2 controls and 10 embolized sheep were 4.2 and 4.7 $\pm$ .3 g/g dry blood free lung, respectively. Our results indicate that uneven increases in PVR due to microemboli lead to increased fluid filtration and protein permeability. We do not know the site or mechanisms of this response. [Supported in part by HL06285 and HL14201 (Pulmonary SCOR).]

ASZ(DCPB)

SUBMAXIMAL EXERCISE RESPONSE OF PLASMA AND URINARY CATECHOLAMINES IN YOUNG ADULT MALES OF DIFFERENT AEROBIC CAPACITIES. Donald A. Olewine, Michael T. Simpson*, Frank R. Ramsey*, Georgelle Thomas*, and Curtis G. Hames*. Georgia Southern College, Statesboro, Ga. 30458 and Evans County Health Department, Claxton, Ga. 30417.

The Balke submaximal treadmill test was administered to 50 male college students aged 24.9 ± 0.5 yrs. ($\bar{X}$ ± S.E.). The majority of the participants were sedentary as indicated by pedometer readings and activity diaries maintained during the 7 days prior to the treadmill test. During a 3 min. warm-up the subject walked on the treadmill at a speed of 3 mi./hr. at a 2 1/2% grade. After a 2 min. rest the test was begun and thereafter the work load was increased by 1 Met every two minutes until a heart rate of 180 beats/min. was reached. Venous blood samples were obtained after 30 minutes of resting quietly in a supine position, immediately after exercise, and 15 minutes after exercise. Resting, exercise, and recovery urine specimens were also collected. Group I (N=22) achieved a work load of 7-9 Mets and had an estimated maximal oxygen consumption (Est. Max. O_2) of 32.3 ± 0.4 ml/kg/min. Group II (N=28) reached a work load of 10-12 Mets and had a significantly greater ($p < 0.001$) Est. Max. O_2 of 39.7 ± 0.4. Both plasma epinepherine (Epi.) levels (ug/l.) and Epi. excretion rates (ug/hr.) between the two groups were the same at rest, after exercise, and at recovery. In contrast the exercise response of plasma norepinepherine (Nor.) was significantly greater ($p < 0.01$) in the more aerobically fit group: I - 0.61 ± 0.09 v.s. II - 1.02 ± 0.10. However Nor. excretion rates after exercise were the same: I - 1.61 ± 0.20 v.s. II - 1.73 ± 0.18.

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HUMAN-LIKE VENTILATORY ADAPTATION TO CHRONIC HYPOXIA IN THE RAT. E.B. Olson, Jr.*, M.A.B. Wanner* and J.A. Dempsey (SPON: J. Rankin). Dept. of Preventive Medicine, University of Wisconsin, Madison, WI 53706.

We studied the awake unrestrained male albino rat (∿ 250 g) at 1 and 5 hours, every second day during 8 days of exposure to hypobaric hypoxia (P_B ∿ 450 mmHg) and after 1 hour return to normoxia. Arterial blood was obtained from an indwelling femoral arterial catheter, and ventilation was measured in a body plethysmograph. Throughout the 8 days of hypoxia ventilation was maintained at a level approximately 48% greater than control, due solely to an increase in breathing frequency. Arterial blood data, corrected to rectal temperature, is tabled. ($\bar{X}$ ± 95% confidence limits.)

	PaO_2	$PaCO_2$	pH_a	$[HCO_3^-]_a$
Control	85±3	39±1	7.44±.01	26±1
+1 hour hypoxia	50±2	29±3	7.51±.01	23±2
+8 days hypoxia	52±4	23±4	7.48±.05	17±1
+8 days hypoxia +1 hr return to normoxia	93±8	27±4	7.43±.04	18±2

Like man (JAP 38:1067), but unlike other species previously studied, the rat in chronic hypoxia showed a progressive and sustained hypocapnia, continued hypocapnia during acute return to normoxia, and a maintained respiratory alkalosis. Quantitatively, the rat's adaptation to chronic hypoxia differed from man: hyperventilation in acute hypoxia was ∿ 2 times man, percent compensation of pH_a (after 8d) was better in rat (88%) than man (75%), and rat depended equally on renal and non-renal mechanisms for this compensation. The awake albino rat presents a suitable model for the study of mediation of human ventilatory acclimatization to chronic hypoxia.

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ALPHA ADRENERGIC RECEPTORS IN THE CANINE INTRA AND EXTRACRANIAL CIRCULATION. J.T. O'Neill* and R.J. Traystman. Dept. of Environmental Medicine, Johns Hopkins University, Baltimore, MD 21205.

Cephalic hemodynamic responses to intra carotid injections (I.C.) of l-norepinephrine (NE) (0.1, 1 and 10 μg) were studied in 13 anesthetized, paralyzed, ventilated dogs. All three doses of NE were repeated after I.C. dibenzylene (Di) (0.1, 1 and 10 mg). Two simultaneous measurements of cerebral blood flow were made: (1) cerebral venous outflow (CBF) was measured at the confluence of the sagittal, straight and lateral sinuses with the lateral sinuses occluded; and (2) regional cerebral blood flow (r-CBF) was measured using the radioactive microsphere (15 μ diameter) technique. Extracranial blood flow was estimated with electromagnetic flow probes (EBF-emf) placed around each carotid artery and measured with radioactive microspheres (EBF-rm). All drugs, dissolved in saline, were injected I.C. via a set of indwelling catheters. While the doses of drugs differed, the volume delivered remained the same (1 ml). Following each injection of NE, CBF showed no change; however, EBF-emf decreased to 84, 69 and 52% of control with each increasing dose of NE. Injections of Di and the 3 doses of NE had no effect on CBF, but the EBF-emf responses to NE were progressively blocked with each dose of Di. r-CBF (12 areas measured) showed no change with NE (1 and 10 μg); however, EBF-rm was reduced to 70 and 40% of control. We conclude that alpha receptors exist in the extracranial vasculature and that these receptors can be blocked with Di. The lack of response of the intracranial vasculature may be due to: (1) that the drugs administered I.C. cannot cross the "blood brain barrier" to stimulate the receptors; or (2) a lack of alpha receptors in the intracranial vasculature. (Supported by HL-10342, HL-05453.)

AGE-DEPENDENT RESPONSES OF THE CYCLIC-AMP SYSTEM OF THE RAT CEREBRAL CORTEX TO IN VITRO STIMULATION. A. Allen Opalek and Alan Berg (SPON: I.D. Zimmerman). Dept. of Physiology & Biochemistry, Medical College of Pa., Philadelphia, Pa. 19129

It was previously demonstrated that, in vivo, cyclic-AMP levels of the rat cerebral cortex are 4-fold lower between the ages of 6-24 months than at 1-3 months. The present study investigates the cyclic-AMP system of cortical slices from rats aged 1-28 months, this being accomplished through measurements of the conversion of 3H-adenine into 3H-cyclic-AMP in the presence of stimulatory agents as a function of dose and time. In the absence of such agents, this system showed age-dependent declines comparable to those seen in vivo. Norepinephrine and adenosine each caused a time and dose-dependent increase in conversion, with the maximum responses occurring at 10-15 minutes and at 0.01-0.1 mM, irrespective of age. Generally, while stimulation was observed in preparations from all ages, the magnitude of the responses was less in the older than in the younger ones. Various stimulatory agents (norepinephrine, adenosine, histamine, and prostaglandin-E1) were also tested pairwise on old and young preparations in the presence and absence of calcium ions. No age-differentiated response to any pairings, per se, was seen with the exception of a positive response by young, but not old, preparations to the norepinephrine-histamine pair in the presence of calcium ion. It is concluded that these age-dependent decreases in stimulatability may be major factors in the decline in cortical cyclic-AMP levels seen in vivo.

RELATION BETWEEN THE ANATOMIC GASTRODUODENAL JUNCTION AND THE "INSULATORY ZONE". H.S. Ormsbee III*, E.J. Toggart, Jr.* and G.R. Mason*. (SPON: W.D. Blake). Dept. of Surgery, Univ. of Maryland School of Medicine, Baltimore, Maryland 21201.

It has been observed that myoelectric activity with a duodenal frequency occurs in the canine antrum following Heineke-Mikulicz pyloroplasty. Previous work has suggested that there is an "insulatory zone" at the gastroduodenal junction (GDJ). Such findings raise the question, what is the pathway for such abnormal myoelectric recordings? The purpose of this study was to determine histologically if smooth muscle of the antrum and duodenum are separate at the GDJ, and to determine the relationship in specimens from dogs with pyloroplasty. Three dogs served as controls; three dogs underwent Heineke-Mikulicz pyloroplasty. At least two months after pyloroplasty all dogs were sacrificed and the GDJ segment was removed and placed in formalin. Longitudinal tissue blocks were made from the anterior and posterior aspects of each specimen. Multiple histological slides were made using Masson's trichrome stain. Each tissue slice was 3 cm long. In the anterior specimens from pyloroplasty dogs, groups of smooth muscle cells exhibiting non-random configurations were observed within the surgical site and appeared to be in continuity with the external muscle layers of the stomach and duodenum. In addition, no significant interruption in longitudinal or circular muscle layers was noted in the anterior control specimens or in the posterior specimens from control or treated animals. In conclusion, an anatomical pathway for the propagation of myoelectric signals across the GDJ exists in dogs with Heineke-Mikulicz pyloroplasty and in normal dogs. The "insulatory zone" appears to be a functional not an anatomic zone between the stomach and the duodenum.

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ASZ(DCPB)

INFLUENCE OF BOVINE PINEAL EXTRACTS ON LUTEINIZING HORMONE AND PROLACTIN. R.J. Orts. Dept. of Physiological Sciences, Oklahoma State University, Stillwater, OK. 74074

A partially purified extract of bovine pineal glands was examined for its antigonadotropic properties. Bovine pineal glands were defatted in acetone, extracted with 2N, glacial and 1N acetic acid and partially purified on Sephadex G-25 to remove protein and melatonin. The eluate was monitored at 254 and 206 nm and the fractions collected according to the elution profile. Each of the five fractions collected was tested for its ability to inhibit compensatory ovarian hypertrophy (COH) by administering 2.5 g eq (equivalent to starting wet weight of tissue) at the time of unilateral ovariectomy. Animals were necropsied 5 days later and three fractions, F3, F4 and F5 were found to be inhibitory to COH. In order to determine the effects on luteinizing hormone (LH) and prolactin, each of the active fractions was administered to mature male rats at dose levels of either 5 or 10 g eq daily for five days. Animals were bled by cardiac puncture on day 6 and the serum concentrations of LH and prolactin measured by radioimmunoassay. The concentration of serum LH was reduced by each fraction but only F4 reduced this significantly at either dose level. Either dose of F3 or F4 and the lower dose of F5 reduced the serum concentration of prolactin while the higher dose of F5 caused a significant increase. It is concluded that extracts of bovine pineal glands free of melatonin possess antigonadotropic properties. Further, the compounds responsible for this are of small molecular weight, possibly peptides, and inhibit LH and prolactin release or in the case of one, stimulate prolactin release, depending on the dosage. (Supported by subcontract PARFR-67 (USAID) and NIH Grant HD-08745)

MAXIMAL POWER OUTPUT OF BREATHING. A. B. Otis, Dept. of Physiology, University of Florida, College of Medicine, Gainesville, FL 32610.

Breathing efforts with either no external resistance or with infinite resistance yield no external work. Breathing through finite resistances results in external work. The value of the resistance with which maximal external power can be obtained depends on the pressure-flow (force-velocity) characteristics of the breathing system. If one makes an inspiratory effort against a closed shutter and the latter is abruptly opened, flow immediately rises to a peak value and pressure at the mouth decreases in magnitude. The amounts of change in pressure and flow depend on the value of the external resistance through which inspiration occurs. Fenn and Agostoni (J. Appl. Physiol. 15, 349, 1960) found a linear relationship with negative slope between pressure and flow when maximal inspiratory efforts were made through resistances of various magnitudes. Submaximal constant inspiratory efforts appear to give a similar relationship, displaced, of course toward the origin. Such relationships are described by: $P = Po - K\dot{V}$ where P represents pressure associated with peak flow, $\dot{V}$, through a particular resistance, and Po is the initial pressure with infinite resistance. With such a linear relationship, maximal external power output occurs with an external resistance such that $P = Po/2$. If one can assume that the breathing system behaves at the source as a constant pressure generator during the brief periods of measurements, the value of this external resistance is equal to the internal impedance of the breathing system.

EFFECTS OF MODERATE TRAINING ON GLUCOSE METABOLISM, LIPOLYSIS AND HORMONAL RESPONSES IN ISOLATED ADIPOCYTES. J.L. Owens*, E.O. Fuller*, D.O. Nutter and M. DiGirolamo. Depts. of Medicine and Physiology, Emory University School of Medicine, Atlanta, Ga. 30303.

We have compared adipose tissue cellularity and functions [glucose metabolism, lipolysis, intracellular free fatty acids (IFFA), responses to epinephrine (E) and insulin (I)] in a group of sedentary (S) rats to another group (T) subjected to a moderate training program resulting in minimal consequences in body weight and composition. Male Long Evans rats, weighing 300g, were trained to run on a treadmill. Following progressive adaptation to the program for 4 weeks, they ran daily for 8 weeks at 22 m/min on an 8^{o} grade for 45 min. Both T and S groups were fed ad libitum and food consumption was recorded. T rats were found to have similar body weight but 12% smaller epididymal fat pads than S.Fat cell volume but not cell number accounted for this difference. ^{14}C-glucose (UL) metabolism to CO_2 + Triglycerides by isolated adipocytes in KRB-albumin medium at 6 mM glucose was significantly less in T rats than S (2.74 ± .2 vs 3.41 ± .22 μM/10^{7} fat cells/hr, $p < .02$);I (1mU/ml) stimulated glucose metabolism to equal levels, E (1 μg/ml) produced a lesser ($p < .001$) stimulation in the T rats. T rats showed significantly lower ($p < .05$) basal glycerol release but greater ($p < .05$) response to E than S. IFFA levels were significantly higher in T rats than in S ($p < .05$), and this difference persisted with addition of I or E. In conclusion, even though moderate training did not markedly affect body weight and composition,it nevertheless produced significant alterations in adipocyte metabolic functions and hormonal responsiveness. These alterations may reflect adaptive changes in substrate availability and exchanges in trained animals.

TERNARY DIFFUSION OF WATER VAPOR IN O_2-INERT GAS MIXTURES. C. V. Paganelli, H. Rahn, and H.-K. Chang. Depts. of Physiology and Civil Engineering, State Univ. of N.Y. at Buffalo, Buffalo, N.Y. 14214.

Theoretical studies of diffusion in the gas phase (*Respir. Physiol.* 23: 109, 1975) predict that ternary gas mixtures should show composition-dependent deviation from binary diffusion behavior. To provide data on this point we measured diffusion of water vapor in ternary gas mixtures containing O_2 and either He, N_2, or SF_6. Our experimental system, which involves measurement of water vapor loss through eggshells, has been described (*Respir. Physiol.* 25: 247, 1975). Water vapor diffusivity was relatively independent of composition in O_2-N_2 mixtures and was close to the binary diffusivities seen in either O_2 or N_2. In contrast its diffusion in O_2-He mixtures showed a strong composition-dependence, as shown in the table below, and deviated considerably from binary diffusivities. For example, water vapor diffuses two times faster in 80:20 He-O_2 than in O_2 alone, whereas binary theory would predict a 4-fold increase in He as compared with O_2. The ternary system containing SF_6 showed a smaller deviation from binary theory. Our results in the three ternary systems can be explained quantitatively on the basis of multicomponent diffusion theory.

% He in He-O_2:	0	20	40	60	80	100
Relative D_{H_2O}:	1	1.2	1.3	1.6	1.9	2.7

(Supported in part by NIH HL 14414-05.)

AFFERENT SYMPATHETIC NERVE FIBERS WITH RECEPTOR ENDINGS WITHIN HIGH AND LOW PRESSURE AREAS OF THE CIRCULATION. M. Pagani*, F. Lombardi*, and A. Malliani*, (SPON: E. Braunwald), Inst. Cardiovascular Research, University of Milan, CNR, Milan, 20122, Italy

Spinal sympathetic cardiovascular reflexes have been elicited by hemodynamic stimuli acting on both the high and low pressure areas of the circulation. Accordingly, we investigated the electrophysiological properties of sympathetic afferent nerve fibers with sensory endings in the aorta (high pressure) and in pulmonary vein-atrial junctions (low pressure) which are likely to participate in mediating spinal sympathetic cardiovascular reflexes. In cats anesthetized with pentobarbital 35 mg/kg and artificially ventilated, we recorded the activity of 35 single sympathetic afferent fibers with aortic endings (T3-T6); 29 were myelinated and 6 non myelinated. Their spontaneous discharge was characterized by a single action potential in phase with the pressure pulse and was increased secondary to elevation of arterial pressure. Post-mortem studies showed rapid adaptation to sustained aortic stretch. Post-mortem probing indicated that only 11 of 35 fibers had more than one receptive field. We also recorded 19 sympathetic afferent units with single receptor endings, which were localized by post-mortem probing to one pulmonary vein-atrial junction. They discharged spontaneously in phase with atrial systole. Their activity was increased secondary to elevation of the left atrial pressure as occurs with i.v. infusion of blood or saline. These sympathetic afferent fibers may play a role in mediating the circulatory reflex responses induced by hemodynamic stimuli acting on high pressure and/or low pressure areas of the circulation.

WATER PERMEABILITY MEASUREMENTS OF PLANT CELL MEMBRANES AT DIFFERENT TURGOR PRESSURES.

J. P. Palta* and E. J. Stadelmann* (Spon G. E. Duke). Department of Horticultural Science & Landscape Architecture, University of Minnesota, St. Paul, MN 55108

Efflux of tritiated water from Allium cepa epidermis cell membranes was measured at various turgor pressures. A 1.4 cm diameter epidermis disc was soaked in tritiated water (500 μcurie/ml) for about 1 hour. The disc was then mounted in the chamber, where it was held flat and washed with water, containing no radioactivity, at a constant flow rate. Water permeability was calculated after separating different exponentials from the efflux curve. Turgor pressure of the cell could be regulated by soaking the disc in mannitol solutions containing tritiated water and washing it in the chamber with same concentration mannitol solution containing no radioactivity. Water permeability values were found to change less than 8% when the turgor pressure was decreased from 8 atmospheres (full turgor) to zero. Turgor pressure had no significant effect on the water permeability of onion epidermal cells. Our results are contradictory to the findings of Zimmerman and Steudle (1974, J. Memb. Biol. 16:331-352) but are similar to the findings of Tazawa and Kamiya (1966, Aust. J. Biol. Sci. 19:399-419).

MECHANISM OF LITHIUM TRANSPORT IN RED BLOOD CELLS. G.N.Pandey*, J.I.Javaid*, J.M.Davis*, D.C. Tosteson. Dept. of Psych., Pharm. & Physiol Univ. of Chicago & Ill. State Psychiatric Inst., Chicago, Illinois

Lithium salts are useful in the treatment of manic states and in the treatment of a subgroup of depressed patients. It has been reported that the ratio of the Li^+ concentration in red blood cells (RBC) to the Li^+ concentration in plasma is higher in patients who respond to Li^+ than in non-responders. We have recently reported the presence in human RBC membranes of a Na^+-Li^+ counterflow system which is insensitive to ouabain but promotes net uphill transport of lithium driven by an oppositely directed electrochemical potential gradient for sodium ions. We now report three components of Li^+ influx. Washed cells were incubated in a buffer containing 40mM LiCl, 100mM NaCl, 5mM glucose and 10mM glycyl glycine, pH 7.4 at 37°C and Li^+ in RBC determined samples taken from time to time. Li^+ influx is inhibited additively by both ouabain and phloretin. Ouabain-sensitive Li^+ influx is inhibited completely by external K^+ and partially by external Na^+ . Phloretin-sensitive Li^+ influx is inhibited by external Na^+ but not by external K^+. Phloretin but not ouabain inhibited the Li^+-Na^+ counterflow system. These data clearly indicate three different pathways for Li^+ influx. These pathways may be mediated by three different membrane molecules but also may involve different parts and/or conformations of the same membrane molecules. The ouabain-sensitive pathway for Li^+ influx is probably the same as that used by K^+ in the normal operation of the Na^+-K^+ pump. Lithium distribution between human red cells and plasma in vivo seems to depend mainly on the quantitative balance between phloretin-sensitive Li^+-Na^+ counterflow and phloretin-insensitive, ouabain-sensitive Li^+ transport. It is now important to determine which of these moieties of Li^+ transport is abnormal in patients with affective disorders.

AIRWAY SENSITIVITY TO HISTAMINE IN ASCARIS ALLERGIC RHESUS MONKEYS. P.D. Pare*, M.-C. Michoud* and J.C. Hogg. (SPON: R. Martin) Depts. of Medicine and Pathology, McGill University, Montreal, Canada H3A 2B4

Rhesus monkeys with a natural sensitivity to ascaris suum antigen (AA) have been advocated as an animal model of human asthma. Since one of the characteristics of human asthmatics is a lowered threshold for bronchial reactivity to non specific stimuli such as histamine, we measured the sensitivity to inhaled histamine in 8 anesthetized monkeys with varying bronchial reactivity to AA. The animals were initially graded according to AA sensitivity by measuring pulmonary resistance (R_L), breathing frequency and plethysmographically-determined subdivisions of lung volume after inhalation of this antigen. Four animals showed consistent responses to a 100 g/ml AA, two responded only to 350 g/ml and two showed no response. The same parameters were measured after 2-minute inhalations of aerosol containing serial 2 fold dilutions of histamine diphosphate (0.016, 0.032....8 mg/ml). The animals demonstrated reproducible thresholds to histamine defined as the dose producing a 50% increase in R_L and the two most ascaris responsive monkeys were also most histamine sensitive. However, when the animals were ranked according to histamine and AA sensitivity and compared by Spearman rank correlation no significant relationship could be demonstrated. Total lung capacity (TLC) and functional residual capacity did not change but residual volume increased 53 $\pm$ 24% at the highest histamine dose. This "gas trapping" was largely reversed by one inflation to TLC and was not more pronounced in AA sensitive monkeys. We conclude that AA allergic monkeys do not show the degree of airway hyper-irritability demonstrated in human asthmatics.

ESTIMATION OF PULMONARY INTERSTITIAL FLUID PRESSURES. J.C. Parker*, A.C. Guyton and A.E. Taylor. (Spon. J.W. Crowell) Dept. Physiology & Biophysics, University Medical Center, Jackson MS 39216.

Equilibration pressures in small fluid filled segments of lung and isolated fluid filled lobes were used to estimate pulmonary interstitial fluid pressure (ISFP) in closed chest dogs. Right upper lobes were chronically cannulated, filled with saline and allowed to equilibrate over a 2 week period. In other dogs, acutely respired on pure O_2 for 2 min, plasma filled Swan-Ganz balloon catheters were inserted down the trachea and wedged in small airways near the periphery of the lung. A fluid filled lung segment of 2-3 cm^3 was obtained in this way. After flushing out residual gas with plasma or other fluid the pressure was set at zero and allowed to equilibrate. Prominent inspiratory excursions of up to -20 mm Hg were noted. Equilibration bronchial wedge pressure (BWP) averaged -6 mm Hg (N=15) after 40 min with plasma filled catheters, and -15 mm Hg (N=16) for Tyrode's filled catheters. A pressure gradient between superior and inferior portions of lung was noted approximately corresponding to the hydrostatic gradient. Three chronic lobe preparations averaged -12 mm Hg after 2 weeks. In 6 experiments edema was caused by a previously implanted aortic snare, and saline infusion. BWP increased from -5.8 $\pm$ 1.0 to +1.8 $\pm$ 1.6 mm Hg during infusion. Final wet/dry lung weight was 7.16 $\pm$ .26 compared to a control ratio of 4.6. The contribution of pulmonary ISFP to BWP in plasma filled catheters remains uncertain, but transient changes closely follow those predicted for ISFP. The pressures measured in isolated lobes may better represent ISFP due to the longer equilibration time for fluid constituents. Supported by NIH grant HL 11678.

Histochemistry of Canine Myometrium and Its Vasculature. R.E. Parker*, D.N. Granger, B.H. Cook*, H.J. Granger, and A.E. Taylor (Spon. T.G. Coleman). Dept. Physiology, Univ. Miss. Med. Cntr., Jackson MS 39216.

The metabolism of myometrial smooth muscle of various species has been extensively studied by both biochemical and histochemical techniques. To our knowledge, no published data exists which deals with the metabolism of myometrial vascular smooth muscle. The purpose of this study was to determine whether differences in metabolic profiles exist between the two smooth muscle types in the canine myometrium. Histochemical techniques were utilized to demonstrate various substrates and representative rate-limiting enzymes of the major metabolic pathways. Lactate dehydrogenase activity was used as an indicator of anaerobic glycolysis, while isocitrate and succinate dehydrogenases were used as indicators of the Krebs TCA cycle. The hexose monophosphate shunt and respiratory chain were represented by glucose-6-phosphate dehydrogenase and cytochrome oxidase activities, respectively. β-hydroxybutyrate dehydrogenase and lipase were used as indicators of lipid metabolism. The substrates studied were glycogen, free fatty acids, cholesterol, and neutral fat. The results of this study indicate that, in the non-gravid state, while the myometrial smooth muscle exhibits a high potential for anaerobic glycolysis as indicated by the strong lactate dehydrogenase activity, there is a virtual absence of histochemically demonstrable lactate dehydrogenase in the vascular smooth muscle. Further metabolic differentiation was observed in the gravid and postpartum states. (Supported by NHLI grant HL 15680)

STUDIES ON MEMBRANE STABILIZING EFFECTS OF SUBSTITUTED QUINAZOLONES (SQL). S.S. Parmar,* S.J. Brumleve, R. Kumar* and B. Ali*Dept. Physiology & Pharmacology, University of North Dakota Medical School, Grand Forks, N.D. 58202 and Dept. Pharmacology & Therapeutics, King George's Medical College, Lucknow 226003, India.

Nonsteroidal antiinflammatory agents stabilize and thus protect erythrocyte membranes during inflammation. SQL [2-methyl-3(3-cyclohexylaminopropyl)-4-quinazolones] possessing antiinflammatory activity (100 mg/kg,ip) against carrageenin-induced edema (29-44%) and formaldehyde-induced arthritis (22-81%) were evaluated for in vitro antihemolytic activity. SQL protected heat-induced and hypoosmotic hemolysis. ED_{50} values ranged from 0.17-1.58 mM, 0.16->2 mM and 0.07-0.18 mM for protection of heat-induced hemolysis of rat, dog and human erythrocytes respectively. Similar ED_{50} values were 0.11-0.88 mM and 0.12-0.69 mM for protection of hypoosmotic hemolysis of rat and dog erythrocytes respectively. The degree of protection was concentration dependent, reversible and biphasic in nature. Reduction in antihemolytic activity in the presence of BSA indicated possible preferential binding affinity of SQL for albumin. SQL also stimulated heat-induced denaturation of BSA where a parallelism exists with their antihemolytic activity. These studies have indicated that antihemolytic activity possibly accounts for membrane stabilizing property and some correlation exists between antiinflammatory and antihemolytic activities of SQL. (Supported in part by USPHS NIH Grant 5-T01-HL005939-03 and NIDA Grant 1-R01-DA00996-01 and the State CSIR (Uttar Pradesh), Lucknow, India.)

ASZ(DCPB)

INFLUENCE OF CIRCULATION ON OSMOTIC WATER UPTAKE BY RANA PIPIENS. R.H. Parsons and T.M. Mahany*, Dept. Biology, Rensselaer Polytechnic Institute, Troy, N.Y. 12181

The effect of circulatory alterations on THO water fluxes across leg skin was assessed. Sciatic artery ligature reduced THO clearance by 2.60±0.9(5) $ml \cdot hr^{-1}$, while producing a visible decrease in foot web circulation. Severing the sciatic nerve increased THO clearance by 2.7±0.5(10), while increasing foot web circulation. This is interpreted as an indication that THO exchange across frog skin is circulation limited. Frogs showed a diving bradycardia in a bath mixed with air. This was reduced in an oxygen mixed bath. Likewise, THO clearance decreased more upon submergence in air mixed medium (0.039±0.009(16) $ml \cdot hr^{-1} \cdot cm^{-2}$) than in an oxygen mixed medium (0.015±0.006(16) $ml \cdot hr^{-1} \cdot cm^{-2}$). Similarly osmotic water uptake declined more on submergence into an air mixed medium (0.023±0.05(16) $g \cdot hr^{-1} \cdot 100cm^{-2} \cdot 200mOsm^{-1}$) than in an oxygen mixed medium (0.10±0.04(16) $g \cdot hr^{-1} \cdot 100cm^{-2} \cdot 200mOsm^{-1}$). The results are interpreted as indicating that osmotic water exchange is circulation limited.
(Supported by grant GB-40816 from NSF.)

BRAINSTEM AND HYPOTHALAMIC PROJECTIONS TO HIPPOCAMPUS IN THE RAT: ANTEROGRADE DEGENERATION AND HORSERADISH PEROXIDASE STUDIES. Daniel A. Pasquier* and Fernando Reinoso-Suarez*(SPON: P.J.Morgane). Worcester Foundation for Experimental Biology, Shrewsbury, Mass 01545 and Department of Morphology, UAM, Madrid 34 (SPAIN).

Anterograde degeneration and retrograde transport of horseradish peroxidase(HRP) have been used to demonstrate direct connections from locus coeruleus (LC), raphe nuclei (RN), supramammillary (SUP) and submammillothalamic (SUB) hypothalamic nuclei to hippocampus.

The LC projects by way of the cingulum and superior fornix to dorsal hippocampus, mainly to its dorsoposterior region. Terminal degeneration was found primarily in the stratum lacunosum moleculare in CA1-CA2 of this hippocampal region. The RN project through cingulum, superior fornix and fimbria to dorsal and ventroposterior hippocampus. Terminal degeneration was observed in the stratum lacunosum moleculare and in the stratum radiatum of areas CA3-CA4, and in the stratum polymorphe of the dentate gyrus.

The hypothalamic nuclei project along the same paths as those of the raphe. The SUP projects primarily to dorsoposterior hippocampus and, to a lesser degree, to dorsoanterior and ventroposterior hippocampus. The SUB nuclei send projections to dorsoposterior hippocampus. The projections from LC and the hypothalamic nuclei are primarily ipsilateral.

Furthermore, the LC and RN project to the SUB and SUP hypothalamic nuclei, diagonal band, and septal nuclei, which, in turn, project to hippocampus. Therefore, the latter three structures serve as relay stations for ascending and descending brainstem-hippocampal connections.
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EFFECTS OF PURIFIED PARATHYROID HORMONE (PTH) ON PHOSPHATE (P) REABSORPTION ALONG THE NEPHRON IN ACUTELY THYROPARATHYROIDECTOMIZED (TPTX) RATS. E. Pastoriza-Muñoz*, C. Lechène, W. E. Lassiter and R. E. Colindres*. Dept. of Med., Univ. of N. C., Chapel Hill, NC 27514, and Dept. of Physiol. Harvard Medical School, Boston, MA 02115.

The nephron segments involved in P reabsorption were studied in two groups of TPTX rats with volume expansion. In group I, after a control period (C), PTH (2 U/hr) was given. Group II was studied during constant volume expansion without PTH. In group I (n=13) the fractional excretion of P increased from 6.8±1% S.E.M. to 28.6±3%* after PTH. SNGFR, filtered P load and tubular fluid:plasma ($\overline{TF/P}$) inulin ratios at late proximal (LP), early distal (ED) and late distal (LD) sites were unchanged after PTH. Other micropuncture results were as follows:

	LP		ED		LD	
	TF/UF P	F.D.	TF/UF P	F.D.	TF/UF P	F.D.
C	0.61±0.05	36±3%	0.73±0.1	24±3%	0.93±0.2	13±3%
PTH	0.78±0.04*	48±2%*	1.29±0.1*	42±3%*	2.19±0.2*	36±3%*

UF=Ultrafiltrable plasma P. F.D.=Fractional delivery of filtered P to each nephron site. *$p<0.01$. n=Number of animals.

After PTH absolute P reabsorption ($pMol \cdot min^{-1}$) decreased from 71±5 to 54±5* in the proximal tubule, from 13±2 to 5±2* in the loop of Henle and from 13±2 to 6±2* in the distal convolution. In group II (no PTH, n=7) P reabsorption was unchanged after 3 hrs and was similar to C in group I. We conclude: 1) P reabsorption in superficial nephrons occurs in all segments. 2) PTH inhibits P reabsorption in all segments proximal to the collecting duct (CD). An effect of PTH in CD could not be excluded.

EPOCH AVERAGE OF ELECTROENCEPHALOGRAM IN PHOTIC STIMULATION. S. M. Peacock, Jr. and A. Yanovski*. Div. of Electroencephalography and Clinical Neurophysiology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, Pa. 19129

Utilizing repetitive samples of ? or 4 seconds duration during train or continuous photic stimulation, an epoch electroencephalogram (EEG) average has been obtained. These electrical potentials suggest that at least three systems are activated by flashing light which provide input to the cerebral cortex. These systems overlap in distribution and are differentially sensitive to changes in stimulus parameters or levels of awareness on the part of the experimental subject. Two systems are suppressed during sleep while the primary radiation system is not. Of the two, one is frequency dependent, the other is not, responding in the alpha range to all flash frequencies.

EFFECT OF INGESTA COMPOSITION ON IN VIVO ABSORPTION OF A PESTICIDAL CARBAMATE. Jerome C. Pekas and Jane L. Giles*, Metabolism and Radiation Research Laboratory, ARS, USDA, Fargo, ND 58102

The lipophilic insecticide, carbaryl (naphthyl-[^{14}C]N-methyl carbamate), was premixed into gastric contents and administered to the stomach of a fasted rat. The ^{14}C in portal blood gradually increased to a peak concentration after 10 hr. The ^{14}C was associated mainly with the intact carbamate the first 20-30 min but with polar metabolites thereafter. The same quantity of carbaryl-[^{14}C] in a small volume of alcoholic solution was administered to the empty stomach of the same rat 20 hr later. The ^{14}C in the portal blood reached a peak concentration within the first minute and was associated mainly with the intact carbamate the first 5-10 min. The ^{14}C concentrations of portal blood was 15 times greater 1 min after the alcohol than after the ingesta dose. The effect of various media on absorption of carbaryl-[^{14}C] (10^{-5}M) was investigated under more controlled conditions by 60-min perfusions of isolated loops of cranial small intestine of etherized rats. The disappearance of ^{14}C from the perfusates was as follows: isotonic saline, 38%; Ringer (pH 6.5), 37%; milk (4% fat), 14%; triolein, 5%; and simulated meal, 3%. The evidence supports the following conclusions: carbaryl appears in portal blood rapidly and intact after gastric doses in alcohol; carbaryl in gastric contents was extensively metabolized and the ^{14}C label slowly appeared in portal blood. Dilution, surface exposure and lipid retention appear to be important parameters. The slower absorption from the simulated meal than from triolein was probably because of distension of the loop, poor volume exposure to the epithelial surface, poor mixing and reduced diffusion with the semiliquid meal.

EFFECTS OF HYPOCAPNIA ON THE PCO_2 GRADIENT BETWEEN CISTERNAL CSF AND CEREBRAL CAPILLARY BLOOD. D.A. Pelligrino* and J.A. Dempsey (SPON: W.E. Stone). Dept. of Preventive Medicine, University of Wisconsin, Madison, WI 53706.

Arterial, cerebral venous and cisternal CSF samples were obtained in anesthetized, paralyzed dogs during 2-7 hours of normal acid-base conditions, metabolic alkalosis and hypocapnia at varying levels of plasma [HCO_3^-] and [H+]. In order to obtain a representative venous effluent, cerebral venous samples were taken from the venous confluence of sinuses after careful elimination of diploic and emissary contamination. The $P(CSF\text{-}\overline{cap})CO_2$ was predictable by the Krogh diffusion model (1-2 mmHg) during < 2 hours of normocapnic control conditions. Normocapnic metabolic alkalosis had no effect on $P(CSF\text{-}\overline{cap})CO_2$. However, under all hypocapnic conditions $P(CSF\text{-}\overline{cap})CO_2$ increased significantly $\geq$ 3-fold [$P(CSF\text{-}\overline{cap})CO_2$ = 4.0-6.4 mmHg]. This effect of hypocapnia was readily reversed, as $P(CSF\text{-}\overline{cap})CO_2$ decreased to control values upon return from hypocapnia to normocapnia. $P(CSF\text{-}\overline{cap})CO_2$ also increased significantly ($\leq$ 2-fold) when normal acid-base conditions were prolonged > 3 hours. The widened $P(CSF\text{-}\overline{cap})CO_2$ was clearly independent of wide variations in capillary or CSF [H+]; but was closely associated with a widened $C(a\text{-}v)O_2$ [i.e. $C(a\text{-}v)O_2$ (ml/100 ml) = 5.4-5.8 (2 hours control); 7.2 (7 hours control) and 10.3 (7 hours hypocapnia)]. The significant increases in $P(CSF\text{-}\overline{cap})CO_2$ during conditions of widened $C(a\text{-}v)O_2$ (and presumably decreased CBF) are probably explained by an increased cerebral intercapillary distance. (Supported by NIH Grants 15469 and 00149.)

NASAL PRESSURE-FLOW RELATIONSHIPS IN MAN. L.D. Pengelly, D.W. Cockcroft* D.W. McCormack‡ S.M. Tarlo* and F.E. Hargreave* Department of Medicine, McMaster University and St. Joseph's Hospital, Hamilton, Ontario, Can.

The relationship between transnasal pressure and flow is markedly curvilinear, even during tidal breathing in man and there is poor agreement between different methods attempting to define nasal resistance with a single number. We made use of Rohrer's theoretical equation ($P = K_1\dot{V} + K_2\dot{V}^2$) and calculated values for K_1 and K_2 from 474 nasal inspiratory P/$\dot{V}$ curves obtained from 34 human subjects by a standard method of posterior rhinometry. Nasal airway inspiratory resistance at 0.4 l/sec ($NAIR_{0.4}$) was also calculated. Rohrer's equation was found by regression analysis to fit each curve well ($0.86<r<1$, av. = 0.983) and in repeat measurements on the same subjects, the average coefficients of variation were: K_1, $\pm$ 22.0%, K_2, $\pm$ 19.6%, $NAIR_{0.4}$ $\pm$ 9.3%. There was a strong correlation between $NAIR_{0.4}$ and K_2: $NAIR_{0.4} = 0.91K_2 + 0.39$ ($R = 0.97$) but less so between $NAIR_{0.4}$ and K_1 ($R = 0.56$). Nasal congestion induced in 7 normal subjects with histamine resulted in larger changes in K_2 and $NAIR_{0.4}$ than in K_1. Patients given an intranasal corticosteroid aerosol, (beclomethasone dipropionate) in a double-blind crossover trial showed a symptomatic improvement in nasal congestion ($p<0.01$) and significant decreases in K_2 ($p<0.02$) and $NAIR_{0.4}$ ($p<0.05$), but no change in K_1 ($p>0.2$). We conclude that Rohrer's equation is a valid description of the nasal P/$\dot{V}$ curve, that K_2 correlates better with nasal obstruction than does K_1 and that $NAIR_{0.4}$ provides a reproducible and simpler estimate of K_2.

(Supported by the Medical Research Council of Canada.)

PULMONARY TISSUE PERFUSION IN DOGS DURING ALVEOLAR HYPOXIA. B.T. Peterson*, M.F. Petrini*, V. Lam*, B.F. Schreiner, R.W. Hyde, Depts. of Biophysics and Medicine, Univ. of Rochester, Rochester, N.Y. 14642

In order to investigate mechanisms that cause hypoxic pulmonary edema we measured airway exchangeable tissue volume (V_t), pulmonary extravascular water volume (PEWV), cardiac output (C.O.), and post mortem lung wet weight to dry weight ratios (W/D) in 3 dogs. The dogs were anesthetized, paralyzed, and ventilated to maintain constant arterial CO_2 tensions and pH throughout the experiment. V_t was measured by rebreathing with a mixture of dimethyl ether and SF_6. PEWV was measured by the Chinard double indicator dilution technique. Pulmonary artery pressure (PA) was recorded and inspired O_2 was decreased to the lowest concentration possible that avoided elevation of "wedge" pressure. The results ($\pm$ SD) are shown on the following table:

	Arterial O_2 (mm Hg)	C.O. (l/min)	PA (mm Hg)	V_t (ml/Kg body weight)	PEWV (ml/Kg body weight)
CONTROL	75 $\pm$ 9	4.1 $\pm$ 0.6	15 $\pm$ 2	12 $\pm$ 2	2.9 $\pm$ 0.5
HYPOXIA	23 $\pm$ 5**	4.7 $\pm$ 0.2	28 $\pm$ 5**	12 $\pm$ 2	1.9 $\pm$ 0.6**

** $p<0.05$ when compared to control values.

The W/D of 4.3 $\pm$ 0.2 was compared to 4.3 $\pm$ 0.2 measured in control dogs indicating that hypoxia did not elevate the water content of the lung. These results show that 1-3 hours of severe hypoxia does not elevate V_t in dogs. Since the volume of tissue perfused by the pulmonary circulation decreased despite an increase in C.O. hypoxia caused an increase in perfusion to those capillaries that remained open. These data support the concept that hyperperfusion of contracted vascular beds may be the initial event of hypoxic pulmonary edema.

INFLUENCE OF ASCORBIC AND FOLIC ACIDS ON TYROSINASE ACTIVITY IN THE COCKROACH, LEUCOPHAEA MADERAE. Leon L. Pierre and John Fabianek, Dept. Life Sciences, New York Tech. 888 Seventh Ave. New York, N.Y. 10019.

Tyrosinase activity was followed spectrophotometrically (Beckman DU) with aliquots(10, 20, 30, and 40 mcg.) of ascorbic and folic acids according to the method of Prota 1961(J.N.Y.Ent. Soc,49:59-67).

Comparable activities resulted when each aliquot of the vitamin was used or any combination of the two except the 20 mcg + 40 mcg. combination. Besides, melanin production occurred in time ranging from 35-315 mins.

Activities and time for product formation when 20 mcg.+ 40 mcg. of ascorbic and folic acids were used respectively with materials of the symbionts and fat bodies of normal adult and nymphal insect were 1.461..(30 mins); 1.390.. (25 mins); and 1.460..(35 mins) respectively. Respective corresponding activities for aposymbiotic insects were 1.435..(32 mins) and 1.444...(55 mins). The reverse combination in amount of the two vitamins showed the following results for symbiont materials and materials of the normal adult and nymphal insect respectively: 1.452..(32 mins); 1.454..(32 mins); and 1.569..(34 mins). Aposymbiotic adults and nymphs showed the following respective results: 1.449..(33 mins) and 1.472..(55 mins).

Since aposymbiotic nymphal materials showed the slow-activity, it would appear that the activity of normal nymphal fat body is boosted by that of symbiont materials.

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MATHEMATICAL SIMULATION OF RESTITUTION OF BLOOD VOLUME FOR FIRST 24 HOURS AFTER HEMORRHAGE. J.C. Pirkle, Jr. and D.S. Gann, Johns Hopkins Univ. School of Medicine, Baltimore, Md. 21205

The restitution of blood volume after hemorrhage has been examined experimentally and by simulation. Experiments on splenectomized dogs show that restoration of plasma volume and protein by 24 hours after hemorrhage average 14±1 ml/kg and 0.9±0.1 g/kg, respectively, for hemorrhages between 10.5-25.5 ml/kg. Plasma osmolality increased for 4 hr(5.4±1.3 mOsm/kg,$p<0.05$) after 10.5 ml/kg hemorrhage and for 12 and 24 hr(10.6±2.1 mOsm/kg,$p<0.01$) after 18.0 and 25.5 ml/kg hemorrhage, respectively. We hypothesized that the increase in extracellular osmolality was associated with a shift of fluid from the cells to the interstitium, resulting in an increased interstitial pressure and accelerated lymphatic movement of interstitial protein to the vascular system. To test this hypothesis, a mathematical model of body fluid dynamics was developed that included transcapillary exchange, lymphatic flow, urinary output and insensible water losses. ICF-ECF exchange was expressed in terms of Nernst-Planck equations, aqueous phase electroneutrality, osmotic gradients and active Na^+-transport. Simulation indicated that ICF-ECF shifts approximated rectangular pulses of 6,6 and 14 hr duration and 4.25,6.25 and 3.17 ml/kg-hr magnitude for 10.5, 18.0, and 25.5 ml/kg hemorrhage, respectively. These different shifts of fluid, mediated by differential changes in extracellular osmolality,lead to nearly identical restitution of plasma volume and protein at 24 hours despite the differing magnitude of hemorrhage.

(Supported in part by NIH grant AM 14952).

