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PROCEEDINGS

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BAYLOR UNIVERSITY COLLEGE OF MEDICINE
AND
THE UNIVERSITY OF TEXAS DENTAL BRANCH

ABSTRACTS OF PAPERS

An asterisk following an author's name denotes "by invitation." Abstracts are arranged in alphabetical order by first-named authors.

INFLUENCE OF POSTURE, PASSIVE TILTING, ANESTHESIA, AND ARTIFICIAL RESPIRATION ON VENOUS RETURN AND CARDIAC OUTPUT. Francis L. Abel and John A. Waldhausen,* Depts. of Physiology, Surgery, and the Heart Research Center, Indiana Univ. School of Medicine, Indianapolis, Ind.

Venal caval flow and cardiac output have been studied in 9 dogs with chronically implanted light weight electromagnetic flow probes. The changes in venal caval flow patterns and in mean flows were observed during normal postural responses, passive tilting, during and following the induction of anesthesia, and with artificial respiration. Zero flow levels were obtained by the injection of acetylcholine in the anesthetized animal or by the comparison of "magnet off" zeroes in the unanesthetized animal with a later true occlusive zero. Inferior vena caval (IVC) flow varied from 37% to 85% of cardiac output, averaging 56%; the azygous vein was ligated. IVC flow and cardiac output decreased uniformly on 20^{o} head-up tilting, but was not consistent on head-down tilting. Cardiac output uniformly increased in the standing versus prone positions, generally by means of a change in heart rate rather than stroke volume. Output decreased in about one-half of the animals in the sitting position. Sodium pentobarbital decreased cardiac output, but methohexital sodium and fentanyl-droperidol (Innovar) increased it or produced no change. Placing the animal on a respirator decreased cardiac output. Pulsatile flow patterns were generally similar in the two cavae. (Supported by USPHS grants HE-08042 and HE-6308).

NITROGEN AND ARGON TENSIONS IN URINE: POSSIBLE EVIDENCE FOR COUNTERCURRENT MULTIPLICATION. J. D. Abernethy, L. E. Farhi, and H. Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

In 6 normal male subjects breathing air urinary nitrogen tension (measured by gas chromatography) was significantly lower (1.5%) than that of blood, and also significantly lower (2%) than the nitrogen tension predicted from simultaneous urinary argon measurements. To account for these absolute and relative differences of the two gases the following hypothesis is proposed: Inert gas tension, P, in the urine equilibrates with that in the inner zone of the medulla and is determined largely by events in this zone. P is a function of two variables: concentration, C, and solubility, α, i.e., $P = C/\alpha$. In the inner zone α is reduced by the increased salt concentration, the "salting-out effect," which alters α for both argon and nitrogen by the same fraction. This would tend to increase P in the same proportion for both gases. C, in the inner zone, is reduced as a by-product of the countercurrent multiplication of sodium by Henle's loop. This would tend to lower P in this zone. The relative magnitude of this reduction in C depends on the diffusivity, d, of the gas, and since $dA/dN_2 = 0.84$, the effect on C argon would be smaller. The final partial pressure for each gas in the inner zone of the medulla will thus depend on these two changes in α and C, P_A perforce being higher than P_{N_2}. These partial pressures will be reflected by the tensions of each gas in the urine with some modifications depending on the rate of urine flow. (Supported by the U. S. Air Force.)

PATTERNS OF UNIT RESPONSE IN THE CAT SUPERIOR COLLICULI ELICITED BY NON-VISUAL STIMULI. V. C. Abrahams and S. Falchetto*. Department of Physiology, Queen's University, Kingston, Ontario, Canada.

Although the superior colliculus of the cat is usually regarded as part of the central visual pathway, 95% of the units from which recordings were made in the chloralose anaesthetized cat responded to one or more non-visual stimuli. These stimuli include electric shocks applied to the skin, clicks, and electrical stimulation of the central end of a cut muscle nerve. Units responding to skin stimulation respond when stimuli are applied over a wide area of the skin. In such experiments examination of post-stimulus histograms has shown that the pattern of cell discharge is usually related to the area being stimulated. Commonly a brisk, short latency (6 m.sec. or so) discharge may be obtained from a single unit when a restricted area of skin is stimulated, whereas the same unit may discharge weakly after a much longer latency when other skin areas are stimulated. Similarly units responding to muscle afferent stimulation may show a brisk early discharge to stimulation of a particular muscle nerve, but respond weakly and at a longer latency to stimulation of a number of other muscle nerves. (Supported by the Defence Research Board and Medical Research Council of Canada)

GLUCOSE AND IMMUNE ERYTHROCYTOPENIA AND LYSIS. V.W. Adamkiewicz and P.J. Sacra*. Physiology, School of Medicine, Montreal, Canada.

An acute (24 h.) syndrome (erythrocytopenia, hemolysis, jaundice, splenomegaly, death) was produced in mice by rabbit anti-mouse-erythrocyte serum. Increasing the blood glucose level of mice from 50 to 190 mg/100 ml, at the time of antiserum injection, resulted in a decreasing of mortality from 90 to 0%, and in an increase of LD_{50} of antiserum from 2,900 to 10,200 agglutine units/kg, i.p. Following a small dose of antiserum (1,200 agg.u./kg) erythrocytopenia changed from 4×10^6 to 8×10^6 r.b.c./ml., and recovery from the syndrome was accelerated from 15 days to 2 days. The blood sugar level at time of antiserum injection in this case was increased from 55 to 220 mg/100 ml. "In vitro" speed of hemolysis of whole blood (diluted 1:8 in saline-heparine-antiserum-complement system) was decreased from 90% to 20% as the glucose level in the blood was changed from 45 to 200 mg/100 ml. But no protection was obtained by adding glucose to washed erythrocytes. It is suggested that glucose bound in plasma protects erythrocytes against the antiserum-complement toxicity. (Grants: MT-640 - The Medical Research Council of Canada, and AM-05684 - The U.S. Department of Health, Education and Welfare).

INCREASED CORONARY SINUS BLOOD FLOW PRODUCED BY COMBINATION OF DIPYRIDAMOLE (PERSANTIN®) & ATP. S. Afonso*& G. S. O'Brien. Cardiovascular Res. Lab., Univ. of Wisc., Madison, Wisc.

Persantin® is a well known coronary vasodilator. In addition it has been reported that previously administered Persantin® I.V. augments adenosine induced increase of coronary blood flow. In the present study a combination of Persantin® and ATP at doses which alone are relatively ineffective was examined for its effect on coronary sinus blood flow. Adult dogs anesthetized with Morphine-Dial-urethane-Pentobarbital-Na were used. Heart rate, arterial blood pressure, cardiac output, left ventricular work and coronary sinus blood flow were measured before and during 20 minute constant rate infusions of 1) ATP alone 1 mg./min., 2) a combination of ATP 1 mg./min. and Persantin® .005 mg./Kg./min. and 3) a newly developed thermodilution flowmeter (Afonso, S. and Crumpton, C. W., Fed. Proc. 25: 699, 1966). Consistently during the infusions of ATP or Persantin® alone coronary sinus blood flow changed little or not at all whereas during the combined infusion a very marked and sustained elevation occurred. These results indicate a potentiating capacity of Persantin® for ATP to increase coronary blood flow.

This work was supported in part by a grant from the Wisconsin Heart Association.

ELEVATION GRADIENT OF LUNG DENSITY. J. Altobelli, R. Ackerley, S. E. Ketner, M. A. Tattersall and J. L. Patterson, Jr. (intr. by J. L. Patterson, Jr.), Depts. of Medicine and Biometry, Medical College of Virginia, Richmond, Virginia.

In an earlier study, intrapleural pressure in the anesthetized dog, held vertical, was found to increase 0.21 cm H_2O for each cm of vertical distance. Mean lung density in the end-tidal position was 0.22 gm/cc lung. The mechanism for the intrapleural pressure (Ppl) gradient is uncertain, but among the possibilities are (1), the lung behaves as a homogenous fluid, or (2), a vertical gradient of lung density exists which affects the Ppl. The present investigation explored this second possibility. Ten anesthetized (pentobarbital) mongrel dogs were studied after 45 minutes in the vertical head-up position, 1 in the horizontal and 1 in the vertical head-down position. Circulation was stopped by electrical fibrillation and the trachea clamped, the thorax entered, pulmonary vessels clamped, lungs removed en bloc, wrapped in polyethylene sheet, and immersed in liquid nitrogen (T -197°C). The trachea was was unclamped to admit air as lung gas shrank. Later, the completely frozen lung was cut from apex to base into cubes 1-2 cm on each edge and the position of each cube measured. The density (wt/vol) of each cube was determined. A composite curve, fitted by least squares to the density vs. vertical distance data, had the formula: Density = $0.094\ c^{0.078H}$, where H = vertical distance from the apex in cm. This indicates a density at the apex of 0.094 Gm/cc and at the base 0.41 Gm/cc, for an apex-to-base distance of 20 cm. The apex-to-base density gradient was absent in the horizontal position, and was anatomically reversed in the head-down position. This density gradient indicates major differences in ratios of lung gas to tissue plus blood at different elevations. It cannot be solely responsible for the linear gradient of Ppl vs. elevation.

CONDITIONS FOR SPONTANEOUS ACTIVITY BELOW 5° C FOR AN ISOLATED ATRIUM OF A NON-HIBERNATOR. E. T. Angelakos and J. T. Maher*. U. S. Army Research Institute of Environmental Medicine and Boston University School of Medicine, Boston, Massachusetts.