GRAVITATIONAL EFFECTS ON HEMITHORACIC AND HEMIDIAPHRAGMATIC BEHAVIOR
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The gravitational effects of different body positions on changes in hemithoracic circumference and hemidiaphragmatic excursions were investigated in 9 normal male subjects during quiet breathing. Positions studied were: (a) horizontal: supine, left and right lateral decubitus; (b) 15° head down: supine, left and right lateral decubitus; (c) 15° head up: supine. Hemithoracic circumferential changes were measured at the level of the xiphoid with mercury-in-silastic resistance gauges and hemidiaphragmatic excursions with radiography. End-inspiratory and end-expiratory diaphragmatic positions were captured by means of an electronic unit which received an airflow signal from a WEDGE spirometer, and triggered a Franklin programmer to fire the x-ray at zero airflow and to change the film rapidly. Hemidiaphragmatic excursions were also measured with diagnostic ultrasound (2.25 megaHz cylindrical pulsed transducer, A-mode display) for validation of this non-injurious technique. Comparison of the ultrasound data, corrected for slight geometric distortion, with the radiographic data, indicated that ultrasound is an accurate method for measurement of diaphragmatic excursions.

Insignificant statistical differences existed between right and left hemithoracic circumferential and hemidiaphragmatic tidal excursions in all supine positions. On the other hand, highly significant differences existed between the upper and lower sides in all lateral decubitus positions, with 48% less circumferential movement in the lower hemithorax, contrasted with 38% greater excursions in the lower hemidiaphragm. These differences can be explained by differences between the high and low sides of the body with respect to contact forces on the thorax, intrathoracic pressures, and transdiaphragmatic pressure gradients.

NON-IDENTITY OF UTERINE AND RENAL RENINS IN THE DOG. D. Mark Potter,* Walter J. McDonald,* and James A. Metcalfe. Univ. of Ore. Health Sci. Ctr. and Vet. Adm. Hosp., Portland, OR 97201.

In 1970 Carretero reported the kinetic constant (K_m) of renal renin (RR) to be the same as uterine renin (UR) in the dog, but that an endogenous substrate (S) susceptible to UR but not RR existed. We confirm the latter observation but find different K_ms. Crude renin extract was prepared from dog kidney and myometrium at 50 days' gestation by aqueous extraction and NH_4SO_4 precipitation. A nephrectomized, hysterectomized bitch was the source of S-rich plasma. This plasma was diluted with 0.9%NaCl and 1.25gm% egg lysozyme to yield 200-1800 ng angiotensin-I (A-I)/ml, determined by exhaustive incubation with RR. Plasma and lysozyme incubated without added extract yielded no detectable A-I. 100µl dilute plasma with 3.5mM diisopropylfluorophosphate and 5.2mM EDTA was pre-warmed 4 min. 5µl of either RR or UR was added and incubated under conditions which satisfied initial velocity requirements at lowest S. A-I was measured by radioimmunoassay. Recovery of A-I was 90% at 60 min. in the presence of extract. For both RR and UR at least 4 independent Lineweaver-Burk plots were constructed by computer and K_ms compared by unpaired t-test. For either extract, combined plots of all data yielded K_ms not different from their respective independent means. K_m of UR was 1570±280ng A-I/ml and of RR 720±90 ($F_{10.53}$, $p<.001$). pH dependence of reaction velocities were similar for both extracts; neither resembled "pseudorenin." Specific activity of UR did not change after transient acidification. Plasma exhaustively incubated with RR yielded additional A-I in small concentration when reincubated with UR. It appears that the renin of the gravid uterus of the dog is kinetically different from renal renin. Lack of increased activity after acidification suggests that it is not "big" renin.

ASZ(DCPB)

AN EFFECT OF THE CELL CYCLE PERIOD ON FLAGELLAR REPLACEMENT RATE
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The rate of flagellar replacement($k = \ln c_1 - \ln c_2 / t_2 - t_1$) for the first ninety minutes in the pre-S period (G_1) and the post-S predivision period (G_2) in a synchronous cell cycle of Chlamydomonas was significantly different. The slower rates of flagellar replacement in the post-S predivision period (G_2) as compared with the pre-S period (G_1) occurred throughout the ninety minute period, a time previously thought to have been sufficient enough to utilize the precursor pool microtubulin for one-half flagellar replacement, and a time prior to a direct synthesis of the tubulin protein for continued replacement. The initial and the midpoints were highly significant slower rate intervals during the post-S predivision period (G_2). This evidence suggests that there may not have been a sufficient amount of the precursor for one-half flagellar replacement; and probably during the post-S predivision period (G_2) flagellar replacement comes to be more dependent on a direct synthesis of the tubulin protein, and not so dependent on the precursor pool substance. Since the replacement phenomenon in the synchronous cell cycle at this time comes close to mitosis, and since mitosis depends in part structurally on a system of spindles(three types) the precursor pool substance, microtubulin, might have been redirected and involved in the structural arrangement of the system of spindles or the precursor pool substance might have become involved in what we commonly call molecular turn-over. All in all flagellar replacement, in a synchronous cell cycle of Chlamydomonas(cells) or a non-synchronous cell cycle,showed that a definite different was involved in the rate during the pre and post periods.

IN VITRO ARTERIAL PERFUSION OF THE DOG ADRENAL GLAND: ALTERATIONS IN C-AMP FOLLOWING ACTH AND PROLACTIN ADMINISTRATION.
Timothy P. Powers* and John W. Lloyd and C. Cooper Bell, Jr.*, The Eastern Virginia Medical School, Norfolk, Virginia 23501; The Dept. of Biology, Old Dominion University, Norfolk, Virginia 23508 and The Veterans Administration Hospital, Hampton, Virginia 23667

The dog adrenal gland was arterially perfused in vitro as described by Redmond and Bell (Endocrinology 94:822, 1974). Perfusion was maintained at 30 mm Hg throughout a 90 min. period. No effect on adrenal gland weight or swelling was observed. Initial perfusate flow varied from 0.8-2.3 ml/min. Following a 20 min. control perfusion with Krebs-Ringer Bicarbonate (KRB) buffer containing glucose and aminophylline, the adrenal gland was stimulated over a 1 min. period with 10 U of purified porcine ACTH. The perfusate was collected over 3 min. intervals for 30 min. Prolactin (8 U) then was administered over a 1 min. period and the perfusate was collected for an additional 60 min. The C-AMP concentration of the perfusate was determined by the method of Gilman (Proc Natl. Aca. Sci. 67:305, 1970). A significant increase in the concentration of C-AMP in the perfusate was observed within 10 min. after the administration of ACTH. Peak increases occurred within 20 min. and varied from 336% to 1590% of the baseline value. Prolactin stimulation resulted in a further increase in C-AMP concentration. This second increase was observed within 6 min. after the administration of 8 U of prolactin and reached peak values of 9.9% to 290% of the ACTH stimulated peaks. Prolactin alone did not cause significant changes in C-AMP concentrations from baseline levels. These data suggest that prolactin may enhance the action of ACTH on C-AMP production by the adrenal gland.

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REGULATION OF EXPERIMENTALLY INDUCED EPILEPSY. S.R. Quint and R.N. Johnson, Div. of Biomedical Engineering and Dept. of Neurology, University of Virginia, Charlottesville, Virginia 22901

The cerebellum, ventrolateral thalamus (VL), and sensorimotor cortex (MC) have been implicated in epilepsy and its control. Numerous areas of the mammalian brain, including cerebellum, have been shown to have regulatory effects on epileptic activity. We have recently demonstrated the suppressive action of the paramedian lobule on the thalamocortical motor system of the cat. In the study reported here, computer generated sequential pairs of pulses were delivered to VL in anesthetized cats, varying either pulse internal or amplitude. Evoked responses from sensorimotor cortex, analyzed on-line with a computer, were plotted as an excitability curve (mean response amplitude as a function of pulse internal) or a family of threshold curves (mean response amplitude as a function of stimulus amplitude at various fixed intervals) forming a 3 dimensional response profile. A mirror focus was produced on homotopic motor cortex following the establishment of an active penicillin induced epileptogenic focus in contralateral cortex. Response profiles were generated before and after the induction of the mirror focus and compared to those observed during stimulation of the paramedian lobule of cerebellum. With the development of extensive spiking in the mirror focus, the thresholds, slopes, and saturation levels of the response profiles were frequently shifted from the control values in a qualitatively similar manner to that characteristic of cerebellar stimulation. When the profile alteration occurred, spiking stopped or the frequency diminished. Where the shift failed to occur, generalized seizures were frequently seen. These results graphically demonstrate regulatory action in response to epileptic activity within the mammalian brain and suggest that this regulation may be mediated by the cerebellum.

THE THREE DIMENSIONAL REDOXSTRUCTURE OF THE NORMOXIC AND HYPOXIC RAT BRAIN. B.Quistorff, B.Chance and E.Benshelter. Johnson Foundation, University of Pennsylvania, Philadelphia 19174, USA. Spon.: M.Reivich.

The redox state of the mitochondrial compartment is indicated by the ratio between flavine- and pyridine nucleotide fluorescences (1). Taking advantage of the general fluorescence intensity increase at low temperatures (a 10-15 fold increase at $77^{o}K$ as compared to $310^{o}K$) the FP/PN ratio can be read from single-tissue-volumes of about $10^{-3}mm^{3}$ in a frozen brain sample. The recording technique involves a microfluorometer coupled to the surface of the frozen tissue via an 85u light guide (2,3). The sample is scanned in two dimensions by moving the light guide across the tissue surface in steps of 100 u, giving about 10,000 data points over the cross section of the brain.The brain samples scanned were obtained by guillotine-freezeclamping of the brain(4) of unanaesthetized rats breathing 20% - and 6% oxygen. The hypoxic group was sampled after 10, 30 and 60 seconds of hypoxia. In the normoxic group the redox ratio variation was greater than in any of the hypoxic groups. The average redox ratio increased with time of hypoxia. There was no right-left differences in any of the groups.

(1) Chance et al., Proceedings of the APS Meeting, Anaheim, April 76. In Press.
(2) Chance et al., FEBS Meeting, Abstract, Paris 75.
(3) Quistorff and Chance, Proceedings of the APS Meeting, Anaheim, April 76. In Press.
(4) Quistorff, Anal. Biochem. 68, 75.

Supported by NINDS Grant, 10939.

INHIBITION OF BRAINSTEM NEURONAL ACTIVITY BY ELECTROCHEMICAL STIMULATION (ECS) OF THE DORSAL HIPPOCAMPUS IN THE FREELY MOVING RAT.
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We have recently obtained data showing that application of ECS (iron deposition by anodal direct current through stainless steel electrodes) to the dorsal hippocampus blocks the LH surge and ovulation in the freely moving proestrous rat. The aim of the present work was to study cortical EEG and multiple unit activity (MUA) in the medial preoptic area (MPO) and the mesencephalic reticular formation (MRF) following bilateral ECS of the dorsal hippocampus (HPC) on the afternoon of proestrus. Continuous recording was begun on the morning of proestrus, and at 12:00 hr ECS was applied to the HPC (50 μA for 2 min on each side) of chronically implanted freely moving rats showing regular 4 day vaginal cycles. As a result of this treatment at approximately 1 hr after ECS a decrease of MUA in the MPO and MRF was observed when compared with prestimulation levels. A further and significant decrease of MUA was observed by 5 to 7 hrs after ECS in both structures. Presumably due to the irritative effect of iron deposition, episodic focal spiking activity was observed starting at 60 to 80 min after stimulation. The spiking episodes lasted for several hours, but never manifested in generalized seizures and they did not necessarily interfere with the ongoing neuronal activity in the MRF or MPO. No alterations in MUA or EEG were observed following application of anodal DC to the HPC through platinum electrodes, using the same stimulation parameters. These observations confirm previous findings that the hippocampus exerts an inhibitory influence on neuronal and endocrine events and lead us to conclude that the lack of tonic activation of MRF and MPO on hypothalamic mechanisms may be related to the blockade of ovulation.

ARGININE- AND GASTRIC INHIBITORY POLYPEPTIDE (GIP)-INDUCED INSULIN RELEASE: EVIDENCE FOR A COMMON MECHANISM IN MAN.
G.S. Raizes*, D.K. Andersen*, D.Elahi, J.D. Tobin* and R. Andres. Gerontology Research Center, National Institute on Aging, NIH, Baltimore, MD 21224

It is well known that arginine (ARG) potentiates glucose-stimulated insulin release without being a potent insulin secretagogue during euglycemia. Recently, GIP has also been shown to induce insulin release, again, however, only during hyperglycemia. To study a possible common mechanism of ARG- and GIP-induced insulin release, 6 normal men were studied using the glucose clamp technique (J.Clin.Invest.53:1481,1974). A square wave of hyperglycemia 125 mg/dl above basal was created for 2 hr. At 60 min, one of the following stimuli was administered while blood glucose was held stable: (a) 40 g/m^2 oral glucose (OG), followed in 1-2 mos by (b) 15 g/m^2 IV ARG in a primed continuous infusion lasting 60 min, and (c) both OG and 15 g/m^2 IV ARG; studies (b) and (c) were done 2 wks apart in random order. Results: (1) Plasma immunoreactive GIP (IR-GIP) remained unchanged after IV glucose alone, but rose to 5 times basal levels after OG. There was no effect of IV ARG on IR-GIP. (2) Plasma immunoreactive insulin (IRI) rose after OG to 4 times the elevated levels produced by hyperglycemia alone. (3) IV ARG resulted in an IRI response of 7 times that seen after hyperglycemia alone, while no further augmentation of this IRI response was seen when OG was simultaneously administered. We conclude that while this dose of IV ARG and endogenous GIP individually result in IRI release during hyperglycemia, they do not act additively. Since, in other studies with other stimuli to IRI release much higher levels of IRI can be achieved than we have seen with IV ARG alone, GIP alone, or GIP and IV ARG in combination, the absence of an additive affect of GIP and ARG in this study suggests a common mechanism of action.

THE EFFECT ON METABOLIC ASSAYS OF TEMPORAL DELAY IN FREEZING SAMPLES OF CANINE MYOCARDIAL TISSUE IN LIQUID NITROGEN. C.A. Ramey* and J.W. Holsinger, Jr., (SPON: R.B. Tobin). V.A. Hospital, Newington, CT. 06111

In the investigation of tissue metabolites, the use of liquid gases for tissue freezing is a frequently used technique. In studying the transmural metabolism of the posterolateral wall of the left ventricle, we have designed a study to determine the effect on metabolic assays of temporal delay (sample time) in immersing samples of dog myocardium into liquid nitrogen to test the hypothesis that sampling time may affect metabolic assay results. Tissue samples were obtained using a stainless steel biopsy device attached to a variable speed electric drill. Sampling time was determined from the initial moment of biopsy until the sample contacted liquid nitrogen. Frozen transmural tissue samples were divided into subepicardial (S-EPI), midmyocardial (MID) and subendocardial (S-ENDO) layers. Phosphocreatine (PCr), ATP and lactate were utilized as sensitive indicators of hypoxia in the heart. Metabolite levels were determined by standardized assays. Tissue metabolite data over the range of sample times, 1.5 to 19.4 seconds, demonstrated no significant evidence of a linear trend associated with changes in the concentration of PCr, ATP or lactate with delayed sampling time. Correlation coefficients, determined by standardized techniques, are expressed as S-EPI→MID→S-ENDO. PCr(-0.06)→(-0.36)→(-0.29), ATP(-0.05)→(-0.28)→(-0.06) and Lactate(-0.17)→(-0.04)→(+0.14). In summary, delays in immersion of tissue samples into liquid nitrogen of up to 20 seconds appears to have no adverse effect on tissue metabolites sensitive to myocardial hypoxia.

EFFECTS OF GASTRIN, OP-CCK, AND SECRETIN ON OPOSSUM LOWER ESOPHAGEAL SPHINCTER IN VITRO. N. Rana*, J.R. Chowdhury*, M. Praissman*, J.M. Berkowitz, and J.W. Fara. Nassau County Medical Center, East Meadow, N.Y., and State University of New York, Stony Brook, N.Y. 11794.

Sequential circular strips of opossum esophagus and lower esophageal sphincter (LES) were dissected out from adult opossums of either sex that were anesthetized or recently sacrificed. Strips measured 2mm X 1-1.5 cm and were mounted with mucosa intact in a Krebs solution bath to record isometric tension. After 45 min equilibration, length-active tension relationships were obtained by acetylcholine (Ach) stimulation (10^{-5} M). Using the passive stretch tension at which peak tension was developed by Ach, dose-response curves were obtained for human synthetic gastrin I, OP-CCK, and pure natural or synthetic secretin, given alone or in combination at the same time. The three peptides either produced small responses or were ineffective on esophageal strips. On LES, Ach (10^{-5} M) gave the greatest response (4 gm) and all peptides were stimulatory:

	Threshold and Dose Range Studied	Peak Response Dose	Maximum Tension Developed
gastrin	1×10^{-17} - 5×10^{-10} M	1×10^{-12} M	1 gm
OP-CCK	1×10^{-14} - 5×10^{-9} M	5×10^{-12} M	250 mg
secretin	0.05 - 0.75 Units/ ml	0.5 Units/ml	250 mg

Contrary to other literature reports, we found no evidence that secretin or OP-CCK antagonize the effect of gastrin, and furthermore, atropine (3×10^{-6} M) which blocked the response to 10^{-5} M Ach did not alter the peptide dose-response curves. Thus, the peptides act through a non-cholinergic receptor mechanism.

A QUANTITATIVE ANALYSIS OF THE GAS EXCHANGE OF THE MIDDLE EAR CAVITY: PRELIMINARY FINDINGS. A. Ranade* (SPON: S. Takashima), Institute for Environmental Medicine, University of Pennsylvania, Philadelphia, Pa. 19174.

A mathematical model of the parameters governing the gas exchange dynamics of the middle ear cavity with blood and environment was formulated. The model incorporates diffusion, solubility, and perfusion characteristics of both the tympanic membrane and the mucosal layer of the middle ear cavity. It can also simulate the venting function of the eustachian tube. In a cat saturated with air in an air environment, uptake of nitrous oxide after an abrupt change to this breathing gas was simulated by the model for a representative set of geometric parameters. The remaining parameters were chosen so that they were within the most probable range of their values and generated a transient response very close to that reported for the cat by previous investigators. The behavior of the model was then studied by varying each parameter through a wide range. Large variations in the values of tympanic blood supply and/or mean diffusion distance for the mucosal layer cause insignificant changes in the overall response of the model. Experiments were conducted on cats to verify these inferences. They confirmed that inert gas exchange across the mucosal layer of the middle ear cavity is perfusion-limited and that diffusion across the tympanic membrane is not critically affected by its blood supply.

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IMMEDIATE CARDIOVASCULAR EFFECTS OF CORONARY ARTERY OCCLUSION AND EMOTIONAL STRESS IN MONKEY. D.C. Randall & D.M. Hasson* Dept. Physiology & Biophysics, Univ. Kentucky College of Medicine, Lexington, Ky. 40506

Hemodynamic and ECG changes occurring within 1 to 2 hours of coronary occlusion (CO) were studied in 10 unanesthetized rhesus monkeys and 1 baboon. Left ventricular pressure (LVP), d(LVP)/dt, left ventricular end-diastolic pressure (LVEDP), heart rate (HR) and the ECG were measured using chronically implanted devices. A snare was placed loosely around the left anterior descending (LAD) coronary artery (8 monkeys) or marginal branch (MB) of the left circumflex coronary artery (3 monkeys) for eventual CO. The animals were classically conditioned to a one minute tone (CSs) followed by shock. Presentation of CSs evokes an "emotional" response in healthy monkeys with increases in LVP, d(LVP)/dt and HR. One month or more after surgery, the monkeys were placed inside an isolation booth and, 30 minutes later, blood flow through the coronary artery was occluded by pulling the snare. LVEDP became elevated within 1 to 2 minutes after LAD occlusion. Ventricular arrhythmias lasting from 1 to 8 minutes occurred very suddenly. LAD occlusion also induced a semi-sustained increase in LVP, d(LVP)/dt and HR in 7 monkeys which may have resulted from a compensatory, reflexly induced increase in cardiac sympathetic stimulation. Ventricular arrhythmias of varying severity occurred in 6 monkeys about 1 hour after LAD CO, and progressed to fibrillation in 4 monkeys. Each animal responded to CSs with increased LVP, d(LVP)/dt and HR, demonstrating that their hearts possessed an additional reserve, in spite of the CO. However, emotional stress had demonstrable deleterious effects in several animals. MB coronary occlusions, which produced smaller infarctions, had less serious cardiovascular consequences. (Supported by NIH grants HL 17680 and HL 19343.)

EFFECTS OF ANOXIA ON SODIUM EXCHANGE IN MAMMALIAN MYOCARDIUM. Eric E. Rau*, Glenn A. Langer and Kenneth I. Shine. Dept. Physiology Cardiovascular Res. Lab., UCLA, Los Angeles, California 90024.

Effects of anoxia on ^{24}Na movement and ^{51}Cr-EDTA space were studied in the isolated, arterially perfused, interventricular rabbit septum at 42 bpm and 28°C. Septa were perfused at 1.8 ml/min/gm with solution containing (mM): Na 142, K 4, Ca 1.5, Mg 1, H_2PO_4 0.4, HCO_3 12, Cl 117 and equilibrated with 98/2% - O_2/CO_2 or N_2/CO_2 The 25-min ^{51}Cr-EDTA space was 50 ± 1% wet wt, n = 6. Anoxia induced a 9% increase in the ^{51}Cr-EDTA space. The sodium contents attributable to the anoxic-induced increases in the space were calculated. The maximal tissue sodium gains were independently determined by asymptotic ^{24}Na labeling. The mean alterations in tissue ion contents ±SEM (n), were:

Anoxic stress	Calc. Δ↑Na in ^{51}Cr space (mm/Kg dry wt)		Observed max. ^{24}Na gain (mm/Kg dry wt)		Max. ^{42}K loss (mm/Kg dry wt)§	
20 min	40 ± 5	(6)	46 ± 6	(8)	31 ± 2	(8)
60 min	49 ± 11	(4)	54 ± 9	(6)	90 ± 14	(7)

During anoxic periods up to 60 min, these data indicated: 1) the gain of tissue sodium, measured by ^{24}Na labeling, was attributable to the increased space measured by ^{51}Cr-EDTA and 2) cellular sodium content did not increase in proportion to potassium lost from the cells. In view of lack of evidence for stimulation or inhibition of the Na-K pump (§) these results suggest that membrane sodium permeability was not significantly altered by anoxia while permeability to potassium was increased. §Fed. Proc. 35:536, 1976.
(Supported by a Grant from USPHS HL-11351-09)

CEREBRAL HEMODYNAMIC EFFECTS OF CAROTID ARTERY INFUSION OF ACETYLCHOLINE, THEOPHYLLINE, ADENOSINE AND AMP IN THE DOG. Richard M. Raymond*, Todd P. Burns*, and Thomas E. Emerson, Jr. (SPON: W. Doyne Collings), Dept. of Physiol., Mich. State Univ., East Lansing, Mich. 48824

It has been postulated that adenosine and acetylcholine (ACh) may be involved in local and remote control of cerebral blood flow (CBF), respectively. Since adenosine apparently does not cross the blood-brain barrier, the adenosine blocking agent theophylline was given to uncover any cerebral vascular effect of endogenous adenosine. Cerebral venous outflow was measured from the sinus confluens with the lateral sinuses occluded in 11 dogs anesthetized with nembutal and heparinized. Each agent was infused bilaterally into the carotid arteries (vertebral arteries ligated) as follows: ACh (N=8), adenosine (N=11) and AMP (N=11) at 2-100 μg/min and theophylline at 0.002-0.02 μg/min (N=11). ACh had no significant effect on CBF, arterial blood pressure (ABP) or cerebral vascular resistance (CVR); at the highest infusion rate, ABP was decreased in 4 dogs, increased in 3 and unchanged in 1. The increased ABP could be ameliorated by chemically blocking the carotid sinus nerves. CBF and CVR responses were equally varied. Adenosine had no effect at any infusion rate, but AMP significantly increased CBF 3.7% at the highest rate, due to an increase in ABP. Theophylline had absolutely no effect on CBF, CVR or ABP at the lower infusion rates, but at the highest rate increased CBF 15% due to a decrease in CVR with no change in ABP. These data support the belief that the cerebral vasculature is relatively unresponsive to many vasoactive agents when compared to their effects in systemic organs. These data do not suggest a role for adenosine in local control of CBF or for ACh in remote control of CBF.
(Supported by the Mich. Heart Assoc.)

CORRELATION BETWEEN CONTROL RENAL FLOW AND RENAL AUTO-REGULATION. J.J.Rechtien*, R.F.Bond and L.C.Peissner*, Dept. Physiology, Kirksville College of Osteopathic Medicine, Kirksville, MO 63501. (SPON: Guy Bond)

Renal vascular autoregulation was studied in 6 pentobarbitalized dogs before and during drug induced dilation. The preparation included: 1) bilateral ureter cannulation to monitor urine flow; 2) isolation of the left renal artery from which renal flow (RF) was monitored utilizing an electromagnetic flow probe and associated amplifier; 3) central systemic pressure taken from a cannula in a carotid artery, and 4) renal perfusion pressure (RPP) from a cannula in a femoral artery and directed up into the abdominal aorta. Vascular dilation was accomplished by intrarenal artery infusion of various doses of prostaglandin E_1, acetylcholine, dopamine and isoproterenol. RPP was reduced incrementally by gradually tightening a vascular occluder positioned around the aorta about 1 cm proximal to the renal artery. The vasculature was allowed to stabilize between pressure steps. Analysis of the data suggest severe autoregulatory impairment when renal flow corrected to 100 mm RPP exceeds 2.9 ml/min/gm kidney regardless of the dilating agent used, indicating a physical rather than a specific drug effect.
(Supported in part by a research grant from the AOA.)

CYCLIC AMP-DEPENDENT PROTEIN KINASE PHOSPHORYLATION OF CARDIAC NATURAL ACTOMYOSIN. Y.S. Reddy* and L.E. Wyborny* (SPON: J.C. Norman). Cardiovascular Surgical Research Laboratories of the Texas Heart Institute, St. Luke's Episcopal and Texas Children's Hospitals, Houston, Texas, 77025.

Guinea pig cardiac and skeletal muscle natural actomyosins (NAM) were isolated as described by Honig (Am. J. Physiol. 241, 1968) with slight modification. In the absence of NaF cardiac NAM pretreated with Mg^{2+}-ATP, protein kinase (Pkase) and 10^{-5} M cAMP had no effect on the ATPase activity. Similar treatment of skeletal NAM yielded the same results as in cardiac NAM. Cardiac and skeletal NAM ATPase activity was completely inhibited with 20 mM NaF and this inhibition was released upon the removal of NaF. Washed cardiac NAM phosphorylated with NaF possessed less ATPase activity at all Ca^{2+} concentrations ($p<0.005$). When phosphorylated NAM was dephosphorylated with either E. coli alkaline phosphatase or commercial Pkase, the ATPase activity increased between pCa 5.0 and 6.5 ($p<.01$). In contrast, phosphorylation had no effect on skeletal muscle actomyosin ATPase activity. Commercial Pkase and cardiac NAM contained phosphatase activities (15.0 and 0.42 nanomoles pi/mg/min) which were inhibited by NaF. SDS gel electrophoresis of phosphorylated proteins shows that most of the radioactive ^{32}P was incorporated into heavy chain and 28,000 dalton fractions. Conclusion: NaF inhibits the phosphatase activities present in both cardiac actomyosin and commercial Pkase. Phosphorylation carried out in the presence of NaF results in a decrease in actomyosin ATPase activity.
(Supported by NIH Grant HL20015).

IMIDAZOLE AND PRESENT STATUS OF THE EVIDENCE FOR THE ELECTROGENICITY OF THE GASTRIC H^+ PUMP IN Cl^--FREE MEDIA. W. S. Rehm, S. G. Spangler,* S. S. Sanders, and R. L. Shoemaker. Dept. of Physiology & Biophysics, University of Alabama in Birmingham, Birmingham, AL 35294

Previous work has shown for the frog gastric mucosa that in Cl^--free media the PD is inverted (the nutrient side is negative) and that following H^+ secretory inhibitors (e.g., DNP) there is in Cl^--free media a precise linear relationship between the PD and H^+ rate (they both go concurrently to about zero). This linear relationship is predicted on the basis of the H^+ pump being electrogenic. It is almost impossible to explain on any other basis except the possibility that the inverted PD is due to a liquid junction potential (LJP) in the lumina between the fluid in the lumina and the secretory fluid where the pH is > 4. Calculations on the basis of available microscopic dimensions of the lumina and the H^+ rate reveal that the $[H^+]$ in the lumina is < 0.01 M and that the LJP (calculated on the basis of standard equations) would be oriented to make the nutrient side negative but would be substantially less than the magnitude of the inverted PD. The LJP over a range of $[H^+]$ from 0.1 M to zero is non-linear but over a small range is about linear so if the actual diameter of the lumina is smaller than that used in the calculations of $[H^+]$ then $[H^+]$ and LJP could be greater and LJP might be solely responsible for the inverted PD. Hence the linearity would not argue for electrogenicity of the H^+ pump. It will be shown that imidazole does not appreciably change the magnitude of the PD but reduces the H^+ rate by neutralization of H^+ in lumina and hence essentially eliminates LJP. Conclusion: LJP does not appreciably contribute to the inverted PD and linearity of PD versus H^+ rate is solid evidence for electrogenicity of the H^+ pump. (NIH and NSF support)

THE EFFECTS OF BODY AND LEG POSITIONS ON SIGH FREQUENCY IN MAN. E. J. Reininger, Dept. of Med. Sciences, Southern Illinois University, Springfield, Il. 62708.

Sigh frequency is almost twice as great in the sitting position (lungs vertical) as in the supine position (lungs horizontal), (Fed. Proc. 30:327, 1971). To evaluate the factors influences sigh frequency, 16 subjects were placed on a tilt table in the supine, head-up (36^o) and head-down (36^o) positions. Respiratory activity was monitored using a pneumograph -- breaths counted as sighs were more than twice the average tidal volume. There was no significant difference between the supine and head-up positions, 8.8 and 8.2 sighs/hr respectively; however, in the head-down position the sigh frequency increased significantly 66% to 14.5 sighs/hr. Further tilting in the head-down position to 62^o augmented the sigh frequency. To translocate blood, without changing the orientation of the lungs, modified supine positions with the legs raised or lowered were used with 6 subjects. The sigh frequency was 20% greater in the feet-up position. The increased sigh frequency in the head-down position can be explained using a model to illustrate the gravitational effect on lung mass; alveolar size is determined by the resultant of mechanical tensile forces, surface tension, transpulmonary pressure, and mechanical attachment to surrounding structures. Translocation of blood volume, abdominal compression and ventilation may affect sigh frequency. The sigh frequency was not the same in the head-up and head-down positions. The results are consistent with the hypothesis that the head-down position produces alveoli of the smallest size which are more likely to exhibit atelectasis resulting in more intense stimulation of pulmonary mechanoreceptors, which in turn are responsible for the increased sigh frequency. Sighing serves to reverse atelectasis.

COMPARISON OF STEADY STATE AND PACEMAKER RELATED CONDUCTANCE CHANGES IN CARDIAC PURKINJE FIBERS. J. Reiser*, G. Anderson*, and A.R. Freeman, Dept. of Physiology, Temple Univ. Sch. of Med. and William Likoff Cardiovascular Institute, Hahnemann Med. College & Hospital, Phila., Pa. (SPON: S.H. Lorber).

The steady state current-voltage profile (V/I_{SS}) of cardiac Purkinje fibers (PF), as determined by the double microelectrode technique, approximates an S-shaped configuration with non-linearities in the slope conductance occurring in the voltage region of the resting potential (RP). In spontaneous Purkinje fibers (SPF) the input resistance (R_{IN}) increased significantly over the voltage range covered by the slow diastolic depolarization. The purpose of this study was to determine the relationship of R_{IN} during spontaneous diastolic depolarization to V/I_{SS} over a similar voltage excursion. Values of R_{IN} during diastolic depolarization ranged from $1.26 \pm .17 \times 10^5$ Ω at the most negative potential to $2.35 \pm .22 \times 10^5$ Ω at the most positive potential ($n = 10$), the mean decrease in diastolic potential being 16.8 mV. Variations in slope conductance obtained from V/I_{SS} over a similar voltage excursion (± 20 mV from RP), ranged from a minimum of $1.21 \pm .25 \times 10^5$ Ω to a maximum of $2.28 \pm .13 \times 10^5$ Ω in 10 experiments, the latter values having been obtained from depolarizing current pulses. This apparent similarity was substantiated by studies which compared the relationship of V/I_{SS} with changes in R_{IN} in the same cells ($n = 8$). Studies employing current ramps and double pulse techniques to compare R_{IN} of SPF at similar membrane potentials throughout slow diastolic depolarization were not in support of a voltage-independent change in R_{IN}. These results suggest that the changes in membrane conductance occurring in SPF may not be the primary mechanism involved in initiation of spontaneous diastolic depolarization.

TUBEROINFUNDIBULAR NEURONS : ELECTROPHYSIOLOGICAL STUDIES ON AFFERENT AND EFFERENT CONNECTIONS. L.P.Renaud, Dept.Medicine, Div.Neurology, Montreal General Hospital, Montreal, Quebec, H3G 1A4, Canada.

Hypothalamic regulation of adenohypophyseal secretion is mediated by peptide messengers secreted into the pituitary portal circulation from median eminence terminals of tuberoinfundibular 'peptidergic' neurons. In experiments on pentobarbital anesthetized male rats, extracellular recordings were obtained from 195 hypothalamic and preoptic tuberoinfundibular neurons identified by antidromic invasion from stimulation on the surface of the median eminence. Basomedial hypothalamic (BMH) tuberoinfundibular cells ($n = 117$) in the ventromedial nucleus displayed synaptic excitatory or inhibitory responses from stimulation in the amygdala, while periventricular tuberoinfundibular cells were responsive to dorsal hippocampus stimulation. Medial preoptic (MPOA) tuberoinfundibular cells ($n = 78$) were generally unresponsive to stimulation in the amygdala. Antidromic invasion from sites other than the median eminence indicated the presence of axon collaterals of MBH tuberoinfundibular neurons to the anterior hypothalamic area (2 cells),MPOA (3 cells),thalamic midline nucleus medialis dorsalis (3 cells) and amygdala (2 cells); evidence for recurrent inhibition implied the existence of local intrahypothalamic axon collaterals in both MBH and MPOA tuberoinfundibular neurons. These observations not only confirm earlier studies on localization of tuberoinfundibular neurons but introduce some of the complexities in the organization of afferent and efferent connections in this system, data that may help to clarify the functional nature of this putative peptidergic neural network.
(Supported by the Canadian MRC)

THE EFFECT OF ENDOTOXIC SHOCK AND FLUID EXPANSION ON REGIONAL BLOOD FLOW IN THE BABOON. D. G. Reynolds, M. J. Zinner*, D. L. Wickline*, D. Locke*, and N. J. Gurll*. Division of Surgery, Walter Reed Army Institute of Research, Washington, D. C. 20012

Eight adult baboons were studied under light pentobarbital anesthesia. Following a control period, the animals were given E. coli endotoxin intravenously (approximately LD_{25}). Arterial pressure fell from 122 ± 5 to 80 ± 9 mm Hg and cardiac output (CO) from 2.75 ± 0.31 to 1.43 ± 0.24 L/min. After 4 hours of endotoxemia, the animals were resuscitated over 2 hours by fluid expansion to return CO to control values. Regional blood flow was determined by radioactive microsphere injections during the control period and at the end of each experimental period:

Organ	Control	Shock	Resuscitation
	ml/min-100 gm	% Control	% Control
Heart	183 ± 58	102 ± 16	134 ± 31
Brain	50 ± 8	147 ± 18	157 ± 33
Kidney	641 ± 59	22 ± 7	30 ± 10
Adrenals	200 ± 38	75 ± 16	110 ± 25
Liver	72 ± 7	42 ± 5	61 ± 20
Pancreas	92 ± 15	30 ± 7	54 ± 17
Stomach	19 ± 4	59 ± 20	88 ± 24
Small bowel	56 ± 9	84 ± 21	148 ± 48
Large bowel	20 ± 4	66 ± 13	158 ± 41

When these data are evaluated in terms of % CO distributed to the circulations, there was an increase in the fraction distributed to the heart, brain, adrenals, and total GI tract during shock. This increase persisted in the brain, heart, and GI tract following resuscitation.

MEASUREMENTS OF THE BALANCE BETWEEN OXYGEN DEMAND AND SUPPLY IN PERFUSED SEPTUM. T.L. Rich* and J.R. Williamson. Dept. Biochemistry and Biophysics, University of Pennsylvania, Philadelphia, Pa. 19174

A technique for measuring the balance between oxygen demand and delivery in the isolated, vascularly perfused, interventricular mammalian septum has been developed utilizing a 4-channel dual wave length spectrophotometer equipped with flexible light guides and appropriately selected filters. Isometric tension, corrected pyridine nucleotide (PN) fluorescence, cyt b and c redox and myoglobin oxygenation-disoxygenation states are measured simultaneously. For equivalent O_2 delivery rates isometric tension is similar in hypoxia (constant flow, decreased PO_2) and ischemia (constant PO_2, decreased flow) until O_2 delivery rates are clearly inadequate for the O_2 demands. Tension then falls more rapidly in ischemia than hypoxia, and cyt b and c are slightly more oxidized and myoglobin more oxygenated in ischemia. This indicates a greater O_2 availability during advanced ischemia when tension and intracellular pH are significantly more depressed than in hypoxia for similar O_2 delivery rates and cyt oxidation states. When PN, myoglobin, cyt b and c signals are poised at any degree of full anoxic reduction, perturbations which increase O_2 demand (catecholamines, increased perfusate Ca^{2+} and stimulus rate) cause further reduction, while agents which reduce O_2 demand (slowed stimulus rate, lowered perfusate pH and Ca^{2+}) allow oxidation of these signals. Thus, it is now possible to measure continuously the balance between O_2 delivery and demand in this isolated myocardial preparation in which experimental parameters can be independently and carefully controlled. (Supported by Grants HV-52995 and HL-18708).

OCCURRENCE OF INSULIN INDUCED FEEDING BUT ABSENCE OF 2-DEOXY-D-GLUCOSE INDUCED FEEDING IN THE HAMSTER. Robert C. Ritter* and Olin K. Balch* (SPON: W.M. Dickson). Dept. of Veterinary Science, University of Idaho, Moscow, ID.

Hamsters appear to lack the feeding response to 2-deoxy-D-glucose (2DG). Adult male and female hamsters did not increase their food intake in response to subcutaneous 2DG (200, 350, 500, 750, 1500mg/kg). For example, hamsters ate 2.2 ± 0.19gs of food over a 5 hr period following saline injection and 2.1 ± 0.18gs following 2DG (500mg/kg). These animals were refractory to 2DG whether tested in the light or dark. Extension of the test period to 12 or 24 hrs also failed to produce any response. Absence of feeding in response to 2DG is probably not due to failure of 2DG to produce glucoprivation since the 2DG treated animals displayed a 2°C fall of colonic temperature. Furthermore treatment of hamsters with 2DG (500mg/kg) elicited a marked hyperglycemia. Blood glucose rose from 67 ± 6mg% prior to 2DG to 271 ± 31mg% within 2 hrs after 2DG. Therefore, 2DG induced glucoprivation appears to be detected and responded to by the central nervous system. In contrast to 2DG, insulin (2, 4, or 8 units/animal) caused hamsters to significantly increase their 5 hr food intake by an average of 40% (control 2.0 ± 0.12gs; insulin, all doses 2.8 ± 0.15gs). Since the hamster seems to lack a feeding response to directly produced glucoprivation, it seems unlikely that insulin elicits feeding via the glucoprivic control in the hamster. The results suggest (1) that hamsters lack the glucoprivic control of feeding behavior, as exercised by 2DG, (2) that 2DG and insulin treatments are not equivalent ingestive challenges and (3) that insulin may be capable of stimulating ingestive behavior independently of any glucoprivic effect.
(Supported in part by NIH grant MH26760).

BLOOD FLOW IN THE CAPILLARIES OF THE OPTIC NERVE. C.E.Riva*, M. Loebl* and G.T. Feke*(SPON: A.Adolph). ERI of Retina Foundation and Harvard Medical School, Boston, MA.02114.

The technique of Laser Doppler Velocimetry has been used to study blood flow in the capillary bed of the optic nerve. In this technique, Doppler-shifted frequency spectra of laser light scattered from erythrocytes flowing in the capillary bed of the optic nerve can be measured. The widths of the spectra are proportional to the average flow velocity of the erythrocytes at the site of measurement. We have measured such spectra in normal human subjects and in anesthetized owl monkeys. Investigation of the effect of elevation of the intraocular pressure (IOP) on the average velocity of the erythrocytes moving in the capillary bed of the optic nerve of monkeys showed the following results: a)No significant change in the widths of the spectra was observed until the IOP approached the diastolic ophthalmic artery pressure. b)When the IOP was maintained between diastolic and systolic ophthalmic pressure, the widths of the spectra decreased and varied markedly from one measurement to the next at fixed IOP. c)With elevation of the IOP above systolic ophthalmic artery pressure, the widths further decreased but did not vary in successive measurements. This technique is rapid and non invasive and offers a promising tool for the examination of the microcirculation of the optic nerve.

DISTRIBUTION OF THE REDUCED CARDIAC OUTPUT INDUCED BY CONTINUOUS POSITIVE-PRESSURE BREATHING. C.H. Robertson, Jr.,* and S.S. Cassidy* (SPON: J.H. Mitchell). Department of Medicine, University of Texas Health Science Center, Dallas, Texas.

A reduction in cardiac output commonly occurs with high levels of continuous positive-pressure breathing. A critical issue is the distribution of this reduced output to the vital organs. Nine closed-chest anesthetized, intubated dogs were ventilated at 15 ml/Kg tidal volume. Cardiac output by dye dilution and regional blood flow by the radioactive microsphere method were measured at 0, 5, 10 and 15 cm H_2O positive end-expiratory pressure (PEEP). Arterial blood gases were monitored and respiratory rate adjusted to maintain a constant P_{CO_2}.

CARDIAC OUTPUT AND DISTRIBUTION (% OF THAT DURING SPONTANEOUS BREATHING)

	PEEP (cm H_2O)			
	0	5	10	15
Cardiac Output	91	75	54	51
Ventricle (Left/Right)	71/84	61/73	49/53	43/48
Brain	65	73	67	56
Kidney	80	66	51	40
Stomach	40	34	26	17

Blood flow to the stomach, intestines, pancreas, adrenals, spleen, and skin decreased much more than the cardiac output. Brain blood flow was relatively well maintained. Flow to the kidneys and heart fell slightly more than the cardiac output. It is unclear whether the fall in myocardial perfusion is a partial cause or effect of the falling cardiac output.

LUNG VOLUME HISTORY EFFECTS ON PATHWAYS FOR COLLATERAL VENTILATION. N.E. Robinson* and P.R. Sorenson* (SPON: L.F. Wolterink). Depts. of Physiology and Large Animal Surgery and Medicine, Mich. State Univ., E. Lansing, MI 48824.

Exsanguinated lower lobes of dog lungs were suspended in a pressure plethysmograph. A double lumen catheter (2.5mm O.D.) obstructed a peripheral airway. Air was delivered to the isoalted segment via a flowmeter and the outer lumen of the catheter, and flowed into the remainder of the lung through collateral channals. The inner lumen measured segment pressure (P_S) while lung inflation pressure (P_l) was recorded from the lobar bronchus. Driving pressure (P_S-P_l) was recorded against lobar volume during deflation, (P_S-P_l)defl, to a variety of lobar volumes and reinflation, (P_S-P_l)infl, to TLC at a series of constant collateral flows ($\dot{V}_{col}$). At a given lobar volume, 1)(P_S-P_l)infl was less than (P_S-P_l)defl at low $\dot{V}_{col}$, 2)(P_S-P_l)infl and (P_S-P_l)defl were equal at moderate $\dot{V}_{col}$, and 3)(P_S-P_l)infl was greater than (P_S-P_l)defl at high $\dot{V}_{col}$. Several animals only demonstrated 2) and 3) at low and moderate $\dot{V}_{col}$ respectively, while one dog exhibited only 3) at all $\dot{V}_{col}$. Lobar volume at the end of deflation did not alter the relationship of (P_S-P_l)infl to (P_S-P_l)defl. These effects may be due to changes in segment volume relative to lobe volume at the different $\dot{V}_{col}$. Isovolume pressure flow curves derived from the P_S-P_l/lobe volume plots were alinear. At all lobe volumes, as flow increased, P_S-P_l increased, decreased and increased again. The magnitude of the pressure gradients was less at high lobe volumes than at low lobe volumes. When lobar volume was held constant for 4 minutes, P_S-P_l increased with time at 25 and 50 but not at 75% of vital capacity. These results suggest that the caliber of collateral channels is a function of both the compliance of the tissues within the isolated segment and surface tension forces within the collateral pathway. Supported by USPHS grant #HL11168.

NONINVASIVE FETAL ELECTROCARDIOGRAPHY BY DIGITAL ADAPTIVE FILTERING.
S. E. Robinson* (SPON: C. A. Snipes). Dept. of Physiol. & Biophysics, Hahnemann Medical College, Philadelphia, PA 19102

The transabdominal fetal electrocardiogram (FECG) of goats has been separated from corrupting noise by means of a general purpose digital computer programmed to perform digital adaptive filtering. The FECG was obtained from subcutaneous stainless steel suture electrodes about the maternal abdomen. Filtering was accomplished by generating a signal average based upon the temporal alignment provided by performing a pseudo-autocorrelation of the incoming signal with the current average. The filtering may be performed in real time. The FECG when first detected was extracted from a noise-to-signal ratio as extreme as 3:1. That is, the FECG was not visible. Fetal ECG was first quantitatable in the range of 49 to 62 days into gestation (N = 6). The mean $\pm$ standard deviation for the group was 54.8 $\pm$ 4.9 days. Gestation in goats is 5 months. QRS complex amplitudes at day of first detection ranged from 3 to 6 microvolts. This method is currently being applied to the quantitative developmental study of the FECG in goats. (Supported by NIH grant HD 09461.)