Cardiac pacemaker activity in isolated preparations from non-hibernating species is known to cease at temperatures from 20-15°C. By contrast similar preparations from hibernators (even when not in hibernation) continue to beat at temperatures below 5°C. Ionic and neurohumoral conditions were investigated that would maintain spontaneous cardiac activity of a non-hibernator at low temperatures. Isolated right atria of the rabbit were perfused as described previously (Arch. Int. Physiol. Biochim. 71:155, 1963). In the controls spontaneous propagated activity ceased at a mean ($\pm$SD) temperature of 18.9 $\pm$ 1.4 C. When the K of the perfusion fluid was reduced to one-half (replaced with Na), spontaneous atrial activity was maintained to a mean of 14.5 $\pm$ 1.1°C. At this point perfusion with acetylcholine (1 μg/ml) re-initiated activity which was maintained for an additional decrease of 3-4°C in bath temperature. However, after arrest at low K, perfusion with catecholamines (epinephrine or norepinephrine, 1 μg/ml) re-initiated and maintained spontaneous activity to temperatures below 5°C (mean 4.2°C). Thus it appears that spontaneous cardiac activity can be maintained at low temperatures in non-hibernators in certain ionic and neurohumoral environments.

EFFECTS OF VARIOUS DRUGS ON THE TRANSMISSION OF WAVES IN THE VENA CAVA. Max Anliker* and Eric Ogden, NASA, Ames Research Center, Moffett Field, California

The wave transmission properties of the vena cava, inferior and superior, of anesthetized dogs are described by measurements of the diameter and wall thickness of the vessel at autopsy and the speed of artificial pulse waves. The waves were generated by injecting 0.5 or 1.0 cm^3 saline into the femoral or external jugular vein with a spring-loaded syringe. The speed of the waves was determined with the aid of two catheter tip manometers. Their placement was verified by X-rays. The manometers and recording system allowed a resolution of 0.5 mm H_2O and 0.5 millisecond, respectively. The speed of transmission varies greatly with location. It is smaller in segments closer to the heart and appears to be increased in the proximity of major branches. The intravenous administration of various doses of drugs including epinephrine, KCN, $MgCl_2$, KCl, $CaCl_2$ and pentobarbital is followed by a marked increased in wave speed. In some cases this phenomenon is temporary. Lethal doses of pentobarbital and the minerals produce a two to five-fold increase in speed that persists for hours after death. In such cases the rise of venous pressure has been demonstrated as insufficient to account for the increased speed and no change in caval diameter could be seen. A theoretical consideration of the factors likely to influence the transmission speed indicates that these marked speed changes must primarily be due to an increase in the effective Young's modulus of the vascular wall.

EFFECT OF HYPOXIA UPON LEARNED PERFORMANCE. Zoltan Annau, Stephen Weinstein, (intr. by Richard Riley). Johns Hopkins University, Baltimore, Maryland.

In this study we have investigated the effect of hypoxia upon electrical self-stimulation of the hypothalamus. Four rats with chronically implanted bipolar electrodes in the hypothalamus were trained to press a lever in order to stimulate this area. The performance in 21% oxygen was observed and the animal was then exposed to four other oxygen concentrations (14%, 12%, 10%, and 8% O_2). Each of these hypoxic levels produced a suppression of lever pressing, with the greatest suppression being produced by the lowest oxygen level. The experiment was then repeated, with the strength of the electrical stimulus decreased to a level that produced response rates approximately one half of those during the first experiment. The animals were then once again exposed to the four low oxygen levels. In this instance there was a more marked depression of response rate in mild hypoxia than had previously been observed. There is a marked interaction between the level of motivation (as estimated by self-stimulation rates) and the degree of impairment in performance in hypoxic environments. A weakly motivated animal, with a low rate of lever pressing, is severely depressed by a level of hypoxia (14% O_2) which produces only mild impairment when the motivational level is high. Severe hypoxia (below 8% O_2) will produce near complete suppression of self-stimulation even in highly motivated animals. (Supported by: U.S.A. Medical Research and Development Command Contract Number DA-49-193-MD-2726 and by Public Health Service Grants HE 01929, TG-HTS 5453, and HE 06945 and by ONR contract NR 102-101 and Wallace Laboratories).

GONADOTROPIN ACTION ON OLFACTORY RECEPTOR. Hugo Aréchiga and Carlos Alcocer-Cuarón. (Intr. by J. J. Izquierdo) Nat. Univ. of México, Sch. of Med.

Although the influence of sex hormones on olfactory sensitivity is a matter of common observation (i.e. hyperosmia during pregnancy, heat periods, etc.) satisfactory explanation of the underlying physiological mechanisms is still lacking. In a preliminary series of experiments in male autum frogs (Rana moctezuma) anesthetized with 10 per cent urethane, capillary glass microelectrodes were placed on eminentia olfactoria, to lead off electro-olfactogram (EOG) induced by short puffs of air odorized with amyl acetate. Injection of chorionic gonadotropin (500-1000 I. U.) into the dorsal lymphatic sac, after a latency period of 15-30 minutes, resulted in a rise in EOG amplitude which became 50-100 per cent greater than in previous responses and reached its maximum in 10-15 minutes, lasted for more than one hour and not infrequently up to 3-5 hours. In controls, spontaneous fluctuations of EOG amplitude were lesser than 10 per cent. Injections of Ringer solution did not modify EOG amplitude. From the long latency of the effect observed, an indirect action, mediated by gonads is suggested, rather than a direct gonadotropic influence on olfactory receptor, and considering the nature of EOG, it seems clear that peripheral receptor modulation is at least one level of sex hormones influence on olfactory sensitivity.