VARIATION OF THIN FILAMENT LENGTH IN HEART MUSCLE.
T. F. Robinson* and S. Winegrad. Dept. of Physiology, Univ. of Penna. Medical School, Phila., Penna. 19174.

The range of lengths of thin filaments of frog and rat atrial trabeculae have been measured by analyzing electron micrographs of serial transverse sections through a major portion of a sarcomere. In order to eliminate sources of artifact regions within serial sections were used only when 1) the Z band was flat and entirely included within one section, 2) all filaments were absolutely perpendicular to the plane of the section without using any tilting, and 3) at least 400 thin filaments and 200 thick filaments could be followed in a given region. The ratios of thin to thick filaments were determined in each transverse section and the total lengths of thin filaments from the Z band determined from the filament ratios, which varied between values of 0 and 2. In frog and rat atrium the ranges of lengths were respectively 0.9 to $>$1.4μm and 0.6 to $>$1.3μm. The functional significance of such considerable variation in thin filament lengths was ascertained by computing the corresponding sarcomere length-developed tension curves using the inferences established by Gordon, et al (1966) for the sliding filament theory in skeletal muscle. Curves were computed for filament lengths throughout the range, weighted by the appropriate factors from the distribution histogram, and summed. The composite sarcomere length-tension curves had shapes distinctly different from that of skeletal muscle: the plateau or near-plateau regions were 0.7μm wide. It appears that over the physiological range changes in filament organization have little effect on force generation.
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THE CAROTID SINUS REFLEX IN LOW AND HIGH SALT STATES. A.P. Rocchini*, J.R. Cant* and A.C. Barger, Department of Physiology, Harvard Medical School, Boston, Mass. 02115.

The magnitude of the pressor response to carotid sinus hypotension in 3 salt states was evaluated by bilateral carotid artery occlusion (CAO) in 4, chronic, unanesthetized dogs. Dogs were surgically prepared with bilateral carotid artery loops, and catheters were chronically implanted in the carotid artery distal to the loop, and in the abdominal aorta and vena cava. Each dog had CAO performed for at least 20 min on 6 consecutive days while on a diet containing 8 (low Na^+), 70 (normal Na^+), or 110 meq/day of Na^+ (high). The diets were randomized to eliminate bias, and 2 weeks allowed for stabilization befored experiments were started. The increase in mean arterial pressure (MAP) to CAO was significantly less in animals on a low Na^+ diet (12.1 ± 3.8 mm Hg, mean ± SD, $P < 0.01$) than in the same dogs on either normal or high Na^+ diets (23.5 ± 7.2 mm Hg and 25.4 ± 7.5 mm Hg, respectively). With bilateral aortic nerve section the MAP rise with CAO was greater, but the differential between high and low Na^+ persisted. The smaller pressor response in the low Na^+ dogs was shown not to be related to differences in response of the renin-angiotensin system, to the degree of carotid hypotension, or to the cardiovascular reaction to infused norepinephrine. However, the dose-response to infused tyramine was shifted significantly to the right in low Na^+ dogs, suggesting that release of catecholamines was decreased. Thus, chronic Na^+ depletion resulted in a reduced response to CAO which may be due to a decrease in the responsiveness of the efferent sympathetic nervous system.

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CHEMICAL ANALYSIS AND PRELIMINARY PHARMACOKINETICS OF THE ACROSIN INHIBITOR PARA-AMINOBENZAMIDINE IN RATS. Lester L. Rolf, Jr. and Donivan Hudgins. Dept. Physiol. Sci., Col. Vet. Med., Okla. St. Univ., Stillwater, 74074

It is generally accepted that ovum fertilization in many mammalian species requires an active acrosomal enzyme, acrosin. Stambaugh and Buckley (Biochim. Biophys. Acta, 284:473, 1972) have shown that rabbit acrosin can be inhibited by para-aminobenzamidine (PAB) though with marked toxicity. Chemical detection of PAB was effected on 11% trichloracetic acid (TCA) extracts of plasma, red cells and selected tissues by diazotization and coupling with N-(1-napthyl)-ethylenediamine. PAB was stable in these extracts for at least 1 week. The diazotized colored complex, with an absorption maximum at 540 nm, was stable for at least 24 hours at 23-26°C. TCA was 92-100% effective in extracting spiked plasma containing between 5 and 100 µg/ml PAB. Time dependent blood concentrations of PAB were determined in male and female rats weighing between 265 and 398 gm after intravenous administration of 40 mg/kg. One ml blood samples were taken for 140 min at 10 and 20 min intervals. It appears that the α phase half-life is 8 ± .6 min while the β phase half-life is 98 ± 13 min. Extrapolation of plasma decay curves to zero time allows for the calculation of an apparent volume of distribution of 330% of total body weight. Erythrocyte levels of PAB are always greater than the plasma during these intervals but the slope of decay is not significantly different from plasma. At 60 minutes, PAB tissue levels(heart, lung, spleen, intestine, testes, uterus, liver pancreas, adrenal and kidney) were greater than plasma levels. At 140 min all tissue levels exceeded the plasma level by factors of 1.01 (testes) to 14 (adrenal). PAB is not concentrated in the fetus. Supported by in-house grant, Dept. Physiol. Sci., Col. Vet. Med.

CHOLINE TRANSPORT ACROSS THE MUCOSAL MEMBRANE OF GUINEA PIG INTESTINE. R.C. Rose, F.J. Kuczler† and D.L. Nahrwold* Departments of Physiology and Surgery, The Pennsylvania State University, Hershey, Pennsylvania.

Choline influx across the brush border of guinea pig jejunum was measured in vitro to determine if a specialized transport mechanism exists. Segments of intestine were mounted mucosal surface upward in Lucite chambers which exposed six areas of mucosa to Ringer solution containing ^{14}C-choline and ^{3}H-inulin, which served to indicate the volume of adherent fluid in the extracellular space. The appearance of ^{14}C-choline in the tissue was found to be a linear function of time for at least 10 min., indicating that this method gives a reliable measure of choline uptake by the epithelium. Subsequent experiments were performed with 5 min. exposure times. With low concentrations of choline (0.024-4.0 mM) in the mucosal solution, influx rate followed saturation kinetics; at choline concentrations above 4 mM absorption was approximately linearly related to the mucosal choline concentration. The possibility that choline influx is a metabolically dependent process was tested by preincubating tissue samples in NaCN (2 mM) and 2,4-DNP (0.1 mM) for 20 min. Choline influx from a mucosal concentration of 0.024 mM was unaffected by the metabolic inhibitors (control: 2.4±0.2 nMol/cm^{2}hr; test: 2.3±0.2 nMol/cm^{2}hr). Similarly, choline influx was unaffected by tissue preincubation in 0.1 mM ouabain (control: 2.7±0.4 nMol/cm^{2}hr; test 2.8±0.3 nMol/cm^{2}hr). Elimination of Na from the mucosal solution by substitution with Tris or mannitol did not significantly alter the rate of choline influx. Also, lowering the intracellular Na concentration by preincubation in a Na-free solution at 0° did not affect choline influx. Thus, choline entry across the brush border into intestinal absorptive cells appears to proceed by a carrier-mediated process which is independent of the transmembrane Na gradient and does not directly use cellular metabolic energy.

EFFECT OF ACIDOSIS ON SODIUM EXCRETION BY THE ISOLATED RAT KIDNEY. S.G. Rostand* and J.B. Watkins* (SPON: J. Schafer). Univ. of Alabama Med. Ctr., Birmingham, Ala. 35294

In order to study the diuretic effect of metabolic acidosis (MA), we perfused isolated rat kidneys at 100 mm Hg with Krebs-Ringer bicarbonate buffer containing 8 gm% albumin and maintained at pH=7.42 ± 0.03 (SEM), pCO_2=39.7 ± 2.8 mm Hg and $[HCO_3^-]$ = 23.6 ± 1.2 mM. During 2 hours of control perfusion, urine flow ($\dot{V}$) was 0.007 ± 0.0001 ml/min, $U_{Na}V$ was 0.48 ± 0.11 µEq/min and U_KV was 0.22 ± 0.05 µEq/min. In paired experiments, MA was produced by adding 1.5 ml of 1N HCl. After 1 hour, perfusate pH was 7.15 ± 0.02 and $[HCO_3^-]$ 13.5 ± 1.1 mM, V increased +0.0184 ± 0.004 ml/min ($p < .01$), $U_{Na}V$ rose +2.46 ± 0.47 µEq/min ($p < .01$). In order to produce acidosis without lowering $[HCO_3^-]$, kidneys were exposed to 88% O_2:12 CO_2 following 1 hour of control perfusion. Perfusate pH fell from 7.43 ± 0.08 to 7.27 ± 0.007, pCO_2 rose from 36.8 ± 1.8 mm Hg to 58.2 ± 2.2 mm Hg and $[HCO_3^-]$ rose from 23.4 ± 0.7 mM to 32.1 ± 1.2 mM. V did not change from control values, but $U_{Na}V$ rose +0.293 ± 0.082, which was a significant change but of much less magnitude than that seen with MA. When 1.2 ml of 1N $NaHCO_3$ was added 30 minutes after MA, pH rose from 7.22 ± 0.019 to 7.49 ± 0.02, and $[HCO_3^-]$ rose from 14 ± 0.8 mM to 25.6 ± 1.4 mM. V fell from 0.035 ± 0.01 ml/min to 0.012 ± 0.002 ml/min and $U_{Na}V$ fell toward normal from 3.8 ± 0.86 µEq/min to 1.7 ± 0.5 µEq/min. These data suggest that the effects of MA are reversible and do not represent non-specific toxicity. We conclude that the natriuresis induced by MA, does not correlate well with pH but correlates best with decreases in perfusate $[HCO_3^-]$. These data are in accord with the view that tubular sodium absorption is in part controlled by the tubular fluid $[HCO_3^-]$. (Supported by a VA Research Grant)

RESPIRATORY MUSCLE FATIGUE IN MAN AT FRC AND HIGHER LUNG VOLUMES. C.S. Roussos*, M.S. Fixley*, D. Gross*, and P.T. Macklem. Meakins Christie Laboratory, McGill University Clinic, Royal Victoria Hospital, Montreal, Canada.

We measured the time (t_{lim}) required to produce respiratory muscle fatigue in five normal subjects breathing at FRC against a variety of high inspiratory linear resistive loads. In a given run the subjects generated a mouth pressure (Pm) with each inspiration which was a predetermined fraction of maximum Pm (Pm_{max}) at FRC and continued breathing until they were unable to generate this Pm. The Pm/Pm_{max} that could be generated indefinitely (Pm_{crit}) was ca 60%, equivalent to the power of ca 6.6 Kg.m/min ($\dot{w}_{crit}$). In two subjects the same experiment was conducted at FRC + ½ inspiratory capacity (IC). The subjects actively maintained increased lung volumes by watching end-expiratory transpulmonary pressure on an oscilloscope. For any fraction of the maximum mouth pressure at FRC + ½ IC (Pm_{max}), t_{lim} was shorter than at FRC. Pm_{crit} decreased to 30% Pm_{max} and the $\dot{w}_{crit}$ to 2.6 Kg.m/min. Thus active hyperinflation markedly increases the susceptibility to respiratory muscle fatigue. This probably is due to decreased energy supplies to the muscles and/or to decreased muscular efficiency. (Supported by the MRC of Canada).

CORONARY VASCULAR RESISTANCE DURING PROLONGED ISCHEMIA IN THE ISOLATED RAT HEART: EFFECT OF METHYLPREDNISOLONE AND HYALURONIDASE. Michael J. Rovetto, Department of Physiology, Jefferson Medical College, Philadelphia, PA 19107.

Prolonged ischemia in the isolated rat heart resulted in a progressive reduction of coronary flow when flow was provided by a constant perfusion pressure. The initial coronary flow provided at this perfusion pressure was 25% of the control aerobic value. Coronary flow remained relatively constant during the first hour of perfusion, but decreased about 20% during the next half-hour of ischemia. The decrease in coronary flow was prevented by addition of 4 U/ml hyaluronidase (hyal) or 0.25 mg/ml methylprednisolone (MP) in the perfusion media. Coronary flows were 65, 97 and 85% of the initial values after 2 hours for hearts perfused with Krebs-Henseleit bicarbonate buffer (KH), KH plus hyal and KH plus MP, respectively. Glucose utilization was not altered in either aerobic working hearts or in ischemic hearts by either hyal or MP. The higher coronary flows at 2 hours in the presence of hyal resulted in lower tissue concentrations of lactate and higher concentrations of creatine phosphate than ischemic hearts not receiving hyal. Tissue concentrations of lactate and creatine phosphate were not significantly different from control values for hearts perfused with MP ($p<0.05$ and $p>0.05$, respectively). Despite the observation that hyal was effective in maintaining coronary flow during ischemia, post-ischemic mechanical performance was depressed to the same extent as that of KH perfused hearts. (Supported in part by NIH grant #HL-17895)

FACTORS AFFECTING ADRENAL MICROSOMAL DRUG AND STEROID METABOLISM IN THE GUINEA PIG. R.C. Rumbaugh*, J.W. Greiner*, R.E. Kramer*, M.E. Wilson* and H.D. Colby, West Virginia University Medical Center, Morgantown, WV 26506.

Previous studies demonstrated that guinea pig adrenal microsomes metabolized several drugs (ethylmorphine, hexobarbital) more rapidly than hepatic tissue. Experiments were carried out to compare the effects of various factors on oxidative drug and steroid metabolism by the guinea pig adrenal cortex. Ethylmorphine (EM) demethylation proceeded more rapidly in adrenals from adult males than females (266 vs 139* nmoles/min/g)(*$p < 0.05$). Metabolism of EM was also greater in mature than immature animals of both sexes. In contrast, adrenal 21-hydroxylase activity was similar in adult males and females (158 vs 140 nmoles/min/g) but like EM metabolism, increased with maturation in males and females. Adrenal microsomal cytochrome P-450 concentrations did not vary with age or sex. However, differences in the magnitude of substrate-induced type I spectral changes paralleled differences in enzyme activities. ACTH administration to young male guinea pigs decreased EM metabolism (221 vs 85*) but did not significantly affect 21-hydroxylase activity (93 vs 81). Administration of testosterone to females increased EM demethylation (144 vs 204*) but decreased the rate of 21-hydroxylation (101 vs 68*). Addition of prostaglandins E_1, E_2 or A_1 to adrenal tissue *in vitro* decreased EM metabolism but did not affect 21-hydroxylase activity. These observations indicate that the activities of adrenal microsomal mixed function oxidases are affected by various factors and that adrenal drug and steroid metabolism are independently regulated. (Supported by NSF grant GB-41215).

HUMAN CARDIORESPIRATORY RESPONSE TO EXERCISE DURING WEIGHTLESSNESS. J. A. Rummel*, C. F. Sawin*, E. L. Michel*, M. C. Buderer*, R. C. Croston*, and D. G. Fitzjerrell* (SPON: W.E. Hull). NASA-Johnson Space Center, Houston, Texas 77058.

Understanding the physiological response of man to long duration space flight requires a quantitative knowledge of alterations in organ systems together with knowledge of how integrated control of the systems is maintained. Exercise is an excellent stressor for studying these interactions, and the study of exercise response during space flight was one of the major medical experiments flown on each of the three long duration (28, 59, and 84-day) Skylab missions.

High levels of *ad libitum* personal exercise engaged in by the crews as an inflight countermeasure to cardiovascular deconditioning complicated the interpretation of our experiment data. The present study attempts to evaluate the interaction of conflicting physiological processes (deconditioning and conditioning) through an integrated analysis approach.

The integrated analysis proceeded in the following manner: first, response indices were calculated for the measured variables (work load, heart rate, blood pressure, oxygen consumption, cardiac output, carbon dioxide production, and minute volume). These were compared during the preflight, inflight, and postflight phases. Significant changes were observed in several aspects of mechanical, respiratory, and cardiovascular efficiencies. Second, the changes were correlated with experiment data from other organ systems by use of an automated data base containing all of the Skylab biomedical data. Third, an integrated hypothesis was derived in the form of a quantitative computer model. This paper will present each of these steps in detail.

RESPONSES OF AIRWAY SMOOTH MUSCLE TO ELECTRICAL STIMULATION AND ACETYLCHOLINE. J.A. Russell* and R.E. Hyatt. Mayo Clinic and Foundation, Rochester, MN 55901

Tracheal smooth muscle (TSM) strips and spiral strips of airways with inside diameters of 5 mm and 1 mm were excised from dog lungs, mounted between platinum electrodes and placed in a chamber filled with Krebs-Ringer bicarbonate solution. All preparations were placed at L_{max} by determining the length at which a standard electrical stimulus produced maximum active tension. Tetrodotoxin (10^{-6} g/ml) abolished the response to maximum electrical stimulation (15v, 25Hz, 0.5msec) in all three preparations but did not alter acetylcholine concentration-effect curves. Atropine also abolished the responses to maximum electrical stimulation. We conclude that electrical stimulation contracts airway smooth muscle via release of neurotransmitter from autonomic nerve endings rather than by a direct effect on smooth muscle cells. In contrast, acetylcholine has a direct effect on smooth muscle membranes. Maximum tensions produced by acetylcholine (Ach) are compared to the tensions produced by maximum electrical stimulation (E.S.) in the following table:

	1 mm airways (N=12) g/g of tissue ± S.E.	5 mm airways (N=10) g/g of tissue ± S.E.	TSM (N=15) g/g of tissue ± S.E.
Ach.	94.4 ± 4.6	49.3 ± 4.9	373 ± 16
E.S.	44.7 ± 3.8	32.5 ± 2.7	371 ± 17

The maximum tensions produced by acetylcholine versus electrical stimulation are significantly different ($p < .001$) in both 1 mm and 5 mm airways but not in TSM suggesting a basic difference between the innervation of intrapulmonary and extrapulmonary airways. (Supported by grant HL-17103 from NHLI.)

BMES

ON-LINE DETECTION PROCEDURE OF PVC RATE CHANGES BASED ON A POISSON MODEL. Urs E. Ruttimann and Ramez Bassir.* Dept. of Clinical Engineering, George Washington University, Washington, D.C. 20037.

The observation that premature ventricular contractions (PVCs) frequently heralded more serious arrhythmias strengthened the view that the data relative to PVC occurrence were of great importance for induction or termination of preventive drug therapy. In an effort to reduce the amount of data provided by either hardware or software PVC detectors, this study is concerned with the detection of significant changes in the rate of the PVC occurrence, enabling the recognition and assessment of trends. Single-lead EKG signals from 21 patients hospitalized in the CCU were recorded in parallel to the patient care display, and a total of 5278 PVCs flagged by a commercially available PVC detector. The intervals between verified PVCs were stored in computer for a subsequent time series analysis. For 86% of the patients the PVC occurrence could be adequately described by a locally stationary renewal process, and in particular, statistical consistency with a Poisson process was demonstrated in 52% of the cases. Adopting the Poisson process as a pertinent model, an algorithm for a statistically efficient test enabling the on-line detection of PVC rate changes was developed. The resulting detection procedure performed without significant loss of efficiency for the much wider class of patients for which the data could be summarized by a nonspecific renewal process. Hence, for the majority of patients, the PVC occurrence may be viewed as a locally stationary renewal process for which the Poisson model provides a satisfactory test scheme to detect changes of the average rate. As a result, the PVC data may be reduced by partitioning into segments of constant rate, enabling the display or possible warning of dangerous trends. (Supported by HEW grant HS-01449.)

VASOACTIVE INTESTINAL PEPTIDE (VIP) INHIBITS CHOLECYSTOKININ STIMULATED GALLBLADDER CONTRACTILITY. J. Ryan and S. Cohen., Dept. of Physiology, Temple Univ. Sch. of Med., 3420 N. Broad St., Phila., Pa. 19140 and Dept. of Medicine, University of PA, Phila., Pa. 19104.

We have recently suggested that the regulation of gallbladder motor function and pressure generation depends upon both the interaction of cholecystokinin (CCK) with gastrin and secretin and the intraluminal volume of the gallbladder (FED. PROC. 34 (3):422, 1975). In an attempt to extend this concept, we examined the effects of continous intravenous infusion of Vasoactive Intestinal Peptide (VIP) on the pressure-volume response of the oppossum gallbladder. Each gallbladder was cannulated via the cystic duct with a saline filled catheter and connected to a pressure transducer. The transducer monitored bladder pressure as intraluminal volume was increased by the continuous infusion of saline at 0.38 cc/min for 10 minutes. As expected, when compared to control values, CCK (2.0 μg/kg/hr) significantly increased the maximal pressure recorded from the bladder upon completion of filling. On the other hand, VIP (1.0, 2.0 and 4.0 μg/kg/hr) had no effect on the pressure-volume response of the gallbladder. Similarly, VIP at 1.0 μg/kg/hr, when infused simultaneously with CCK (2.0 μg/kg/hr), had no effect on the increased pressure response. However, VIP at 2 and 4.0 μg/kg/hr produced a dose-related inhibition of the CCK stimulated pressure-volume response We feel this finding adds further strength to our proposal that gallbladder contractility is regulated via G.I. hormone interaction rather than soley in response to CCK.

ELECTROIMMUNOASSAY OF SERUM ALPHA-2-OPSONIC PROTEIN AS AN INDEX OF RETICULOENDOTHELIAL CLEARANCE: RE FAILURE AND TRAUMATIC SHOCK. Thomas M. Saba, Frank Blumenstock*, Peter Weber* and John E. Kaplan*, Departments of Physiology and Biochemistry, Albany Medical College, Albany, New York 12208.

Reticuloendothelial (RE) involvement in survival following shock has been well-documented (Circ. Shock 2:91,1975) and speculated to be due to clearance of blood-borne toxic and damaged cellular debris. RE failure following shock is, in part, mediated by a humoral opsonic deficiency, i.e., a depletion of an RE stimulatory alpha-2-globulin (α_2-RE glycoprotein) as detected by bioassay. The present investigation resulted in the isolation and characterization of this protein from rats and development of an immunoassay (rocket electroimmunoassay) with monospecific antiserum for its quantification. The protein was isolated by a combination of ammonium sulfate fractionation, free flow electrophoresis, and gel filtration with purity tested by gradient gel electrophoresis and immunoelectrophoresis. The isolated protein is thermolabile at 60°C and dependent on heparin. It has a molecular weight of 800,000 daltons at 4°C and 400,000 at 37°C. Reduction of the protein yields a polypeptide of approximately 200,000 daltons. The protein will stimulate hepatic RES clearance of particulate matter and antiserum to the glycoprotein will inhibit RE phagocytosis and decrease resistance to traumatic shock. Serum concentration correlates (r=0.98) with RE capacity and the assay can detect dynamic disturbances following shock. The data document a relationship between serum levels of α_2-RE glycoprotein and Kupffer cell function. This electroimmunoassay can provide a sensitive index of RE function. The findings emphasize the role of systemic defense as mediated by this opsonic protein in the homeostatic response to shock (GM-21447, CA-16011, T32-GM07033).

ENDOCRINE AND PATHOLOGICAL EFFECTS OF SIMULATED-SUBWAY STRESS (SSS) IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). A.M.Sackler*, A.S. Weltman, L. Johnson*, S.C. Sommers*, R. Garcia*, Lab. Therapeutic Res., B'klyn. Col. Pharm., B'klyn, N.Y. 11216 and Lenox Hill Hosp., N.Y.,N.Y. 10021

Effects of environmental SSS on male SHR consisting of tape recordings of train noises ranging from 68-112db, horizontal vibration with an ampl. of 2½" and a freq. of 150 cpm & crowding were noted after 8,16 & 53 wks of stress on test vs control groups. The test SHR were exposed twice daily for 1 hr at 9:00 AM & 3:30 PM during weekdays. During the studies & at sacrifice, all 3 test groups, in general, showed patterns of decreases in body wts & wt gains, signif. increases in rel. adrenal wts, signif. thymic involution & increased heart wts compared to control SHR. In the 53 wk study, testes wts and sizes were signif. decreased. Signif. elevations in peripheral plasma corticosterone due to SSS were only noted in test SHR sacrificed ½-1½ hrs after stress (16 wk study). Histological evaluations in the 53 wk study showed pathological changes usually noted in the SHR. In accord with organ wt changes due to SSS, test SHR showed signif. and/or marked increases in myocardial hypertrophy and sclerotic vascular changes. In accord with adrenal hypertrophy, test rats showed signif. smaller islets of Langerhans and thymic atrophy. In the testes, an approx. doubling was noted in the freq. of periarteritis nodosa in the blood vessels of the test vs control SHR (9.2% vs 5.3%). Test rats showing decreases in testes wts displayed evidence of atrophy in the seminiferous tubules & decreased spermatogenesis. The present findings indicate that in the SHR, acute and chronic exposure to SSS caused significant adrenal hypertrophy and augmented hypertensive pathologies.

REESTABLISHMENT OF RHYTHMIC RESPIRATION IN DECEREBRATE CATS HAVING BILATERAL PNEUMOTAXIC CENTER LESIONS AND SECTIONED VAGI.
W.M. St. John and S.C. Wang. Dept. of Pharmacology, College of Physicians and Surgeons, Columbia Univ., New York, N.Y. 10032

In decerebrate animals, bilateral pneumotaxic center lesions and bilateral vagal section result in apneusis, characterized by marked increases in tidal volume (V_T) and inspiratory duration (T_I). Any one of the following lesions greatly decreased V_T and T_I and reestablished a rhythmic respiratory pattern: midline lesions at the pontomedullary junction, bilateral lesions in the lateral reticular formation of the caudal pons, or rostral medullary lesions encroaching upon the rostral extremes of the dorsal or ventral respiratory nuclei. In cats having bilateral pneumotaxic center lesions, prior lesions within these sites prevented the development of apneusis upon vagal section. Large lesions in the rostral pons were ineffective in preventing or altering apneusis. Subsequent to the reestablishment of rhythmic respiration, no frequency elevation was obtained in response to hypercapnia; hypercapnia-induced tidal volumes approximated those of pneumotaxic lesioned animals. Qualitatively comparable changes in T_I, in terms of phrenic nerve discharge, were obtained following these caudal pontile or medullary lesions in decerebrate, paralyzed and ventilated cats; however, large rostral pontile lesions resulted in a shortening of T_I. These results imply that apneusis is not simply a quantitative phenomenon dependent upon the relative number of certain respiratory neurons but may reflect a synchronization of brainstem controller discharge. These data further suggest that, in addition to the pneumotaxic center and the vagal nerves, another mechanism within the brainstem controller promotes phase-switching of the respiratory cycle. (Supported by Grants HL 18009 and NS 00031, N.I.H.)

NON-INVASIVE MONITORING OF THE HEAD INJURY PATIENT. A. Sances, Jr., S. J. Larson* and J. J. Ackmann*, Department of Neurosurgery, The Medical College of Wisconsin, Milwaukee, Wisconsin 53226

Many of the critical descriptors in the head injury patient are late indicators of adverse clinical changes. The physiologic evaluation of the patient with trauma depends greatly upon clinical assessment and intrusive techniques. An automated computerized system has been developed to monitor various physiologic parameters in the head injury patient. In over 50 patients we have recorded on-line somatosensory evoked potentials, transcranial impedance, EEG and transthoracic impedance. A nuclear magnetic resonance blood flowmeter has also been developed which is capable of measuring limb flow. In patients with volume occupying lesions, the somatosensory evoked potential changes preceded clinical signs by more than 24 hours. Changes in EEG were observed 20 hours prior to clinical detection. Transthoracic impedance has been useful in the detection of pulmonary edema. Marked changes in cerebral impedance are observed in patients with tumors. The routine clinical methods are compared with the non-invasive techniques.

REVERSAL OF THIOCYANATE INHIBITION OF H^+ SECRETION IN FROG GASTRIC MUCOSA BY IMIDAZOLE. S. S. Sanders, J. A. Pirkle,* R. L. Shoemaker, and W. S. Rehm. Dept. of Physiology & Biophysics, University of Alabama in Birmingham, Birmingham, AL 35294

Thiocyanate (SCN) (10-15 mM) added to either nutrient (N) or secretory (S) side of in vitro frog gastric mucosa in Cl^- media (100% O_2 S — 95% O_2 — 5% CO_2 N) markedly reduces H^+ secretion, often to zero and increases the potential difference (PD) and resistance (R). These effects occur regardless of whether pH of (S) is 4.5 or 8.0 and are readily reversible upon removal of SCN. We have previously reported that imidazole (20 mM) in N decreases measured H^+ rate with pH 4.5 (S) but that normal H^+ rates are obtained if pH (S) is raised to 8.0 and concluded that the apparent H^+ decrease at pH 4.5 (S) is due to neutralizing action of imidazole. In present work we find that imidazole reverses SCN inhibition of H^+ secretion. At pH 8.0 (S) with imidazole (20 mM) in N, the SCN effect on H^+ rate, PD and R is attenuated. When SCN (15 mM) was added to S first, its usual effects were seen with H^+ rate greatly reduced. Subsequent addition of imidazole (20 mM) to N (SCN still present in S) restored H^+ rate to near control or above it. In Cl^--free media ($SO_4^=$ and sucrose, or isethionate for Cl^-) [95% O_2 — 5% CO_2 on both sides, pH 4.5 (S)] the PD is reversed (N is negative) and H^+ secretion ≈ 30% of that in Cl^-. Addition of SCN (15 mM) to S abolishes H^+ rate and PD goes to about zero and then the addition of imidazole (10 mM) to N results in a rapid return of PD to its negative value. Imidazole (10 mM) to N in Cl^--free media has little effect on PD and subsequent addition of SCN to S (imidazole still in N) then has little effect on the negative PD. (NIH and NSF support)

STRESS-INDUCED ALTERATIONS IN CORONARY ARTERY BLOOD FLOW IN MINIPIGS. T.M.Sanders, F.C.White*, T.Peterson*, J.F.Andres*, C.M.Bloor, Department of Pathology, School of Medicine, UC San Diego, La Jolla, Calif. 92093.

We studied the characteristics of left circumflex coronary artery blood flow (CBF) in Yucatan minipigs simultaneously with electromagnetic flow probes and tracer microspheres. Determined by flow probe, stroke systolic/diastolic flow ratios (SS/SD) varied from 0.2-0.4 at rest. Sustained subtotal occlusion (SO) or adenosine infusion (AI) at rest caused abrupt and significant systolic shift in CBF, increasing the SS/SD significantly, often to 1.75. The shift was not caused solely by reduced contractility, as reflected by aortic dF/dT, shortened diastolic filling time, or a change in aortic perfusion pressure. Heavy exercise (HE), requiring 75-90% of maximum heart rate, also increased the SS/SD ratio, to 0.7-0.8. HE reduced systolic time about 30-35% and diastolic time about 60-70%. SO or AI during HE further increased the SS/SD ratio above HE values. Transmural myocardial blood flow (MBF) was determined with tracer microspheres at HE, HE+SO or HE+AI. Endo/epicardial MBF ratios at HE remained greater than 1.2. During HE+SO, endo/epi MBF dropped to 0.5-0.7. This reduction was due primarily to decreased endocardial flow,and a systolic shift occurred. HE+AI increased both endo and epicardial MBF and the SS/SD ratio. With AI epicardial MBF tended to increase more than endocardial MBF. Our data suggest (1) the endocardium is preferentially perfused during rest and HE; (2) the reduction in endocardial MBF is in concert with a reduced diastolic CBF during subtotal occlusion; and (3) adenosine infusion increases both endocardial and epicardial MBF, but preferentially to the epicardium, and increases both diastolic and systolic CBF, but preferentially systolic. Thus, the systolic shift observed during subtotal occlusion may preferentially perfuse the epicardium, and the reduced diastolic flow may cause decreased endocardial flow. (Supported by the San Diego County Heart Association.) ASZ(DCPB)

EFFECTS OF TSH, CYCLIC AMP AND THEOPHYLLINE UPON IN VITRO THYROID ACTIVITY OF AGING RATS. J. L. Sartin*, J. F. Pritchett and D. N. Marple*, Depts. Zoology-Entomology and Animal Science, Auburn University, Auburn, AL. 36830

This investigation was conducted to assess indices of thyroid activity in young and mature (60 and 340 days of age respectively) male rats. Thyroid accumulation of 3',5' cyclic adenosine monophosphate (cyclic AMP) after in vitro exposure (30 min) to thyroid stimulating hormone (TSH) (100 mU/ml), theophylline (10 mM), or a combination thereof was determined by radioimmunoassay. Additionally, secretion rates of triiodothyronine (T-3) and thyroxine (T-4) were assessed by radioimmunoassay of incubation media following exposure of thyroid lobes to TSH (100 mU/ml) or cyclic AMP (30 mM) for 120 min. Plasma levels of T-3 and T-4 at the time of sacrifice were also determined. Mature animals exhibited significantly lower plasma T-3 and T-4 levels but slightly elevated in vitro secretory rates of T-3 and T-4. TSH stimulation enhanced cyclic AMP accumulation and thyroid hormone release in the young but not in the mature group. However, cyclic AMP significantly elevated in vitro thyroid hormone release in both age groups. The data suggest an age-related alteration in the thyroidal adenylate cyclase-cyclic AMP-phosphodiesterase system. Additionally, since cyclic AMP treatment appeared to induce greater increases in T-3 than in T-4, the data indicate a possible role of this nucleotide in the conversion of T-4 to T-3.

PERIBRONCHIAL PRESSURE IN ISOLATED DOG LUNG. H. Sasaki* & F.G. Hoppin, Jr. Dept of Physiol, Harvard School of Public Health, Boston, MA 02115.

Pressure surrounding large airways, Px, is not securely known and can be expected to change with lung vol, intrabronchial pressure, and airway muscle tone. In lobes from 6 dogs, we inferred Px from the difference between intrabronchial pressures in a segment of intrapulmonary airway at the same dimensions and dimension history before and after dissection from the lung. With the segment isolated by beads (Takishima et al, JAP 38:875), we could control segment and lung dimensions separately; first (Fig 1) we studied Px as bronchial diameter, Dbr, was changed at constant P(L). Then (Fig 2) we studied Px during deflation with the airway constricted (C) or relaxed (R) (using Dbr for C and R determined by radiograph in these and other lobes after airway lavage with constrictor or dilator).

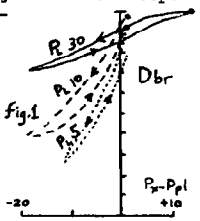

fig.1

When Dbr was varied at constant P(L) (Fig 1), Px showed static hysteresis (about twice that shown by the dissected airway). The overall slope was roughly .7 to .3x that predicted by Mead et al (JAP 28:596). Abolishing tone widened airways only slightly but increasing tone narrowed airways up to 60%: corresponding Px are shown in Fig 2 relative to Ppl. In the relaxed state (control was nearly similar) Px was near Ppl except at high V(L). The difference between C and R represents smooth muscle tone. With constriction, Px was lower than Ppl; at P(L)30, in the example shown, Px was 56 below Palv or Pbr! Although this high degree of interdependence stabilizes airway diameter, it may also promote entry of fluid or gas into the interstitial space. (Supported by NIH Grant HL 14580.)

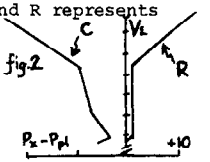

fig.2

ASZ(DCPB)

METABOLIC ADAPTATION OF PALAEMONETES PUGIO LARVAL STAGES CULTURED AT CONSTANT AND CYCLIC TEMPERATURE REGIMES. A. N. Sastry and John P. Laczak*, Graduate School of Oceanography, University of Rhode Island, Kingston, R.I. 02881

Metabolic compensation to temperature has been demonstrated in a variety of adult ectothermic organisms. This phenomenon may occur instantaneously, or with acclimation or over the evolutionary time scale. In contrast, capacities for metabolic adaptation in developing larval stages of benthic invertebrates have been examined in only a few instances. Both interspecific and interstage variation in temperature ranges for metabolic compensation have been observed in larval stages of two sublittoral brachyuran crabs, Cancer irroratus and C. borealis cultured at optimum constant temperatures for their survival. Culture of C. irroratus larval stages at a favorable daily cyclic temperature regime altered the temperature range for metabolic compensation and shifted the resistance zone to higher temperatures compared to that of larvae cultured at constant temperature. Pelagic larval stages of an estuarine shrimp, Palaemonetes pugio, cultured at daily cyclic and constant temperatures, showed both inter and intrastage variation in their metabolic responses to temperature, but interstage variation between the two culture conditions had no consistant or predictable pattern. Culture at cyclic temperatures enhanced the respiration rate in some stages and reduced the rate in other stages. These differences in metabolic responses of P. pugio larvae from the two culture conditions were not consistant as observed with Cancer. Thus, although metabolic temperature adaptation of larval stages may be altered by culture conditions, the manner in which these phenotypic changes are expressed appear to differ with the species and habitat. (Supported by Grant R800981 from EPA)

BMES

DEPOSITION OF A CHARGED AEROSOL IN A STRAIGHT TUBE, B.J. Savilonis, S.E. Fu* and J.S. Lee. Div. of Biomedical Engineering, Univ. of Virginia, Charlottesville, Va. 22901

An analytical model has been developed to establish the mechanisms affecting the deposition of charged particles on a tube wall. The theory is used to analyze the experimental results of charged aerosol flowing through a variety of long straight tubes, as well as through an excised dog trachea. It was found experimentally that the fraction of aerosol deposited onto conducting tubes such as steel or trachea is much smaller than for an insulating tube. Analytical results indicate that the charge concentration down a conducting tube should roughly vary as $C/CO = 1/(BSz' + 1)$ where C/CO is the ratio of the local to the entrance aerosol concentration, z' is the distance down the tube normalized with the tube radius, S is the Stokes number, and B is a parameter indicating the ratio of electrical to inertial forces. This distribution agrees well with experimental measurements. Experiments with an insulating tube yield time-dependent concentration profiles. As charged particles deposited on the vessel wall collect, an additional electrical field is developed which markedly increases aerosol deposition. It is concluded that for charged aerosol flow in straight pulmonary airways deposition is mainly due to the interaction among charged particles; charge deposition on the vessel walls does not influence particle behavior.

(Supported in part by grant HL-16812 from NHLI.)

ASZ(DCPB)

PROLINE AND THE HYPERPLASTIC RESPONSE IN FASCIOLIASIS. Terry Sawma*, David Reino* and Hader Isseroff, Biology Dept. SUNY College at Buffalo, Buffalo, N.Y. 14222

Fasciola hepatica, is a large flatworm parasitizing the main bile duct of ruminants and occasionally man. In fascioliasis an enormous hyperplasia of the bile duct occurs resulting in its enlargement to over 20X normal. Histologically, the hyperplasia of the duct becomes evident while the worms are still migrating through the liver parenchyma and makes possible their eventual entry and establishment in the main duct. Earlier studies had shown that free proline occurs in the bile fluid of infected animals at levels 10,000X normal. The increase of proline in the bile correlated well with the onset of bile duct hyperplasia. Furthermore, Fasciola had been shown to be the source of the proline. These and related studies suggested that the worm might induce the enlargement of the bile duct through the release of proline. The present investigation was undertaken to test this hypothesis. Male Wistar rats were infused with one of the three treatment infusates: 20.0 mM proline in physiological saline; a mixed amino acid infusion of alanine, valine, methionine, leusine, tyrosine, phenylalanine, and histidine all at 2.0 mM in physiological saline; and a physiological saline infusion. Infusion pathways were via flow rated tubing and "T" cannulae, constructed of Polyethylene-50, surgically implanted into the abdominal cavity. All animals were sacrificed after 7-14 days of infusion, blood samples drawn, and bile ducts excised, fixed and prepared histologically. Histologic comparison of bile duct tissue between treatments indicate that proline can cause a significant hyperplasia of the bile duct endothelium mimicking that observed in fascioliasis.

(Supported in part by grant AI-0991 from the NIH)

AN EXPERIMENTAL STUDY OF DIFFERENT FACTORS INFLUENCING THE ELECTROPHORETIC MOBILITY (EM) OF HUMAN LYMPHOCYTES. P. N. Sawyer, D. Venkataraman*, W. W. Wrezlewicz*, and N. Ramasamy*. Electrochemical and Biophysics Laboratory, Department of Surgery, S.U.N.Y., Downstate Medical Center, Brooklyn, New York 11203.

Electrophoretic mobility (EM) of charged particles and cells in an electric field depends on the net charge density on the surface. Determination of this property under various experimental conditions yields information about the effects of chemical, enzymatic and antibody reactions on the surface charge characteristics of the cells. The present communication reports the effect of storage time, mercurial inhibitor, compatibility of blood group, and autologous and cytotoxic sera on the EM of lymphocytes using Seaman's electrophoretic apparatus. The EM increases with storage time after an initial period indicating probable deterioration of cells with time. Toxicity of mercurial inhibitors is indicated by an increase in EM of lymphocytes treated with mercuric chloride. EM of the mixture of lymphocytes from ABO incompatible pairs shows a marked increase, whereas for the compatible groups a significant decrease is observed. Autologous serum does not alter the EM of lymphocytes to any significant degree; but cytotoxic serum increases the EM. The toxic influence of cytotoxic serum on lymphocytes is further confirmed when heat inactivated complement-cytotoxic serum does not significantly alter the EM of lymphocytes. These studies demonstrate that EM can be used to discriminate between normal and abnormal lymphocytes. Prediction of histo-compatibility seems possible. Therefore, further extensive studies have been completed using histo-compatible and histo-incompatible rats as well as humans undergoing kidney transplantation. The EM data has been compared to conventional MLC & HLA data.

SODIUM FLUXES IN RAT LIVER SLICES IN HEMORRHAGIC SHOCK. M.M. Sayeed, J.P. Connors,* and B.J. Henton,* Dept. of Surgery, Washington University School of Medicine and The Jewish Hospital of St. Louis, St. Louis, Missouri 63110.

Unidirectional fluxes of ^{24}Na were measured in liver slices from rats subjected to hemorrhagic shock. Animals were bled to a mean arterial pressure of 40 mm Hg and maintained at this pressure by returning 30% of shed blood over a period of 1-1½ hrs. Remaining blood was then reinfused rapidly and one-half hour later animals were sacrificed. 0.3-0.5 mm thick liver slices from control or shock animals were incubated at 0.5 C for 90 minutes in a Krebs-Ringer bicarbonate medium (KRB) containing a trace amount of ^{24}Na and with or without 1 mM ouabain. Cold incubation caused elevation of liver slice sodium. Sodium-rich liver slices were then incubated at 37 C in an isotope-free KRB with or without ouabain. In some experiments the isotope-free medium was modified by replacing 85% of Na^+ (118 mmoles) by either choline or lithium. Slices were removed after various time intervals at 37 C and their radioactivity determined. An initial rapid loss of ^{24}Na from slices occurring at about the same rate in all experiments probably represented loss of isotope from the extracellular space. This was followed by a slower loss of ^{24}Na, representing efflux from the cellular space. The rate of efflux, measured as Δ log cpm/0.5 hr, in liver slices from shocked animals was about one-half of that found in controls. Addition of ouabain decreased efflux in control but not shocked animal liver slices. Replacement of medium sodium had no effect on control efflux but significantly decreased ^{24}Na efflux by liver slices of shocked animals. These results suggest that ^{24}Na efflux in shocked animal liver slices was due to an ouabain-insensitive Na-Na exchange diffusion and was not related to ouabain-sensitive Na-K exchange.

PULSATILE PRESSURE-FLOW DYNAMICS IN RESTING SKELETAL MUSCLE. R. W. Scearce, Jr.* and L. R. Yonce, Research Triangle Institute, Research Triangle Park, N.C. 27709 and Physiology Dept., UNC Medical School, Chapel Hill, N.C. 27514.

Various sine-wave pulse pressures and mean perfusion pressures applied to the isolated denervated gracilis muscle of a dog produced a vasoconstrictor response if mean perfusion pressure was 100 mmHg with pulse pressure amplitudes of 20 and 40 mmHg, and if mean perfusion pressure was 125 mmHg with pulse pressure amplitudes of 20,40 and 60 mmHg. A vasodilator response was seen at all other mean perfusion pressures (50,75,100 mmHg) and pulse pressure amplitudes (80, 100 mmHg). In vascular beds exhibiting no reactive hyperemia, resistance was low and the vasoconstrictor response continued at all mean perfusion pressures and pulse pressure amplitudes. The vasoconstrictor response to a particular pulse pressure amplitude produces a nearly identical percent change from zero pulsation flow at all mean perfusion pressures. The vasodilator response overwhelms the vasoconstrictor response at a critical combination of vascular tone, mean flow, and mean perfusion pressure. In a plot of the vascular resistance versus the pulse pressure amplitude, the resistance values coinciding with the appearance of vasodilation approximate a straight line. Myogenic response to high mean perfusion pressures causes the vasodilator response to appear at lower pulse pressure amplitudes. If the mean pressure is high enough, the vasoconstrictor response disappears. The vasodilator response appears to be caused by the vascular smooth muscle's greater demand for oxygen produced by the increased vascular tone that has resulted from the vessel's myogenic response to increased mean perfusion pressure and pulse pressure amplitude.