EFFECTS OF WATER STRUCTURE ON OSMOTIC FLUX IN APLYSIA NEURONS. G. Austin, M. Sato‡ H. Yai‡ Univ. of Oregon Med. Sch., Portland, Oregon.

In this presentation we present a model which further considers the structure of H_2O as determined experimentally by Buijs and Choppin, (1963) and modified theoretically by Vand and Senior (1965) to include an energy band form. Water molecules exist in three species: monomeric singly or doubly H-bonded each with a mean energy $\bar{E}_0$, $\bar{E}_1$, and $\bar{E}_2$.

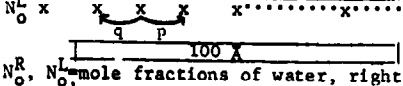
$J = J_{LR} - J_{RL}$ = net flux

$$J_{LR} = (N_o^L \cdot O_f \cdot P_M \cdot \frac{kT}{h} \cdot \delta)\ (V_f + O_f' \cdot P_e)\ P_{LR}$$

$$J_{RL} = (N_o^R \cdot O_f \cdot P_M \cdot \frac{kT}{h} \cdot \delta)\ (V_f + O_f' \cdot P_e)\ P_{RL}$$

$$P_{LR} = \frac{(q/p) - 1}{(q/p)^n - 1} \qquad p = \tfrac{1}{2}\left(\tfrac{1}{2} + \frac{N_o^L}{N_o^L + N_o^R}\right) \qquad q = \tfrac{1}{2}\left(\tfrac{1}{2} + \frac{N_o^R}{N_o^L + N_o^R}\right)$$

Model 'Pore'-single file



8.9 Å effective diameter

N_o^R, N_o^L=mole fractions of water, right and left

O_f, O_f'=fraction of sites occupied by H_2O molecule in solution & in pore

P_M=probability of monomeric form outside 'pore'; f=steric factor;

V_f=fraction of vacancies in 'pore'; P_e=probability of energy of activation.

P_{LR}, P_{RL}=probability of molecule that enters from left and occupies first site, will exit from right and vice versa

p=probability of moving one site to right; q=probability of moving one site to the left

We calculate $J = 10^7$ molecules/second/'pore'/osmol/liter. The order producing effect of Ca^{++} on water (Buijs and Choppin) may decrease the flux rate and provide some explanation for our experimental findings of Ca^{++} producing hyperpolarization.

DYNAMICS OF MAMMALIAN MUSCLE CONTRACTILE COMPONENT. Alan S. Bahler* and John T. Fales, Department of Environmental Medicine, Johns Hopkins University, Baltimore, Md.

The dynamic characteristics of the contractile component of rat gracilis anticus muscle at 17.5 C have been determined by isotonic loading. For a fixed starting length these characteristics are represented either as a family of length-velocity phase trajectories at various isotonic afterloads or a series of force-velocity curves taken at isopleths of length. These 2 families of curves are combined to generate a 3-dimensional function of length, external load, and velocity. When the muscle is allowed to shorten from different starting lengths, the functions are different for each starting length, with the greatest discrepancies appearing at heavy external loads. Separation of the function is not caused by simple fatigue or by changes in internal elastic elements. Therefore, the contractile component is said to have been influenced by its past history. When the behavior at different stimulating frequencies is investigated, the affecting factor is the number of stimulating pulses received by the muscle for a given amount of shortening.

(Supported by USPHS grants 5-Fe-GM-23, 697-02, AM-05524 and Am. Heart Asso. Established Investigatorship.)

CHANGES IN VASCULAR VOLUME, RESISTANCE AND $Rb^{86}Cl$ RECOVERY WITH CONTROLLED PERFUSION PRESSURE OF THE DOG FORELIMB. Carleton H. Baker, Medical College of Georgia, Augusta, Ga.

In isolated dog forelimb preparations perfusion pressure was increased over the range from 75 to 200 mm Hg in steps of 25 mm Hg. Changes in blood flow, peripheral resistance, limb weight, $Rb^{86}Cl$ recovery and vascular volume estimated by albumin-I^{131} injections were determined. With each elevation of perfusion pressure the peripheral resistance declined until the perfusion pressure reached 150 mm Hg. The resistance then stabilized for the remaining pressure increments to 175 and 200 mm Hg. Limb weight (fast change) and vascular volume as determined by albumin-I^{131} increased by approximately equal amounts with each pressure increment and both weight and volume increased with every pressure increment on a parabolic type curve. $Rb^{86}Cl$ recovery increased with each pressure increment to the 150 mm Hg level and then remained at this level for the remaining perfusion pressure increases. The venous time-concentration curves after intra-arterial slug injections of albumin-I^{131} had uniform downslopes up to the 125 mm Hg level but then a second concentration peak appeared on the downslope of the succeeding curves. These data seem to indicate the opening of a second circulation, not capillary in nature, when the perfusion pressure passes a certain level (ca. 125 mm Hg).

(Supported by USPHS grant HE-4573)

EFFECTS OF NEUROHYPOPHYSEAL POLYPEPTIDE HORMONES AND OF AMINO ACIDS ON THE MICROCIRCULATION. Theodore A. Baloundas,(Intr. by E. M. K. Geiling) Dept. of Pharmacology, Medical School, Howard Univ., Washington, D.C.