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ACID BASE REGULATION AND BONE BUFFERING IN CHRONIC HYPERCAPNIA

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Animal and human experiments with prolonged exposure to CO_2 have demonstrated that the time of adaptation as determined by partial compensation of respiratory acidosis increases with lower CO_2 concentrations suggesting that acid base regulations in chronic hypercapnia are dominated by fast acting mechanisms (kidney) at higher CO_2 concentrations and slow acting mechanisms (bone CO_2 storage) at lower CO_2 concentrations. Guinea pigs exposed for 4 weeks to 1% CO_2 showed a consistent increase of 2-3mm Hg P CO_2. Blood bicarbonate did not change indicating that the well known renal response to higher CO_2 concentrations was not operating. Bone CO_2 increased during prolonged exposure to 1% CO_2, bone Ca and bone H_2O decreased; bone K and Mg increased. A similar pattern of bone electrolyte exchange in connection with CO_2 uptake in the bone was observed during exposure to 15% CO_2 in rats and guinea pigs. Time course of intracellular ph and electrolyte changes in bone during chronic hypercapnia will be discussed.

CONVECTIVE MIXING IN THE BRONCHIAL AIRWAYS

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It has recently been shown experimentally (Scherer et al, J. Appl. Phys. 38:4, 719, 1975) that the mixing of gases in the upper, larger branches of the human bronchial tree is 3 orders of magnitude larger than would be expected on the basis of molecular diffusion alone. An effective longitudinal dispersion coefficient, D, was measured which was noted to be larger for inspiratory flow than for expiratory flow by a factor of approximately 3. It was postulated that the mixing for large Péclet numbers was mostly due to convection and that the difference between inspiration and expiration could be explained by the difference in velocity profiles observed experimentally at bronchial bifurcations. (Schroter, R.C. and M.F. Sudlow, Rev. Physiol. 7, 341, 1969)

In this paper it is shown that if one considers gas convection alone as the mixing process in a tube of the upper airways, the transport equation becomes $\partial c/\partial t + u \cdot \nabla c = 0$ and the second moment, σ^2, of an injected tracer concentration profile averaged over the tube cross-section is related to the steady velocity distribution across the tube by the equation $\sigma^2 = [\overline{u^2} - (\overline{u})^2]t^2$ where $u(r,\theta)$ is the steady axial velocity distribution across the tube. $\overline{u^2}$ and $(\overline{u})^2$ represent the mean of the square and the square of the mean axial velocity profiles respectively averaged over the tube cross section. From the above relation for σ^2, the difference in the experimental dispersion coefficients for inspiration and expiration is explained by the difference in axial velocity distributions across the tubes for the two breathing modes. Although only crude analytical estimates of the axial velocity distributions in tube bifurcations are available (Scherer, P.W., J. Biomech. 5, 223, 1972), use of these in the equation to calculate σ^2 gives reasonably good agreement with the experimentally measured dispersion coefficients mentioned above.

HIGH FREQUENCY EVENTS IN THE ELECTROCARDIOGRAM FOLLOWING BLUNT CLOSED-CHEST TRAUMA IN RABBITS. T.D. Schick*, H. van der Zee*, S. Powers*, and W. McCafferty*, (SPON: L. Grumbach), Departments of Physiology and Surgery, Albany Medical College, Albany, N.Y. 12208.

Previous studies have demonstrated that high frequency events occur in the ECG following myocardial infarction. The present study was conducted to determine if myocardial contusive lesions produced by blunt closed-chest trauma result in high frequency events in the ECG. Rabbits (3-6 kg) were initially anesthetized with sodium pentobarbital (50mg/kg), intubated and maintained on a free-flow mixture of nitrous oxide (70%) and oxygen (30%) while breathing spontaneously. Trauma was delivered to the sternal area at the level of the fourth intercostal space by dropping a cylindrical brass weight from a known height through a plexiglass tube. The average trauma was 1.75 Joules/kg. ECG limb leads I,II, and III were recorded on a Grass polygraph and a Hewlett-Packard wide band FM tape recorder. Posttrauma recordings played back on a storage oscilliscope revealed marked high frequency notching and slurring especially along the R-wave. Of the rabbits autopsied, all exhibited anterior myocardial contusive lesions and most demonstrated increases in serum myocardial creatine phosphokinase (MB-CPK). In one chronic study notching and slurring in the QRS complex became more pronounced daily from day 1 to day 10. Power spectrum analysis of the high frequency electrocardiograms (HF-ECG) is underway. These studies have disclosed that high frequency events in the form of notching and slurring appear following blunt closed-chest trauma associated with contusive lesions of the myocardium. In preliminary investigations, two of three animals tested had high frequency events which persisted while the standard ECG record appeared normal. (T32-GM07033 and GM-15426)

TISSUE OXYGEN CONCENTRATION TRANSIENTS DURING FLOW AUTOREGULATION: POSSIBLE EVIDENCE FOR CAPILLARY DENSITY CHANGE. Roy W. Schubert*, W.J. Whalen and P. Nair*, St. Vincent Charity Hospital, Cleveland, Ohio 44115.

We have observed the behavior of tissue O_2 concentration during a change in perfusion pressure with our 2-3μ tip O_2 electrode inserted approximately 1-2 mm into the left ventricular free wall of a paced, isovolumic cat heart. In this autoregulating preparation the transient tissue O_2 resembled the flow transient in that there was an overshoot followed by a return towards control. However, while the steady-state flow always increased above control (8 ± 3% [SD]) with increased perfusion pressure (35%), the steady-state before and after tissue O_2 decreased (steady-state) when perfusion pressure was increased. This observation could be due to spatial movement of the O_2 electrode since perfusion pressure can alter the dimensions of the myocardium. However, a specially designed electrode suspension minimized this possibility. Additionally, the cardiac action potential was monitored, and those records which showed a change in action potential character during perfusion pressure change (position change) were eliminated from the data base. Another possible explanation for the observation is that capillary density underwent active adjustment during changes in perfusion pressure in this modified Krebs-Hensleit perfused, isolated heart. In contrast, the non-autoregulating group of hearts displayed flow and tissue PO_2 transients that always varied directly with perfusion pressure, possibly reflecting a lack of intrinsic microvascular control. Supported by HL 11906 from the USPHS.

ASZ(DCPB)

THE INSECT GOBLET CELL CAVITY MATRIX: ITS POSSIBLE ROLE IN MAINTAINING THE TRANSPORT CAPACITY OF THE LARVAL HORNWORM MIDGUT, Manduca sexta. T. Wayne Schultz and Arthur M. Jungreis. Dept. of Zoology, University of Tennessee, Knoxville, Tennessee 37916

The midgut epithelium of larval Lepidoptera is composed of two cell types: goblet and columnar. The high rate of K^+ transport characteristic of the larval midgut is thought to result from active transport via the goblet cells. When K^+ transport is measured in vitro, the midgut exhibits a characteristic decay profile not present in vivo. The cause of the decay is unknown. We have obtained evidence for the presence of a matrix plug within the cavity of the goblet cells of the larval hornworm midgut. While the composition of the matrix plus is unknown, it contains little muccopolysaccharide as evidenced by a failure of the goblet cells to selectively incorporate N-Acetyl-Galactosamine. Extrusion of these plugs is stimulated by stretching. In response to stretching, columnar cells lost contact with adjacent goblet cells at their apical-lateral borders with resultant reduction in electrical coupling. A model is presented to account for the in vitro cation transport decay profile characteristic of the midgut epithelium. In this model, the loss of matrix material is hypothesized to be directly related to the in vitro loss of cation transport capacity exhibited by this tissue. The loss of matrix material is also associated with separation of the apical-lateral membrane interactions between goblet and columnar cells. Supported by NSF Grant #PCM75-23456 and Biomedical Science Support Grant #07088.

BMES

LINEAR AND NONLINEAR BEHAVIOR OF ELECTRODE POLARIZATION: A TIME DOMAIN ANALYSIS. H. P. Schwan and B. Onaral *. Dept. of Bioengineering, University of Pennsylvania, Phila., PA 19174

Electrode polarization is characterized in the frequency domain by a polarization capacitance Cp in series with a polarization resistance R_p. Fricke's law states that the capacitance and resistance change as power functions of frequency $C_p \sim f^{-m}$ and $R_p \sim f^{-n}$ with the loss tangent $\tan \delta = R_p 2\pi f C_p$ where $\delta = m\pi/2$. Extensive measurements have shown that m changes somewhat with frequency but the rule $\delta = m\pi/2$ still applies. The limit of linearity of the polarization impedance is frequency dependant (Schwan, 66, 68) with the limit current density given by $j_\ell = j_o f^{1-m}$ (Schwan, 66, 68, Geddes 71).

This paper extends these concepts into the time domain. The linear response of the electrode boundary potential to a current step is of the form $V = i(at + bt^a)$ if the electrode boundary region is modeled as a Warburg element in series with a blocking capacitor. More generally the boundary potential $V = iAt^m$, which is the time domain equivalent of the Fricke's law with m slowly varying in time. The nonlinearity is enforced by the fact that the steady state boundary potential is a weak function of current density and is approached as time proceeds. The time domain equivalent of the frequency limit law of linearity is formulated as $j_\ell = j_o t^{-m}$ (limit current of linearity as a function of pulse duration) or as $t_\ell = t_o j^m$ (limit time of linearity). Experimental evidence supports these relationships.

THE ANALYTIC STRUCTURE OF THE RETINOTOPIC MAPPING OF THE STRIATE CORTEX. Eric L. Schwartz* Brain Research Laboratories, New York Medical College, 105 St. and Madison Ave., New York, 10029, N.Y.(Spon: E. Roy John)

The retinotopic mapping of the striate cortex is characterized as a (conformal) mapping of the visual field onto the cortical surface under the complex logarithm function. This summarizes in a concise way the curve of cortical magnification, the scaling of receptive field size with eccentricity, and the mapping of global visual field landmarks (meridians, octants, circles of constant eccentricity). The natural size invariance properties of the complex logarithm function is suggested as a possible basis for psychological size invariance in visual perception. The local functional architecture (hypercolumn structure) of area 17 is discussed in the light of the global retinotopic structure. It is suggested that the local (hypercolumn) intracortical projection of cortical afferents to simple cells is a recapitulation of the global retino-striate projection. The cortical mosaic is thus a concatenated logarithmic structure; the developmental consequences of this analysis are briefly discussed.

INCREASED SENSITIVITY OF STREPTOZOTOCIN-TREATED DOGS TO THE DIABETOGENIC EFFECT OF GROWTH HORMONE(GH). Jessica Schwartz*and Norman Altszuler. Dept. Pharmacology, NYU Med. Ctr., NY, NY 10016

GH-diabetes is characterized by high plasma insulin levels and marked insulin resistance. To investigate the influence of GH on insulin secretion and on insulin sensitivity in the development of diabetes, low doses of GH were given to normal dogs before and after treatment with Streptozotocin (Stz), which has been used to produce graded degrees of insulin deficiency. A regimen of GH alone (1 mg/kg per day) for 3 weeks did not produce diabetes, but induced resistance to injected insulin (0.1 U/kg). Postabsorptive plasma glucose rose moderately and persisted despite a 3-fold increase in plasma insulin. Glucose tolerance was impaired despite enhanced insulin secretion in response to iv glucose (150 mg/kg) or to iv tolbutamide (5 mg/kg). A subdiabetic dose of Stz (15 mg/kg) did not alter insulin sensitivity, but blunted insulin secretion in response to glucose or tolbutamide. Administration of GH 2-3 weeks after Stz could then induce diabetes with fasting plasma glucose above 200 mg/100 ml and glucosuria. Nevertheless, plasma insulin rose to levels comparable to those in GH-treated animals before Stz, suggesting diminished effectiveness of insulin. Insulin secretion in response to glucose or tolbutamide was not as great as with GH alone. While Stz produced variable degrees of impairment in glucose tolerance, susceptibility to the diabetogenic action of GH appeared to correlate with severity of response to Stz. These observations indicate that Stz-primed prediabetic animals may become hypersensitive to diabetogenic actions of GH, and suggest that diminished effectiveness of insulin and inability to augment insulin secretion are involved.

Q-T INTERVAL PROLONGATION AS PREDICTOR OF SUDDEN DEATH IN PATIENTS WITH MYOCARDIAL INFARCTION

P. J. Schwartz, M.D., and S. Wolf, M.D., Cardiovasc. Res. Inst., CNR, Univ. of Milan, Italy & Marine Biomed. Inst., UTMB, Galveston, Texas.

In an earlier study an imbalance in cardiac sympathetic innervation which prolongs the Q-T interval was shown to increase the arrhythmias associated with coronary artery occlusion and to lower the ventricular fibrillation threshold. The present study focuses on whether or not a prolonged $Q\text{-}T_c$ (>440msec), irrespective of its many possible causes, is associated with sudden death (SD) in patients with myocardial infarction (MI).

53 patients with recent MI and 53 healthy controls, matched for age, sex, race, height, weight, education and job, had an electrocardiogram taken every 2 months for 8 years. 28 patients and 1 control had a sudden cardiac death. The $Q\text{-}T_c$ (mean of all values recorded) was found prolonged in 1 control (2%), 5 of 25 surviving patients (20%) and in 16 of 28 patients who had SD (57%). The difference between surviving and SD patients is significant ($p < 0.01$). It is interesting that the only control with a long Q-T is the one who died suddenly of MI. Among patients with previous MI a prolonged $Q\text{-}T_c$ constitutes a 5.33 times greater risk for SD.

It is concluded that a constant prolongation of $Q\text{-}T_c$ in patients with MI may help, with other risk factors, in defining a sub-group at higher risk for SD.

APICAL LUNG FUNCTION IN THE SUPINE POSTURE

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The apices of the human lungs are perfused in the supine but not in the upright posture. In order to examine apical function, two aspects of gas exchange have been measured in the supine posture in normal subjects and in patients with lung disease. (1) the pulmonary diffusing capacity for carbon monoxide and (2) regional distribution of inhaled and injected Xenon^{133} and regional differences in the washout of injected Xenon^{133}. The pulmonary diffusing capacity increased on moving from the upright to the supine posture in healthy subjects but not in certain patients with lung disease. The perfusion of injected Xenon^{133} in healthy subjects in the supine posture was greater at the apices than at the bases but inhaled Xenon^{133} and Xenon^{133} washout were evenly distributed. In patients breathing mainly with the diaphragm due to costovertebral ankylosis, inhaled Xenon^{133} was preferentially distributed to the bases and injected Xenon^{133} to the apices. In cigarette smokers and in patients with primary (non-bronchitic) emphysema, inhaled Xenon^{133} was preferentially distributed to the bases and the washout of Xenon^{133} was better at the bases than at the apices of the lungs. In emphysema, but not in the smokers, injected Xenon^{133} was also distributed mainly to the bases.

AN INCREASE OF ARTERIAL CONTRACTILE PROTEIN CONTENT WITH MATURATION AND HYPERTENSION.

C.L. SEIDEL and R.A. MURPHY, Depart. Cell Biophysics, Baylor, Houston, Texas 77025 and Depart. Physiol., U. of Virginia, Charlottesville, Va. 22901.

These experiments were designed to determine if an increase in arterial contractile protein content occurs with maturation or in association with hypertension. The media from rat thoracic aorta was isolated, weighed and DNA content was determined by the indole method. The contractile protein was extracted in a phosphate buffer containing 1% sodium dodecylsulfate (SDS). Aliquots of this extract were applied to 5% acrylamide-SDS gels. Similar gels were loaded with known amounts of purified skeletal actin and myosin (standard curve gels). After electrophoresis, all gels were stained with Coomassie blue, destained, and the density of the myosin heavy chain and actin bands determined. The amount of myosin plus actin (CP) in gels loaded with smooth muscle protein was calculated from the relationship between density and protein content of the standard curve gels. The total protein content of media increased from 126.5 mg/g at 4 wks of age (6 pooled media) to 258.6 $\pm$ 14 ($n = 6$; $P < 0.02$) at 16 weeks. The CP content increased from 3.64 mg/g at 4 wks to 9.57 $\pm$ 0.96 ($n = 6$; $0.10 > P > 0.05$) at 16 wks. The amount of CP/mg DNA increased from 0.9 mg/mg at 4 wks to 2.62 mg/mg at 16 wks. After eight weeks of 2-kidney renal hypertension, the CP content was 16.5 mg/g media. Age matched controls (16 wks) had 9.6 mg/g. These data suggest that the amount of CP/smooth muscle cell continues to increase up to 16 wks of age and that 8 wks of hypertension is associated with a stimulation of contractile protein synthesis.

(Supported by grants from the AHA, Texas and Virginia affiliates).

AORTIC BLOOD FLOW IN HIBERNATING AND HYPOTHERMIC WOODCHUCKS, MARMOTA MONAX. J.B. Senturia and C.M. Ferrario, Department of Biology and Health Sciences, Cleveland State University and Research Division, Cleveland Clinic Foundation, Cleveland, Ohio.

Electromagnetic blood flow transducers (Narco Biosystems "c" type 4.5 mm or 5.0 mm) were affixed to the root of the ascending aorta of adult woodchucks. Miniature radiotelemetry capsules for recording body temperature (Minimitter Model JW) were implanted in the same animals. The following variables were measured through daily recording of the output of the transducer and the transmitter; Cardiac output (estimated by aortic blood flow), Heart rate, Stroke volume, Body temperature, and Ejection time. For two to three weeks postoperatively daily control readings were taken. Animal #1 entered hibernation spontaneously and was recorded at daily intervals during hibernation. Animal #2 was artificially cooled to a temperature of 15°C using a helium hypothermia technique. The animal aroused spontaneously from this temperature in approximately 12 hours when placed in a 15°C environment. This animal was recorded continuously during this process. It appears, from these two animals that cardiac output in this species is regulated primarily by heart rate at lower body temperature, that stroke volume is relatively constant and that ejection time increases markedly at lower body temperatures. (Supported by a grant from the American Heart Association, Northeast Ohio Affiliate).

HYPEROSMOTIC DECARBOXYLATION OF GLUCOSE AND HISTIDINE IN RAT GASTRIC MUCOSA. Thomas J. Sernka and Anne F. Jackson*. Department of Physiology and Biophysics, LSU Medical Center, School of Medicine in Shreveport, Shreveport, Louisiana 71130.

Metabolic pathways that relate to the secretion of acid by isolated gastric mucosa were studied to determine the mediation for hyperosmotic inhibition of this function. Paired slices of gastric mucosa from the rat were incubated in sealed flasks with an oxygen atmosphere and isosmotic or three-fold hyperosmotic media containing (1-^{14}C) glucose, (6-^{14}C) glucose or (carboxyl-^{14}C) histidine. The rate of (1-^{14}C) glucose oxidation to $^{14}CO_2$ in isosmotic medium was reduced by 74% in hyperosmotic NaCl and by 28% in hyperosmotic KCl. The rate of (6-^{14}C) glucose oxidation to $^{14}CO_2$ in isosmotic medium was reduced by 64% in hyperosmotic NaCl and 53% in hyperosmotic KCl. Reductions in hyperosmotic ethanol were not significant. The ratio of $^{14}CO_2$ formed from (1-^{14}C) glucose to that formed from (6-^{14}C) glucose was not significantly changed by hyperosmotic NaCl or ethanol but was significantly raised by hyperosmotic KCl. The rate of (carboxyl-^{14}C) histidine decarboxylation in isosmotic medium was reduced significantly by 48% in hyperosmotic NaCl, by 30% in hyperosmotic KCl and by 27% in hyperosmotic ethanol. We conclude that hyperosmotic solutions reduce glucose oxidation and histidine decarboxylation by rat gastric mucosa in the order of potency NaCl > KCl > ethanol. Hyperosmotic solutions inhibit both the source of metabolic energy for stimulated acid secretion, the citric acid cycle, and the formation of the secretagogue, histamine.

COMPARISON OF SPONTANEOUS AND EVOKED AROUSALS FROM HIBERNATION IN THE WOODCHUCK, MARMOTA MONAX. J.N. Sexton*[1], T.F. Albert[1], A.L. Ingling*[1], L.W. Douglass*[2]. [1]Dept. of Veterinary Science and [2]Dept. of Dairy Science, University of Maryland, College Park, Md. 20742

With the aid of implanted thermocouples an attempt has been made to compare spontaneous (SA) and evoked arousals (EA) from hibernation in the woodchuck (T_A 6°C). Monitored tissues were: supraspinatus muscle (SU), axillary brown fat (BF), pectoral muscle (P), subcutaneous white fat over the scapula (AF), subcutaneous white fat of the flank (FF) and semimembranosus muscle (SM). SA and EA were compared with regard to: 1. thermal gradients within the animal during arousal; 2. times required for SU and SM to increase through 5°C increments from 15 to 35° (last SM increment is 30-34°); and 3. total time for completion of the arousal process, (time interval between which SU reached 15° and SM reached 34°). Three animals provided data on 11 SA while 12 woodchucks provided data on 28 EA. During SA and EA, there were no significant differences in times required for 5° increases in SU or in the thermal gradients between SU and BF, P, AF, FF, SM. Differences ($P<.01$) were found in minutes required for 5° incremental SM increases between SA and EA respectively: 15-20°, 32, 20; 20-25°, 31, 15; 25-30°, 32, 18; 30-34°, 40, 25. Times from beginning of arousal until onset of caudal vasodilation were SA 99 min. and EA 94 min. (N.S.). Total times for SM rewarming were different ($P<.001$), SA 136 min. and EA 73 min. Total arousal times were SA 233 min. and EA 143 min. ($P<.001$). It therefore appears that times for 5° incremental increases in SM are shorter in EA than in SA and that total time for EA is shorter than SA due to more rapid rewarming of SM during EA once caudal vasodilation has been initiated.

PHARMACOLOGICAL STUDY OF EVOKED POTENTIALS IN THE OLFACTORY BULB. M. Seyal*and W.J. Freeman. Dept. Physiology-Anatomy, University of California, Berkeley, CA 94720

A study was made of the effects of synergists and antagonists of putative neurotransmitters on the rabbit olfactory bulb. Drug effects were determined by measuring changes from control in the averaged evoked potential (AEP) induced in the bulb by lateral olfactory tract stimulation. AEP's were measured by using a non-linear regression program to generate best fitting curves. Differential equations describing synaptic feedback interactions define the fitted parameters. Drug induced changes in these parameters were interpreted as changes in synaptic feedback interaction strength among various neuron populations (Freeman, W.J. Mass Action in the Nervous System. New York: Academic Press, 1975). Muscarinic cholinomimetic agents caused a decrease in decay rate, initial amplitude and phase of onset and increase in frequency of the AEP. Nicotine caused an initial transient reduction in frequency with increased decay rate followed by a more persistant reduction in decay rate with frequency approaching control values. These effects suggest a selective increase in forward gain of the mitral cells. The concomitant increase in frequency with muscarinic agents suggests an increase in baseline interaction strength. Atropine, scopolamine and dihydro-β-erythroidine caused a reduction in frequency, increase in decay rate and phase of onset suggesting a reduction in excitation bias. Noradrenaline and the early effects of dexamphetamine caused a reduction in frequency, decay rate and initial amplitude and increase in the phase of onset suggesting an increase in inhibitory bias. Reserpine, picrotoxin and phenoxybenzamine caused a reduction in frequency and decay rate and increase in phase of onset, interpreted as a reduction in forward gain of the granule population. GABA effects suggested multiple sites of action. (MH06686)

ASZ(DCPB)

ENZYMATIC ASPECTS OF THERMALLY-INDUCED METABOLIC REORGANIZATION IN THE GREEN SUNFISH, Lepomis cyanellus. James B. Shaklee, James A. Christiansen*, Bruce D. Sidell*, C. Ladd Prosser, and Gregory S. Whitt, Depts. of Genetics & Development and Physiology & Biophysics, Univ. of Illinois, Urbana, IL. 61801.

The molecular aspects of thermal acclimation were investigated by determination of the levels of catalytic activity and the isozymic forms present for more than ten different enzymes in tissues of fish acclimated to 5° and to 25°C. Many enzymes, including glucose-6-phosphate dehydrogenase, malate dehydrogenase, fructose-biphosphate aldolase, and pyruvate kinase exhibited significant changes in activity in one or more tissues in response to temperature. Generally, enzymes in a particular metabolic pathway responded in a parallel fashion in any given tissue. Enzymes in different pathways, however, frequently exhibited non-parallel changes, so that the response of any given enzyme was tissue-specific. These results are interpreted as indicating that important restructuring of intermediary metabolism (based on changes in enzyme activities) occurs during thermal acclimation. Starch gel electrophoresis of tissue homogenates revealed no changes in the isozyme patterns of lactate dehydrogenase, creatine kinase, fructose-biphosphate aldolase, malate dehydrogenase, phosphoglucomutase, or glucosephosphate isomerase in any of the tissues examined. There were, however, changes in the isozyme patterns of esterases in both liver and eye tissue. These results suggest that changes in isozyme patterns may play a minor role in the thermal-acclimatory response of species such as the green sunfish.
(Supported by grants GB 43995 and BMS 01587 from NSF).

RESPONSES OF MUSCLE FIBERS TO IONTOPHORETICALLY APPLIED GLUTAMATE AND ASPARTATE. R.P. SHANK* , M.B. WANG and A.R. FREEMAN (SPON. J.D. DURRANT), Dept. of Physiology, Temple Univ. Sch. of Medicine, Phila., Penna. 19140.

Neuromuscular excitation in the limbs of lobsters may be mediated by glutamate and aspartate acting in concert. We have iontophoresed these amino acids separately and together from double barrel micropipettes onto muscle fibers in the carpopodite of the walking limbs. Our results show that when applied separately glutamate is 10 to 100 times more potent than aspartate. However when iontophoresed simultaneously, the glutamate response is potentiated by aspartate in amounts that are inactive when applied without glutamate. This potentiative effect can be selectively abolished by D-aspartate. Also the excitatory action of glutamate can be selectively abolished by D-glutamate and kainic acid. These observations provide additional evidence for the concept that glutamate and aspartate combine with different binding sites within the same receptors. Furthermore the principal function of aspartate apparently is not to initiate receptor activation, but to modulate the action of glutamate in a manner analogous to the way that positive modulators influence the activity of allosteric enzymes. (Supported by AHA-Grant-in-Aid #584-218-01.)

RESPIRATORY RESPONSES TO THORACIC DORSAL RHIZOTOMIES (1-4, 5-9, 10-13) IN THE ANESTHETIZED CAT. Roger Shannon. Dept. of Physiology, Univ. of So. Florida, Col. of Med., Tampa, Florida 33612

Elimination of chest wall afferents by thoracic dorsal rhizotomies (TDR, 1-12) produces changes in the spontaneous breathing pattern ($\downarrow V_T$, $\uparrow f$, $\downarrow t_i$, $\downarrow t_e$), suggesting that these afferents do reflexly influence central respiratory activity (Shannon, Physiologist 18:386, 1975). Experiments were conducted to determine if the changes in respiratory pattern with TDR(1-12) could be correlated with known reflexes from the middle and lower intercostal muscles or lungs, which travel via thoracic dorsal roots. Afferents from these sources were eliminated by sectioning the thoracic dorsal roots 5-9, 10-13, and 1-4, respectively. The effects of TDR on V_T, f, t_i, t_e, and blood gases were studied in 22 vagotomized, anesthetized (Dial) cats. EMG's were monitored to test intercostal activity prior to the rhizotomies; only animals with EMG activity were used. TDR(1-4) had no significant effects on the respiratory pattern or blood gases. TDR(5-9) produced small changes similar to TDR(1-12) with exceptions that t_e was inconsistent and Pa_{CO2} increased. TDR(10-13) caused changes similar in direction and magnitude to TDR(1-12); there were negligible alterations in Pa_{CO2}. The results indicate that: (1) afferents (1-4) from neither the upper intercostal muscles nor lungs (sympathetic afferents) contribute significantly to the control of the normal respiratory rhythm, (2) afferents via the middle thoracic roots (5-9) have a small degree of influence on the rhythm, and (3) afferents via the lower thoracic roots (10-13) contribute substantially to the rhythm. The results do not completely correlate with known intercostal reflexes, but it is suggested that elimination of intercostal muscle proprioceptor afferents is responsible for the observed effects of thoracic deafferentation. (Supported by USPHS, NIH Grant HL-17715)

EVIDENCE FOR THE NEUTRALIZATION BY IMIDAZOLE OF H^+ SECRETED BY FROG GASTRIC MUCOSA, IN VITRO. R. L. Shoemaker, S. S. Sanders and W. S. Rehm. Dept. of Physiology and Biophysics, University of Alabama in Birmingham, Birmingham, Alabama 35294

Alonso, Rynes and Harris reported that imidazole inhibited H^+ secretion of in vitro frog gastric mucosa (Am. J. Physiol. 208:1183, 1965). With normal Cl^- solutions and the pH of secretory (S) side maintained at 4.5 (100% O_2 S — 95% O_2 & 5% CO_2 N) we found that imidazole (10-30 mM) added to nutrient fluid (N) markedly reduced the measured H^+ rate. On basis of following evidence we conclude that imidazole (Imz) does not inhibit H^+ secretion but diffuses from nutrient (pH 7.3) to secretory side in neutral form and combines with H^+ in lumina (pH low < 4.5). After reduction of measured H^+ rate with pH (S) at 4.5 changing to pH (S) 8.0 resulted in a restoration of measured H^+ rate (pK of Imz = 7.0 so at pH 8.0, 90% of charged form of Imz releases H^+ while at pH = 4.5 < 1% H^+ released). Addition of imidazole to N with pH (S) 8.0, increased H^+ rate and then anoxia reduced H^+ rate to zero and return to O_2 restored H^+ rate. With pH (S) at 4.5, flux of imidazole from N to S (with ^{14}C imidazole) accounted for decrease in measured rate. With imidazole (20-30 mM) on N, measured H^+ rate often went to zero and a titratable alkalinity was seen; the decrease in H^+ rate (ΔH^+) plus the alkalinity rate (alk) equaled the flux of ^{14}C imidazole (Q_{Imz}) into S. In 10 exps. $(\Delta H^+ + alk)/Q_{Imz} = 1.09 \pm 0.16$. Anoxia and other evidence indicates that imidazole diffuses from N to S in neutral form, i.e., amount that diffuses across mucosa in charged form is negligible. When imidazole reduced measured H^+ rate (pH (S) = 4.5) to zero there was no change in electrical resistance but potential difference (PD) increased. Relation between measured H^+ rate and PD is complicated. (NIH and NSF support)

EFFECT OF NICOTINE AND SODIUM PENTOBARBITAL ON SERUM SECRETIN AND EXOCRINE PANCREATIC SECRETION IN DOGS. Laurence S. Shore, N. Essa-Koumar* and G. Boden*. Dept. of Medicine, Temple UHSC., Phila., Pa. and Dept. of Surgery CMDNJ, Rutgers Medical School, Piscataway, N.J.

The effect of Na pentobarbital anesthesia or nicotine on serum secretin concentration and exocrine pancreatic secretion was investigated in dogs with chronic gastric and pancreatic fistulas. Na pentobarbital was found 1) to reduce basal pancreatic flow rate, bicarbonate and protein secretion without affecting basal immunoreactive secretin (IRS) concentration; 2) to have no effect on HCL (9.6 mEq/30 min, intraduodenally) mediated IRS release, pancreatic flow rate and protein secretion while moderately suppressing bicarbonate output; 3) to have no effect on pancreatic responsiveness to stimulation by exogenous secretin (0.5 IU/kg/30 min); 4) not to affect blood concentration of IRS following secretin infusion. Nicotine (100 ug/kg/30 min) was found not to affect basal pancreatic secretion or pancreatic excretory function stimulated by either HCL or exogenous secretin. It did however, delay the appearance of peak IRS concentration in response to intraduodenal HCL by about 20 min. The infusion of HCL intraduodenally for 30 min and the secretin infusion both resulted in an IRS concentration of approximately 150 pg. The excretory peaks of volume and bicarbonate following HCL stimulation were 19.7 ml/15 min and 2.29 mEq/15 min and following secretin 14.9 ml/15 min and 1.84 mEq/15 min. These data suggest that neither nicotine or Na pentobarbital anesthesia have a significant effect on IRS release or stimulated pancreatic secretory function.

PRESSURE-FLOW AND PRESSURE-VOLUME RELATIONS IN THE ENTIRE PULMONARY VASCULAR BED OF THE DOG DETERMINED BY TWO-PORT ANALYSIS. A.A.Shoukas and K. Sagawa. Dept. of Biomedical Engineering, The Johns HOpkins University, Baltimore, Md. 21205

In nine dogs with a fixed endotracheal pressure of 5 mm Hg, the arterial pressure-flow and pressure-volume relations were determined while venous pressure was fixed at constant values of 2, 5, and 8 mm Hg. The venous pressure-flow and pressure-volume relations were obtained when arterial pressure was fixed at constant values of 15 and 20 mm Hg. The arterial and venous pressure-flow relations could be regarded as linear around the physiological ranges of arterial and venous pressures; however, at very low pressures, these relations became nonlinear. The arterial and venous pressure-volume relations were also approximately linear within the physiological pressure ranges. The mean arterial compliance was 0.1798 ml/mm Hg kg^{-1} and was independent of venous pressures. The venous compliance values were 0.1236 and 0.0955 ml/mm Hg kg^{-1} for arterial pressures of 15 and 20 mm Hg, respectively. The sums of the arterial and venous compliances were 0.3034 and 0.2753 ml/mm Hg kg^{-1} for arterial pressures of 15 and 20 mm Hg, respectively. These values were nearly identical to the mean total compliance, 0.3265 ml/mm Hg kg^{-1}, measured in a separate series of experiments in the same dogs. The data obtained in these experiments using two-port analysis techniques represent the compliances and the resistance of the entire pulmonary vascular bed around the normal operating pressures and flows.

(Supported by Grant HL-14529 from NHLI)

TIME COURSE OF ATP AND PHOSPHORYLCREATINE (PCr) BREAKDOWN DURING A SINGLE ISOMETRIC TETANUS IN MAMMALIAN SMOOTH MUSCLE. M.J. Siegman, T.M. Butler*, S.U. Mooers,* and R.E. Davies. Jefferson Medical Col., Phila., PA 19107 and Sch. Vet. Med., Univ. of Pa., Phila., PA 19174.

Strips of rabbit taenia coli under 2 g-wt for 2 hr at 20°C were adjusted to 85% ℓ_o. Treatment with 0.5 mM iodoacetate, 5 mM fluoroacetate, glucose-free Krebs soln (95% N_2-5% CO_2) for 30 min at 5°C was followed by rewarming to 18°C for 3.5 min, electrical stimulation under isometric conditions, and quick freezing. The results (experimental minus unstimulated control ±SEM) are expressed as mole/mole total creatine vs. duration of tetanus (sec). (2.7±0.1 μmole total creatine/g wet wt, N=18)

Duration	N	ΔPCr	ΔATP	Total ΔcP	Force/Max Force
5	5	+0.024±0.024	-0.030±0.047	-0.005±0.048	0.23±0.02
10	6	-0.004±0.031	-0.066±0.018	-0.065±0.026	0.71±0.02
20	6	-0.113±0.034	-0.009±0.020	-0.130±0.054	0.95±0.01
25	5	-0.165±0.024	0.000±0.033	-0.166±0.049	0.98±0.01
35	6	-0.092±0.044	-0.039±0.029	-0.131±0.026	0.97±0.02
60	5	-0.217±0.024	-0.037±0.036	-0.256±0.037	0.91±0.04

ATP breakdown occurred (P=0.02) at 10 sec with resynthesis (P=0.05) between 10 sec and 20-25 sec. No significant change occurred in PCr at 10 sec, but an increase (P=0.05) in the rate of PCr usage took place between 10 and 25 sec, followed by a decrease in rate between 25 and 60 sec. These results are consistent with a delayed activation of creatine kinase. The rate of total energy usage did not change significantly with time (≈0.01 μmole/g-sec, and about 150 times less than that of frog sartorius at 18°C), and this suggests that similar rates of crossbridge cycling occur during force development and its subsequent maintenance in this smooth muscle stimulated under isometric conditions at 18°C. Supported by HL 15835 to the Penna. Muscle Inst. and HD 06074 to MJS.

CARDIORESPIRATORY FUNCTION OF DOGS DURING TWO METHODS OF LUNG LAVAGE AND DURING UNILATERAL HYPOXIA. S.A. Silbaugh,* B.A. Muggenburg, J.L. Mauderly, and C.R. Crain,* Inhalation Toxicology Research Institute, Lovelace Foundation, Albuquerque, New Mexico 87115

The method of saline instillation and unilateral hypoxia imposed by filling one lung with saline affect cardiorespiratory function during lung lavage. In one method of lavage, the dog was hyperventilated and saline was instilled relatively rapidly through a single lumen tracheal tube. In another method of lavage, a double lumen tube separated right and left bronchi and saline was instilled more slowly into the dog's right lung. Unilateral hypoxia was produced by directing right lung airflow to a rebreathing bag. Few blood gas or shunt changes occurred during the single lumen lavage, but blood oxygen decreased and shunt increased during both double lumen lavage and unilateral hypoxia. Heart rate, cardiac output, and systemic arterial pressure decreased during single lumen lavage, but not during double lumen lavage or unilateral hypoxia. Apparently, most alveoli were gas filled during single lumen lavage and unilateral hypoxia was not imposed. Hyperventilation may have been the major change-producing factor during single lumen lavage. The similar changes observed during double lumen lavage and unilateral hypoxia suggested unilateral hypoxia was the major change-producing factor during double lumen lavage. (Research performed under U.S. Energy Research and Development Administration Contract E(2-2)-1013.)

MYOCARDIAL REVASCULARIZATION WITH BOVINE EMBRYONIC SKIN. A.N. Silvetti* and B. Cortis* (SPON: A.A. Hakim). Embryonic Tissues Transplantation Laboratory, Biologic Resources Laboratory, University of Illinois at the Medical Center, Chicago, Illinois 60612.

Saphenous vein by-pass is the most commonly applied procedure for revascularization of the cardiac tissue. This technique has proven to be helpful in limited cases, it requires extra-corporeal circulation and could be accompanied with post-operative by-pass thrombosis. The present studies report on an effective and simple new method for myocardial revascularization. Acute myocardial infarction was induced in dogs by ligature of the anterior descending branch of the left coronary artery. Immediately thereafter, the infarcted area and normal surrounding myocardium were covered with fresh bovine embryonic skin (B.E.S.). At 24 hours post-operatively, the chest tube was removed, and sutures were removed at the end of 14 days. All dogs tolerated the procedure well and most of the dogs are alive and are 6 months post-embryonic skin graft. The chest cavity of one of the dogs was opened on the 5th day post-surgery for early evaluation. There were no local signs of inflammation, infection and/or tissue rejection. The B.E.S. looked "fresh", undegraded and shining. Its original color and luster were still present. B.E.S. was intimately and firmly ahdered to the underlying epicardium, blending smoothly with surrounding cardiac tissue. Abundant, highly vascularized capillary networks could be seen in the surrounding myocardium and advancing towards the bovine embryonic skin graft. Normal and infarcted areas with and without B.E.S. were histologically examined. Therefore, B.E.S. stimulated and induced the formation of a highly vascularized granulation tissue over and beyond the infarcted area.

EFFECTS OF A 2% CHOLESTEROL DIET ON BILE FLOW AND COMPOSITION IN MALE RATS. David Simon*, Trudy M. Stillman* and Janet S. Kerr. Dept. of Biology, Rutgers University, Camden, N.J. 08102

Effects of 1.5% and 2.5% cystine, niacin and taurine on total and free liver and serum cholesterol levels in 5-month-old male rats maintained on a 2% cholesterol diet have been reported (Simon and Kerr, N.J. Acad. Sci. Bull. Vol. 20). 2.5% cystine, 1.5% niacin and 1.5% taurine have been shown to reduce significantly both total and free liver and serum cholesterol levels. The effects of this dietary regime on bile flow and composition have now been investigated. Normal controls received a diet without cholesterol. Bile was collected anaerobically for 3 hours. Bile flow in cholesterol controls (4.25 ± .15 µl/min/100 g body weight) was higher than in normal controls (3.25 ± .25 µl/min/100 g) ($P < .05$). Rats on a 2.5% niacin diet maintained bile flow higher than normal controls (4.32 ± .25 µl/min/100 g) ($P < .05$). Total bile acids were 22% higher with cholesterol (410 ± 40 µg/ml bile) than in normal control animals (319 ± 34 µg/ml). Total bile acid levels in rats fed 1.5% taurine were higher (403 ± 12 µg/ml) ($P < .05$) than in normal controls. 2.5% niacin and 1.5% taurine animals showed increased protein levels in bile (39.4 ± 4 mg/ml and 47.2 ± 10 mg/ml respectively), compared with normal (23.4 ± 3.0 mg/ml) and cholesterol controls (21.5 ± 2.3 mg/ml) ($P < .05$). HCO_3^- levels showed the greatest decrease with 1.5% taurine compared with normal controls (17 ± 1.0 mEq/l and 24.8 ± 1.1 mEq/l respectively) ($P < .05$). Changes were also found in levels of cholesterol and individual bile acids. The effects of this type of dietary regime on bile flow and bile composition have not previously been reported.

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VENOUS CHANGES IN RENAL HYPERTENSIVE RATS: ROLE OF HUMORAL FACTORS. G. Simon* (SPON: R.L. Malvin). Hypertension Section, University of Michigan, Ann Arbor, MI 48109.

Previously, we have shown that the venous pressure-volume (VP-V) curves of rats with two-kidney Goldblatt hypertension (2-KGH) are shifted toward the pressure axis. To investigate the role of humoral factors in the pathogenesis of venous changes, 4-wk-old male Sprague-Dawley littermate rats were united in parabiosis. In 13 parabionts (Group 1), one renal artery of one rat (A1) was constricted to produce 2-KGH; the other rat (B1) was untouched. In 11 parabionts (Group 2), one rat (A2) underwent sham surgery; the other (B2) was untouched. Two months later, femoral vein pressure (FVP) of pentobarbital-anesthetized parabionts was measured, then the lower-body vascular beds of rats were perfused through the aorta with oxygenated Krebs-Ringer (K-R) sol. containing dextran (7 gm/100 ml) at 37° C. Perfusion was stopped every 9 min for 60 sec to record FVP rise during rapid infusion (19.3 ml/min) of K-R sol. into the inferior vena cava. Results were as follows:

	Rats	Type	N	SBP (mm Hg)†	FVP (mm Hg)†
Group 1	A1	2-KGH	13	163 ± 6.8***	2.2 ± 0.18
	B1	untouched	13	122 ± 2.1	2.5 ± 0.17*
Group 2	A2	sham surgery	11	118 ± 4.0	2.1 ± 0.18
	B2	untouched	10	115 ± 4.0	2.2 ± 0.17

† mean ± SE; *** $p<0.001$, A1 vs A2; * $p<0.05$, B1 vs A1 (paired t-test)

Compared to A2 rats, lower-body VP-V curves of A1 rats were shifted toward the pressure axis ($p<0.01$). The shift persisted following killing the rats and stopping perfusion. VP-V curves of B1 rats were similar ($p>0.5$) to those of B2 rats. Increased FVP in B1 rats suggests fluid shift from hypertensive to normotensive parabionts. Results confirm our previous findings but do not provide evidence for the role of humoral factors in the pathogenesis of venous changes in 2-KGH.

CHANGES IN METABOLISM OF DOPAMINE, NOREPINEPHRINE AND SEROTONIN, AND RELATION TO GONADOTROPIN SECRETION IN AGING MALE RATS. J.W. Simpkins*, G.P. Mueller*, H.H. Huang* and J. Meites. Dept. of Physiology, Michigan State University, East Lansing, MI 48824.

Content and turnover of dopamine (DA), norepinephrine (NE) and serotonin (5HT) were measured in the medial basal hypothalamus (MBH), remaining hypothalamus, and brains of young and old male Wistar rats. In 21 month old males, DA content was 41% less in MBH ($P<.02$), 14% less in hypothalamus and not different in the olfactory tubercles as compared with 3-4 month old males. NE content was reduced 19% in MBH and 33% in hypothalamus ($P<.01$) in old as compared to young males. One hour after injection of 250 mg α-methyl-para-tyrosine/kg, DA was reduced by 37% in the MBH of young males and by 23% in old males, and NE in the hypothalamus was decreased by 48% in young and by 23% in old males ($P<.02$). Hypothalamic and brain content of 5HT were the same in young and old male rats. By 30 min after injection of 75 mg pargyline/kg, hypothalamic 5HT rose 20% in young and by 34% in old males ($P<.02$) and brain 5HT increased 28% in young and 37% in old rats. Brain 5HIAA was 25% higher in old than in young males ($P<.001$). Basal serum levels of prolactin were significantly higher and serum LH and FSH were significantly lower in old than in young rats. Serum TSH was the same in both age groups. These data indicate that a decreased turnover of DA and NE and an increased turnover of 5HT may account in part for the increase in basal levels of prolactin and the decrease in LH and FSH in old male rats. (Aided by NIH grant AG00416).

EFFECT OF REDUCTION OF CARDIAC OUTPUT ON SUBENDOCARDIAL AND TRANSMURAL MYOCARDIAL FLOWS IN RIGHT HEART BYPASS PREPARATION H.Singh,* M. Swank,* R. Flemma,* D.Mullen* and D. Lepley, Jr.*(SPON. C. Dawson) The Medical College of Wisconsin, Milwaukee, Wisconsin.

Stepwise reduction of cardiac index from normal to 30% of normal on right heart bypass produced decrease of left ventricle subendocardial flow and total coronary sinus flow directly proportional to the cardiac index. A 15 cc. bolus of cold blood at 2 to 3°C. was injected into the left atrium of 15 dogs. Myocardial isothermy was maintained by incorporating a heat exchanger in the perfusion circuit monitored by Yellow Springs thermistor probes (0.1 sec. response time) placed at precise depths and location in the myocardium. Coronary sinus flows and simultaneous transmural epicardial and endocardial flows were measured by previously reported thermal washout methods (coefficient of correlation to direct known flows was 0.998 and microspheric measurement was 0.977). At a cardiac index of 50% and 30% of normal (mean aortic root pressures 49.8 mm Hg and 33.5 mm Hg respectively), endocardial flows were 44% ± 12% (SD) and 28% ± 14% and epicardial flows were 40% ± 14% and 26% ± 8% of maximal flow obtained at normal cardiac indices. Endocardial/epicardial flow ratios did not vary significantly in the right heart preparation studied. Significant elevation of coronary sinus lactate levels occurred at a cardiac index of 50% below normal ($p<.05$). We conclude that in the right heart bypassed and working left ventricle preparation, left ventricular subendocardial flows were directly proportional to cardiac indices (equation $y = 1.12x - 9.28$) and that at a cardiac index of 30% below normal, transmural endo/epicardial flow ratios were not altered.

IDENTIFICATION OF CONSTITUENTS OF CHYME RESPONSIBLE FOR POSTPRANDIAL INTESTINAL HYPEREMIA IN DOGS. S.P. Sit*, P. Kvietys*, J. Post*, and C.C. Chou. Dept. Physiology, Mich. St. Univ. E. Lansing, MI 48824

To identify which constituents of intestinal chyme are responsible for postprandial intestinal hyperemia, we compared the vascular effects of luminal placement of the following substances: 1) undigested homogenized dog food (UDF), 2) pancreatic enzymes (Viokase^R) (PE), 3) UDF digested by PE (DF), 4) supernatant of DF (SUPNT), 5) precipitate of DF (PPT), 6) 1:2 diluted gallbladder bile (BI), 7) DF plus BI and 8) normal saline. These substances were paired into 6 combinations (see below). Venous outflows from two adjacent in situ jejunal segments were simultaneously measured; one segment contained one of the paired substances and the adjacent segment the other such that the vasoactivity of the paired substances could be compared (D=A-B). As a control, normal saline was placed in both segments before and after the comparison. Changes in blood flow from precontrol (Δ flow) were:

	Segment A		Segment B		D = A - B
(N)	Contents	Δ flow in %	Contents	Δ flow in %	%
(11)	DF	+11.5±1.8*	UDF	+2.0±2.3	+9.5±1.5*
(6)	SUPNT	+11.3±4.4*	PPT	-1.4±4.0	+12.7±4.2*
(6)	SUPNT	+11.3±4.1*	DF	+13.4±3.4*	-2.1±2.1
(6)	SUPNT	+12.1±3.8*	PE	+4.8±4.8	+7.3±2.0*
(6)	BI	+1.1±2.6	NaCl	-4.1±4.8	+5.2±2.6
(9)	DF + BI	+54.8±12.9*	DF	+17.8±5.6*	+37.0±10.3*

* = $p<0.05$. Although pancreatic enzymes and bile per se did not alter jejunal flow, the hyperemia required the digestive action of the former and was markedly enhanced by the latter. The study indicates that the substances responsible for postprandial hyperemia are in the supernatant of the digested food and likely to be the digestive products of food. (Supported by USPHS Grant #HL15231).

CHOLINERGIC INFLUENCES ON THE HYPOTHALAMO-HYPOPHYSEAL-ADRENOCORTICAL (HHA) RESPONSE OF RATS TO ACUTE STRESSES. N. Sithichoke* and S. F. Marotta. (SPON: R. Greenberg). Dept. Physiology and Research Resources Center, University of Illinois at the Medical Center, Chicago, IL 60680

Cholinergic agonists and antagonists were employed to ascertain the influence of the neurotransmitter, acetylcholine (ACh) on the function of the HHA system of stressed and non-stressed male rats. The cholinergic agents were injected IP and an hour later the animals (9/group on 12L;12D lighting schedule) were subjected to either ambient air, 10% O_2 or 10% CO_2 for one hour prior to decapitation at 1000 hrs. Trunk blood was collected and the plasma analyzed for corticosterone. The following results were obtained:

Agent	Dose (mg/kg)	Pl. Cort. (µg/100 ml) air	10% O_2	10% CO_2
Saline	-	3.9	37.1	35.0
Atropine(A)	4	8.8	35.4	34.4
Mecamylamine(M)	1.5	2.8	31.7	25.5
A + M	4+1.5	6.4	42.3	30.8
Methyl Atropine(MA)	4	9.2	31.6	22.4
Eserine(E)	1	6.5	37.8	14.2
E + A	1+4	6.7	42.3	35.3
E + M	1+1.5	2.9	36.1	15.2
E + MA	1+4	8.2	35.1	29.2
NVP(ChAT Inhibitor)	100	7.3	43.3	29.6

These data demonstrate a partial stimulatory nicotinic effect of ACh on the HHA system, in contrast to the muscarinic effect which is stimulatory peripherally but inhibitory centrally. Activation of the HHA system during some stresses may be the result of modifying the action of cholinergic neural inputs. (ONR contract NR 201-020.)

EFFECT OF CHRONIC CO EXPOSURE ON RAT PAPILLARY MUSCLE. R. A. Slonek* and D. G. Penney. Univ. of Ill. at Chicago Circle, Chicago, Ill. 60680.

Studies with isolated right ventricle (RV) (J. Appl. Physiol., 40, 324, 1976) and left ventricle (LV) of chronically CO-exposed rats demonstrate increased tolerance of anoxia and more rapid aerobic recovery. We now report on similar studies carried out with papillary muscle. Wet weights of LV anterior papillary muscles were elevated 86% by 38-50 day continuous exposure of young adult male rats to 500 ppm CO (36% COHb). Cross-sectional area (mm^2) increased from 1.37 ± 0.08 to 2.09 ± 0.11. Tension was monitored isometrically in an apparatus similar to that of Blinks (J. Appl. Physiol., 20, 755, 1965) using a Grass force displacement transducer (FT-03C) with a micrometer adjustment to allow use of various rest tensions. The bathing medium (Krebs-Ringer-Bicarbonate) was maintained at 22° C, gassed with 95% O_2-5% CO_2, and contained no glucose. Maximal developed tension (DT) for treated and control preparations occurred at rest tensions of 3.33 and 2.66 g respectively. All subsequent preparations were set at these values of rest tension. Initial aerobic DT of treated preparations both on the basis of dry wt. and cross-sectional area was somewhat depressed. During anoxia (95% N_2-5% CO_2) DT of treated preparations declined more slowly than that of controls, DT falling to 50% of preanoxic DT in 7.5 minutes in the former group and 3.5 minutes in the latter group. Time to 50% recovery of DT upon re-introduction of oxygen was less than 1.5 minutes in the treated group and greater than 14 minutes in the control group. These data are consistent with our earlier findings that while prolonged CO exposure appears to compromise cardiac aerobic contractility, it also results in increased anoxia tolerance and aerobic recovery.
(Supported by grant HL-16367 from NHLI.)

LIGHT STIMULATED CALCIUM RELEASE BY BOVINE ROD DISK VESICLES.
H. Gilbert Smith*, Burton J. Litman*and Roger S. Fager* (SPON: Brian R. Duling). University of Virginia Medical School, Ch'ville, Va. 22901

Purified bovine photoreceptor disks were fragmented by sonication in the presence of Ca^{45++} and allowed to reseal. They were placed on a filter in a flow system and the calcium external to the disks washed out. Light exposure at this point induced calcium release between 0.5 and 1.2 Ca^{++}/rhodopsin bleached. Calcium release was found to be proportional to the amount of rhodopsin bleached in the range of 20% to 100% bleaching. With increasing calcium trapped, calcium release plateaued at approximately one calcium per rhodopsin bleached. Incubation of sealed vesicles with external Ca^{45++} leads to very little Ca^{++} release on bleaching, implying that only calcium inside the vesicles is released by light and there is actually transport of calcium across the membrane, rather than a release of bound calcium. Lowering the temperature to 3°C (which suppresses the Meta I to Meta II transition) also suppresses calcium release. Hagins and Yoshikami have suggested that calcium serves as a transmitter for visual transduction. The above evidence is consistent with rhodopsin functioning as a light-activated one-shot calcium carrier.
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PARATHYROID HORMONE AND RENIN SECRETION. *Jacquelyn M. Smith, David R. Mouw, and Arthur J. Vander, Dept. of Physiology, University of Michigan, Ann Arbor, Michigan

These experiments were designed to determine whether parathyroid hormone (PTH) can induce changes in renin secretion. After control clearances, a prime (18μg) and sixty-minute infusion (1.12μg/min) of synthetic PTH (Bovine 1-34 Beckman) was given intravenously to hypropenic anesthetized dogs; clearances were performed during* last thirty minutes of PTH infusion. A 1-hr recovery period followed the PTH infusion. The biologic activity of PTH in this prep was substantiated by the phosphaturia produced by PTH infusion. Arterial plasma renin activity (ng/ml/hr) was elevated approximately two-fold during PTH infusion and returned toward normal during the recovery period. The rise in renin was associated with a significant increase in sodium and potassium excretion. There were no significant changes in plasma calcium, sodium or potassium, or in calcium excretion, glomerular filtration rate or renal blood flow. Mean arterial blood pressure decreased an average of 7mmHg, from 120 to 113 mmHg. In one experiment, renin secretory rate was determined at 5-minute intervals and found to be markably elevated during PTH infusion. These experiments show that exogenous PTH induces renin secretion in the dog. Although the mechanism by which renin release is stimulated remains unclear, direct stimulation of the juxtaglomerular apparatus or an alteration in renal calcium are two likely possibilities.

INFLUENCE OF AGE AND CORONARY DISEASE ON POSTURAL AND VALSALVA RESPONSES. James J. Smith, Felix E. Tristani*, John H. Kalbfleisch* and Karel J. Kotrly*, Medical College of Wisconsin, Milwaukee, WI and Veterans Administration Center, Wood, WI 53193.

To investigate the effect of age and heart disease on stress response, 11 ambulatory male patients with proven coronary heart disease (CHD) and 11 normal male subjects of similar age were subjected to a test battery and results compared with our previous studies using younger normal subjects. The tests were monitored by non-invasive methods and cardiac output estimated with the Minnesota Impedance Cardiograph.

In the 20 minute, 70° head-up tilt there was a lesser heart rate (HR) and lesser diastolic pressure response in the older subjects. In CHD patients there was a greater decline in systolic and pulse pressure and a lesser rise in total peripheral resistance than in age-matched controls. In the valsalva, the HR response was determined during a 15 sec. intrathoracic pressure rise of 40 mmHg; the HR increments between successive valsalva phases were diminished with increasing age. In CHD patients the HR increments from phases I to II, II to III and III to IV were less than in normal subjects of similar age.

The results indicate that with both advancing age and CHD, there is a lessened HR and peripheral resistance response to graded hypotensive stresses such as head-up tilt and valsalva.

ON-LINE EVALUATION OF STEADY STATE RESPIRATORY GAS EXCHANGE. R.T. Smith,* S.F. Sullivan, R.W. Patterson. Dept. of Anesthesiology, UCLA School of Medicine, Los Angeles, CA 90024

Recognition of steady-state periods of respiratory gas exchange is a requirement in many areas of physiologic investigation. For example, our investigations concerned with oxygen consumption of patients during induction and emergence from anesthesia, in recovery rooms and intensive care units, requires an evaluation of steady-state respiratory gas exchange to distinguish changes in body gas stores from metabolic changes. The same holds true for gas exchange studies during hyperalimentation, during hemorrhage and shock, and in studies on the effect of acid/base disturbances on oxygen consumption. Real time measurement of oxygen uptake or gas exchange during a change in environmental conditions or during subject movement requires an open circuit measurement technique. Open circuit techniques that measure $\dot{V}O_2$, $\dot{V}CO_2$, R, and $\dot{V}_E$ on-line should be designed to simultaneously evaluate the reliability of data in terms of steady-state conditions; a condition defined by a constant FEN_2/FIN_2 ratio. A prototype system consisting of a volume displacement spirometer adaptable to either spontaneous or controlled respiration, Perkin-Elmer MGA-1100 gas analyzing mass spectrometer and digital computer has been developed, tested, and used in a number of settings, in animal studies in the experimental laboratory, human studies in exercise physiology, and data collection in the intensive care unit. A comprehensive computer program schedules calibration sequencing with other phases of the data collection. When total system reliability was measured with a model during constant ventilation and with constant inspired and expired gas concentrations, the coefficient of variation for measured $\dot{V}O_2$ was 0.3%.

ESTROGEN-INDEPENDENT DAILY DECREASE IN GONADOTROPIN-RELEASING HORMONE (GnRH) CONTENT IN THE HYPOTHALAMUS OF LONG-TERM OVARIECTOMIZED RATS. Michael C. Snabes*, Robert P. Kelch* and Fred J. Karsch, Departments of Physiology, Pediatrics and Pathology, Reproductive Endocrinology Program, The University of Michigan, Ann Arbor, Michigan 48109.

We examined the possibility that a change in hypothalamic content of immunoassayable GnRH occurs independent of ovarian hormones. Female rats were ovariectomized and 6 wks later treated for 2 days sc with Silastic capsules containing estradiol-17β (E2). Control animals were either untreated or treated with empty capsules. Rats were decapitated every 3 hrs between 8AM and 8PM and trunk blood was collected for determination of GnRH, LH, FSH and prolactin by radioimmunoassay. Hypothalami were removed rapidly, snap frozen, and separated into an anterior and posterior region by a transverse cut made at the caudal aspect of the optic chiasm. Each region was homogenized in acetic acid and the neutralized homogenate was assayed with the #42 antisera of Niswender. Hypothalamic content of GnRH was similar in all groups throughout the day. A positive correlation was found between GnRH content of the anterior and posterior regions during the period studied ($r=.74, p<.001$). There was a precipitous 70% drop in content of GnRH in both regions between 11AM and 5PM. This drop occurred regardless of whether E2 was administered. However, only in the E2 treated group was a surge of LH, FSH, and prolactin observed during the late afternoon. Serum GnRH was uniformily low at all times examined (<5pg/ml). If an acute drop in hypothalamic GnRH content reflects secretion, these results suggest that the pituitary may respond to the daily increase in GnRH secretion in the surge mode only in the presence of estrogen. Thus, the positive feedback effect of estrogen may be to elicit an increase in pituitary responsiveness to GnRH. (Program Project HD08333)

METABOLIC AND MECHANICAL RESPONSE OF RABBIT PAPILLARY MUSCLE TO TRANSIENT HYPOXIA. T. Russell Snow* and Frans F. Jöbsis, Departments of Physiology and Medicine, Duke University; Durham, NC 27710

To determine the metabolic impact of transient periods of hypoxia, the changes in intracellular NADH and mechanical performance in rabbit papillary muscles were monitored. The protocol was: HCO_3^- Ringer with 10 mM butyrate as substrate, T=23°C, fifteen twitches were ellicited at each of the five separate frequencies (.1-.5 Hz). Following the control (pO_2=523 Torr), the muscles were exposed to fifteen minutes low oxygen Ringer (pO_2=187), after which oxygen was reintroduced. The effects of this transient period of hypoxia, determined thirty minutes after reoxygenation, were as follows. There was a consistant decrease in the peak twitch tension (T), with maximal change at the higher frequencies. However, neither the maximum nor the minimum time derrivative of the tension ($\dot{T}_{mx}$ or $\dot{T}_{mn}$) decreased significantly. The change in the time to peak tension was marginal. The metabolic effects of this transient hypoxic episode, as demonstrated by the maximal change in NADH fluorescence (P_{mx}), paralled those of T. At the lower frequencies, the relation between T and P_{mx} did not appear to be altered. However, at the higher frequencies, there were definite indications of greater susceptability to development of hypoxia as a result of the hypoxic episode. Since the availability of oxygen is the same in the two control situations, the data suggest an impaired ability to utilize oxygen following a hypoxic episode.
(Supported in part by NIH grants HL-02285 and HL-16828)

MEASUREMENT OF SINGLE BREATH CO_2 RESPONSES IN MAN BY IMPULSE RESPONSE DETERMINATION. S. Sohrab* and S. M. Yamashiro, Biomedical Engineering Department, USC, Los Angeles, CA 90007

Single breath CO_2 responses were measured in 7 normal men by estimating the unit impulse responses of breathing pattern variables to inhaled CO_2. Impulse responses of minute ventilation, tidal volume, frequency, inspiratory duration, expiratory duration, and end-tidal CO_2 were estimated by cross-correlating these outputs with an input consisting of pseudo-random inhalations of 6-8% CO_2 or air on a breath-to-breath basis. Random inhalations were applied for 500-1300 consecutive breaths to permit averaging of responses. Testing and data processing were performed on-line with a PDP/11-20 mini computer. Tidal volume and minute ventilation responses reached a peak 15-30 seconds following a single breath CO_2 inhalation. CO_2 response sensitivities estimated from peak changes in end-tidal CO_2 and tidal volume or minute ventilation ranged from .0059-.0212 liters/mmHg for tidal volume and .122-.210 liters/min/mmHg for minute ventilation. Changes in breathing frequency, inspiratory duration, and expiratory duration were consistent within but not between subjects. These single breath responses are probably mediated primarily by the peripheral chemoreceptors. Thus, impulse response determinations appear to provide a reliable means of measuring peripheral chemoreceptor response.

PERCEPTUAL AND PHYSIOLOGICAL RESPONSES TO EXERCISE IN WOMEN. R.G. Soule and J.M. Watras.* Exercise Physiology Laboratory Sargent College of Allied Health Professions, Boston University, Boston Massachusetts 02215.

In an attempt to determine the relationship between perceived exertion and several selected physiological parameters in college age women the following study was conducted. Seven normal adult female subjects exercised on a bicycle ergometer at four consecutive power outputs of 25, 50, 75, and 100 watt. Each exercise bout lasted five minutes, and there was a ten minute rest interval between bouts. Mean results were:

Power Output	25	50	75	100	(watt)
Metabolic Rate	198.0	298.9	389.3	492.3	(watt)
Heart Rate	112	127	148	174	(bpm)
Ventilation	15.1	20.5	28.0	38.6	(l/m)
Perceived Exertion	10	12	14	17	(RPE)

At each increased power output the physiological values were significantly higher. The ratio of HR to RPE did not change with an increased power output supporting the data of Brog and others. The regression equation (5 Sub.) HR = 44.3 + 7.25 (RPE) has significant slope. The correlations were: HR vs RPE = 0.82, $\dot{V}e$ vs RPE = 0.726 and $\dot{V}O2$ vs RPE = 0.710 all of which are significant at < 0.001. Thus a HR/RPE ratio of 10 is reasonable at progressive power outputs above 50 watt, whereas at lower outputs RPE is not as good a predictor of HR. The results of the study indicate that females respond to bicycle ergometer exercise in terms of HR, $\dot{V}e$ and $\dot{V}O2$ and their relationship to RPE in approximately the same manner as males.

FACTORS INFLUENCING THE EXCRETION AND RETENTION OF FLUORIDE IN MAN. Herta Spencer, Emilie Wiatrowski*, Dace Osis*, and Clemontain Norris*. Metabolic Section, Veterans Administration Hospital, Hines, IL. 60141

The intestinal absorption and retention of fluoride has been shown to be affected by certain inorganic elements in several animal species and most of the substances used inhibited the uptake and retention of fluoride. Only very little information is available on this subject in man. In order to investigate whether the changes in fluoride metabolism observed in animals also apply in man, studies were carried out under strictly controlled dietary conditions during the intake of added calcium and phosphorus, used singly and combined and during the intake of added magnesium used alone and in conjunction with calcium and/or phosphate. Fluoride balances were determined in control and experimental studies by analyzing the fluoride intake derived from the diet and drinking water and by analyzing the excretions of fluoride in urine and stool. Increasing the calcium intake 4- to 10-fold from 200 to 800 and 2000 mg/day, and increasing the phosphorus intake similarly, from 800 to 1400 or to 2000 mg/day, did not change the urinary fluoride but increased the fecal fluoride excretion, however, the fluoride balance did not change. Increasing the magnesium intake by a factor of about 3, from 250 to 800 mg/day, did not change the urinary fluoride but increased the fecal fluoride 2- to 3-fold. Despite the increase in fecal fluoride, the fluoride balance remained unchanged as the fecal fluoride excretion was very low in the control study and the increase during the intake of calcium, phosphorus, and magnesium accounted only for a very small fraction of the excreted fluoride in relation to the considerably greater urinary fluoride excretion and in relation to the fluoride intake. (Supported by USPHS grant DE-02486.)

REGIONAL HEMATOCRIT: THEORY, RESULTS WITH PHANTOMS AND INITIAL HUMAN STUDIES. Richard P. Spencer, Harold L. Atkins*, Powell Richards*, Johannes F. Klopper*, Suresh C. Srivastava*, George E. Meinken*, Prantika Som*. Univ. Connecticut Health Ctr., Farmington, CT and Brookhaven National Laboratory, Upton, N.Y.

Ability to estimate the hematocrit of body areas during life would be of use in evaluating shock and documenting splenic red cell trapping in hemodilutional anemias. A technique for determining regional hematocrit (RHC) has been evolved. When a red cell tag is counted in vivo, there are problems of gamma ray absorption and scattering. These are compounded if a plasma radiolabel has a gamma ray of different energy (since absorption and scattering are energy dependent). With a constant geometry of the area, the difficulties are overcome if the red cell and plasma labels bear (in sequence) the identical gamma ray energy. Cr-51 tagged red cells can be used, followed by Cr-51 albumin; the radiolabels of choice appear to be Tc-99m red cells and Tc-99m albumin. Models were made of organs, surrounded by a "body background". When a gamma camera is used with nonfocused collimators, we must refer to the calculated value as RHC rather than a hematocrit of a specific organ; the higher the radioactivity in an organ, and the lower that in the background, the more closely does RHC approach that of a true organ hematocrit. We administer tagged red cells, count the region in vivo and draw a blood sample (radioactivity in the red cells R, corrected for background B). Tagged plasma is given and the in vivo region again counted. A second blood sample (S-B) represents R+P (P=plasma), and the radiohematocrit is R/(R+P). A plasms correction factor is used so that the blood radiohematocrit matches the known hematocrit. This factor is then used in calculating RHC. Initial human studies with Cr-51 as the label have shown a splenic RHC higher than that of the liver. (Supported by USPHS CA 17802).

ENDOTOXIN INFLUENCE ON THE LIPOLYTIC RESPONSE OF ISOLATED RAT FAT CELLS FROM VARIOUS TISSUE SITES. J. A. Spitzer and I. Hikawyj-Yevich, Dept. of Physiology, Louisiana State University Medical Center, New Orleans, La. 70112

It has been previously demonstrated that metabolic adjustments brought about by hemorrhagic hypotension are not uniform at all adipose tissue sites [R. Storck and J. A. Spitzer, J. Lipid Res. 15, 200 (1974)]. Recently we studied the influence of E. coli endotoxin on the in vitro lipolytic response of adipocytes isolated from epididymal (E), perirenal (PR), omental (O) and subcutaneous (SC) tissue sites of 24 hr. fasted Fisher and Sprague-Dawley rats (250-300 g.). Basal and norepinephrine (NE)-stimulated (0.1 µg/ml) free fatty acid (FFA) and glycerol (G) release by control and endotoxin pretreated (0.20 µg/0.5 ml cell suspension for 10 min.) cells were determined. Incubations lasted for 1 hr. and the results were expressed per 10^6 cells. Basal FFA release of E cells of Fisher rats, and O and SC cells of Sprague-Dawley rats was significantly elevated by endotoxin. NE-stimulated FFA and G release of endotoxin treated PR cells derived from Fisher rats was significantly higher than that of untreated cells. Endotoxin treatment of E cells of Sprague-Dawley origin resulted in significantly greater NE-stimulated FFA response than NE-stimulation of control cells. The results indicate that modulation by endotoxin of the lipolytic sensitivity of isolated rat fat cells varies with the strain and tissue site of origin. (Supported by ONR contract #202-501).

THE INFLUENCE OF THE MATERNAL PITUITARY-ADRENAL SYSTEM ON THE DEVELOPMENT AND FUNCTION OF FETAL ADRENAL GLANDS. M.G. Sproul* and S. Levine* (SPON: J.M. Davidson). Dept. of Psychiatry, Stanford University, Stanford, CA. 94025

Adrenal development in fetuses of adrenalectomized (Fadx) and control (Fco) rats was studied over the last four days of gestation (G). Adrenals of Fadx were significantly heavier from day 19G on; however, adrenal corticosterone concentration ([B]) did not differ as a function of day of gestation or maternal adrenalectomy. Fetal adrenal [B] was similar to adult stress levels (87% adult values) and nearly 4 times adult base levels. Thus maternal adrenocortical hormones do retard the growth of fetal adrenal glands; however, fetal adrenal [B] indicates that the glands are quite active. Can fetal adrenal glands respond to further stimulation? The adrenocortical response to a physiological stress was studied in fetuses on day 21G. Adrenals were obtained either before, or 20, 40 or 60 min. after exposure of fetuses to ether for two min. Adrenal [B] increased in both Fadx and Fco; however, the response patterns differed markedly as a function of maternal adrenalectomy. Fadx response peaked at 40 min., and levels remained elevated at 60 min. Fco response peaked at 20 min., and dropped to sub-basal levels by 60 min. Thus fetal adrenals are not maximally stimulated during gestation, and different response patterns found in Fadx and Fco indicate that maternal adrenocortical hormones do influence fetal adrenal function. (Supported by BSTG MH-8304 (NIH) and NICH&HD 02881 (NIH))

ARTERIAL INSTABILITY DEMONSTRATED BY VARIABLE PERFUSION CONDITIONS.
E. Stanley* and H. Krause* (SPON: P. Kezdi). Cox Heart Institute, Dayton, Ohio 45429

Variable resistance of the dog's hind limb was determined by simultaneously recording femoral flow and pressure. Mean flow, pressure, and complex impedance (I) (0-30 Hz) were interpreted during intact (I), nonpulsatile (N), and sinusoidal extracorporeal perfusion (P). Peripheral resistance (R) during (N) correlated inversely with flow acceleration (FA) independent of flow rate. It was R = 1.38 mmHg cm^{-3} for FA = 9.37 $cm^{3}min^{-2}$, R = 0.72 for FA = 21, and R = 0.95 for FA = 13.3. Resistance valves changed abruptly. Extrapolation to zero flow yielded back pressures of 48, 68, and 48 mmHg respectively (water fall proposal). Decelerated flow (Olson's method) confirmed sudden R changes at critical closing pressures (218, 147, 105, and 48 mmHg). The decelerated flow condition confirmed the inverse relation between FA and R. Controlled sinusoidal pulsatile flow (P) produced detailed and dense impedance spectra. Nyquist plots were not continuous. Discontinuities occurred at 2.6 Hz and 11.2 Hz producing three curve segments apparently belonging to three different systems. In conclusion, R does not change gradually, FA is highly correlated with R changes and may be important to explain the Bayless effect. Blood accumulation or depletion in the microcirculation may determine the number of collapsed vessels and R. Variability of R and discontinuous impedance spectra make the application of Fourier techniques questionable. Sudden changes vascular state occur in both continuous and pulsatile perfusion.

EMOTIONAL ALTERATIONS IN THE CIRCULATION DURING CARDIAC CATHETERIZATION.
I. Starr and J.C.Shelburne* Univ. of Pa. Hospital, Phila. Pa. 19104.

In 121 cardiac patients admitted to the University Hospital for diagnostic cardiac catheterization (CC), resting pulse rates (PR) and systolic blood pressures (SBP) were measured after the subjects had rested supine for 1/2 hour or longer, both during CC and in a parallel noninvasive test, the ballistocardiogram (Bcg), made a day or two before. The emotional background of the 2 tests was very different; before Bcg, the subjects were assured that the procedure was free from danger, that they would suffer no discomfort, and that they could go to sleep during the test if they wished. Before CC, all were warned that the procedure was not without danger and signed a statement of their willingness to assume the risk involved. While some had no complaint, many found CC to be a most disagreeable experience. About 1/3 underwent the rigors of CC without significant increase of PR and SBP. In the remaining 2/3 evidence of excitement during the invasive test was clear; significantly larger mean values for PR and SBP being found (t=3.0 and 2.0). But even in this group the mean differences were small, 5.4 per mm and 7.3mmHg, although the scatter was almost 3 times larger in the invasive test. In only a few cases did major increments of PR, +34%, +31%, and +63%, and of SBP, +31%, +54%, +41%, occur during CC. Routine comparison of the PR and SBP found during CC, with the values found when the subject lies at rest in comfort and without apprehension, would permit the identification of those in whom emotion may play a large part in the levels of physiological data secured at CC.
(Supported in part by NIH Grant CVB HE-625.)

THE EFFECT OF TAURINE ON THE INOTROPIC EFFECT AND WORK LOAD IMPOSED ON THE DOG HEART BY ISOPROTERENOL. R.P. Steffen* and W.O. Read. Dept. of Physiology and Pharmacology, The Univ. of South Dakota School of Medicine, Vermillion, South Dakota 57069.

Cardiac performance, as measured by the Time Tension Index (TTI) and rate of intraventricular pressure development during the isovolumetric phase of the cardiac cycle (contractility), was determined in anesthetized vagotomized dogs. Four treatment groups were studied (n = 4/group): 1) taurine, 2-aminoethansulfonic acid, 5 mM/kg i.v.; 2) saline in a volume comparable to that of the taurine treatment; 3) taurine plus isoproterenol; 4) saline plus isoproterenol. All treatment solutions were infused over a 90-minute period and the isoproterenol was titrated to achieve a 10-15% increase in cardiac contractility. During each treatment records were taken with and without stress. The stress was produced by the inflation of a balloon catheter placed fluoroscopically in the ascending aorta juxtaposed to the aortic valve. Taurine had no effect on cardiac contractility in either the stressed or non-stressed condition, but in the stressed condition the TTI with the taurine treatment was less than the TTI with the saline treatment ($P < .01$). Isoproterenol is known to have a positive inotropic effect and to increase the work of the heart. Taurine minimized the inotropic effect of isoproterenol under the stressed condition ($P < .01$) and minimized the increase in TTI produced by isoproterenol in the non-stressed condition ($P < .01$). These data indicate that taurine has a modifying effect on changes in cardiac performance induced by isoproterenol.
(Supported by South Dakota Heart Association Fellowship 74-SD-107.)

THE ASSESSMENT OF ETHANOL VAPOR AS A MEANS FOR INDUCING LIVER INJURY T.E. Stege*, J.D. Hanby*, J.A. Cook* and N.R. Di Luzio, (Spon: J.C. Pisano), Dept. Physiology, Tulane University School of Medicine, New Orleans, La. 70112

The search for an adequate animal model of alcoholism is particularly important in the field of hepatic physiology, since the abuse of alcohol accounts for nearly two-thirds of all cases of cirrhosis. Recently both tolerance and dependence to ethanol have been induced in mice and rats by inhalation of ethanol vapors. Therefore, the chronic inhalation of ethanol vapor was evaluated as a possible method of inducing liver injury in rats. Animals were exposed to ethanol vapor in conjunction with daily injections of pyrazole (6.9 mg/kg), an inhibitor of alcohol dehydrogenase, in order to enhance blood ethanol levels. Animals exposed to ethanol vapors with concomitant administered pyrazole or saline developed classic ethanol-induced fatty livers after 3, 6, and 9 days exposure. However, the ethanol-induced fatty liver was reduced to normal levels after 26 days exposure. Liver triglyceride results correlated directly with blood alcohol levels. After 3, 6, and 9 days exposure blood ethanol levels were significantly elevated. However, blood ethanol levels were markedly reduced at 26 days indicating the development of tolerance to ethanol. Measurement of plasma GOT and plasma triglyceride levels, as well as the clearance of BSP were all normal after 6 days of ethanol vapor exposure. Rats, therefore, after mild transient liver alterations, appeared to adapt after 26 days exposure to ethanol vapor, as reflected by decreasing blood ethanol levels and normal liver triglycerides. Since chronic liquid ethanol diets have been demonstrated to induce significant hepatic alterations, the value of the ethanol vapor technique appears limited in assessing ethanol induced liver injury.

EFFECTS OF SYNTHESIZED THYROXINE ANALOGS ON BASAL METABOLIC RATE OF WHITE RATS. 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 alteration in Basal Metabolic Rate in white rats, and to formulate a possible mechanism for thyroxine activity based on the correlation between the nature of the chemical change in the molecule and the corresponding alteration in BMR. Another possibility which the results of this study might point to is a normal biochemical transformation of the thyroxine molecule into another chemical species at respective target organs. This second possibility might explain the delay in observing thyroxine effects after injection of exogenous thyroxine. Carworth CFE strain rats were allowed to consume food and water ad liberatum. The rats were divided into three major groups, with the third group broken down into several subgroups. Each group received a daily injection of either: 1) 0.9% sterile saline, 2) thyroxine, 20 micrograms, 3) one of the analogs, 20 micrograms. The analogs were synthesized, dissolved in 0.9% saline and passed through sterilized Micropore filters. The analogs were: (1) tetra bromo -L- Thyronine (2) 4 - (4 - hydroxy-3, 5-diiodophenoxy) - 3, 5-diiodocinnamic acid and (3) 4 - (4-methoxy-3, 5-diiodophenoxy)-3, 5-diiodocinnamic acid. The relative effects for each group and subgroup were plotted on a single graph, using the average BMR increase for each injectable obtained by the least squares method. Conclusions drawn were that the iodines at the 3, 5, 3', 5' positions are not critical for activity. The alanine side chain is not essential. The hydroxyl group can be replaced with methoxy group. The key site on the molecules is the halogenated diphenoxy ether linkage which interacts with receptor sites in some fundamental way.

EFFECTS OF RENAL ARTERIAL INFUSION OF SODIUM LACTATE AND POTASSIUM LACTATE ON RENIN SECRETION. G.A. Stephens*, J.O. Davis, R.H. Freeman, and B.E. Watkins*. Dept. of Physiology, Univ. of Missouri, School of Medicine, Columbia, Mo. 65201.

Studies were conducted in 12 dogs with thoracic inferior vena caval constriction with a high rate of renin secretion. After two 15-minute control periods, hypertonic sodium lactate or hypertonic potassium lactate was infused into the renal artery for 1 hour, and renin secretion was measured at 15-minute intervals. Sodium lactate infusion in 6 dogs increased renal venous plasma sodium concentration from 142 to 166 mEq/liter and produced a significant decrease in renin secretion (3073 to 1512 ng angiotensin/min, $P<0.005$); no significant change in arterial blood pressure (BP) or renal blood flow (RBF) occurred. During Na lactate infusion, sodium excretion increased from 8 to 447 μEq/min ($P<0.001$), while chloride excretion fell during the first three 15-minute infusion periods (34 to 22, 22 and 22 μEq/min, $P<0.05$). Potassium lactate infusion in 6 dogs increased renal venous plasma potassium concentration from 4.1 to 6.2 mEq/liter with a significant decrease in renin secretion during the first three 15-minute periods of infusion (3465 to 2537, 1792 and 2213 ng angiotensin/min, $P<0.01$). Potassium lactate infusion produced no significant change in BP but RBF was significantly elevated during the second 15 minute period. Renal venous plasma sodium and chloride concentrations were unchanged. Excretion of sodium (4 to 25 μEq/min, $P<0.001$), potassium (32 to 112 μEq/min, $P<0.001$) and chloride (10 to 60 μEq/min, $P<0.001$) increased significantly during the infusion. These results show that renin secretion decreased with Na lactate without a chloruresis but the response to K lactate was associated with increased chloride excretion.

ASZ(DCPB)

ROLE OF THE CIRCADIAN PACEMAKER IN ESTROUS CYCLICITY IN HAMSTERS: CYCLIC GONADOTROPIN RELEASE IN THE PRESENCE AND ABSENCE OF OVARIAN NEGATIVE FEEDBACK. Milton H. Stetson, Marcia Watson-Whitmyre* and Kathleen S. Matt*, University of Delaware, Newark, Delaware 19711

Two or three weeks after ovariectomy adult hamsters housed on 14 hrs of light per day (lights 0600-2000 EDT) a) received a 5mm Silastic implant containing crystalline 17-B-estradiol, b) received an empty implant or c) received no implant. Following decapitation 1, 3 or 5 days later, serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were measured by radioimmunoassay. The animals in every group demonstrated a daily release of LH and FSH between 1300 and 1800 hrs EDT. Basal LH levels were near-normal in all groups whereas "basal" FSH levels were elevated by a factor of 50-100. Estradiol induced 1 day later the release of normal "preovulatory" levels of LH while "preovulatory" FSH release was elevated X5. Prolonged retention of estradiol implants was correlated with reduction of peak LH and FSH release and reduction of "basal" FSH levels. Peak LH levels in castrates with or without empty implants were 35-40% of normal at 3 or 4 weeks post-castration. Peak FSH levels in these animals were 6-10X normal and out of phase with LH release. The biphasic proestrous-estrous FSH release requiring 31 hrs in intact females appears to be compressed to a 24 hr periodicity in castrates. These results suggest that an endogenous pacemaker times gonadotropin release in reproductively mature female hamsters and that ovarian steroids act merely to effect the levels of each hormone released.

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BMES

UNIQUE INOTROPIC EFFECT OF FREE FATTY ACID ON CARDIAC MUSCLE: EXPERIMENTAL AND ANALOG SIMULATION ANALYSIS. P.J. Stoll, A.F. Salel*, T.A. Brandon*, C.J. Drake* and D.T. Mason*. Cardiology, UC Davis, CA 95616.

Free fatty acid-albumin solutions (FFA) have recently been shown in our laboratory to enhance the contractile properties of cardiac muscle. In order to understand the mechanism underlying this change in the force-velocity relationship, the physiological properties of isometric and isotonic right ventricular papillary muscle preparations under the influence of known myocardial stimulants [digoxin (DIG), isoproterenol (ISO)] and depressants [propranolol (PRO) and pentobarbital (PEN)] were compared with those changes caused by FFA. As FFA concentrations (conc) were increased to 1 mM, peak contractile element velocity (Vmax, from Hill's equation) rose 35-50% above control but maximum developed tension (S_0, gm/cm^2 muscle) fell to 30% below control. However, with classic inotropic agents, S_0 and Vmax were concordant. Measured tension-time curves were fitted to computer simulations using a generalized form of Hill's equation, where t_m is time-to-peak tension; λ is an amplitude constant independent of curve shape; $\gamma = a/S_0$; a and b are Hill's original constants. The increase (↑), decrease (↓) or absence of change (→) in the magnitudes of the simulation parameters are shown below:

	t_m	λ	b	γ	Vmax	S_0
FFA	→	↓	↓	↑	↑	↓
DIG	↑	↑	→	→	↑	↑
ISO	↓	↑	↑	→	↑	↑
PRO	→	↓	→	→	↓	↓
PEN	→	↓	→	→	↓	↓

Since the simulation analysis of FFA influence on cardiac muscle is markedly dissimilar from that of known inotropic agents, a previously unrecognized mechanism of dissociated action on force and shortening is demonstrated.

INTRAMITOCHONDRIAL LACTATE OXIDATION IN HYPOTONICALLY TREATED RABBIT EPIDIDYMAL SPERMATOZOA. B.T. Storey* and F.J. Kayne* (SPON: M.M. Civan). Depts. of Obstetrics and Gynecology, Physiology, and Biochemistry and Biophysics, University of Pennsylvania School of Medicine, Philadelphia, PA 19174.

Glycolysis yields either lactate with no cytosolic redox imbalance, or pyruvate plus cytosolic NADH whose reducing equivalents must be transferred to the NADH-impermeable mitochondria to maintain cytosolic redox balance. We have found that suspensions of hypotonically treated rabbit epididymal spermatozoa (HTRES), in which the mitochondria are fully intact and accessible to added reagents, oxidize added lactate more rapidly than added pyruvate; there is no detectible oxidation of added NADH. Lactate oxidation is equally rapid in the absence of or in the presence of either added NAD+ or NADH. Redox studies of mitochondrial pyridine nucleotide (MPN) using fluorescence show that both lactate plus malate and acetyl-L-carnitine plus malate give comparable MPN reduction in the aerobic steady state, and the same maximal reduction in the presence of rotenone, which blocks reoxidation of MPN. Addition of lactate to rotenone-treated HTRES in the presence of acetyl-L-carnitine plus malate gives no further MPN reduction, showing that MPN is the only pyridine nucleotide pool in HTRES accessible to lactate. Addition of pyruvate causes reoxidation of reduced MPN in the presence of rotenone. An intramitochondrial LDH must therefore be present to equilibrate the redox state of MPN with pyruvate/lactate. The rabbit sperm cell apparently handles cytosolic redox imbalance from glycolysis by the unique route of direct intramitochondrial lactate oxidation. (Supported by USPHS grant HD-06274 and NSF grant GB-43235).

REGIONAL MYOCARDIAL ISCHEMIA IN THE PIG:A MODEL FOR MECHANICS AND METABOLISM. DF Stowe*, JV Tyberg, DG Mathey*, WY Moores*, RM Townsend*, P Kabra*, K Chatterjee*, and WW Parmley. Cardiovascular Research Institute, Univ. of California, San Francisco, CA 94143.

Because ischemic heart disease involves partial coronary stenosis and heterogenous perfusion, we have developed a model to analyze regional (R) left ventricular (LV) performance and metabolism during periods of controlled, graded ischemia (I). In 16 open-chest anesthetized pigs, blood flow (BF) to a R supplied by the 1. ant. descending art. (LAD) was fixed by means of an arterial (a) bypass and constant volume (V) pump at either 100, 75, 50 25 or 0% of the basal flow rate for up to 90 min. 19±6(SD)% of the total heart mass was perfused. We measured R mechanical work per stroke (S) in both ischemic (IRSW) and control (CRSW) segments of the LV by on-line computer integration of approximations for R wall stress (LVP·length (l)/thickness (t))xdl/dt. l and t were measured by ultrasonic crystals. Global measurements were: LVP, dP/dt, SV and LVSW. Metabolic indicators, assessed in the IR coronary vein (cv) blood, were: pH, PCO_2, O_2 content, lactate (Lac)and inosine (Ino). $[Ino]_a$ was 11.3±3.6(SD) μM. Means at 15 min represent percent of controls before LAD bypass:

RBF	Δl_I	Δt_I	Δl_C	IRSW	CRSW	LVSW	Ino(a-cv/a)	Lac(a-cv/a)	n
100	84	103	121	109	100	98	9	10	2
75	71	-17	77	68	82	86	10	-7	3
50	29	-16	109	61	103	105	-59	-27	3
25	-32	-11	132	23	---	77	-314	-72	4
0	-17	-53	90	11	70	78	-366	-83	4

Ino(a-cv) varied with Lac(a-cv) ($r=.80$, $p>.01$). R-DO_2 varied with % IRSW ($r=.78$, $p>.01$) and with Lac(a-cv) ($r=.60$, $p>.05$). Thus, because R function and metabolism vary linearly with the degree of I, this model should be sensitive to the effects of interventions.

DIELECTRIC PROPERTIES OF RABBIT CEREBRAL CORTEX IN THE RADIO FREQUENCY RANGE. R. D. Stoy* and H. P. Schwan. Dept. of Bioengineering, University of Pennsylvania, Philadelphia, PA 19174.

Virtually no dielectric data on brain tissue has been made available in the radio frequency range. There is considerable need for such data in order to better understand the interaction of RF electromagnetic fields with man and the possible health hazards involved. The equivalent parallel conductivity and permittivity of excised rabbit brain cerebral cortex were measured over the range from 100 kHz to 100 MHz. All measurements were performed within one hour of excision and did not vary significantly during the period of measurement. The permittivity relative to vacuum changes as a power function of frequency from about 4000 at 100 kHz to about 75 at 100 MHz. The conductivity at 100 kHz is about 1.6 m mho/cm and changes with frequency at first slowly but then more rapidly to a value of about 6 m mho/cm at 100 MHz. The data connect well with data obtained previously at lower and higher frequencies. A summary of available data is presented.

Mechanism responsible for the data are characterized by a broader spectrum of time constants than characteristic for other tissues of high water content such as muscle. This spectrum probably originates to a large extent from Maxwell Wagner type dispersion phenomena caused by charging of cellular membranes.