Vasoactive amino acids and polypeptides as catabolic hydrolytic protein products in malnutritional states and subnutritional edema, and directly administered by intravenous injection or topical application were found inducing changes in microvessels of rat mesentery (Baloundas, T.A., Fed. Proc. 12:9, 1953, Proceedings of 5th Intern. Congress on Nutrition, Washington, 1960). In the present in vivo studies on rats the same bioassay technique was used for direct observation of the meseappendiceal vasculature under the microscope. The neurohypophyseal hormones ocytocin and vasopressin were intravenously injected or locally applied. Results: Ocytocin in desage 8-10 µg produced vasodilatation, slowing blood flow, many stases in dilated microvessels, venoconstriction, some petechial hemorrhages, increased permeability and increased vascular reactivity to vaseconstricter epinephrine threshold test. Vasopressin caused vasoconstriction, increased capillary permeability, microvascular hyperreactivity, considerable slowing bleed flow, many stases and hemorrhages. Vasodepresser activity of ocytocin and vasopresser effect of vasopressin have also been shown in determining the bleed pressure (BP) in rats and dogs. The phenomenon of tachyphylaxis was observed with ocytocin in regard to BP response. Similar functional and structural effects on the microvessels were observed with amino acids especially with aliphatic ones containing sulfur. The findings support the concept that the vasoactive effects of octapeptide amides of posterior pituitary hormones might be considered similar to those produced by other polypeptides. Possible mechanisms of action and physiological role of these hormones will be discussed.(Supported by a grant from National Institutes of Health).

UPTAKE OF NON ESTERIFIED FATTY ACID (NEFA) BY DOG KIDNEY IN VIVO: RELATIONSHIP TO THE PAH TRANSPORT SYSTEM. M. Barac-Nieto*[7] and Julius J. Cohen. Univ. of Roch., Rochester,N.Y.

Uptake of NEFA by dog kidney has been shown to be markedly specific for palmitate and may be a major source of energy for the organ. NEFA inhibits p-aminohippurate (PAH) accumulation in renal cortical slices; α-Ketoglutarate, also an inhibitor of renal PAH uptake, suppresses the net renal uptake of NEFA ($\dot{Q}$-Nefa) in vivo. We have studied the possible relationship between the PAH transport system and $\dot{Q}$-Nefa in the intact dog. In 5 experiments $\dot{Q}$-Nefa was measured in fasted anaesthetized (Na pentobarbital) female dogs during continuous mannitol infusion, first under control conditions and then during constant infusion of probenecid. Under control circumstances it was observed that $\dot{Q}$-Nefa was proportional to NEFA arterial concentration ($[NEFA]_A$). Mean control $\dot{Q}$-Nefa was -.79 mEq/hr/100 g kidney (negative values indicate uptake) at a mean $[NEFA]_A$ of .570 mEq/l (n=24). During infusion of probenecid, $\dot{Q}$-Nefa decreased to -.21 mEq/hr/100 g in spite of a rise in $[NEFA]_A$ to .901 mEq/l ($n=19, p<0.01$). In 4 additional experiments, chlorpromazine and heparin were given throughout each experiment in an attempt to achieve maximal and steady $[NEFA]_A$. Associated with the infusion of probenecid a greater rise in $[NEFA]_A$ occurred than was observed when chlorpromazine and heparin were not given. In spite of this rise in $[NEFA]_A$ no changes in $\dot{Q}$-Nefa occurred. These findings are interpreted to indicate that NEFA may enter renal tubular cells through the PAH transport system. [7]Rockefeller Fellow. Supported by USPHS Grant AM-03602.

RENAL FUNCTION FOLLOWING MERCURIC CHLORIDE POISONING OF THE RAT.
R.L. Barenberg*, S. Solomon, S. Papper* and Helen Alpert*. Dept. of Physiol. & Med., Univ. of New Mex. Sch. of Med., Albuquerque, N.M.

Using mercuric chloride treated rats as an experimental model, the sequence of changes in renal function resulting from acute renal failure was studied. Hydrated adult rats (250-350 gms) were prepared with tracheal cannula, rectal thermometer, jugular vein infusion (1.6-1.8 cc/hr of Ringer's solution containing H^3-methoxy-inulin), bilateral ureteral catheters and femoral arterial catheterization for blood pressure monitoring. Experiments were rejected or ended if intraarterial pressure fell below 80 mm Hg. Renal function was studied during 30 minute intervals up to 5 hours following i.m. injection of 15 mgm/kg of $HgCl_2$. Because of functional variation between kidneys during control and experimental periods, results were analyzed for changes in individual kidneys. Pigmenturia developed within 15-35 minutes of mercury injection and gradually diminished after about 3 hours. GFR regularly decreased. Changes in urine flow rates varied. Fraction of the filtered water which was excreted tended to increase. In the urine from 13 kidneys studied, U_{Na} increased in 11, decreased in 1 and did not change in 1. UV_{Na} increased in 9, decreased in 2 and did not change in urines from 2 kidneys. Fraction of filtered sodium which was excreted increased in 12 and did not change in 1 study. Preliminary histologic examination revealed minimal tubular changes. These experiments are interpreted as indicating a change in renal function prior to morphological damage. The changes in sodium and water excretion are not related to changes in GFR. The increasing fractional sodium excretion in the presence of increasing water excretion and decreasing GFR suggest a decrease in transport of sodium.
(Supported by grants from NIH, HE 08477 and T1 HE 5633.)