GASTRIC EMPTYING AT CONSTANT INTRAGASTRIC PRESSURE. U.T. Strunz* and M.I. Grossman. VA Wadsworth Hospital Center, Los Angeles, CA 90073

In 5 dogs with gastric fistulas, gastric emptying of liquids was studied while keeping intragastric pressure constant by means of a barostat, a reservoir 7 cm in diam that dampened fluctuations to less than 1 cm H_2O pressure. An automatic device instilled additional test fluid as required to keep the barostat at a selected level. Reference point for zero pressure was the entry of the cannula into the abdominal wall. 0.5 M $NaHCO_3$ was added at the rate needed to keep pH at 5.5. In calculating vol emptied, vol of gastric juice secreted and vol of $NaHCO_3$ added were taken into account. Vol recovered from the stomach at the end of the test (90 min) served as an index of the distensibility of the stomach at each pressure. With both saline (SAL, pH 5.5, 300 mOsm kg^{-1}) and 10% liver extract (LE, pH 5.5, 500 mOsm kg^{-1}) rate of emptying (ml min^{-1}) increased with increasing pressure. At low pressures, emptying rate and vol recovered did not differ for SAL and LE. At higher pressures, SAL emptied more rapidly than LE and recovered vol was greater with LE than with SAL.

Intragastric pressure (cm H_2O)	Emptying rate (ml min^{-1})		Recovered vol (ml at 90 min)		N
	SAL	LE	SAL	LE	
0	1.6± .34	2.1±.34	88±13	82± 8	10
2.5	3.1± .58	3.1±.47	78± 5	73± 9	9
5	9.3±1.3	5.7±.90	89±10	246±50	10
10	20.0±1.4	8.2±.89	227±50	1297±191	7

CONCLUSIONS: Increasing intragastric pressure causes increasing rates of gastric emptying of fluids. Factors other than intragastric pressure also regulate emptying because at the same pressure saline empties more rapidly than liver extract.

NON-EXCISED BLOOD-PERFUSED CANINE PAPILLARY MUSCLE PREPARATION AND ITS PEAK-SYSTOLIC FORCE AND LENGTH RELATIONSHIPS IN TRANSIENT AND STEADY STATES. Hiroyuki Suga, Kiyoshi Nakayama*and Kiichi Sagawa Dept.Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, Md. 21205

This study was undertaken to analyse contractile behaviors of the papillary muscle in more physiological conditions than those for the conventional excised preparations. A mechanoelectric servocontrol system was devised for analyses of the mechanical contractile properties of a non-excised blood-perfused papillary muscle. The muscle preparation (unstressed length l_0 = 9 ± 1(SE) mm, cross-sectional area = 8.5 ± 0.8 mm^2) was selected from the anterior papillary muscles of the right ventricle of the excised, cross-circulated canine heart. Preparations' temperature was kept at 37 C. Heart rate was 110 ± 4 /min. The peak-systolic force-length relationship curves of such preparations were compared between isometric and isotonic modes of contraction over a wide range of muscle length (l_0 to 1.4 l_0). The steady-state (1 - 2 min)peak-systolic force-length relationship curve for isotonic contractions was somewhat lower (24 ± 11 % at comparable lengths) than the isometric one obtained under a given inotropic background. However, the isotonic relationship curve obtained from the first beats after switching from the isometric to isotonic mode at identical peak-systolic muscle lengths was identical with the steady-state isometric curve. The difference in the steady-state relationship curves of the two modes was found to be due to 1)a relatively rapid (5 - 10 sec) shift of the resting force-length relationship curve because of a creep phenomenon in the isotonic mode and 2) a relatively slow (0.5 - 2 min) reduction of the amount of shortening.

(Supported by grant HL - 18912.)

PROLONGED DEPRESSION OF REGIONAL MYOCARDIAL FUNCTION FOLLOWING TRANSIENT ISCHEMIA IN CONSCIOUS DOGS. J.A. Swain*, H.G. Hanley*, K.R. Genth*, R.M. Lewis*, C.J. Hartley*, and A. Schwartz. Departments of Cell Biophysics, Medicine and Surgery, Baylor College of Medicine, Houston, Texas 77030.

The effects on regional myocardial function of short (3 minute)coronary artery occlusions followed by reperfusion were evaluated to delineate the time course of the recovery of contractile function of ischemic myocardium. Conscious unsedated dogs instrumented 2-6 weeks prior to study with circumflex coronary artery flow probes and occluders, a left ventricular pressure gauge, and 3 pairs of subendocardial ultrasonic crystals for measurement of segment length in the ischemic zone were observed for 21 hours after a 3 minute coronary artery occlusion. Regional function expressed as end diastolic length (EDL) minus end systolic length (ESL) divided by EDL was evaluated for 9 pairs of segments in 5 dogs. Coronary occlusion produced an 88 ± 4% decrease in function in the ischemic zone. Upon release of occlusion there was a return to near control by 1 hour that persisted until 4 hours. Late depression of function then occurred, was maximum at 6 hours (-16.6 ± 1.8%), with subsequent gradual improvement (-10.7 ± 1.5% at 12 hours) and a return to control by 15-21 hours. Two other parameters of contractile function; ESL, and EDL-ESL (shortening),also reflected decreased function at 6 hours (ESL increased 5.3 ± 1.0% and EDL-ESL decreased 15.7 ± 2.5%). These results are consistent with our biochemical studies of regional ischemia in open chest anesthetized animals demonstrating prolonged defects in mitochondria. Therefore, transient coronary artery occlusion in the conscious dog produces a prolonged period of depression of myocardial function that has not been previously recognized.

RESPIRATORY FUNCTIONS OF BLOOD FROM THE LESSER MOUSEDEER, TRAGULUS JAVANICUS. G.K. Synder* and W.W. Weathers. (SPON: W.O. Wilson). Dept. of EPO Biology, Univ. of Colorado, Boulder, CO 80302

Respiratory characteristics and selected hematological parameters of whole blood from the lesser mousedeer were studied. Oxygen-hemoglobin equilibrium curves, determined with a mixing technique at 37°C and 10, 36 and 71 torr P_{CO_2}, have the same configuration observed in blood from mammals in general. The P_{50} of mousedeer blood at a P_{CO_2} of 40 torr is 34 torr; the Bohr effect, $\Delta \log P_{50}/\Delta pH$, is -0.483; and the slope of the P_{CO_2} titration curve, $\Delta \log PCO2/\Delta pH$, is -3.76. The red corpuscle dimensions, determined under oil immersion with an ocular micrometer, averaged 2.2μ, while the cell counts averaged 53 million/ microliter blood and the packed cell volume averaged 29.8%. Blood hemoglobin concentration averaged 11.2 g % and the calculated mean cell hemoglobin concentration was 38 g %. The hematological features are consistent with the observation that small corpuscle size is compensated by high cell counts, resulting in a relatively constant packed cell volume. The mean cell hemoglobin concentration is higher than mammals in general but similar to other artiodactyls. The relative viscosity of the mousedeer plasma was 1.97. The viscosity increased in a non-linear manner with hematocrit to 100 at 80% packed cell volume. The shape of the viscosity curve is similar to those prepared with blood from a variety of mammals. These data suggest that the small size and spherical shape of the mousedeer erythrocytes are not significant factors in altering the respiratory functions of whole blood, at least under the conditions employed in these studies. (Supported by NSF grant BMS 75-02343)

RESPIRATORY RESPONSES OF UNANESTHETIZED CATS TO THERMAL STRESS. M. Tabatabai*, A. Ovassapian* and M.S. Shahid Salles* (SPON: J. R. Brobeck). Dept. Physiol., Sch.Med., Pahlavi University, Shiraz, Iran.

One of the thermoregulatory mechanisms in some animals on exposure to heat is panting. The question verified in this study was whether in cats the increased respiratory rate during panting affects only the dead-space ventilation or increases the alveolar ventilation as well. Ten cats, lightly anesthetized with open-drop halothane were tied to the operating table, and in each the left femoral artery was cannulated. Respiration and rectal temperature were recorded. Two arterial blood samples were drawn at 15-minute intervals after the cats had become fully conscious. Then they were exposed to ambient temperature of 47-49 C. The third blood sample was obtained at the onset of panting and seven more samples thereafter at 15-minute intervals. The animals were removed from the hot environment when their rectal temperature reached 41 C. The blood samples were analyzed for PO2, PCO2 and pH and the values were corrected for the animal's temperature at the time of the blood withdrawal. Control experiments were carried out on five cats to separate the effects of thermal stress from those of general stress induced by restraining the animals. In the test group, the mean respiratory rate increased from 28 to 365 per minute as the mean rectal temperature rose from 38.2 C to 41.2 C. The initial mean arterial PO2 of 95 mm Hg went up to 111 mm Hg, while the mean arterial PCO2 dropped from 34 mm Hg to 21 mm Hg, and the mean arterial pH of 7.31 increased to 7.44 at the peak respiratory rate of 365 per minute. The increase in the arterial PO2 and pH and the decrease in the arterial PCO2 during panting indicate increased alveolar ventilation. In the control group, the mean respiratory rate of 29 per minute rose to 44 one hour after restraining when the animals were untied.

ELECTRICAL PROPERTIES OF PASSIVE NERVE AXON MEMBRANE, S. Takashima, Dept. of Bioengineering, University of Pennsylvania, Philadelphia, Pa. 19174

In the measurement of membrane admittance of nerve axons, there are two sources of major errors. One of them is the series resistance due to the presence of electrolyte solutions between the membrane and electrodes. The other is the fringe effect at the tip of the internal electrode. Currently there are two methods to correct for the fringe effect. 1) Use of guarded internal electrode and 2) Use of internal electrodes with varying lengths. The fabrication of guarded internal electrodes is cumbersome and difficult to use. Using the second method, we found the magnitude of the fringe capacitance to be 0.06-0.07μF. After subtracting this value, the membrane capacity reduces to 0.75μF/cm^2 from the well known value of 1μF/cm^2. Membrane conductivity reduces, after the correction, to 0.1-0.2 mmho/cm^2 instead of the widely accepted value of 1mmho/cm^2. Resting membranes are partially active and a truly passive membrane can only be obtained by hyperpolarizing the membrane to -120mV. At this potential, membrane capacity further decreases to 0.6-0.65μF/cm^2 and only slightly frequency dependent. Membrane conductivity with hyperpolarization reduces even below 0.1m mho/cm^2. Under these conditions, the analogy "Leaky Condensor" may not be suitable for passive membranes. This research is supported by ONR N00014-76-C-642, NSF GK-40119 and NIH HE-012-53.

THE EFFECT OF CHANGING THE TEMPORAL PATTERN OF FCO_2 IN THE INSPIRATORY GAS FLOW OF BIRDS. R. D. Tallman* and A. L. Kunz, Dept. of Physiol., The Ohio State Univ. College of Med., Columbus, Ohio 43210.

Kunz and Miller (Resp. Physiol. 22: 167-177, 1974) have shown that the ventilatory movements of a unidirectionally-ventilated chicken lock in synchrony onto the frequency of forced FCO_2 oscillations in the lung gas. The event in the FCO_2 oscillation which sets the time of the next breath in this situation is FCO_2 beginning to rise after passing thru a minimum. The present study examines what this phenomenon in the unidirectionally-ventilated chicken means in a bird which is breathing in a normal manner. Awake chickens are used. The trachea is cannulated and connected to the side arm of a "T" tube carrying an air stream of 5 L·min^{-1}. The FCO_2 in the air stream is controlled by a computer. Ventilatory movements are monitored with a whole body plethysmograph. Tracheal FCO_2 is continuously sampled and measured with a Beckman Medical Gas Analyzer. The time between the beginning of inspiration and the arrival and departure of a pulse of "fresh air" (0% CO_2) at the trachea is varied. In the steady state, respiratory period was found to be a function of the time between the beginning of inspiration and the beginning of the rise of FCO_2 in the inspired gas. This supports the hypothesis that the respiratory period in avian ventilation is determined by the length of time after an inspiration before FCO_2 again begins to rise. (Supported in part by the National Heart and Lung Institute Grant HL 14870-05 and Office of Naval Research Grant NR 201-001.)

LACTATE AS RELATED TO EXHAUSTION: EFFECTS OF EXOGENOUS K^+-ASPARTATE. S. Tangsakul*, Z. Kendrick*, A. Goldfarb*, and P.A. Molé *(SPON: L. Toth). Biokinetics Research Lab, Temple University, Philadelphia,PA

Dose-response studies established that injecting (IP) 12.5 mg/kg K^+-aspartate (K-asp) 1 hr prior to work maximally increased swim time to exhaustion (STE) 90% in female rats. In a second study, animals were sacrificed at rest or following work to exhaustion after saline, KCl, or 12.5 mg/kg K-asp injections 1 hr prior to the swim. As found before, STE was increased 90% by the K-asp treatment. Exogenous K-asp, however, did not alter the levels of lactate (lac), pyruvate (pyr), alanine (ala), and aspartate (asp) in blood or muscle at rest or at exhaustion. STE was not significantly correlated with pyr or ala in either muscle or blood. STE was positively correlated with muscle asp and lac, but negatively correlated with blood asp and lac. K-asp treatment shifted the relationships such that animals had a longer STE for a given level of blood asp and lac. Lac accumulated over 2 times slower in blood and 46% slower in muscle with K-asp treatment. These effects of exogenous K-asp may reflect a reduced rate of glycogenolysis in muscle and/or an increased rate of lac uptake by extramuscular tissue. The 90% increase in STE produced by exogenous K-asp could have been due to a reduced rate of glycogen depletion. This interpretation is consistent with other research showing that work is prolonged either by having high initial muscle glycogen stores or by reducing the rate of glycogen depletion in muscle and liver. Further studies are needed to elaborate on this possibility.

EVIDENCE OF REFLEXIVE BETA ADRENERGIC MOTOR STIMULATION IN THE CANINE STOMACH AND SMALL INTESTINE. M.F. Tansy, J.S. Martin*, W.E. Landin* and F.M. Kendall, Dept. of Physiol. and Biophys., Temple Univ. Hlth. Sci. Ctr., Philadelphia, Pennsylvania 19140

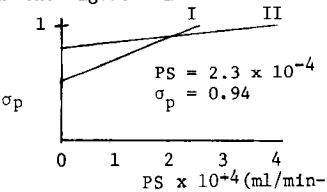
The expected gastrointestinal motor responses to central vagal stimulation (CVS) in bilaterally vagectomized dogs include relaxation of the stomach and small bowel. However, occasionally, an excitation of motor activity is observed. The purposes of this study were to determine whether the inhibitory response could be consistently converted to an excitatory effect by the use of appropriate pharmacological blockade, the nature of the excitatory motor response which resulted after blockade, the afferent and efferent limbs subserving the excitatory effect, and the possible nature of the neurotransmitter(s) which mediate the motor response. Ten nightly fasted adult mongrel dogs of either sex were anesthetized with a mixture of chloralose-urethan. Surgical preparation included the placement of balloons in the stomach and small intestine and bilateral cervical vagectomy. CVS in untreated dogs always produced a reduction in gastric and small bowel activity. CVS following administration of phenoxybenzamine resulted in increased propulsive and segmenting activity of these two organs. These excitatory responses were abolished by bilateral section of the sympathetic chains and could be reproduced by electrically stimulating the chains. Similar responses were observed in dogs that had been chronically reserpinized. The excitatory effects of either CVS or peripheral sympathetic stimulation could be abolished by dichloroisoproterenol. It is concluded that a sympathetic pathway exists which is excitatory to the stomach and small bowel, and that these excitatory effects are mediated by beta adrenergic neurotransmission.

CONTRACTILE ACTIVATING SUBSTANCE RELEASED FROM ISOLATED SINGLE FROG ATRIAL CARDIAC CELLS. Merrill Tarr and John W. Trank. Dept. Physiology, Univ. Kansas Med. Ctr., Kansas City, Kans. 66103

Microprobe impalement of isolated frog cardiac cells produces immediate cell death. Surprisingly, neighboring cells not in direct contact with the impaled cell often give twitch contractions after the death of the impaled cell. A plot of the time interval of cell impalement-neighboring cell contraction versus the square of the cell separation distance gives a straight line having a slope of $1.9 \times 10^4 sec/cm^2$. This suggests that a substance is released from the impaled cell which diffuses to neighboring cells and activates contractile activity. A diffusion coefficient of 8.8×10^{-6} cm^2/sec for the substance can be calculated from the time versus distance squared relationship assuming that 1) the substance diffuses away from the impaled cell as from an instantaneous point source of strength Q, and 2) the neighboring cell contracts when the peak of the concentration wave propagating away from the point source contacts the cell. The nature of the substance is unknown. Its ability to activate contraction was abolished by the absence of calcium in the bathing medium, but was not abolished by the presence of high extracellular potassium (28 mM). Considering the small volume contained by a single cardiac cell (5-10 picoliters) and that contractile activation of neighboring cells can occur at cell separation distances as great as 350 μm, it seems that the substance must be effective in small concentrations; an instantaneous point source of Q = 1 picomole (intracellular concentration of 100 mM) would produce a maximum change in concentration of 5 μM at 300 μm from a point source located at the center of the base of a hemisphere. (Supported by grant HL-18943 from NHLI and a Kansas Heart Assoc. Grant-in-Aid).

Estimation of PS Products and Reflection Coefficients for Plasma Proteins Across the Microcirculatory Exchange Barrier. A.E. Taylor and D.N. Granger*. Dept. Physiology, Univ. Miss. Med. Cntr. Jackson MS 39216.

The Kedem and Katchalsky equation describes a steady-state relationship between the permeability surface area product (PS) and the reflection coefficient (σ_p) that is linear. If lymph flow, lymph protein concentration and plasma protein concentration can be measured at two different lymph flow-tissue steady states, then a unique σ_p and PS may be determined for the experimental conditions. A plot of σ_p vs PS is shown in the figure below for the data of Chen et al. CIRC. RES. 1976.



Curve I represents data calculated from a dog hind paw preparation at a venous pressure of 5 mm Hg and Curve II represents data obtained at 35 mm Hg. The point at which the two curves intersect yields a solution that will describe both sets of protein flux data in terms of a single σ_p and PS. This approach is a very simplistic approach that allows an approximation of σ_p and PS for two experimental conditions, and more importantly, if the curves do not intersect at a common point, then the analysis will indicate what physiological changes have occurred which alter σ_p and PS in certain experimental maneuvers. Supported by NIH grant 11477.

TRACE ELEMENTS IN HUMAN ARTERIAL HYPERTENSION. Gurdarshan S. Thind, Grace M. Fischer and Nancy C. Flowers*, Hypertension Unit of Cardiology Section, University of Louisville School of Medicine, Louisville, Kentucky 40201.

Imbalance of cadmium and zinc has been implicated in the pathophysiology of human and experimental hypertension. Plasma cadmium and zinc (ug/l) was determined by atomic absorption spectrophotometry in inferior vena caval or peripheral venous specimens obtained from 30 hypertensive patients and 15 normal subjects (volunteers); none of whom had significant clinical renal failure. All hypertensive medications were discontinued 7-10 days prior to the collection of plasma specimens. There was no difference in the age and sex distribution, BUN and serum creatinine of normal subjects and hypertensive patients. The mean arterial blood pressure of hypertensive patients (143 $\pm$ 4 (SEM) mm Hg) was significantly higher ($P < 0.001$) than normal subjects (96 $\pm$ 2.0 mm Hg). The plasma cadmium (mean $\pm$ SEM) of hypertensive patients (2.92 $\pm$ 0.31 ug/l) was significantly higher ($P < 0.05$) than that of normal subjects (1.90 $\pm$ 0.19 ug/l). The cadmium/zinc ratio X 10^3 was significantly higher ($P < 0.015$) in hypertensive patients (3.02 $\pm$ 0.03) than in normal subjects (1.72 $\pm$ 0.02). There was a significant direct correlation of the cadmium/zinc ratio with the level of mean arterial blood pressure of hypertensive patients and normal subjects ($P < 0.015$). The data suggested that elevated plasma cadmium and elevated cadmium/zinc ratio is associated with arterial hypertension. It is conceivable that public health measures to limit the environmental exposure to cadmium may reduce the risk and/or severity of arterial hypertension and its complications.

BMES

COMBINED OPTICAL AND ELECTRONIC ANALYSIS OF CELLS WITH THE AMAC TRANSDUCER. R.A. Thomas, T. Yopp, B.D. Watson B.F. Cameron, S.B. Leif and R.C. Leif

The amount of information utilized by flow transducers to discriminate between classes of cells must be at least equal to, and preferably greater than, that obtained with pattern recognition systems, since any uncertainty in classification with a flow analyzer requires the additional costs of sorting and consequent slide preparation and analysis. The solution to this problem for flow analysers is to increase both the precision and the dimensionality (numbers of parameters) of the data. The optimal solution to this problem is the fabrication of a small square orifice with sensing electrodes located at both ends. This has been accomplished by constructing an orifice out of quartz. This combined electro-optical transducer has been utilized for both fluorescence and electronic cell volume measurements. The diffraction effects due to the orifice appear minimal and should not interfere with the scattering produced by the cells. Results will be reported both with visible argon ion laser and ultraviolet excitation. The fluorescence emission is both dispersed and separated from the scattered light by a holographic grating. Previous studies with a round but otherwise electronically similar orifice have indicated that it was possible to determine the shift in phase produced by the presence of a particle in the orifice.

(Supported by NIH Grants CA13441, GM18671 and HL15999).

Dr. B.F. Cameron is an Established Investigator of the American Heart Association.

ASZ(DCPB)

MONOAMINE-AFFECTING DRUGS AND CONDITIONED AVOIDANCE LEARNING IN THE BLACK-CHINNED MOUTHBROODING TELEOST. R.F. Thomas and L.R. Aronson, Dept. of Animal Behavior American Museum of Natural History, N.Y., N.Y.

Intracranially and intramuscularly injected drugs were tested for the acquisition and performance of a conditioned avoidance response (CAR) with light as the conditioned stimulus. Two classes of drugs were used: 1) drugs which inactivate the monoamine neurotransmitter at synapses (Alpha-m-tyrosine, Chlorpromazine, p-Chlorophenylalanine, Reserpine and Tetrabenazine); 2) drugs which increase levels of monoamines or potentiate their effects (Imipramine, Iproniazid and L-Dihydroxyphenylalanine). Acquisition group fish, Sarotherodon melanotheron, (formerly Tilapia macrocephala) were given a single dose of drug, after which the learning of the CAR was monitored until a specific criterion was or was not reached. Drugs were given to performance group fish, i.e., animals which had acquired and maintained the CAR at a criterion level of at least 80% avoidances for 5 consecutive daily sessions. Results show that drugs which reduce the effects of catecholamine (CA) have a disruptive effect on the maintenance of a well-established CAR, but not on acquisition. Drug-induced reduction of 5-HT did not suppress the overall performance of the CAR, but relative decreases in 5-HT produced deficits in acquisition. The ratio of neuronal CA/5-HT activity plays a role in the acquisition of the CAR.

AN AUTOMATED FREEZING PROCEDURE FOR STUDIES OF METABOLISM OF MAMMALIAN MYOCARDIUM DURING A SINGLE CONTRACTION. C.I. Thompson,* R. Rubio and R.M. Berne. Dept. of Physiol. University of Virginia School of Medicine Charlottesville, Virginia 22901.

Previous studies of cardiac metabolism during a single contraction have been limited to the amphibian heart at low temperatures. Similar studies in the mammalian heart are lacking because the time for enzyme inactivation by freezing (approx. 50 msec) can be as long as the time to peak tension (80-100 msec). A technique was developed for precise sampling at specific moments of the mammalian cardiac cycle which were prolonged in order to reduce freezing time to a small fraction of the duration of the contractile process. In isolated, Krebs-Henseleit-perfused guinea pig hearts, contraction was prolonged by lowering the temperature to 33°C and by replacing Ca^{2+} by Sr^{2+} (5mM). This divalent ion substitution increased the duration of contraction and time to peak tension from 546 and 221 msec. to 1519 and 355 msec., respectively. These values are considerably larger than the minimum freezing time. To increase the precision of sampling, an automated system was designed allowing the point of time of tissue freezing to be predicted within 10 msec. The system involves electronically triggered modified Wollenberger clamps. The electronic triggering device can be activated by any mechanical or electrical event. By means of a variable triggering level and the use of a variable time delay (0-1.5 sec), it is capable of tissue sampling at predetermined points in the contractile cycle. The resulting tissue waffers are 0.5-1.0 mm thick and weigh approximately 1.7 g. Using this technique, the improved time resolution for tissue sampling and the prolonged contraction will permit metabolic studies to be carried out in the mammalian myocardium during a single contraction.

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RELEASE OF GASTRIN FROM AN ANTRAL POUCH BY LIVER EXTRACT BATHING OXYNTIC AND INTESTINAL MUCOSA. M.R. Thompson*, H.T. Debas*, J.H. Walsh* and M.I. Grossman. VA Wadsworth Hospital Center, Los Angeles, California 90073

In 3 dogs with gastric fistulas (GF) and innervated pouches of the entire antrum (IAP), 10% liver extract was instilled into the GF at 100 ml/hour for 2 hours under 3 conditions: 1) IAP filled with 0.15 M $NaHCO_3$, 2) IAP filled with 0.15 M HCl, and 3) after surgical removal of the IAP. Serum gastrin was measured by radioimmunoassay.

		Serum gastrin (pg/ml)		
			During	
Antral pouch	N	Before	1st hour	2nd hour
$NaHCO_3$	14	73	98	99
HCl	14	66	79	101
after antrectomy	9	47	52	52

The increases in serum gastrin above basal were statistically significant ($p<0.05$) before antrectomy and the $NaHCO_3$ and HCl conditions did not differ significantly ($p>0.05$). After antrectomy serum gastrin did not increase above basal significantly ($p>0.05$). Thus instilling liver extract into the oxyntic part of the stomach and thereby into the intestine (without contact with the antrum) caused release of antral gastrin that was resistant to inhibition by acid bathing the antrum. Release of antral gastrin by the peptide bombesin is the only other form of gastrin release known to be resistant to antral acidification. Therefore we speculate that liver extract might release a bombesin-like peptide that in turn releases antral gastrin.

REDUCED DIPSOGENIC RESPONSIVENESS TO VARIOUS STIMULI IN RATS TREATED WITH AN ESTROGENIC AGENT. T. N. Thrasher and M. J. Fregly, Dept. of Physiol., Univ. of Florida, College of Medicine, Gainesville, Florida 32610.

Administration of the estrogen, ethinyl estradiol (36 µg/kg/day), alone, and in combination with the progestogen, norethynodrel (165 µg/kg/day), significantly attenuated the dipsogenic response characteristically induced by acute s.c. administration of the β-adrenergic agonist, d,l-isoproterenol (50 µg/kg). Attenuation was apparent within 1 week of steroid treatment and remained during the 4 weeks of testing. After 16 weeks of steroid treatment, the drinking response to acute i.p. administration of renin (2 and 4 Goldblatt Units/rat) was tested. The groups receiving ethinyl estradiol alone, and in combination with norethynodrel, but not norethynodrel alone, showed a reduced water intake compared with untreated controls. Drinking induced by administration of hypertonic saline (1% of body wt. of 1 M NaCl solution, i.p.) was also reduced in rats treated with the estrogenic, but not the progestational, agent. However, estrogen treatment did not affect drinking following a 24-hour period of dehydration. Although the reduced dipsogenic response to isoproterenol observed in estrogen-treated rats may reflect a reduced renin secretion, drinking could not be induced in these animals by administration of renin. In addition, the reduced dipsogenic response to hypertonic NaCl loading suggests that estrogens may inhibit thirst mechanisms centrally. Dehydration, which combines hypovolemic and osmotic thirst stimuli was, however, sufficient to overcome the reduced dipsogenic responsiveness of estrogen-treated rats. (Supported by grant HL 14526-05 from the National Institutes of Health).

GASTRIC MUCOSAL BARRIER (GMB) FOLLOWING THERMAL INJURY. A. M. Tichy (SPON: G. A. Courtney). Depts. General Nursing and Physiology, University of Illinois at the Medical Center, Chicago, IL 60612.

The GMB impedes diffusion of acid from the gastric lumen into the mucosa. Disruption of the GMB is characterized by an altered mucosal permeability with resultant back diffusion of H^+. This investigation was undertaken to study the effects of cutaneous burn on the integrity of the GMB. H^+ back diffusion and peptic activity of gastric aspirate were determined in burned and sham burned rats. Twenty-four hr after a 30% body surface contact burn (Brevital anesthesia) and a 48 hr fast with saline and 10% dextrose ad lib, gastric secretions were collected for 2 hr following pyloric ligation under Urethane anesthesia. The following was studied: 1) basal secretion; 2) histamine stimulation; 3) glycine instillation; 4) saline instillation, and 5) a combined glycine instillation with histamine augmentation. Significant reductions in acid secretion occurred in burned rats unless the secretion was stimulated by histamine and/or glycine. Following stimulation, acid values in the burned rats exceeded those of unburned rats. GMB disruption, as determined by glycine trapping, was not an apparent pathogenetic mechanism of gastric erosion in 24 hr post burn rats. Peptic activity was elevated in those burned rats with mucosal erosions suggesting a contributory role for this proteolytic enzyme.
(Supported in part by PHS NU 5020)

THE EFFECT OF LOWER BODY NEGATIVE PRESSURE ON BLOOD PRESSURE CHANGES IN RATS. C.M. Tipton, R.D. Matthes*, P.M. Gross* and A.C. Vailas*, Exercise Physiology Lab, Depts. of Physical Education and Physiology-Biophysics, University of Iowa, Iowa City, Iowa 52242.

Preliminary results with lower body negative pressures (LBNP) indicated its effectiveness in differentiating normal and immunosympathectomized groups (Physiologist, 17:346, 1974). Preliminary studies have also been conducted with anesthetized adult male rats assigned to normotensive (WKY), hypertensive (SHR) or anti-hypertensive (A-SHR) groups. This latter group had resperine, hydralazine and chlorothiazide added daily to their drinking water for ten weeks. The systolic blood pressure results were evaluated as a percentage change from their pre-test value ($\bar{X}$,SE):

Group	N	-2.5 mmHg	-5.0 mmHg	-7.5 mmHg
WKY	5	14 ± 2.4	49 ± 2.5	69 ± 6.2
SHR	9	10 ± 1.9	24 ± 3.9	39 ± 5.9
A-SHR	5	16 ± 2.9	52 ± 6.0	86 ± 3.1

These changes suggest that the vasoconstricting ability of the SHR to resist the effects of "pooling" were greater than the two other groups. The results also indicated that the anti-hypertensive regimen was able to "normalize" the response to a LBNP stress. Similar studies have also been performed using trained and nontrained groups and it appears that endurance training reduced the resting vasoconstricting capability of rats, a trend similar to that reported for humans. To what extent these differences are due to alterations in chemoreceptors, low or high pressure baroreceptors, baroreceptor reseting, or resting sympathetic tone remains to be determined. (Supported in part by HL-014388-5)

ASZ(DCPB)

Effects of Estradiol and Calcitonin on Rat Plasma Calcium and Osteocyte Lacunar Size. A. Tolvo* and A. Saxena. Department of Biological Sciences, Fairleigh Dickinson University, Teaneck, New Jersey 07666

The combined and individual effects of 17-beta-estradiol and salmon calcitonin were observed on plasma calcium and osteocyte lacunar size in 25-30 day old Sprague-Dawley female rats. Estradiol treatments (12 mg. for 6 days) alone resulted in an 8% decrease in plasma calcium compared to the control group receiving no hormone. Calcitonin treatment (120 MRC mU for 140 minutes) alone produced a 28% decrease in the plasma calcium level. Animals pre-treated with estradiol, when given calcitonin, showed a 38% decrease in plasma calcium. The effect of the hormones on osteocyte lacunar size along tibial shaft segments collected from each hormone treated and untreated control group was also observed. The decrease in lacunar width by 18% and length by 29% in the estradiol treated group was more pronounced than the decrease observed in the calcitonin group. The combined effect of both hormones on lacunar size was of greater magnitude than the separate effects of estradiol or calcitonin. These data have established the synergistic effects of estradiol and calcitonin as hypocalcemic and anti-bone resorptive hormones in young female rats. Further studies are in progress to show the age-specific change in estrogen influencing the hypocalcemic action of calcitonin.

A STUDY ON THE CON A-INDUCED STIMULATION OF THE SODIUM EFFLUX IN OUABAIN-INHIBITED BARNACLE MUSCLE FIBERS. E.Y. Tong and M.B. Aarons*. Biology Dept., Wheaton College, Norton, MA. 02766

In a previous study using single barnacle muscle fibers (Tong & Coyle, The Physiologist. 18: 423, 1975), it was observed that externally applied concanavalin A (Con A) at 200 μg/ml augmented the extrusion of Na-22 after pretreatment with 5 x 10^{-5}M ouabain. A similar percent increase (43 ± 7 SE, N=18) was obtained in the present investigation when the concentration of Con A was raised to 300 μg/ml in experiments lasting about 2 hr. The peak effect occurred between 40 to 85 min following the Con A application. However, after the fibers were treated with a higher concentration of ouabain (10^{-4}M), Con A at 200 μg/ml (N=6) or at 300 μg/ml (N=6) failed to produce a stimulation of the ouabain-inhibited Na efflux. It was concluded that Con A may be acting directly on the ouabain-sensitive Na-K pump to potentiate the Na efflux. These results are in agreement with the findings from human lymphocytes in which Con A was reported to stimulate the ouabain-sensitive Na-K ATPase (Averdunk & Lauf, Exptl. Cell Res. 93: 331, 1975). The Con A-induced stimulation of 5 x 10^{-5}M ouabain-inhibited Na efflux was blocked by α-methyl-D-mannopyranoside (α-MDM) at a concentration of 2.1 x 10^{-6}M (N=7). The saccharide itself had no effect on 10^{-4}M (N=7) or 5 x 10^{-5}M (N=5) ouabain-inhibited Na efflux. In addition, α-D-glucose (N=6) produced no change in the sodium efflux of fibers treated with the same concentrations of ouabain. Thus, it is highly possible that the Con A-induced stimulation of the ouabain-inhibited Na efflux may be a consequence of the binding of Con A to the glycoprotein or glycolipid receptors on the cell surface.

ANALYSIS OF THE BEHAVIOR OF THE LUNG IN RESPONSE TO TRANSIENT INPUTS OF INERT GASES. V. T. Tornabene*, S. M. Lewis, P. D. Wagner and J. W. Evans*. Departments of Medicine and Mathematics, University of Calif. San Diego, La Jolla, California 92093.

The description of the behavior of a lung in response to transient inputs of inert gases requires knowledge of the ventilation ($\dot{V}_A$), perfusion ($\dot{Q}$) and volume (V_o) of the functional respiratory units making up the lung. Techniques which analyze measurements of these responses using gases with differing solubilities offer the hope of characterizing the lung in those terms. A computer model has been used to investigate the feasibility of this approach. The lung model was generated as a continuous surface of the distribution of V_o as a function of log ($\dot{V}_A/V_o$) and log ($\dot{Q}/V_o$). It was constructed as the sum of 1 to 3 bivariate normal distributions set to have a given total, $\dot{V}_A$, $\dot{Q}$ and V_o. Solubility in lung tissue was considered, and tissue volume was taken to be proportional to gas volume (V_o). Steady-state inert gas elimination, insoluble gas washouts (sampled in both expired gas and arterial blood), and step injections of gases with varying solubilities were modeled. The ability to infer the distribution of $\dot{V}_A/\dot{Q}$ from both the known distributions of $\dot{V}_A$ and $\dot{Q}$ as functions of $\dot{V}_A/V_o$ and from distributions recovered from data generated by the model was examined, particularly as a function of the number of test gases. Combination of both transient and steady-state measurements of several inert gases in both arterial blood and expired gas shows promise as a tool for investigating the functional distribution of ventilation, perfusion and volume.

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EFFECTS OF HYPOXIA ON ERYTHROPOIETIC TISSUE PYRIMIDINE NUCLEOTIDE BIOSYNTHESIS. D.E. Troike* and M.T. Nishikawara, Dept. Physiology, The Ohio State University, Columbus, OH. 43210.

To detect changes in the de novo and salvage pathways of pyrimidine nucleotide biosynthesis in developing erythroid cells, male Wistar rats were subjected to an hypoxic environment. Over a period of four days the bone marrow and spleen were assayed for three enzymes shown to be at the control points of these pathways: de novo, aspartate carbamyl transferase (ACTase); thymidine salvage, thymidine kinase (TKase); and uridine salvage, uridine kinase (UKase). The spleen of a normal rat is not actively erythropoietic, but when stimulated, it responds with a wave of erythropoiesis. In this way, activity changes in the enzymes of early stage erythroblasts were studied. The marrow activity changes represent those of predominantly late stage erythroblasts. Early stage erythroblasts (spleen) responded with an increase in all three enzymes, but only after a one to two day delay. Late stage erythroblasts (marrow) responded with an immediate increase in ACTase and TKase activities, but UKase did not increase until day three. An hypothesis is presented which explains these differences between early and late stage erythroblasts.

SUBSENSITIVE BETA RECEPTOR ACTIVITY IN THE SMALL BLOOD VESSELS OF THE HUMAN PLACENTA. T. N. Tulenko and J. A. High*., Dept. of Physiology, Temple Univ. Sch. of Med., 3420 North Broad St., Phila., Pa. 19140.

This study was undertaken to compare the beta adrenergic receptor activity reported in the nerve-free human placental vessels (Tulenko, Fed. Proc. 35:843, 1976) with beta adrenergic activity of blood vessels from a more typically innervated vasculature. Helically cut strips of blood vessels from the human placenta (.75-1.25 mm O.D. N=6) and left coronary artery (.75-1.5 mm O.D., N=4) were suspended together in a common muscle chamber containing Krebs-Henseleit solution equilibrated with 95% O_2-5% CO_2 under a passive tension of 300 mg and 600 mg respectively. The strips were contracted with 40 mM KCl, and phenoxybenzamine (10^{-6}M) was added to the bath to block alpha adrenergic activity. After sufficient equilibration time, dose-response curves were constructed for the relaxing action of the beta agonist isoproterenol (ISO) alone and in the presence of the beta antagonist propranolol (PRO) (10^{-6}M). The results of these experiments indicated that the beta activity of the coronary arteries was significantly more sensitive to the action of ISO ($ED_{50} \approx x\ 10^{-9}$M) than the placental vessels ($ED_{50} \approx 1 \times 10^{-7}$M). In the presence of 10^{-6}M PRO, the ED_{50} for ISO shifted approximately 4.2 log units to the right for the coronary artery strips whereas the placental vessel ED_{50} shifted only 0.7 log units to the right. We take these finds to suggest that, under these conditions, the beta adrenergic receptor activity of the small blood vessels of the human placenta are qualitatively different than their counterparts in the neurally innervated dog coronary artery, being subsensitive to both beta receptor stimulation with ISO and beta receptor antagonism with PRO.

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MICROVASCULAR RESPONSES TO SULOCTIDIL. Ronald F. Tuma*, Mary P. Wiedeman and Harvey N. Mayrovitz*, Dept. of Physiology, Temple Univ. School of Medicine, 3420 N. Broad Street, Phila., Pa. 19140.

The effect of suloctidil, a new experimental drug, on the inhibition of vasospasm and platelet aggregation was tested in-vivo using two preparations, the bat wing and the hamster cheek pouch. The microvascular beds of both models were prepared for direct microscopic observation at magnifications up to 1,200 diameters. Localized vasospasm was produced in arterial vessels 20-80 microns diameter by stimulation with microelectrodes. Vasospasm in untreated vessels persisted for over 20 min. Following topical or intra-arterial administration of suloctidil, the duration of vasospasm was reduced to less than 10 minutes. Exposure of unstimulated vessels to suloctidil did not cause vasodilation. The action of suloctidil on platelet aggregation induced by electrical and laser stimulation was also studied. Although administration of suloctidil did not inhibit the formation of platelet aggregates following laser or electrical stimulations, the results suggest that the duration of activity of the aggregates following intravenous, intra-arterial, and topical application of suloctidil was shortened.

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STUDY ON POST-GLUCOSE HYPERINSULINEMIA AFTER BURN INJURY. J. Turinsky, L.D. Loose and W.A. Scovill*. Albany Medical College, Albany, N.Y. 12208

Our previous studies demonstrated that 20% body surface burn in the rat results in initial inhibition of insulin secretion which is followed by a period of exaggerated hyperinsulinemic response to i.v. glucose. To evaluate the role of glucagon and corticosterone in the etiology of this latter response, rats fasted overnight were studied 1 to 7 days after 20% body surface burn. At each daily interval, groups of rats were sacrificed 0, 15, and 40 min after i.v. glucose load (1 g/kg b.w.) and the average hyperinsulinemic and hyperglycemic responses were expressed as area under the curve with those of timed controls representing 100%. The insulin response of burned rats was 101% on day 1, 185% on day 2, reached its peak of 209% on day 3 and decreased to 140% on day 4, 108% on day 5, 115% on day 6, and 128% on day 7. The exaggerated hyperinsulinemic response cannot be explained by decreased ability to cope with the glucose load since in burned rats the area under the glucose curve did not differ appreciably from control at any of these times. Nor was there any clear relationship to fasting serum glucose which was 68±7 (SE) mg/100 ml higher than control on day 1 and returned almost linearly to control level on day 4. Fasting plasma glucagon was 179±44 pg/ml higher (2-fold elevation, $p<0.01$) and plasma corticosterone was 192±21 ng/ml higher (4.7-fold elevation, $p<0.001$) than control on day 1 when the hyperinsulinemic response of burned rats was normal. Both hormones virtually returned to control level on day 3 when the post-glucose hyperinsulinemia of burned rats was maximal. This lack of correlation seems to suggest that the development of the exaggerated post-glucose hyperinsulinemia after burn is not directly due to the presence of these two anti-insulin hormones in blood. (GM 15426 and AI 12839)

EFFECT OF NICOTINIC ACID ON CHOLERA TOXIN-INDUCED INTESTINAL SECRETION AND LEVELS OF CYCLIC AMP. N. Turjman*, G.S. Gotterer* and T.R. Hendrix, Depts. of Physiological Chemistry and Medicine, Johns Hopkins University School of Medicine, Baltimore, Md. 21205.

Based on the knowledge that nicotinic acid (N.A.) is an inhibitor of the adenylate cyclase (A.C.) system in vitro, studies were undertaken to examine the effect of N.A. on secretion and rises in cyclic AMP (cAMP) levels induced by cholera toxin (C.T.) in rabbit intestinal loops. Intestinal secretion was determined by measuring fluid accumulation in closed intestinal loops. Four loops were constructed in each animal. An isotonic electrolyte solution was instilled in two control loops and purified C.T. (50 ug/10 cm loop) in the same electrolyte solution in the remaining loops. cAMP levels in TCA extracts of full thickness biopsies were measured by a binding assay. In a group of 9 rabbits, 100 mg/kg of N.A. in saline were administered subcutaneously prior to the introduction of C.T. In a group of 6 control rabbits, saline alone was administered. In the control group C.T. stimulated intestinal secretion (0.014 ±0.10 SEM vs. 0.29 ±0.09 SEM ml/cm/3 hrs; $p < 0.001$) and caused a rise in cAMP levels (8.56 ±2.49 SEM vs. 15.15 ±2.22 SEM picomoles/mg protein; $p < 0.0025$). In the N.A. group the C.T.-induced secretion and the rise in cAMP were both blocked completely (0.063 ±0.098 SEM vs. 0.103 ±0.072 SEM ml/cm/3 hrs, n.s.; 8.17 ±2.95SEM vs. 8.33 ±2.19 SEM picomoles/mg protein, n.s.). These findings suggest that N.A. should prove useful in examining the relationship of the A.C. system to the mechanism of C.T.-induced secretion.

THE COMPARATIVE EFFECT OF HYPERBARIC OXYGEN EXPOSURE ON THE IN VITRO ELECTRORETINOGRAM. John L. Ubels* and J. Russell Hoffert. Dept. of Physiology, Michigan State University, East Lansing, MI 48824.

ERG's were recorded from frog, rat, goldfish and trout eye cup preparations during exposure to 100% oxygen at 740 Torr and 3800 Torr. The frog ERG was significantly attenuated during 6 hours exposure to hyperbaric oxygen, the b-wave often being abolished. No change was seen in the control preparation. Similar results were obtained for the rat ERG after 90-100 minutes exposure to hyperbaric oxygen. The control preparation could be maintained for 2-3 hours although some decline in the b-wave was observed. The results indicate that hyperbaric oxygen has a toxic effect on the neural elements and supporting tissues of amphibian and mammalian retinas, the mammal being more susceptible to oxygen toxicity. No significant change in the goldfish ERG was seen during 6 hours exposure to hyperbaric oxygen. A normal response was also maintained in the control preparation. Similar results were obtained for the trout ERG. The teleost retina is normally exposed to oxygen tensions above 400 Torr generated by the counter-current oxygen multiplier of the choroidal rete. Our results indicate that the teleost retina is well adapted to these high oxygen tensions and that no toxic effect is seen from exposure to oxygen tensions well above those normally encountered. (Supported by NIH Grant EY00009.)