Functional Reinnervation of the Spinal Cord by ACh Synapses
Charles D. Barnes. Dept. of Anatomy and Physiology, Indiana University, Bloomington, Indiana.

The mammalian neuromuscular junction is probably the best understood site of synaptic transmitter action, and it is generally agreed that acetylcholine is the transmitter. By directing motoneurones back into the cord any synaptic contacts established would be cholinergic. The present study investigates the existence of cholinoseptive neurones in the spinal cord by establishing ACh synapses by regenerating ventral root fibers into cut dorsal roots. The left L_7 ventral root was grafted to the right L_7 dorsal root and the remaining right L_7 dorsal root ganglion removed. The cats were then allowed six to eight weeks for regeneration. On the final exposure recordings were taken from right L_6 and L_7 ventral roots and right L_6 and L_7 (grafted) dorsal roots were used for stimulating. The grafted fibers were not found to make any monosynaptic connections with motoneurones but did produce polysynaptic discharge when recorded from the L_7 ventral root and facilitate or inhibit L_6 monosynaptic reflexes. When recording from L_6 dorsal root and stimulating the graft a dorsal root reflex could be produced.

ETHANOL-INDUCED ANEMIA IN THE DOG. James D. Beard and David H. Knott (intr. by R. R. Overman). University of Tennessee Medical Units, Memphis, Tennessee.

Anemia has been frequently observed in association with chronic alcoholism. Many investigators attribute the anemia in alcoholics to vitamin deficiency states, particularly with respect to folic acid and vitamin B_{12}. In the present study the hematocrit, hemoglobin concentration, erythrocyte count, reticulocyte count, red cell mass, plasma volume and body weight were measured on a weekly basis. Twenty-six dogs received via gastric tube a daily dose of 4 g ethanol/kg body weight as a 33% solution (v/v) for two weeks alone (11 dogs), or in combination with daily intramuscular injections of vitamin B_{12} (100 μg) and folic acid (15 mg - 8 dogs) or with folic acid alone (7 dogs). During the experiment the body weights remained relatively constant. After two weeks of either daily ethanol alone, or with vitamin B_{12} and/or folic acid, all three groups of animals were found to have comparable and significant reductions in erythrocytes below control values, e.g., range of per cent decrease for all groups, hematocrit (17-22%), hemoglobin concentration (16-21%), erythrocyte count (16-21%), reticulocyte count (75-83%) and absolute number of reticulocytes (85-90%). The mean corpuscular values were not altered; these data in combination with the characterization of the peripheral blood smear indicate that the type of anemia found in this study was of the normochromic normocytic variety. There was no evidence of a functional deficiency of vitamin B_{12} or folic acid. These data suggest that in the dog the ethanol-induced anemia is not prevented by the doses of intramuscular vitamin B_{12} and folic acid used in the study.

EFFECTS OF ACCLIMATION ON THRESHOLD SKIN TEMPERATURE FOR SWEATING IN RESTING MAN. E. Behling, V. Corroll, L. Oscai (intr. by F. Sargent II) Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

Belding and Hatch (Fed. Proc. 22:881, 1963) have emphasized the importance of the downward shift in threshold skin temperature for sweating to explain the improved tolerance to heat by acclimation. To investigate directly the magnitude of this shift, we have determined the threshold for sweating in three resting male subjects immersed to the neck in warm water before and after ten daily bouts (100 min.) on a level treadmill walking (5.6 km/hr) in the heat, (49°C D.B., 27°C W.B.). Well stirred water fixes skin temperature precisely (Burton and Bazett, Am. J. Physiol. 117:36, 1936). Thus it was possible to determine within 0.1-0.2°C the skin temperature associated with barely detectable sweating. Weight change per 15 min. (by load cell, sensitive to one gram; Transducers, Inc.) and moisture on the forehead were used as criteria for sweating. Thresholds in all subjects were lowered: L.O., 1°C; V.C., 0.1-0.2°C; and E. B. only slightly less than 0.1°C. A fourth subject who was not exposed to heat showed no change in threshold.

EFFECTS OF DEHYDRATION AND SODIUM LOADING ON THE RENAL LYMPH CONCENTRATION OF Na^+, K^+ AND UREA. Richard D. Bell* and M. Jack Keyl, Dept. of Physiol. Univ. of Okla. Med. Ctr., Oklahoma City, Oklahoma.

Published data concerning concentrations of Na^+, K^+ and urea in renal lymph from different laboratories appears inconsistent. Data obtained in our laboratory indicate that the lymph/plasma ratios (L/P) of Na^+, K^+ and urea are changed by altering the experimental conditions. Some laboratories utilized hydrated animals while others did not; some utilized NaCl infusions while others did not. The experiments reported in this paper were designed in an effort to determine if these factors affect the L/P ratio of these substances. The effects of 24 hour H_2O deprivation alone and together with intravenous injections of 0.9% NaCl, 2.7% NaCl or 5.5% NaCl were studied in the dog. Dehydration alone appears to elevate L/P ratio of Na^+, K^+ and urea. Pretreating the dehydrated animals with 0.9%, 2.7% and 5.5% NaCl solution did not further increase L/P ratio for Na^+ and urea. In contrast, pretreatment with 2.5% and 5.5% NaCl increased L/P ratio for K^+ above that due to dehydration alone, whereas 0.9% NaCl had minimal effect. (Supported by a grant from NIH)

PURINE SECRETION BY INTESTINAL EPITHELIUM. Richard D. Berlin and Richard A. Hawkins*. Dept. of Physiology, Harvard Medical School, Boston, Mass.

Purine transport has been investigated using sacs of hamster small intestine. The analogue allopurinol was used to inhibit xanthine oxidase. In contrast to other metabolites thus far reported, the purines hypoxanthine, xanthine, and uric acid can be shown to accumulate on the mucosal side of the epithelium. Unidirectional fluxes, serosa to mucosa, are 10 times those in the reverse direction. Accumulation is abolished by DNP and anaerobiasis. The process cannot be saturated due presumably to a high K_m for transport. The site of the secretory pump was also investigated. Xanthine oxidase was shown to be an intracellular enzyme and used as a marker for penetration of its substrates from either mucosal or serosal solutions. Xanthine presented to either side of the epithelium is oxidized rapidly, despite the relatively slow transepithelial flux in the serosal direction. Further, the efflux of uric acid formed intracellularly from exogenous xanthine is more rapid in the mucosal as compared with the serosal direction. Thus, the passage of purines across the basal membrane is probably rate-limiting to their absorption. From changes in the fluxes through both sides of the epithelial cell which occur after poisoning with DNP, it is suggested that at least some of the transport sites are at the basal membrane.

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AN ELECTRON MICROSCOPE STUDY OF THE FORMATION OF PROTEINS ASSOCIATED WITH MINERALIZATION IN MACROCALLISTA MACULATA. G. Bevelander and H. Nakahara (intr. by E. L. Smith). University of Texas Dental Branch, Houston, Texas.

The periostracum, a horny covering, and conchiolin the organic supporting structure of the crystalline shell are scleroproteins derived from the outer mantle fold. A submicroscopic examination of the cells involved in the elaboration of these structures has shown that there are three distinct cell types which make up the investing surface of the fold and further each cell type elaborates a specific protein secretion. At the base of the fold one observes a 'basal' cell which elaborates an electron dense pellicle at the cell junction. The pellicle serves as a boundary for the subsequent secretions elaborated by the distal two-thirds of the mantle epithelium. These latter cells are tall columnar, with prominent microvilli and contain numerous stout tegmental fibers. They elaborate a viscid secretion which undergoes tanning during the formation of the periostracum. The upper one-third of the fold is beset with epithelia differing from those described in several aspects. They are concerned with the formation of conchiolin which serves as a support for the mineral component of the shell. The organic structures associated with protection and support of the mollusc shell are highly specialized both in structure and in the manner in which they are formed - in the example we have cited, three kinds of proteins each elaborated by a specific cell type.

EFFECT OF PROLONGED CONTINUOUS RECUMBENT BED REST ON CIRCULATORY RESPONSE TO TRAINING. N. C. Birkhead, G. J. Haupt,* R. M. Patton.* Div. of Research, Lankenau Hosp. Philadelphia, Pa.

Prolonged continuous recumbent bed rest (RBR) results in decreased physical work capacity. Bicycle exercise at 600 kpm/min for 1 hour daily post-RBR results in return to pre-RBR values for maximum O_2 uptake when determined after 3 weeks. To study the rate of return of physical work capacity, 4 healthy males 18-22 years were hospitalized in a metabolic ward on a weighed diet of 2500 Calories (74 gm protein, 99 gm fat, 341 gm CHO) and subjected to 18 days RBR. For 18 days before and after RBR they trained on a bicycle ergometer for 1 hour daily at 600 kpm/min and performed near maximum exercise on the 18th day of training before and 10th day of retraining after RBR. The post-RBR O_2 uptake to near maximum work was similar to pre-RBR O_2 uptake but heart rates were 8-20 beats/min greater in 3 of 4 subjects. The rate of retraining following RBR was slower as judged by daily heart rate response to similar training loads.