ASZ(DCPB)

HISTOPHYSIOLOGICAL STUDIES OF IONOREGULATION IN THE MARINE CATFISH, PLOTOSUS LINEATUS. Bruce L. Umminger, John Pucke*, and Susan J. Levy. Dept. Biological Sciences, University of Cincinnati, Cincinnati, Ohio 45221

Most species of plotosid catfish living in marine environments possess a highly vascularized accessory "dendritic organ," ventrally located immediately posterior to the anus and comprised of numerous papillae with walls several cell layers in thickness enclosing a lumen which empties to the outside. Both ecological (Lanzing, Pacific Sc. 24: 498) and ultrastructural (Van Lennep, J. Ultrastruct. Res. 25:94) studies indicate the dendritic organ has a salt-secreting function. In the present investigation, both the gills and dendritic organ of six specimens of the marine catfish, Plotosus lineatus, were examined histologically using three techniques (modified Lescke silver test, hematoxylin-eosin, and Pollak trichrome). Using criteria of cellular morphology and histochemistry, we found no evidence of salt-secreting chloride cells in the gills, but found numerous chloride cells in the dendritic organ. The serum chemistry was not unusual for a marine teleost (osmolarity=346 mOsm/l, Na=198 mmoles/l, Cl=149 mmoles/l, K=7.5 mmoles/l). The marine catfish regulates its internal osmotic environment quite well, even though the gills lack chloride cells, due to the presence of the salt-secreting dendritic organ. (Supported by NSF grant GB 26321.)

ARTIFICIAL LUNG BASED ON HEMODIALYSIS PRINCIPLES. S.J. Updike and M.C. Shults, Dept. of Medicine, University of Wisconsin Center for Health Sciences, Madison, WI 53706

A new type of extracorporeal membrane oxygenator based on hemodialysis principles has been developed and evaluated in the dog.

Excretion of CO_2 is obtained by dialyzing out bicarbonate ion. This process is associated with tissue retention of buffered hydrogen ion. To prevent acidosis, sufficient hydroxyl ion is dialyzed from the bath into the blood to maintain normal pH. In this manner using venovenous hemodialysis, the dog's entire CO_2 production (2 to 6 mMoles/min) was excreted. These experiments used commercially available hollow fiber, plate and coil dialyzers and lasted 4 to 6 hours. During the experiment, dogs were anesthetized, intubated and allowed to spontaneously ventilate into a closed rebreathing device. Acid-base balance was maintained by continuously transducing ventilation and negative-feedback-controlling addition of alkali to the dialysis bath. The dogs fully recovered and appeared to tolerate the procedure well.

Oxygenation was obtained by transmembrane catalysis of H_2O_2 which is added to the dialysis bath. By impregnating the cellulosic dialysis membrane with catalyst, ruthenium oxide, better than 99.999% of H_2O_2 is broken down to O_2 and H_2O during diffusional transport across the membrane. In vitro studies show the transfer of 400 ml of $O_2/min/M^2$ is easily achieved with dialysis bath concentrations of 0.5% or less H_2O_2.

Using a partial reverse flow (Oxford) oxygenator design, O_2 transfers of over 200 $ml/min/M^2$ were obtained with O_2 hemoglobin saturation increasing 30% with inlet saturation of 65%. The approximate design flow is 3 $liters/min/M^2$.

SEX DIFFERENCES IN THE DEVELOPMENT OF EXPERIMENTAL THROMBOSIS. A. Uzunova*, E. Ramey, and P. Ramwell. Dept. Physiology and Biophysics, Georgetown University Medical Center, Washington, D.C. 20007.

Experimental arterial occlusive thrombi were induced in 1.5, 3, 4, 6 and 12-month-old male and female Wistar rats using a plastic loop inserted in the abdominal aorta (Hornstra and V.-Starrenburg, 1973). The mortality rate, dry thrombus weight and loop obstruction time were used as criteria for the degree of development of thrombosis. Arterial thrombosis was studied also in New Zealand rabbits of both sexes aged 6 months, using the method of Maekawa et al (1974). The mortality rate of 3, 4 and 6-month-old rats was $\sim$ 2X higher in males than in females ($p < 0.01$). Significant differences were found in both thrombus weight and obstruction time between male and female rats aged 3, 4 and 6 months ($p < 0.01$). Differences were not significant in 1.5 and 12-month-old rats. In rabbits, thrombus formation in the femoral artery occurred in 90.9% of males and 56.2% of females and the thrombus weight was significantly higher in males. In vivo, thrombosis was induced in CF1 mice by i.v. injection of arachidonate (60 mg/kg). A higher mortality rate and longer hypoxic response were found in male mice than in the female. These data suggest an association between sex and the development of experimental thrombosis. (Supported by NHLI 17516, Educ. Found. of Am. and Wash. Heart Assoc.)

ESTIMATES OF IN SITU SURFACE TENSION AND AIRSPACE DIMENSIONS BASED ON MULTIPLE PRESSURE-VOLUME CURVES. P.Valberg* and J.D.Brain, Department of Physiology, Harvard School of Public Health, Boston, MA 02115.

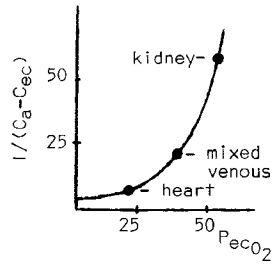
The static pressure-volume (PV) curves of excised rat, cat, and dog lungs were determined in a sequence of 3 conditions: 1) normal-surface, air-filled, 2) liquid-filled, and 3) Tween-surface, air-filled. Wilhelmy balance measurements demonstrated that lung washings containing 2% Tween 20 exhibit constant surface tension (ST or γ) at 32 dy/cm with no ST vs area (A) hysteresis. At a given volume the pressure difference between the air-filled and liquid-filled curves (P_γ) can be interpreted as a measure of the pressure needed to overcome ST forces. This pressure difference is related to ST by $P_\gamma = \gamma(dA/dV)$. Previous estimates of in situ ST relied on a pair of PV curves. Hence an assumption on how lung surface area is related to lung volume had to be made of the form $V = kA^\lambda$ where λ was usually assumed to be 2/3 and k was determined from an assumption about maximum ST. By knowing PV curves in 3 conditions, we need not specify the volume-area function. Rather, we assume it is the same in the two air-filled cases, and thus the normal-lung ST is given by $\gamma_{norm} = \gamma_{Tween}\left[(P_{norm} - P_{liq})/(P_{Tween} - P_{liq})\right]$. We calculated γ_{norm} and found that it varies from approximately 40 dy/cm (TLC) to 34 dy/cm (80% TLC) to 3 dy/cm (<10% TLC). The shape of the calculated ST vs A curve appears closer to the results for lung washings than those of previous in situ estimates. On the deflation limb of the PV curves where the Tween curve crosses the normal curve (90% TLC), we assumed all alveoli to be open and at a ST of 32 dy/cm. P_γ at this point yields estimates of alveolar diameters: cat, 180 μm; dog 117 μm; rat, 85 μm. An elevation of passive and forced expiratory flow was also noted in the Tween-surface lung, reflecting the contribution of increased surface forces to lung recoil.

ADENINE NUCLEOTIDE METABOLITE FORMATION IN VASCULAR SMOOTH MUSCLE DURING HYPOXIA. G.L. Van Harn*, R. Rubio and R.M. Berne. Dept. Physiol., University of Virginia, Charlottesville, Virginia 22901.

Strips of hog carotid artery media incubated in physiological saline and bubbled with 95% O_2 - 5% CO_2 produced 16.4±1.67 ($\bar{X}$ ± S.E.) nmoles/gm wet wt./hr. hypoxanthine (HYX) and 24.25±1.76 inosine (INO) but no significant amounts of adenosine (ADO). During hypoxia (95% N_2 - 5% CO_2) HYX production increased to 50.91±3.98, INO to 41.2±2.82, however there were no measurable amounts of ADO. Increases in HYX and INO during hypoxia were paralleled by a decrease in total adenine nucleotide content of the media strip and the ATP/ADP+AMP+IMP ratio decreased from 0.8 to 0.6. In addition AMP levels were 2.8 times greater than IMP, suggesting a low adenylic acid deaminase activity. ADO (10^{-6}M) added to the bath during or after media strip incubation was recovered as INO after one hour of incubation, whereas with 30 min of incubation of the strips with AMP in the bath, 20% was recovered as INO and 20% as ADO; after 60 min of incubation, 40% was recovered as INO and 25% as ADO. AMP added to baths in which strips had been incubated previously did not appear as nucleoside. The degradation of exogenous AMP to ADO and INO, and the deamination of exogenous ADO to INO indicate the presence of 5'-nucleotidase and adenosine deaminase in media strips and leakage of the latter enzyme into the bath. These results can explain the lack of measurable amounts of adenosine production during hypoxia and indicate that vascular smooth muscle is capable of ADO production. However, the quantity produced and its persistence in the extracellular space necessary to produce relaxation under more physiological conditions remains to be determined.
(Supported by USPHS Grants #HL10384 and F32H105132.)

USE OF THE O_2-Hb DISSOCIATION CURVE FOR CHARACTERIZATION OF O_2 EXCHANGES OF VARIOUS TISSUES. Hugh D. Van Liew. Dept. of Physiology, State Univ. of New York at Buffalo, Buffalo, N.Y. 14214.

Tissue oxygenation involves the intersection of three physiological variables: a) local metabolic rate, b) local blood perfusion and c) blood's carriage of O_2. To deal with this "3-variables-at-once" problem, one can invoke the law of conservation of matter by modifying the Fick blood flow equation so that it applies to exchanges of individual capillary units. One can then apply the information of the Hb-O_2 dissociation curve by turning the curve "inside-out" -- that is, by plotting the reciprocal of the O_2 content difference between arterial and end-capillary bloods, $1/(C_a-C_{ec})$, against end-capillary P_{O_2}, Pec_{O_2}. By the Fick equation, the y axis of the plot equals the perfusion/metabolism ratio. For cardiac tissue the ratio is about 8 ml of blood per ml of metabolized O_2, for kidney cortex the ratio is 60, and other tissues are arranged along the curve between these two extremes. If it is assumed that P_{O_2} of end-capillary blood is a reasonable indicator of tissue P_{O_2}, the x axis gives an idea of the P_{O_2} available to the metabolic machinery. The basic plot can be used to illustrate how P_{O_2} must change with such stresses as halving of perfusion rate, of arterial P_{O_2}, of blood Hb content, or of P_{50} of the blood. (Supported in part by NIH Grant 5 P01 HL-14414).



BIOAVAILABILITY OF CYTOSINE ARABINOSIDE (ARA-C) IN MAN. H.C. van Prooijen* and C. Haanen* (SPON. S.Y. Botelho) University of Nijmegen, Div. of Haematology, Dept. Int. Medicine, Nijmegen, The Netherlands.

Ara-C is a cytostatic drug frequently used in acute myeloid leukemia (AML). In the cell Ara-C is phosphorylated to its triphosphate (ARA-CTP). Only as Ara-CTP the drug inhibits DNA-synthesis. The effect of the drug depends on the amount and duration of Ara-CTP in the cell. For the determination of drug levels in plasma a sensitive bio-assay has been developed and analysed mathematically. The disappearance curve of Ara-C after a bolus injection appeared to be biphasic. The slope of the first part of the disappearance curve turned out to be identical in all patients. The half life time of the second part showed variations from 8.0 - 19.0 min in different individuals.
The effect of Ara-C has been determined "in vivo" by measuring DNA synthesis in the blast cells with tritiated thymidine incorporation in a marrow aspirate taken before and one hour after the bolus injection in a dose of 100 mg/m^2. The measured inhibition of DNA synthesis varied from 50 - 90 %.
The plasma half life times of Ara-C and the "in vivo" sensitivities were compared with the results of remission induction therapy in 10 patients with blastic phase of AML.
Poor response of Ara-C remission induction therapy appeared to relate with short half life times and low "in vivo" sensitivities for this drug

REFLEX CIRCULATORY CONTROL IN RESPONSE TO HEMORRHAGE IN CONSCIOUS DOGS
Stephen F. Vatner, Robert J. McRitchie* and Ronald W. Millard, Department of Medicine, Harvard Medical School, Peter Bent Brigham and The New England Regional Primate Research Center, Southboro, MA 01772

To investigate the relative importance of carotid sinus and aortic baroreceptors in comparison with low pressure vagal afferents in the defense against acute hemorrhage, responses of mean arterial pressure, heart rate, cardiac output, and systemic vascular resistance were monitored during hemorrhage (0.5 ml/kg/min) in conscious dogs instrumented with electromagnetic flow probes on the aorta and pressure catheters. Hemorrhage was repeated after recovery from a) section of carotid sinus nerves, b) bilateral carotid sinus and aortic nerve section, i.e., arterial baroreceptor denervation, and c) after arterial baroreceptor denervation and cervical section of both vagi. Hemorrhage, 25 ml/kg, in intact, conscious dogs reduced mean arterial pressure 6 $\pm$ 3 mmHg and increased heart rate 68 $\pm$ 7 beats/min and systemic resistance .024 $\pm$ .003 mmHg/ml/min. After carotid sinus nerve section hemorrhage reduced mean arterial pressure 27 $\pm$ 4 mmHg and increased heart rate 30 $\pm$ 7 beats/min and systemic resistance .016 $\pm$ .003 mmHg/ml/min. After arterial baroreceptor denervation hemorrhage reduced mean arterial pressure 47 $\pm$ 6 mmHg, and increased heart rate 13 $\pm$ 6 beats/min and systemic resistance .007 $\pm$ .002 mm Hg/ml/min. After arterial baroreceptor denervation and vagotomy hemorrhage reduced mean arterial pressure 69 $\pm$ 8 mmHg but didn't increase heart rate or systemic resistance significantly. Thus, in the conscious dog, the combined carotid and aortic baroreceptor reflexes are of much greater importance in the cardiovascular defense against hemorrhage as compared with low pressure vagal afferents, which exert an effect roughly equivalent to only one set of buffer nerves.

BMES

THE EFFECT OF THE AIRWAYS ON STRESS IN THE LUNG PARENCHYMA. D.L. Vawter, Division of Biomedical Engineering, University of Virginia, Charlottesville, Virginia, 22901

A numerical procedure was used to study the interaction of the parenchyma with the large airways in the lung. In addition to studying the role of tissue elasticity the effects of interfacial tension were analyzed. The parenchyma's elastic behavior was modeled using a strain-energy formulation developed from previous stress-strain tests on the parenchyma. The airway was modeled as an infinitely long circular cylinder composed of a nonlinear elastic material. The parenchyma volume was normalized according to the size of the airway. Surface tension was assumed to be a function of surface area as established by Flicker and Lee in an *in situ* study. The hysteresis of both the surface tension and the elastic response were accounted for in the analysis. The principle findings of the analysis were: 1) there is a concentration of stress at the airway-parenchyma interface which increases with increasing rigidity of the airway, 2) the effect of the airway is localized with stress in the parenchyma becoming uniform a few diameters away from the airway, 3) the effect of surface tension on airway caliber was found to be less during deflation than during inflation.
(Supported by grant HL16812 from NHLI)

ENERGY FLUX IN FREE-RANGING BIRDS. J.H. Veghte. Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio 45433

This study was undertaken to obtain continuous, weekly, diel body temperatures, respiration and heart rates by means of telemetry in free-ranging ravens (Corvus corax). Also, surface temperatures of flying birds were obtained with real-time, color infrared movies. The diel body temperatures varied from 38.5 to 42.7°C with an average thermal differential of 3°C between low, nocturnal levels and high, diurnal values. Rapid temperature increases of 1°C were seen after short flights. Heart rates were extremely labile during the day and varied from resting levels of 180 beats/min to 600 beats/min after several, short flights. At night, heart rates were less variable and ranged from 140 to 160 beats/min. Respiratory rates varied from resting diurnal levels of 20 to 25 breaths/min to 40 breaths/min after short flights. At night, rates fell to 13 to 17 breaths/min. The surface temperatures of flying birds showed that the head, legs, feet, and region of the body under the wings to be much warmer than the rest of the body which remained within 1° to 2°C of ambient temperature (21°C). At rest, these warmer regions, leg, feet, and edge of the marginal covert, remained 5° to 11°C above ambient temperatures while the eye auricular region was 17° to 18°C above ambient conditions. After several flights, these warmer regions rose 10° to 19°C above ambient while the eye auricular and nares regions rose only 1°C. The other feathered regions were 1°C higher than resting values.

ASZ(DCPB)

IONIC AND RESPIRATORY INTERACTION IN BROWN SHRIMP *PENAEUS AZTECUS* IVES. A. Venkataramiah, G.J. Lakshmi, Patricia Biesiot* and John D. Valleau*. Gulf Coast Research Laboratory, Ocean Springs, Mississippi 39564.

The interaction between blood osmoconcentration and chloride levels and the respiratory rate was determined in brown shrimp that were either in the process of acclimation or had been acclimated for three weeks to different salinity and temperature combinations. Test salinity (2°/₀₀ to 36°/₀₀) and temperature (18° to 32°C) ranges approximated their natural habitat conditions. At 25°C it appeared as though there was a positive interaction between ion concentration and respiration. The oxygen uptake increased in proportion to the deviation of the ion gradient from control. But this trend was not consistent in other test conditions although the ion concentration pattern remained essentially the same. The respiratory rates at 18°C were well below and at 32°C far above the control level and maintained no correlation to the blood ion gradient. Evidently these responses reflected the efforts to compensate for temperature changes. The respiratory rates of three week acclimated shrimp were apparently in synchrony with seasonal salinity and temperature rhythms but not with the blood ion gradients. More important is the observation that the respiratory rates often tended to return toward the control level within two hours after transfer while the ionic influx continued to increase for more than six hours as if these processes were unrelated. Data obtained from these and other experiments in our laboratory indicated the absence of a consistent reciprocal relationship between blood ion levels and respiration. On the contrary, the oxygen uptake appeared to be in closer agreement with the overall behavior (including diurnal rhythm) and physiological state of brown shrimp.

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PROTECTIVE EFFECTS OF CARNITINE IN MYOCARDIAL ISCHEMIA. J. Vick*, S. DeFelice*, N. Sanzari* and M. Klein* (SPON: C.C. Hassett). Bio Basics International, New York City, New York.

The possible protective effects of carnitine, a naturally occurring amino acid, on artifically induced myocardial ischemia has been studied. Adult beagle dogs anesthetized with pentobarbital, Na were artifically ventilated and the chest opened to allow access to the anterior descending coronary artery. Electromagnetic flow probes were used to record changes in coronary flow while arterial blood pressure, EKG and heart rate were monitored using appropriate recording devices. Using a micrometer controlled snare device coronary flow was reduced from 38 ± 10 ml/min to 22 ± 5 ml/min which produced significant elevations in the ST segment of the EKG. Flow was further reduced to 10 ± 3 ml/min resulting in ventricular fibrillation in 8 of 8 control animals within 5 minutes. 6 additional dogs were pretreated with 500 mg carnitine I.V. 5 to 15 minutes prior to coronary constriction. The average ST elevation (5.4 ± 2.1 mm) produced by coronary constriction in control animals was significantly reduced (2.1 ± 1.1 mm) in carnitine treated dogs. In addition, the previously observed ventricular fibrillation was prevented in 5 of 6 carnitine treated dogs. Results indicate that carnitine protects the canine heart from both moderate and severe ischemia. These beneficial effects may be due to an increase in the mobilization of fatty acids and/or to the reversal of the inhibition of adenine nucleotide translocase which usually follows myocardial ischemia.

EFFECTS OF SO_2, H_2SO_4, and $AL_2(SO_4)_3$ ON PULMONARY FUNCTION OF RATS AND GUINEA PIGS. A. Vinegar, G.P. Cooper and S.M. Brooks*, Dept. Environ. Health, U. Cincinnati Col. Medicine, Cincinnati, OH 45267.

In one experiment rats were exposed for 90 days to either control (ambient) air, air containing SO_2 (0.90 mg/M^3), or air containing H_2SO_4 mist (2.37 mg/M^3). In another experiment rats and guinea pigs were exposed for 50 days to either control air, H_2SO_4 mist (4.05 mg/M^3) or particulate $Al_2(SO_4)_3$ (2.04 mg/M^3). Only the second set of exposures produced measurable effects on pulmonary function. $Al_2(SO_4)_3$ increased and H_2SO_4 decreased the static compliance of rats, although not significantly.[4] Similar effects were seen in juvenile rats conceived and born in the exposure chambers but the $Al_2(SO_4)_3$ effect was enhanced such that static compliance of these animals was greater than those exposed to H_2SO_4 ($p<.05$). Static compliance of guinea pigs was decreased by H_2SO_4 (N.S.) and more so by $Al_2(SO_4)_3$ ($p<.05$). Pulmonary resistance and dynamic compliance were increased in juvenile and adult rats exposed to H_2SO_4 or $Al_2(SO_4)_3$. However, only the resistance of H_2SO_4-exposed adults was significantly different ($p<.05$). H_2SO_4 increased dynamic compliance and decreased resistance and $Al_2(SO_4)_3$ decreased dynamic compliance and increased resistance in guinea pigs, although not significantly. Thus there are clearly inter- and intraspecific differences in reaction to $Al_2(SO_4)_3$ and H_2SO_4. $Al_2(SO_4)_3$ appears to be more toxic than H_2SO_4. (Supported by EPA contracts 68-03-2335 and 68-03-0492).

BLOCKADE OF MYOCARDIAL SLOW CATION CHANNELS IN LOW pH. Stephen Vogel* and Nick Sperelakis. Dept. of Physiology, University of Virginia, Charlottesville, Va. 22903

Electromechanical uncoupling occurs in isolated perfused embryonic chick hearts at a pH of 6.4. Since mechanical activation depends on an influx of Ca^{++} through slow channels in the sarcolemma during the plateau of the action potential, this finding suggests an effect of H^+ ion on the slow inward Ca^{++} current. Therefore, we examined the pH dependency of slow channel activation in perfused chick ventricles whose fast Na^+ channels were voltage inactivated by partial depolarization to about -40 mV with elevated (25 mM) K^+, resulting in loss of excitability. In this condition, agents which increase the density of slow channels elicit slowly-rising overshooting electrical responses (the "slow response") accompanied by contractions. The rate of rise and overshoot of the slow responses induced by isoproterenol (10^{-6} M) declined as the pH was lowered from 7.4 (15 mM HCO_3^-, 5% CO_2), and were completely abolished at pH 6.4 (15 mM HCO_3^-, 50% CO_2). The slow response produced by theophylline (1 mM) was also abolished at pH 6.4. Therefore, the Ca^{++} influx through the slow channels is supressed at low pH. Since the HCO_3^--CO_2 buffer leads to rapid intracellular pH changes, the present findings could be explained by some intracellular effect. However, since lowering pH by use of other buffer systems which first change extracellular pH also rapidly blocked the slow inward current, low pH may produce a direct blockade of the slow channels (as produced by verapamil, Mn^{++}, La^{+++}), presumably at their outer surface. (Supported by NIH grant HL-18711.)

COMPARISON OF SLOW WAVE ELECTROGENESIS IN NEURONS AND SMOOTH MUSCLE. Howard Wachtel and Nels Anderson. Departments of Biomedical Engineering and Physiology, Duke University, Durham, North Carolina 27706.

The slow waves which underlie burst firing patterns in certain nerve and smooth muscle cells have several features in common. In both systems slow waves can persist in the absence of spikes, and hyperpolarizing (HP) currents cause the slow wave magnitude to increase and its frequency to diminish while depolarizing currents have just the opposite effect. In the extreme, large HP currents result in the abolition of slow waves in favor of a steady V_m, whereas large DP currents cause burst firing cells to approach a continuous firing mode. The actions of metabolic inhibitors, in most cases, can best be explained in terms of the removal of the HP influence exerted by a steady electrogenic pump. Brief disturbances of the slow wave cycle result in a "resetting" of the oscillator lasting many cycles.

These shared properties are explainable in terms of a reciprocal current model that we have evolved from voltage clamp studies of burst firing neurons in Aplysia and have applied to uterine smooth muscle. The model incorporates a regenerative (negative conductance) inward current and a slow outward current. In addition to simulating the voltage clamp data, the model predicts that these slow waves can regeneratively propagate from cell to cell - which is a notion that is attractive for explaining burst synchrony in smooth muscle (or in epileptic foci) in the absence of spike synchrony.

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ROLE OF THE LUNG IN ARTERIAL PRESSURE RESPONSE TO ARACHIDONIC ACID IN DOGS. H. Waldman*, I. Alter*, P. Kot, J. Rose, P. Ramwell, and E. Ramey (SPON: L. Lilienfield). Dept. Physiology and Biophysics, Georgetown University Medical Center, Washington, D.C. 20007.

The lung is known to inactivate PGE_2 and $PGF_{2\alpha}$ and cause attenuation of the systemic vascular response to intravenous administration of these substances. Whether transit through the lung similarly affects the systemic response to arachidonic acid (AA), precursor of these prostaglandins (PGs), has not been explored. AA (100 µg/kg and 200 µg/kg), PGE_2 and $PGF_{2\alpha}$ were administered by bolus injection into the inferior vena cava (i.v.) and left ventricle (i.a.) in spontaneously breathing anesthetized dogs (16). The decrease in femoral arterial diastolic pressure produced by i.a. administration of AA was 7.2 ± 1.5 % and 24.1 ± 3.4 %, respectively, for the two doses of AA. These depressor responses were not significantly different from those following i.v. administration (5.9 ± 1.8 % and 23.7 ± 3.8 %). Under the same circumstances, the vasodepressor response to PGE_2 (1, 2 and 3 µg/kg i.v.) was reduced 12-40 fold by passage through the dog lung. Similarly, the vasopressor response to $PGF_{2\alpha}$ (1, 2, 3, and 5 µg/kg i.v.) was diminished 5-8 fold by lung transit. Our previous studies on AA have led to the conclusion that the cardiovascular responses in the dog are due to intermediate compounds generated in PG formation. These studies support the view that the depressor response to AA is not due to prostaglandins but to other substances in the biosynthetic pathway.

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ASZ(DCPB)

GONADAL FUNCTION OF RATS UNDERFED FROM BIRTH. R. F. Walker and C. L. Bethea. Dept. of Zoology, Clemson University, Clemson, S. C. 29631

Rats were underfed from birth to determine the effects of chronic food deprivation on gonadal function. Pups were allowed to nurse for 12 hours out of 24 until they were weaned. Thereafter, they received 50% of the daily amount of food consumed by controls. Besides being underfed, animals in selected groups were pinealectomized and/or maintained in constant light. Though delayed, vaginal opening occurred in all underfed groups. 2 or 3 extended estrus cycles occurred after vaginal opening, then the animals became anestrus; however, cycling was restored when they were placed in constant light or with a male. Despite irregular reproductive cycles in underfed females, they would copulate, become pregnant and give birth to litters of normal size and composition. Similarly, underfed males impregnated fed females; however, the latency period between introduction and intromission was prolonged. Pinealectomy shortened this period. Continuous illumination or pinealectomy stimulated compensatory hypertrophy in the remaining ovary after hemiovariectomy, however, the latter treatment was not as effective as the former. It did, however, increase ovarian weight prior to surgery. Blood levels of gonadotropins were more profoundly reduced in underfed castrates injected with estrogen than fed controls receiving a comparable dose of the steroid. This indicates that underfeeding causes increased sensitivity of negative feedback sites for gonadotropin secretion. The adverse effects of underfeeding on reproductive function seem to be due to physiologic alteration resulting in a new pattern of control, rather than simply a reduced rate or lack of function due to less available energy.

LIMITING TRANSEPITHELIAL INORGANIC ION CONCENTRATION DIFFERENCES ACROSS THE RAT PROXIMAL TUBULE. R. Warner* and C. Lechene (SPON: T. Wilson). Harvard Medical School, Boston, Massachusetts 02115

Using the standing droplet (stationary microperfusion) technique combined with electron probe microanalysis, we wish to determine how permeabilities and limiting transcellular concentration gradients for Na, K, Ca, Mg, Cl, SO_4 and PO_4 vary along the length of rat proximal tubule *in vivo*. To divide the proximal tubule into discrete segments, droplets having a small volume, 200 pL are required. Injecting 200 pL isosmotic raffinose droplets, and sampling at timed intervals, droplet volume doubles within 30 sec. and remains at this plateau for an additional 30 sec. By 30 sec., concentrations of Na, Cl and K are within 10% of their steady state levels. The remaining ions approach steady state levels within 45 sec. The difference between Na and Cl concentrations increases with time to a constant value, likely indicating preferential reabsorption of $NaHCO_3$. Limiting concentrations (mM/L) are: Na 114; K 3.7; Ca 1.2; Mg 0.7; Cl 138; SO_4 1.0; PO_4 1.2. Using droplets containing 50 mM/L raffinose and having a composition similar to steady-state levels, droplet volume decreases very slowly for 20 sec. before a more rapid exponential decrease. Limiting concentrations tend to be invariant with time and are similar to those determined using isosmotic raffinose. These limiting concentrations agree well with literature values for Na, K and Cl; limiting concentrations have not previously been reported for the remaining ions. These results also demonstrate the feasibility of using 200 pL volume droplets for segmental analysis of ionic transport along the rat proximal tubule *in vivo*.

PRODUCTION OF RENOVASCULAR HYPERTENSION IN ADRENALECTOMIZED DOGS. B.E. Watkins*, J.O. Davis, R.H. Freeman, and G.A. Stephens* (SPON: D.H. York). Dept. of Physiology, University of Missouri School of Medicine, Columbia, Mo. 65201.

This study evaluated the necessity of adrenal cortical steroidogenesis for the development of renovascular hypertension. Following bilateral adrenalectomy and unilateral nephrectomy, 8 dogs were fed a diet containing 60 mEq sodium per day and were given minimal steroid maintenance (20 mg cortisone acetate, 2 mg deoxycorticoterone acetate per day). Using an adjustable renal artery constricting device, renal blood flow to the remaining kidney was then reduced by 56±2% ($\bar{x}$±SEM) to produce hypertension. Mean arterial pressure rose from 105±3 to 142±5 mm Hg in all dogs within 3 days after renal artery constriction, and remained elevated for the ensuing 30 day observation period. These findings demonstrate that chronic renal hypertension can be produced despite the absence of aldosterone secretion and without excess mineralocorticoid availability. In addition to the pressor response, plasma renin activity (PRA) rose nearly 2 fold for the first 6 days after renal artery constriction, and remained slightly elevated ($P<0.05$) thereafter. Increased urine excretion and decreased hematocrit were associated with the large transient PRA elevation. Also, plasma volume was expanded for the first 3 weeks after the onset of hypertension. These results show that chronic renal hypertension was produced without enhanced mineralocorticoid secretion. Furthermore, chronic one kidney renal hypertension was associated with an elevation in PRA in adrenalectomized dogs.

HEMODYNAMICS OF THE LESSER MOUSEDEER. W.W. Weathers and G.K. Synder*. Dept. Avian Sciences. Univ. of California, Davis, CA 95616

The lesser mousedeer, Tragulus javanicus, has the smallest known erythrocytes of any vertebrate. In addition to their small size, osmotic fragility suggests that the corpuscles are spherical in shape. Fifty percent hemolysis of mousedeer corpuscles occurred in 0.7% NaCL, as compared with 0.6% for spherical human cells and 0.4% for normal biconcave human cells. Spherical shape is correlated with increased rigidity in erythrocytes, and increased rigidity is known to contribute to increased blood viscosity in vitro. At comparable hematocrits the viscosity of mousedeer blood is approximately twice that of human blood, as determined with a glass tube viscometer. To determine whether increased blood viscosity has any in vivo hemodynamic consequences we measured cardiac output (by dye dilution) and arterial blood pressure of three mousedeer ($\bar{X}$ weight 1.18 Kg). Under light Na pentothal anaesthesia, mean arterial pressure averaged 99 torr while cardiac output averaged 145 $ml \cdot min^{-1} \cdot Kg^{-1}$. Total systemic peripheral resistance averaged 4.90 x 10^5 $dynes \cdot sec \cdot cm^{-5}$. All three values compare favorably with data for similar sized mammals. These data suggest that the small size and spherical shape of mousedeer erythrocytes has no significant in vivo hemodynamic effect. (Supported by NSF grant BMS 75-02343)

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CLINICAL ENGINEERING VIEWED FROM THE HOSPITAL. G.N. Webb, Dept. of Biomedical Engineering, Johns Hopkins School of Medicine, Baltimore, MD 21205

Clinical Engineering, a new sub-set of Biomedical Engineering is definately in a growth phase. I define this field as the application of engineering principles and practices to the interface between patients and his/her physical and instrumented environment in the outpatient clinic and the hospital. The growth in the number of engineers working in the clinical setting has come about through: increased use of high technology instrumentation; increased number and complexity of standards, codes and regulations which have to be met; and the active promotion of the field including certification, by professional societies.

Although Biomedical Engineering has been so identified since the '50s, the Clinical Engineering term has been in use for a little more than five years. The approximately 200 individuals who have been certified as Clinical Engineers probably represent a third of those who might be called Clinical Engineers. This number can be expected to increase, perhaps by a factor of five.

The areas in which real engineering work is needed and can be supported are: instrument and system development for optimum clinical use; selection, application and support management for these instruments and systems in the clinical environment; helping to optimize the physical facilities in the best interest of the patient, particularly with respect to instrumentation; adn active work in the code, and standards making and reviewing process. This last, may have the highest priority to assure the best balance among, performance, safety and outside controls.

EVIDENCE FOR EXTERNAL WORK IN WALKING, AS DETERMINED FROM DIRECT CALORIMETRY. Paul Webb, James F. Annis,* and Samuel J. Troutman, Jr.* Webb Associates, Yellow Springs, Ohio 45387.

A number of biomechanical studies over the past 45 years have been interpreted to show that about 20% of the total work in level walking is external (mechanical) work which does not appear as heat in the body. Despite these studies, the term for work (W) in the standard body heat balance equation -- $S = M \pm E - (\pm W) \pm R \pm C \pm K$ -- is usually taken to equal zero for a man walking on a level surface. Using continuous direct and indirect calorimetry, we have measured heat balances in men walking on a level treadmill and found that metabolic free energy conversion (M) is greater than the sum of the heat losses by about 20%, nor is this imbalance recovered during an hour or more of rest following the exercise. Thus in level walking about 20% of M is dissipated in some non-thermal manner, presumably as W. If men exercise on a bicycle ergometer, which permits direct measurement of W, calorimetric data plus W show that the body heat balance equation is fully satisfied. This calorimetric evidence confirms the biomechanical evidence that there is external work in walking.

INSTANTANEOUS FORCE-VELOCITY-LENGTH RELATIONS IN ISOLATED DOG HEART. K.T. Weber* and J.S. Janicki* (SPON: A.P. Fishman). Cardiovascular-Pulmonary Division, University of Pennsylvania, Philadelphia, PA 19104

To investigate the mechanics of left ventricular contraction as a function of instantaneous mural force, mid-wall circumferential shortening velocity (dL/dt) and fiber length (L) the steady state response of 7 servo-regulated hearts were utilized. For a series of variably preloaded or afterloaded allasotonic contractions net wall force and L were derived for a thick-walled sphere from the continuous recording of left ventricular pressure, volume and its derivative. Norepinephrine (0.55-1.38 μg/min) or propranolol (0.07-0.14 mg/min) served to alter inotropic background. For any given contractile state and initial L, maximum dL/dt was not attained instantly but occurred after a finite time (39 $\pm$ 0.2 msec SEM; 24-60) and from a lesser length (92 $\pm$ 0.5% SEM; 83-99) than present at end diastole. Beyond this initial period instantaneous dL/dt was dependent on both instantaneous force and length (e.g. the participation throughout shortening of the reciprocal force-velocity relation with its length dependent characteristics) while independent of time after contraction and initial L. Alterations in contractile state also influenced instantaneous velocity. For example with propranolol, dL/dt was less for any given basal force-length condition (vis a vis norepinephrine). Finally, peak dL/dt was shown to be a function of the extent of shortening. Thus, the three dimensional trajectory describing instantaneous force, velocity and length serves to describe both the mechanical behavior and contractile state of the myocardium and therefore provides the necessary information for elucidating the functional characteristics of a given ventricle. (Supported by NHLI-PPG Grant, HL-08805).

EFFECT OF INTRAVENTRICULAR ANGIOTENSIN II INJECTIONS ON RENAL FUNCTION. J.F. Weet*, W.E. Hoffman*, and M.Ian Phillips. Dept. of Physiology and Biophysics, University of Iowa, Iowa City, IA 52242

Previous studies of intraventricular angiotensin II (IVT AII) injections have shown that animals exhibit increased drinking behavior, increased blood pressure, antidiuretic hormone (ADH) release and increased sodium excretion (natriuresis). Natriuresis is also known to occur in hydrated animals following the intravenous injection of ADH (IV ADH) although this response does not occur in volume expanded but non-hydrated animals. Since the only study to date used water loaded animals as its experimental model, our experiments were completed in saline expanded rats to determine if natriuresis ordinarily might accompany IVT AII injection at a time when ADH release would not alter the response.

In volume expanded animals, IV ADH increases blood pressure but does not lead to increased sodium excretion. Similarly, IVT AII has a pressor effect but does not cause natriuresis. Furthermore, glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were not changed with these treatments. Responses contrast to those following intravenous injection of angiotensin II (IV AII).

It is concluded that IVT AII injection has little primary effect on renal function and that natriuresis in hydrated animals is probably due to ADH release. (Supported by NIH grant #BNS75-16346 to MIP)

ALDOSTERONE STIMULATION OF RENAL AMMONIA (NH_3) PRODUCTION. T.C. Welbourne and D. Francoeur*, Institut de Recherches Cliniques de Montréal, Montréal, P.Q.

Administration of D-aldosterone, 2.5, 5.0 or 7.0 μg $100g^{-1}$ day^{-1} significantly increases urinary ammonium (NH_4^+) excretion producing metabolic alkalosis without hypokalemia. The purpose of this study was to determine the mechanisms of aldosterone's action on NH_3 production. To demonstrate independence of filtered electrolyte exchanges, $Na^+ \rightleftarrows K^+$ and $Na^+ \rightleftarrows H^+$, NH_3 production was determined in slices from aldosterone treated rats incubated in 1 mM L-glutamine; NH_3 production, 74.3 ± 4.3 μ Mol 45 min^{-1} g^{-1} was significantly greater ($P< .05$) in slices from hormone treated rats than from controls, 51.4 ± 4.1 μ Mol 45 min^{-1} g^{-1}. To determine whether an effect of aldosterone on protein induction can be eliminated, rat kidneys were isolated and perfused with carrier L-glutamine, 1 mM, and 2 ucurie L-glutamine-u-C^{14} (sp. act. 127 ucuries μ Mol^{-1}) in the presence of physiological levels of aldosterone (10^{-7} M). Aldosterone stimulated NH_3 production 2 fold, 24.8 ± 4.2 vs 49.5 ± 3.3 μMol $h^{-1}kd^{-1}$ ($P< .005$) and increased the NH_3 produced per glutamine extracted ratio from 1.29 ± 0.07 to 1.62 ± 0.05 ($P< .01$); in addition, the per cent of glutamine uptake converted to CO_2 increased from 2.18 ± 0.15% to 6.14 ± 0.70% ($P< .01$). This effectively eliminates induction of protein synthesis as a mechanism. We suggest that aldosterone stimulates activation of the mitochondrial glutaminase I-glutamate dehydrogenase pathway based on the NH_3/gln ratio and the proportional increase in the oxidative disposal of glutamine's carbon moieties as CO_2.

VENTILATION-PERFUSION RELATIONSHIPS IN THE TURTLE. F.N. White and James Kinney*, Dept. Physiology, UCLA, Los Angeles, Cal. 90024.

$\dot{V}O_2$ consumption ($\dot{V}O_2$, ml/(kg·min)) of resting Pseudemys floridana relates to body temperature (BT) in the manner: log $\dot{V}_{O_2}$=0.047BT***±0.243 log Wt***±1.32;(***=p<.001). $\dot{V}E/\dot{V}_{O_2}$ declines with increased BT (Jackson, D.,Resp.Physiol.12:131,1971) resulting in elevated P_{CO_2}, an adjustment holding arterial pH parallel to the neutral pH of H_2O and $[OH^-]/[H^+]$ constant (Howell,B.,et al.Am.J.Physiol.218:600,1970). Our data follow the expression: log $\dot{V}E/\dot{V}_{O_2}$= -0.017BT***-0.025 log Wt^{ns}+2.01. We estimate O_2 cost (%resting $\dot{V}O_2$) of $\dot{V}E$ (comparison of resting $\dot{V}_{O_2}$ with apnea induced by lung perfusion at low PCO2) for various BT at: 10°C=32%; 20°C=21%; 35°C=11%. Reduced $\dot{V}E/\dot{V}_{O_2}$ with BT reduces O_2 cost of $\dot{V}E$ as BT and $\dot{V}O_2$ increase. Resting pulmonary blood flow ($\dot{V}b$,ml/(kg·min)) by Fick method follows the relationships: $\dot{V}b$=54.9 $\dot{V}_{O_2}$***-2.39 log Wt^{ns} -1.97; log $\dot{V}b$=0.05 BT***-0.51 log Wt^{ns}+0.38 and log $\dot{V}b/\dot{V}O_2$=0.001BT^{ns} -0.143 log Wt^{ns}+1.73. $\dot{V}E/\dot{V}b$ falls with BT: $\dot{V}E/\dot{V}b$=-0.011 BT***+0.54 log Wt*-0.041. This adjustment is via cholinergic vasoconstrictor modulation of muscular segments of the pulmonary artery. No direct effect of O_2 or CO_2 on pulmonary microvessels was seen by direct visualization in intact animals. Rising O_2 extraction with BT associates with decrease in $\dot{V}E/\dot{V}b$ and mixing of lung gas during apnea via cholinergic mediated lung smooth muscle according to the equation:log contractions/min=0.037 BT-1.93. Little change in arterio-venous O_2 difference occurred at rest. Assertion that fall in $\dot{V}E/\dot{V}O_2$ contrasts to the relatively constant $\dot{V}E/\dot{V}_{O_2}$ of mammals (Jackson,D.,Resp.Physiol. 12:131, 1971) as $\dot{V}_{O_2}$ increases is not verified from our measures on 5 exercising turtles where $\dot{V}E/\dot{V}_{O_2}$ remained constant at constant BT. The resting $\dot{V}E/\dot{V}_{O_2}$ appears to be related more to BT than to $\dot{V}_{O_2}$ per se. For P. floridana:$\dot{V}E/\dot{V}O_2$ at 37°C is 0.5-0.6 L/mMO_2; for man:0.57(Dejours,Princ. Comp.Resp.Physiol.,Am.Elsevier Pub.Co.,N.Y.,1975). NSF Grant GB 41390.

DEVELOPMENT OF A NEW ANIMAL MODEL FOR THE STUDY OF ENDOTOXIN SHOCK. G. White*, L. T. Archer*, T. Schroeder*, B. K. Beller*, D. D. Holmes*, R. T. Brantley*, and L. B. Hinshaw. (Intro. by K. Weiss.) V.A. Hospital and Univ. Okla. Health Sci. Ctr., Okla. City, Okla. 73104

Recent work in the canine has demonstrated an accelerated uptake of glucose in the blood following endotoxin administration with certain components of the buffy coat being responsible for the decrease of blood glucose. The purpose of the present study was to determine the role of the leukocyte in accounting for the increased uptake of glucose as well as its possible role in preventing hypoglycemia and death in endotoxin shock. The awake dog was utilized in this study with the endotoxin group receiving 0.003 mg/kg body wt (i.e., 1/1,000 LD_{100}) on days 1 and 2, 3 mg/kg body wt (LD_{100}) on day 3 and a challenge dose of 6 mg/kg body wt (2xLD_{100}) on day 4. The control group received an equal volume of saline on days 1, 2 and 3, but on day 4 received a 6 mg/kg body wt challenge dose of endotoxin. All dogs receiving endotoxin spiked a fever ranging from a mean of +1.4°C to +2.7°C between +1 and +4 hours post-injection with endotoxin levels of 1/1,000 LD_{100}, LD_{100} and 2xLD_{100}. The endotoxin group had a mean WBC count of 12,840 mm^3 at zero time and on day 4 a mean value of 39,000. Blood glucose in this group decreased after 2xLD_{100} endotoxin challenge initially but returned to near control between 4 and 5 1/2 hours. The awake dog spiked an elevated temperature with doses of endotoxin from 0.003 mg to 6 mg/kg. All dogs in the endotoxin group survived a 6 mg/kg challenge of endotoxin while all saline-injected control dogs died with the same dose of endotoxin. Results suggest that although the leukocytes may demand increased amounts of glucose in vivo they may protect the ability of the liver to perform glycogenolysis and gluconeogenesis. (Supported by V.A. Hospital and U.S. Navy Project N00014-76-C-0229.)

A FOUR MODE AUTO-REGULATING ARTIFICIAL LEFT VENTRICLE. R. Whitman* M. McMullen* and S. Furman. Cardiothoracic Surgery, Montefiore Hospital and Medical Center, Bronx, New York 10467.

An Artificial Left Ventricle (ALV) has been designed for post cardiac surgical patients whose needs exceed (in time duration and stroke volume (SV)) the support available from intra-aortic balloon and bypass roller pumps. Hemodynamic tests in acute open-chested dogs are encouraging.

The ALV is capable of synchronous diastolic augmentation for increased coronary artery perfusion, active left ventricular (LV) unloading and auto-regulated SV. The input connects proximal to the occluded ascending aorta. The valved output connects to the descending aorta. During pump systole the input also serves as an output providing elevated perfusion pressure exclusively to the coronary arteries. The ALV is discoid-shaped with rigid shell and tangential ports. It has 2 ellipsoidally-shaped segmented polyurethane diaphragms (D) for minimizing stagnant and turbulent flow areas, reportedly resulting in terminal deposition of blood elements. The four modes of operation unique to this design are: (1) passive conduit mode, (2) maximum pumped volume, (PV) mode using 2 active D's for the critical post operative period, (3) one fixed and one active D mode for normal PV, and (4) one active and one compliant D mode for auto-regulated PV, needed for the recovering LV.

Twelve experiments with 4 hours of pumping in open-chested anaesthetized dogs show healthy LV's and a 75% increase in coronary flow (off to on) in spite of total inflow and outflow occlusion during ALV connections. Heart rate, arterial pressure, RV and LV pressure, pump (P) gas pressure, P vacuum, P timing, and P blood flows in and out were monitored each minute by computer. Urine output and blood chemistries were determined hourly. Chronic dog implants are being planned.

VASCULAR RESPONSES TO THE MONOENOIC PROSTAGLANDIN (PG) PRECURSOR DIHOMO-γ-LINOLENIC ACID (DGLA) IN THE PERFUSED CANINE LUNG. T.C. Wicks*, P.W. Ramwell, J.C. Rose and P.A. Kot. Dept. Physiology and Biophysics, Georgetown Univ. Med. Ctr., Washington, D.C. 20007

DGLA produces systemic hypotension in the dog. Its effect on the pulmonary circulation has not been studied. The effects of DGLA were compared with those of arachidonic acid (AA, the bisenoic PG precursor) and $PGF_{1\alpha}$ in the isolated (in situ) canine lung lobe perfused with autologous blood under constant flow conditions. Lobar arterial and venous pressures were monitored constantly following bolus injections of these agents. DGLA produced pulmonary vasoconstriction in a dose range of 50-500 ug/kg. From 50 to 300 ug/kg the relation was linear. DGLA (100 ug/kg) produced a 26.4 $\pm$ 5.6% (n=7) increase in pulmonary artery pressure whereas the same dose of AA resulted in a mean increase of 62.8 $\pm$ 7.1% (n=13). $PGF_{1\alpha}$ (1 ug/kg) produced a pulmonary pressor response of 28.1 $\pm$ 8.3% (n=7). DGLA responses at 200 ug/kg (n=10) were nearly identical to those with AA at 100 ug/kg. The DGLA and AA vascular responses were blocked by indomethacin. Linoleic acid, used as a control fatty acid, had no pressor action. In three experiments with a cell-free artificial perfusate, the vasopressor response to 200 ug/kg DGLA was at least equal to that in the blood perfused lobe. DGLA has a pulmonary vasopressor action which is qualitatively different from its systemic vasodilator effect. This may be due to conversion to vasoactive endoperoxide intermediates. The conversion is either less efficient than with AA or the intermediates formed are less potent than those produced from AA.

ASZ(DCPB)

EFFECTS OF PARATHYROIDECTOMY AND PARATHYROID HORMONE REPLACEMENT ON RENAL TUBULAR TRANSPORT OF CALCIUM AND PHOSPHATE IN STARLINGS.
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Previous studies in this laboratory have shown the kidney to be a major target organ for the parathyroid hormone regulation of Ca and PO_4 homeostasis in the intact starling, Sturnus vulgaris. It was therefore of interest to study the renal effects of parathyroidectomy (PTX) and parathyroid extract (PTE) replacement therapy in these birds. Starlings were studied using standard clearance techniques. Animals received constant infusion of ^{14}C-inulin and blood and urine samples were collected at regular intervals. After collection of control data, the parathyroids were surgically removed. Three hours post-PTX, bovine PTE was administered (Lilly; 50 IU/100 gbw) and samples were collected for two hours longer. Serum Ca values fell sharply following PTX, to about 60% of normal by 3 hours, while serum PO_4 values increased to 175% of normal during the same period. Simultaneously, relative urine Ca clearance (C_{Ca}/C_{In}) rose dramatically following PTX (from 0.02 to 0.25 by 40 min. post-PTX); PTE returned these levels to near-normal within 2 hours. We found previously that surgical trauma can evoke PO_4 secretion in intact starlings. However, by 40 min. post-PTX, only PO_4 reabsorption is observed, indicating that the original hyperphosphaturia is a consequence of endogenous parathyroid hormone release. Administration of exogenous PTE in PTX birds reestablishes PO_4 secretion within 20 min. PTX decreased the relative clearance of K (C_K/C_{In}) by nearly 50%; PTE greatly elevated these values in PTX animals. In many cases, secretion of K was noted. In normal starlings essentially all filtered Na is reabsorbed; PTX did not change this pattern. PTE administration produced a brief natriuresis, seen also in intact birds.

THE TOPOLOGY OF REACTION-DIFFUSION SYSTEMS IN THE MITOCHONDRIA. W.A. Wiegand* (SPON: G.D. Ford). Dept. Physiology, MCV-VCU, Richmond, VA. 23298.

The bond graph techniques of Oster and Perelson, Arch. Rat. Mech., Vols. 55 and 57 (1974), are used to model the mitochondrial respiratory cycle first as a stirred tank and then as a spatially organized reaction-diffusion system. These same techniques are then used to model single mitochondria and mitochondrial aggregates with specific spatial topologies. In particular, a model is given for the linear arrangement of mitochondria in the proximal tubules and for the arrangement of mitochondria on the tail of spermatozoa. It is then shown, using topological manifolds, that single mitochondria and aggregates of mitochondria can generate concentration gradients across them as required in the proximal tubules for reabsorption. Using the reaction-diffusion manifolds of B. Bunow, Biosystems, #7, 160-171 (1975), it is shown that these systems can exhibit multiple steady states and thus serve as switches for reaction and diffusion processes. The connection between this work and the chemiosmotic hypothesis of Mitchell is then given. The results imply first that the topology of reaction-diffusion systems determines the overall dynamics of the system and second that Mitchell's hypothesis is realizable in light of the topology of the mitochondria.

SMALL VEIN CONSTRICTION IN THE SPONTANEOUSLY HYPERTENSIVE RAT. D.L. Wiegman*, P.D. Harris, F.N. Miller*, and I.G. Joshua*. Microcirculatory Systems Research Group, Dalton Res. Ctr. and Depts. of Physiol. and Pharmacol., Univ. of Missouri Sch. of Med., Columbia, Mo. 65201

In vivo concentration response curves to topically-applied norepinephrine (NE) were determined for a major small artery and vein pair in the cremaster muscle of 10 spontaneously hypertensive rats (SHR) ($\bar{X} \pm$ SEM, 178 ± 7g) and 8 Kyoto Wistar control rats (C) (180 ± 3g). Rats were anesthetized with urethane and α-chloralose. The cremaster muscle with circulation and innervation intact was suspended in a Krebs bath (31°C; pH 7.2). Vascular diameters were measured via television microscopy. In the following table, diameter is the resting vessel diameter before application of NE, maximal constriction is the % decrease in vessel diameter in response to a supramaximal concentration of NE, and pD_2 (-log ED_{50}) indicates vessel sensitivity to NE. (*$p < .05$)

	Artery diameter (μm)	Artery maximal constric. (%)	Artery pD_2	Vein diameter (μm)	Vein maximal constric. (%)	Vein pD_2
SHR	94±6	72±2 *	6.4±.2	142±6 *	42±3	7.0±.1
C	94±6	64±3	6.4±.1	214±10	46±3	7.1±.1

Mean pressures in the tail artery were measured under light ether anesthesia two days before the NE experiments. SHR gave 137±2 mmHg; C gave 114±3 mmHg. The major findings in the SHR are chronic constriction in the vein and increased maximal constriction in the artery. (Funded by PHS HL05184, HL05810, HL12614, and HL20422.)

STIMULUS VS. RESPONSE IN CATTLE SUSCEPTIBLE AND RESISTANT TO HYPOXIC PULMONARY HYPERTENSION. D.H. Will, I.F. McMurtry*, R. Looga*, E.K. Weir*, A.F. Alexander* and J.T. Reeves. Department of Physiology and Biophysics, Colorado State University, Fort Collins, CO 80523 and CVP Research Lab., University of Colorado Medical Center, Denver, CO 80220.

Do individual variations in the pulmonary vascular response to low oxygen reflect differences in vascular reactivity or differences in the level of hypoxic stimulus? To help answer this question we conducted studies in progeny of two groups of cattle, one bred for susceptibility and the other for resistance to high altitude pulmonary hypertension. At low altitude (1524m), susceptible calves had a lesser hypoxic ventilatory drive over 5 minutes than did the resistant animals indicating that their greater pulmonary hypertension at high altitude may be the result of a relative hypoventilation with augmentation of the hypoxic stimulus. This was not supported, however, by blood gas measurements in the two groups of calves at 2 hours or 2 weeks at a simulated high altitude of 4270m. Although the susceptible animals developed greater pulmonary hypertension at high altitude, their arterial oxygen and carbon dioxide tensions were not different from those of the resistant calves. In addition, the susceptible calves developed a greater pulmonary pressor response than did the resistant calves to iv injections of prostaglandin $F_{2\alpha}$ at low altitude. This indicated a basic difference in pulmonary vascular reactivity between the two groups which was supported by subsequent lung biopsy studies showing qualitatively thicker-walled pulmonary arterioles in the susceptible vs. resistant calves. Collectively the data indicate that the principal basis for susceptibility of cattle to high altitude pulmonary hypertension is probably an increased pulmonary vascular reactivity rather than an increased hypoxic stimulus. (Supported by Colorado Heart Association and NIH Grants HL-14985 and HL-18191).

PARALLEL VARIATION OF PLASMA OCTOPAMINE AND ORTHOSTATIC BLOOD PRESSURE DROP DURING L-DOPA AND SINEMET THERAPY. W.J. Willems, D. Wang*, H.D. Itskovits*, and E.A. Sasse*, Milwaukee County Medical Complex, Milwaukee, Wis. 53226

Simultaneous measurements of serum Octopamine levels and blood pressure (erect and recumbent) were obtained in six patients with idiopathic Parkinson's disease before and during treatment with L-dopa. Similar measurements were made in a second group of nine patients during L-dopa treatment and after switching to Sinemet therapy. Both Octopamine and the orthostatic systolic blood pressure drop, calculated as paired changes from control, increased with incremental L-dopa doses. The increases were significantly different from zero ($p < 0.05$) when values at the maximum L-dopa doses were grouped. Significant decreases in orthostatic blood pressure drop and decreases in plasma Octopamine were noted in the patients who were switched from L-dopa to Sinemet therapy. In the total fifteen patients, a positive corellation was noted between all blood pressure drops and serum Octopamine levels obtained ($n=45$, $R=0.7$). These data are consistent with a peripheral locus for L-dopa's hypotensive action. Since the serum levels of Octopamine paralleled the blood pressure drop in all groups, the hypothesis is entertained that Octopamine may play an etiologic role in the causation of hypotension as a false transmitter in adrenergic neurons exposed to high L-dopa concentrations.

TRANSIENT RESPONSES OF THE CEREBRAL BLOOD FLOW (CBF) TO ACUTELY INDUCED HYPERCAPNIA. D. Wilson* and C.E. Rapela. Dept. of Physiol. and Pharmacol., Bowman Gray School of Medicine, Winston-Salem, N.C. 27103

Most methods used to measure CBF do not allow studying cerebral vascular transient responses to increases in inspired [CO_2]. Only scanty data based on indirect methods of estimating CBF exist (Shapiro et.al., J. Clin. Invest. 45:913, 1966). Dogs were anesthetized with Pentobarbital, paralyzed with Gallamine triethiodide and ventilated at constant rate and volume. CBF was recorded continuously at the confluence of the sagittal and straight sinuses with both lateral sinuses occluded. Blood samples were drawn simultaneously from the femoral artery (a) and confluence of the sinuses (cv) for determination of P_{aCO_2}, $[H^+]_a$, P_{cvCO_2}, and $[H^+]_{cv}$ while breathing air or a 10% CO_2 gas mixture. After achievement of a steady-state CBF, CO_2 was discontinued and blood sampling continued until end-tidal CO_2 ($ETCO_2$) returned to control levels. The half-times ($t_{\frac{1}{2}}$) were determined graphically as a relative measure of the rate of change for each variable:

	$ETCO_2$	P_{aCO_2}	P_{cvCO_2}	CBF
onset phase	52 sec. ±5	75 sec. ±6	140 sec. ±11	222 sec. ±19
offset phase	40 sec. ±5	56 sec. ±11	90 sec. ±11	68 sec. ±9

The delay between the rising $ETCO_2$ and CBF response as determined by the difference between the $t_{\frac{1}{2}}$s cannot be explained by a slow rise of either P_{aCO_2} or P_{cvCO_2} during the onset phase of hypercapnia. During the offset phase the $t_{\frac{1}{2}}$ of the CBF was 3 fold less than during the onset phase and did not differ significantly from the $t_{\frac{1}{2}}$ of the P_{cvCO_2}. These results are not in agreement with the generally accepted concept that increases in $ETCO_2$ are followed immediately by proportional increases in CBF. Supported by NIH Grants NS11953, HL 5392, HL 0487 and N.C. Heart Association.

BINOMIAL RELEASE IN THE RAT DIAPHRAGM CUT MUSCLE PREPARATION. D.F. Wilson, Dept. of Zoology, Miami University, Oxford, O. 45056.

Transmitter release was examined in the rat diaphragm cut muscle preparation. The cutting technique was modified to permit consistent recordings of miniature end-plate potentials (MEPPs) and end-plate potentials (EPPs). Anomalous action potentials were identified by a summation test. The advantage of this preparation is that quantal release can be examined from motor neurons that are not depressed by blocking agents and quantal release can be determined from MEPP amplitudes. Normally quantum size measurements are required to examine quantal release if transmitter release is not depressed and this requires the assumption that release is Poisson. In agreement with previous reports however quantum size estimates obtained from preparations stimulated 0.5 to 2/sec are usually smaller than MEPPs. Hence Poisson assumptions leads to overestimation of quantal release. The present results support the conclusion that transmitter release is binomial rather than Poisson. Binomial analysis suggests that in control solution the statistical store is approximately 134 quanta and the probability of release is 0.57. The available store extrapolated from the initial rundown of EPPs in a tetanic train (150/sec) is 11 times greater than the statistical store. It is suggested that this available store reflects vesicles clumped around the releasing sites. (Supported by USPHS, NIH Grant NS-09042).

ION SPECIFICITY OF PRIMAQUINE-INDUCED CHANGES IN ERYTHROCYTE MEMBRANE PERMEABILITY. J.Winkert, M. Florip*, A.Johnson*, P.Pyle*, E.Winkert* and R.Reba*. Washington Hospital Center, Washington, D.C. 20010.

Evidence for a permissive role for band 7 erythrocyte membrane protein in the primaquine-induced potassium leak included the simultaneous inhibition of potassium efflux and the loss of band 7 protein after incubation with chloroquine.(Winkert, et al,Fed.Proc.35:252,1976). In the erythrocyte membrane model of Nicolson (BBA 457:57,1976), band 7 protein appears on the inner side of the membrane at the base of the permeaphore complex. It has also been found in RBC hemolysates where it appears as the only other major band in addition to hemoglobin (Fairbanks et al, Biochem. 10:2606, 1971). It's molecular weight of 27,000 is about half that of the calcium transport activator which Luthra et al (BBA 419:164,1976) have extracted from RBC hemolysates, suggesting a monomer-dimer relationship between potassium and calcium gating proteins. If potassium and calcium gating proteins were related oligomers, the antimalarials might be expected to alter calcium as well as potassium permeability. Although 5mM chloroquine significantly reduced primaquine-induced potassium leak, neither primaquine at 1.5mM nor chloroquine at 5mM significantly altered RBC calcium levels. It thus appears that potassium and calcium gating are separate processes. Although chloroquine blocks primaquine-induced potassium efflux, chloroquine alone, also induces a small but significant loss of RBC potassium. The chloroquine-induced potassium leak is coupled with an inward movement of sodium whereas the primaquine-induced leak is not. These observations suggest the presence of two separate potassium channels. In one channel potassium efflux is coupled to sodium entry; in the other, band 7 protein may permit uncoupled potassium loss.

A NEW SOLID STATE CHLORIDE-SENSITIVE MICROELECTRODE. W. Wojtkowski*, K. F. Frey*, C. J. Myers* and W. McD. Armstrong. Dept. of Physiology, Indiana University School of Medicine, Indianapolis, Indiana 46202

Conventional micropipettes (tip diameter <0.5 μm) were pulled from Kimax-51 glass tubing (O.D. 1 mm, I.D. 0.7 mm). Their tips were sealed with a microforge under 200X magnification. A layer of silver approximately 3000 Å thick was vacuum deposited on the outside of the sealed glass micropipette which was then shielded by a modification of the method of Lee and Armstrong (J. Membrane Biol., 15:331, 1974) leaving an exposed tip of 2-5 μm. Silver conducting paint was used to make contact between the microelectrode and the input lead to a high impedance electrometer (Analog Devices, 311J; input impedance > 10^{14} ohm). The electrical characteristics of eight microelectrodes of this type were studied. These electrodes gave rapid and stable linear responses in KCl solutions (5-100 mM). The average slope of the electrode potential was 55.2 ±0.9 (SEM) mV/decade change in Cl^- activity (a_{Cl}). Substitution of Na^+ for K^+ did not affect the electrode response which was also unaffected by the addition of 10 mM HCO_3^- or a mixture of 7.4 mM $HPO_4^=$ and 2.6 mM $H_2PO_4^-$ to the calibrating solution. Addition of Br^- (1,5, or 10 mM) caused erratic responses. Average tip resistances were 1.36 x 10^{11} ohm in 10 mM KCl and 7.8 x 10^{10} ohm in 100 mM KCl. Repeated calibrations showed that the electrical properties of the microelectrodes remained essentially unchanged for at least 24 hr. Preliminary experiments with these electrodes suggest that, in isolated frog sartorius muscles equilibrated at 25° with Ringer's solutions (Cl^- concentration 121 mM), intrafiber a_{Cl} exceeds the value predicted if Cl^- is assumed to be in electrochemical equilibrium across the fiber membrane. (Supported by USPHS Grants HL 06308 and AM 12715).

THE EFFECTS OF BURN INJURY ON GLUCOSE OXIDATION, TURNOVER AND RECYCLING IN GUINEA PIGS. Robert R. Wolfe and John F. Burke*, Shriners Burns Inst., Mass. General Hosptl., and Harvard Medical School.

We used the simultaneous primed-constant infusion of (6-^{3}H)- and (U-^{14}C)-glucose to determine true glucose turnover, glucose oxidation and the recycling of glucose carbons in guinea pigs(GP)(n=10) that had been either burned or sham-burned (controls) 48 h earlier. Fasted animals were maintained on a continuous intravenous infusion of lactated Ringer's (1.25 ml/h) from the time of burning (or sham burning) until the experiment began. True glucose turnover was 29.1±3.8 SEM μmole/kg·min in the controls and was elevated approximately 50% in the burned GP, whereas the plasma glucose level was only slightly higher in the burned group. The glucose carbon recycling was increased from 2.3±.8 μmole/kg·min in the controls to 9.7±3.2 μmole/kg·min in the burned GP, but the rates of glucose oxidation were similar in the two groups. When a two hour intravenous infusion of 55 μmole/kg·min glucose was given, hepatic glucose output was reduced to a much greater extent in the controls than in the burned GP. Nevertheless, the mean plasma glucose concentration in the burned GP did not rise to a higher level during the glucose infusion than did that of the controls, indicating a higher metabolic clearance rate in the burned animals. During the glucose infusion the recycling of the glucose carbons remained higher in the burned GP than in the controls. The rate of glucose oxidation and the % of CO_2 due to glucose oxidation rose similarly in each group. We concluded that although burn injury markedly affects the glucose kinetics (turnover and recycling), these alterations may not be reflected in corresponding changes in the rate of oxidation of glucose.

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RENAL AND HEPATIC EFFECTS ON GLUCOSE AND KETONE BODY METABOLISM IN FED AND FASTED EVISCERATED RATS. C.M. Woodbury,* E.F. Spangler,* E.R. Ramey and J.C. Penhos. Dept. of Physiology & Biophysics, Georgetown University School of Medicine, Washington, D.C. 20007.

Fed and 18 hr. fasted male Sprague-Dawley rats (200-350 gms) were eviscerated in four different conditions: 1) with functional liver (L) and intact kidneys (K), 2) with nonfunctional L and intact K, 3) with functional L and nephrectomy, and 4) with nonfunctional L and nephrectomy. At 0 hr. control values for blood glucose (BG) were 124 ± 3.1 mg/dl and 67 ± 3.2 mg /dl; ketone body (KB) levels were 0.8 ± 0.1 mg/dl and 1.9 ± 0.2 mg/dl, fed and fasted respectively. In animals with L and K intact, BG levels are highest; they climb steadily to 702 ± 45.1 and 180 ± 13.6 at 72 hrs. post eviscer-ation. Intermediate levels of BG occur at 6 hrs. in nephrectomized animals with functional L (169 ± 7.2 and 123 ± 10.3) and in functionally hepatectomized animals with K intact (83 ± 3.2 and 17 ± 2.0). With neither L nor K, BG levels drop to 20 ± 3.71 and 8.0 ± 1.0 at 3 hrs.

KB levels at 6 hrs. are highest in nephrectomized animals with intact L (2.3 ± 0.4 mg/dl fed, 14.3 ± 1.1 mg/dl fasted). Intermediate levels occur in rats with both L and K intact (1.8 ± 0.3 and 5.2 ± 0.3) and in rats with no L or K (3 hrs. only - 1.1 ± 0.2 and 5.2 ± 0.3). Levels rise rapidly in animals with functional L and K, especially in fasted rats, up to 72 hrs. (11.2 ± 0.8 and 15.2 ± 1.4).

From our data we conclude that 1) the kidney plays an important role in maintaining BG in both fed and fasted eviscerated diabetic rats, and 2) the kidney's contribution to ketone body level is not detectable in our preparation. (Supported in part by USPHS grant 5R01 AM16342-03).

ACTIVE POTASSIUM TRANSPORT BY THE CHOROID PLEXUS. Ernest M. Wright. Dept. Physiology, UCLA, Los Angeles, CA 90024.

There is a net transport of potassium (0.03 μmoles/cm^2/h) across the frog choroid plexus from the cerebrospinal fluid to the blood. This phenomenon was studied by measuring the intracellular ionic composition and the unidirectional potassium influxes across the apical and baso-lateral plasma membranes of the epithelium. In normal tissues the intracellular sodium and potassium concentrations were 17 and 154 m-equiv/l respectively. Incubation of the plexus in the cold or in the presence of 1 x 10^{-4}M ouabain increased the internal sodium and decreased the internal potassium towards the concentrations in plasma. Tissues incubated in the cold subsequently reaccumulated potassium and pumped out sodium when the temperature was returned to 22°C. The unidirectional influx of K across the apical plasma membrane exhibited a K_m of 1.5 m-equiv/l and a V_{max} of 6 μequiv/cm^2/h. This influx was inhibited over 90% by ouabain, phloretin and ethacrynic acid; the ouabain K_I was 1 x 10^{-7}M. Bicarbonate increased the influx by 100%, and the HCO_3 K_m was 15 m-equiv/l. [3H]-ouabain binding revealed that there was 5 x 10^4 pump sites /μ^2 of the apical membrane, and this estimate together with the V_{max} for the active K influx yielded a turnover number of 125/minute for each pump site. The number of sites and their turnover number are in the range reported for single cells. The ion selectivity of the potassium pump was found to be Rb ~ K > Cs > Li,Na, and active K pumping was only observed in the presence of Na. The rate of active K pumping into the epithelium across the baso-lateral membrane was less than 7% of the active influx across the apical membrane. It is concluded that both the active accumulation of K within the epithelium and the net flux of K across the plexus is due to the presence of a Na/K exchange pump on the apical cell membrane. [Supported by USPHS grant NS-09666.]

THE EFFECT OF SOMATOSTATIN ON ARGININE STIMULATED INSULIN AND GLUCAGON RELEASE IN NORMAL AND SPONTANEOUSLY DIABETIC CHINESE HAMSTERS.
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Diabetes, resembling diabetes mellitus in man, develops spontaneously in the Chinese hamster (CH). Insufficient insulin and excessive glucagon release occur in diabetic man and in the spontaneously diabetic CH. Somatostatin, a hypothalamic tetradecapeptide, inhibits arginine induced insulin and glucagon secretion in normal and diabetic man. Previous studies have shown that plasma insulin and glucagon increase in normal and diabetic CH after treatment with arginine. This study describes the effect of somatostatin on arginine induced changes in plasma levels of insulin and glucagon in normal and diabetic CH. Overnight fasted normal and diabetic CH were injected with arginine or arginine plus somatostatin. Plasma insulin and glucagon were determined 5, 15, and 25 min. after treatment. Somatostatin inhibited arginine induced insulin release at 5 min. and glucagon release at 5, 15, and 25 min. after treatment in the normal but not in the diabetic CH. These data indicate that, unlike the islet α and β cells of normal and diabetic man and the normal CH, the α and β cells of the diabetic CH may be insensitive to somatostatin.

ON-LINE ESTIMATION OF RESPIRATORY RESISTANCE BY FORCED OSCILLATION.
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An on-line digital computer approach to estimating total respiratory resistance by forced oscillation was tried in an attempt at minimizing sources of variability. Combined analog and digital processing methods were utilized for this purpose. Analog filtering was used to separate the perturbation signal from the breathing harmonic, while peak detection, division, and averaging were accomplished digitally using a PDP 11/10 minicomputer. Data in a set of normal subjects suggest that frequency dependence of resistance (3-12 Hz) may have been previously overestimated due to a bias introduced by not filtering out the breathing harmonic. This bias leads to up to a 75% overestimate of resistance primarily at 3 Hz. An analysis of variance performed on data collected over 4 days in 6 normal subjects showed good reproducibility of estimates (4.6-20.7% coefficient of variation) made at 3,6,9, and 12 Hz. All estimates were made during the beginning of inspiration at an airflow level of 0.5 LPS.
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INTERACTION OF OSMOTIC AND NEURAL STIMULI ON NEUROSECRETORY CELLS OF SUPRAOPTIC NUCLEI (SON) OF THE HYPOTHALAMUS. H.Yamashita* and H. Kannan* (SPON: K. Koizumi). Dept. Phys., Kobe Univ.,Sch.of Med.,Japan

In cats anesthetized with Nembutal (30mg/kg), single unit recordings were made from SON of the hypothalamus with glass capillary electrodes. Neurosecretory cells were identified by antidromic excitation following stimulation of the posterior lobe. Stimulation of septal area with a latency of 27 msec., followed by a long lasting (110 msec) inhibition, while repetitive stimulation (10 Hz) of the area produced constant inhibition of SON cells. Stimulation of the midbrain RF with a single pulse also evoked action potentials in SON cells with a latency of 10-30 msec and spontaneous discharges were augmented for the next 50-100 msec. Repetitive stimulation of RF caused a significant increase in firing frequency of SON cells. Intracarotid injection of hypertonic saline (1M:0.3 ml) first excited, then inhibited SON cell activity. Combination of the osmotic and repetitive stimulations of the two neural structures showed that septal stimulation could completely block effect of osmotic stimulus, while excitatory effect of RF stimulation on SON cells summated with osmotically induced effect. Intravenous injection of one of cholinergic blockers, pempidine (5 mg/kg), blocked early excitatory effect of osmotic stimulation on SON cells without affecting late inhibitory response. The result suggests that neural input may greatly alter the response of SON cells to osmotic stimuli, and the latter may act on neurosecretory cells through osmoreceptors, while septal and RF stimulations seem to directly act on neurosecretory cells.

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OSCILLATIONS OF GLUCOSE AND INSULIN IN CONSCIOUS DOGS. F.E. Yates, R.H. Odell* and D.J. Marsh. Dept. Biomedical Engineering, Univ. Southern Calif., Los Angeles,CA 90007

Intravenous infusions of glucose at rates of 0, 5, 10 or 15 mg kg^{-1} min^{-1} were given for 10 to 30 hrs in trained, fasting, conscious dogs. Arterial blood was continuously withdrawn, and analyzed for plasma levels of glucose (G) (mg%) and insulin (I) (ng/ml). Data were analyzed for linear trends and periodicities by a new method (Ann. Biomed. Eng. 3:160,1975). Initial G levels averaged 82; I levels were < 1.0. In the control group (no infusion) spontaneous, small G and I oscillations were usually seen. Infusions (18 exps) caused rapid rises of G and I. This onset transient ended after 3.5 hrs and was followed by a slow, linear decline in both G and I (12/18 exps). For all experiments the mean levels of G and I during this quasi-steady state were both linearly related to G infusion rate, and thus were positively correlated with each other (r=0.81). When mean G levels were between 100 and 130, both G and I oscillated with a common period of 90 mins. The oscillations lasted as long as the infusions. Amplitudes (peak-peak) were: G=15; I=1. G oscillations led I. During oscillations the arterio-venous difference for G across the hind-quarters remained constant at about 5, in spite of the variations in I and G. At G levels > 130, both G and I showed large, slow aperiodic fluxions. We conclude that the glucose regulator has an oscillatory steady-state, possibly determined by hepatic processes.

SINGLE PREMATURE BEAT AND ATRIAL DYSRHYTHMIA IN PUPPIES. M.R. Yelich and S.N. Sinha*, Dept. of Pediatrics, Loyola University Stritch School of Medicine, Maywood, Ill. 60153

Atrial tachyrhythmia is a common clinical phenomenon. This study was undertaken to investigate the role of a premature atrial beat occurring in the vulnerable period in producing atrial tachyrhythmia using the puppy as an experimental model. In open chest anesthetized canine, aged 5-24 wks. (0.7 - 4.1 kg), a single premature stimulus (5m sec.) was delivered during the vulnerable period through an epicardial electrode to the right atrial appendage, with and without simultaneous vagal stimulation. In 10 puppies whose hearts were isolated from normal central nervous control, stimuli from 52-100 ma (82 $\pm$ 4, mean $\pm$ s.e.m.) produced in some animals short runs of tachyrhythmia with no vagal stimulation. With right vagal stimulation, atrial fibrillation could be uniformly induced with markedly reduced stimulation intensity (2.0 $\pm$ 0.5 ma). In eight of the animals, similar results were produced with left vagal stimulation (single premature stimulation intensity of 5.0 $\pm$ 2.2 ma). It is concluded that under strong vagal influence, the heart of even a small animal is susceptible to atrial tachyrhythmia if a premature beat falls in the vulnerable period.

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CORRELATION OF AMOUNT OF OXYGEN CARRIED BY FACILITATED DIFFUSION WITH CYTOCHROME P-450 CONCENTRATION. A. J. Young* and I. S. Longmuir. Dept. of Biochemistry, North Carolina State University, Raleigh, N. C. 27607

The fraction of oxygen carried by cytochrome P-450 in liver slices can be determined by measuring the rise in the ambient partial pressure of oxygen (P_{O_2}) necessary to maintain the respiration rate after exposure to P-450 inhibitors (Longmuir and Pashko, International Society for Oxygen Transport to Tissue, Mainz, 1975, Longmuir, American Physiological Society Colloquium on Oxygen and Physiological Function, Anaheim, 1976). The level of P-450 shows a normal diurnal rhythm (Pashko and Longmuir, Federation of American Societies for Experimental Biology, Abstr. 919, 1974) and can be varied by drug treatment. We have determined that the increase in P_{O_2} necessary to maintain a constant respiration rate of rat liver slices after treatment with nicotinamide shows a good correlation with the concentration of cytochrome P-450.

EFFECT OF PROSTAGLANDIN SYNTHESIS BLOCKERS AND ANTIHISTAMINE ON PROLONGED VASODILATION FOLLOWING EXERCISE. E.W. Young*, M.L. Morganroth*, and H.V. Sparks. The University of Michigan, Ann Arbor, Mi. 48109.

An extended recovery period of vascular resistance follows heavy exercise of dog hindlimb skeletal muscle. Previous work has ruled out K^+, increased osmolality, lactate, damage to vascular smooth muscle, and factors closely related to oxygen consumption (e.g. pO_2) as mediators of this prolonged vasodilation (Am.J.Physiol. 228:38, 1975). To test whether prolonged vasodilation is a graded response to injury mediated by prostaglandins or histamine, the prostaglandin synthetase inhibitors indomethacin (indo) and meclofenamate (meclo), the antihistamine tripelennamine (trip) and indo plus trip together were administered i.v. to anesthetized dogs between two 20 minute direct stimulations of the extensor digitorum longus and tibialis cranialis muscles at 4 twitches/sec. Blood flow was held constant at $\sim$20 $ml \cdot min^{-1} \cdot 100\ g^{-1}$, typically resulting in a venous O_2 content below 2.0 vol% during exercise. Recovery is expressed as the mean time $\pm$ SEM required for resistance to return 90% of the way to its final value(t_{90}).

Intervention	n	Control Run--t_{90}(min)---Drug Run		P
Time Control	7	26.6 $\pm$ 2.6	25.5 $\pm$ 2.0	.7390
Indo (5 mg/kg)	7	27.2 $\pm$ 3.6	16.9 $\pm$ 1.4	.0430
Meclo (3 mg/kg)	3	23.6 $\pm$ 1.6	14.7 $\pm$ 2.3	.0075
Trip (3-4 mg/kg)	5	28.0 $\pm$ 0.9	16.5 $\pm$ 1.3	.0021
Indo + Trip	4	33.6 $\pm$ 3.5	17.9 $\pm$ 2.0	.0183

Whereas all drugs caused a significant decline in t_{90}, indo + trip together had no greater effect than either drug alone. None of the drugs reduced the t_{90} time to that which follows less severe exercise at 2 twitches/sec where t_{90} is <1 minute. Thus prostaglandins and histamine release may be at least partially responsible for prolonged vasodilation. (Supported by USPHS grant HL-14516.)

THERMODYNAMIC ASPECT OF THE MEMBRANE BOUND ENZYME IN THE VAGAL HEART SYSTEM. Wei Young and John A. Parker, Chemical Research Projects Office, Ames Research Center, NASA, Moffett Field,CA.

Earlier we reported the effect of Ca, chlorpromazine and flaxedil on the membrane bound enzyme activity in the vagal heart system (Fed. Proc. 35:1859, 1976). This report is an inquiry of thermoproperties of this particular enzyme. Thepreparation was subject to various temperatures ranging from 12 to 30 °C. The vagus vagus nerve was stimulated with a pair of platinum electrodes through a Grass S 8B stimulator. The relative enzyme activity was determined at 12, 16, 20, 25 °C. The activation energy was found to be 23 Kcal per mole, which is equivalent to the energy of one electron volt. The reaction velocity constant at different temperature can be written as

$$K^* = kh/k_BT$$

where k is the rate constant, k_B is the Boltzman constant, h is the Planck constnat, T is the absolute temperature, and K^* is the equilibrium constant.

F was calculated to be -12,3Kcal which is approximately equal to the energy released by splitting of one mole of ATP to one mole of ADP. Since His very similar to the apparent activation energy, which was determined to be 23 Kcal at lower temperature range. The entropy change can be calculated as 34.5 E.U.

CEREBROSPINAL FLUID (CSF) AND PLASMA CORTISOL (F) LEVELS IN CONSCIOUS CATS DURING BASAL AND STRESS STATES AND FOLLOWING ACTH AND CORTISOL INFUSIONS. M. Yu*, S. F. Marotta and J. P. Marbarger. Dept. Physiology and Research Resources Center, University of Illinois at the Medical Center, Chicago, IL 60680.

To investigate the relationship of F levels in CSF and plasma in the basal state, during hypoxia (10% O_2 + 90% N_2) and hypercapnia, (10% CO_2 + 20% O_2 + 70% N_2) and following intravenous injections of F or ACTH, cats were implanted with cannulae in the external jugular vein and cisterna magna. F was analyzed by radioimmunoassay. Pairs (98) of samples obtained from 28 cats showed mean CSF and plasma F levels of 14 & 62 ng/ml, respectively, and a significant ($p<.001$) correlation ($r=.81$). Exposure to 10% O_2 caused 68 & 31% increases in plasma F levels at 30 & 60 min., respectively, while CSF levels rose 16 & 41% at these times. Exposure to 10% CO_2 elicited essentially the same patterns in CSF and plasma F levels as exposure to 10% O_2, whereas no changes were observed in cats breathing ambient air. Following rapid injection of ACTH (40 U) peak CSF and plasma F levels were reached within 15 to 20 min. Injection of F (1 mg/kg) rapidly increased plasma F to a maximum (1900 ng/ml) at 5 min. and it then declined in the next 10 min. to a relatively steady level (500 ng/ml). Peak F level (15 ng/ml) in CSF was attained at 5 min. and maintained for the next 10 min. before it gradually declined. The steady state CSF/plasma ratio was 0.15. Probenecid treatment (200 mg/kg; IP) 2 hr. prior to F injection did not affect the pattern of plasma F, but the appearance of peak CSF level was delayed and the steady state level depressed. The CSF/plasma ratio was lowered to 0.11. These data suggest that F patterns in CSF generally reflect those observed in plasma.

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INTERACTION OF ADRENERGIC STIMULI, PROSTAGLANDINS AND ANGIOTENSIN II IN DOG KIDNEY. E.J. Zambraski* and G.F. DiBona. Univ. Iowa Coll. Med. and VA Hosp., Iowa City, Iowa 52242.

Anesthetized dogs were studied using renal clearance and electromagnetic flow probe techniques. Intrarenal blockade to angiotensin II (AII) with 1-sarcosine-8-isoleucine AII (AIIA) did not alter renal vascular responses to norepinephrine (NE) or renal nerve stimulation (RNS). After indomethacin (INDO, 2 mg/kg IV), renal vascular responses to NE were significantly enhanced ($P < 0.025$) while responses to RNS were unaffected. Unilateral intrarenal blockade to AII did not alter the renal vasoconstrictor response to INDO (N=7, mean ± SE):

Time (min) after INDO		0	15	30	45	60
Arterial pressure, mmHg		139±1	160±4	154±3	151±4	147±4
Renal blood flow, % control	Left-AIIA	100	75±5	79±5	83±7	86±7
	Right-control	100	78±4	82±5	85±7	87±7

Intrarenal blockade to both AII (AIIA) and alpha-adrenergic agonists (phenoxybenzamine, POB) did not alter the renal vasoconstrictor response to INDO (N=2):

	Control	AIIA/POB	0	20	60 min
Arterial Pressure, mmHg	128	129	141	138	141
	123	122	135	130	137
Renal Blood Flow, ml/min	323	365	255	250	252
	233	235	165	167	176

As with studies in the rat and rabbit, the effect of INDO on renal NE/RNS responses is species dependent. At basal levels of circulating AII, the renal vasoconstrictor response to INDO is not due to unopposed action of AII (or adrenergic stimuli). This response is related to withdrawal of renal vasodilator activity. (NIH AM15843, VA MRIS 1836.07).

DIFFERENCES BETWEEN IRON BINDING AND RETICULOCYTE IRON DONATING PROPERTIES OF HUMAN AND RABBIT TRANSFERRINS. Edward J. Zapolski* and Joseph V. Princiotto. Georgetown University Schools of Medicine and Dentistry, Washington, D.C. 20007

At neutral pH, human or rabbit transferrins randomly bind ferric ions at each iron-binding site. However, each human transferrin iron-binding site exhibits different pH-dependent binding properties; one specific site can bind iron at a lower pH than the other site. This property was not observed for rabbit transferrin iron-binding, each site randomly bound iron at low pH. There was also a difference between iron-dissociation patterns observed for partially iron-saturated human and rabbit transferrin preparations. As the pH was lowered, partially or fully saturated rabbit transferrin solutions exhibited identical dissociation patterns but there was a difference in dissociation patterns observed with human transferrin preparations. A further difference between the two transferrins was apparent from their in vitro reticulocyte iron-donating properties. Rabbit reticulocyte iron uptake does not occur randomly from each binding site of diferric human transferrin and was also dependent upon transferrin iron-saturation levels. Human reticulocyte uptake of human transferrin iron was also saturation dependent. Rabbit reticulocyte uptake of rabbit transferrin iron was neither site or saturation dependent. Supported in part by grants from NIH, NIAMD #AM RO15553 and the Washington Heart Association.

GASTRIC SECRETORY RESPONSE FOLLOWING DIRECT CHEMICAL STIMULATION OF THE SUPRAOPTIC NUCLEUS. Eugene J. Zawoiski and Irwin Koplovitz*. Dept. of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107.

The effect of pilocarpine hydrochloride on basal gastric secretion was examined in 6 chloralose-urethane anesthetized dogs with gastric fistulas and stereotaxically positioned hypothalamic cannulas. Salivary output was followed in all 6 by natural drainage. The pilocarpine was administered via the hypothalamic cannulas at a dose of 3.2 mg/0.02 ml. Pilocarpine produced a significant increase in gastric secretory volume, total acidity, chloride and pepsin output in 5 of 6 dogs when it was instilled into the region of the supraoptic nucleus and preoptic area approximately 21 to 25 mm rostral to the inter-aural line. Concomitant increases in salivary volume were observed in 4 animals and lacrimation in 2. Pilocarpine did not produce any significant gastric secretory changes following bilateral vagotomy but continued to elicit ptyalism and lacrimation. The results suggest that cells located in the supraoptic and preoptic region send projection fibers directly or indirectly to the dorsal motor nuclei of the vagi. The relatively prompt onset of gastric secretory activity (5 to 15 minutes) suggests that the gastric responses were probably neural in nature and not mediated via a hormonal mechanism. The results also suggest that acetylcholine is involved in neurotransmission in the region of the supraoptic nucleus, and that cells located there may play a significant role in regulating gastric secretion.

EFFECTS OF FUROSEMIDE-INDUCED FLUID LOSS ON WATER AND NaCl INTAKE BY SHEEP. M.B. Zimmerman*, E.H. Blaine, and E.M. Stricker* (SPON: R.J. Schimmel). Dept. of Physiology, School of Medicine, Univ. of Pittsburgh, Pittsburgh, PA 15261

To investigate the time course of water and NaCl solution intake after volume depletion, furosemide was administered (60 mg/hr IV for 4 hr) to conscious sheep. This level of furosemide produced plasma volume deficits of betweeen 6 and 12% as estimated by changes in plasma protein concentration. Water intake was elevated above that of controls within one hr of the furosemide infusion onset, and remained elevated throughout the 24 hr test period (cumulative mean water intakes for 24 hr were 900 $\pm$ 401 ml (SEM) and 2140 $\pm$ 308 ml for controls and furosemide-treated animals, respectively). The water intake attributable to isotonic fluid loss was closely correlated with plasma volume deficits (R=0.88). Three percent NaCl solution intakes of depleted sheep did not differ from controls during the first 7 hr of the study despite large losses of NaCl in the urine. Between 7 and 24 hr, NaCl ingestion increased in these animals, resulting in restoration of the volume deficit by 24 hr. Arterial and venous blood pressure and glomerular filtration rate decreased during the initial 7 hr of the study. Plasma renin activity (PRA) increased maximally by the third hr of the furosemide infusion, but only to 3 ng AI/ml/hr above control levels. Previous observations in sheep (Abraham, et al, J Comp Physiol Psychol 88:503, 1975)indicate that the angiotensin II concentrations associated with such increases in PRA cannot account for the augmented water intakes. These data suggest that thirst is rapidly stimulated after furosemide-induced volume depletion but salt appetite is delayed by at least 7 hr despite large extracellular fluid volume deficits. (Supported by USPHS grants HL-16483 and MH-24140).

OXYGEN EFFECTS IN NORMAL AND ANOXIC VENTILATED PERFUSED LUNGS. James Zocco, M.D.*, J. Wilk, M.D. *, Stephen L. Crute * and L.J. Greenfield, M.D. Dept. of Surgery, Medical College of Virginia/Virginia Commonwealth University, Richmond, Virginia 23298

The assumption that hypoxia protects the lung from oxygen toxicity was tested in isogravimetric perfused left lower lobes of 26 dogs anesthetized with pentobarbital. A deoxygenating perfusion system was used with measurement of pulmonary capillary (PCi)pressures, blood gases and continuous weight. Controls consisted of nine lungs ventilated with room air for four hours and showed neither significant weight gain (.004 gm/hr/gm dry lung, $p = < .5$) nor change in pulmonary venous PO_2 (PVO_2) or compliance. Oxygen ventilation ($FIO_2 = 1.0$) for four hours in 13 dogs compared to controls produced a significant weight gain (.280 gm/hr/gm dry lung, $p < .025$) but no change in PVO_2, PCi, or vascular resistance (PVR). The third group of four lungs was ventilated with N_2 for one hour and then O_2 for three hours. Anoxic lungs gained weight comparable to the O_2 lungs for one hour but then more rapidly during O_2 ventilation (.608 gm/hr/gm dry lung)which was greater than the O_2 group ($p < .025$)and controls ($p < .001$). Anoxic lungs showed increased PCi after one hour O_2 ventilation (7.9 to 10.3 mmHg, $p < .05$) and then increased further to 14 mmHg after three hours O_2. No change in PVR, compliance or PVO_2 was seen. Wet/dry weight ratios increased from control of 3.7 to 5.03 in the O_2 group ($p < .001$) and 5.5 in the anoxic group ($p < .001$) which did not differ significantly from each other. The normal canine lung is vulnerable to O_2 toxicity quite early and not only does transient anoxic ventilation fail to protect against O_2 toxicity but there is increased PCi and interstitial edema.

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