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THE STRETCH REFLEX OF THE ABDOMINAL WALL. Beverly Bishop. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

The abdominal muscles resemble limb muscles in their postural role but resemble the internal intercostal muscle in their respiratory role. This study has examined the stretch reflex of the abdominal muscle to determine whether the stretch reflex exerts strong segmental control comparable to limb muscle or whether it is subsidiary to the respiratory center as is the case for the intercostal muscle. The electrical activity (EMG) of the external oblique abdominal muscle of the Dial-anesthetized cat provides the index of alpha-mononeurone activity. A mechanically evoked tendon jerk, elicited by a hammer tap to the linea alba, has a 10 to 15 msec latency and a "dead-beat" ending. Similarly, an electrical shock to the exposed muscle branch of the peripheral nerve evokes a short latency (7 msec), synchronous reflex response. The reflex response to stimulation of the skin or electric shock to the cutaneous branch of the nerve has a long latency (20 to 30 msec) and is polyphasic. In the intact animal over-inflation of the lung excites activity in the abdominal muscle only during expiration. This expiratory activity is a vagal reflex mediated from thoracic receptors via medullary respiratory neurones. Stretching the abdomen by over-inflating the lungs will cause the abdominal muscles to contract during inspiration only after (a) bilateral cervical vagotomy or (b) hyperventilation. This has been interpreted to mean that the respiratory center normally inhibits the abdominal stretch reflex. When the abdominal motoneurone pool is functionally released from respiratory control, a strong segmental reflex is unveiled. Thus it appears that the abdominal muscle like limb muscle is endowed with segmental monosynaptic circuitry, but like the chest wall, respiratory control may predominate. (Supported in part by U.S. Air Force.)

SOME COMPLICATIONS OF STUDYING ENZYME CHANGES IN AGING RED CELLS. Charles Bishop (intr. by Beverly Bishop). State Univ. of New York at Buffalo, N.Y.

The objective of this study was to discover if glucose-6-phosphate dehydrogenase (G-6-PD), 6-phosphogluconate dehydrogenase (6-PGD), and isocitric dehydrogenase (ICD) activities changed as the rabbit or human red cell aged. Red cells were separated by density on bovine albumin gradients, since it is known that red cells become more dense as they age. G-6-PD activity was highest in the least dense rabbit red cells and lowest in the most dense red cells. After bleeding, rabbit red cells had slightly more G-6-PD activity. In humans who had a very low percentage of reticulocytes, only the lightest layers had more G-6-PD activity; the rest of the layers had equal activities. The 6-PGD activity in rabbit red cells was essentially equal in all density layers while in humans the lightest layer had somewhat more activity. The ICD activity in rabbit red cells was highest in the light layers but the activities were about equal in all layers of human red cells. The results indicated a general decrease in enzyme activity with increasing density. The percentage of reticulocytes also decreased with increasing red cell density. When the data were replotted, the enzyme activities were shown to be related to reticulocyte percentage. This suggested that the decline in enzyme activities reported to occur with aging may be primarily those associated with reticulocyte maturation. In any event, reports of enzyme activities of a red cell population should be accompanied by the reticulocyte percentage since the presence of an increased percentage of reticulocytes may be responsible for the high enzyme activities reported in various dyscrasias. (N.I.H. Grants AM-06367 and AM-05581)

A MATHEMATICAL DESCRIPTION OF VENTRICULAR OUTPUT CURVES. Vernon S. Bishop and H.L. Stone. USAF School of Aerospace Medicine, Brooks AFB, Texas.

The mathematical relationship between the changes in cardiac output and mean right atrial pressure (RAP) or mean left atrial pressure (LAP) which occurs during the determination of ventricular output curves can be described by the equation $dc/dp = k\ (C_m - C)$; where dc/dp is the change in cardiac output with respect to the change in atrial pressure, k is a constant of proportionality, C_m is the maximum cardiac output obtained during a ventricular output curve and C is the cardiac output at a given pressure. The solution of the above differential equation (d.e.) is $C = C_m - (C_m - C_o)\ e^{-kp}$. C_o is the initial cardiac output and p is the change in RAP or LAP from control. A plot of C versus p for either RAP or LAP yields a curve which agrees within the S.E.M. of the average ventricular output curves obtained in this laboratory. This equation also describes the ventricular output curves obtained in single animals if the rate of change in atrial pressure with respect to time (dp/dt) is constant, then the above d.e. can be transformed to $dc/dt = k(dp/dt)(C_m - C)$ since $dc/dt = (dc/dp)(dp/dt)$. Using this d.e. the ventricular output curve can be described as a function of time. By knowing the slope dc/dt and the cardiac output C at two different times C_m can be estimated without completion of the curve. We have estimated C_m from the initial portions of ventricular output curves obtained in conscious dogs and have found it to agree within 10% of the experimental value in each animal.

Metabolism of Progesterone and 20α- and 20β-dihydroprogesterone by Human Placentas Perfused in situ at Midpregnancy. A. J. Blair, R. Palmer* and E. Diczfalusy. Hormone Laboratory, Karolinska Sjukhuset, Stockholm, Sweden.

Midterm placentas were perfused with labelled progesterone combined with differently labelled 20α- or 20β-dihydroprogesterone and the metabolites recovered from the placental tissue and perfusate were isolated in a radiochemically homogeneous form. There was an extensive placental conversion of 20α-dihydroprogesterone into progesterone, but hardly any transformation of progesterone into 20α-dihydroprogesterone. No metabolism of 20β-dihydroprogesterone was found. Except for a limited conversion into 6β-hydroxyprogesterone, no significant placental metabolism of progesterone was observed. There was no evidence of 16α- and 17α-hydroxylation, side-chain cleavage, or reduction of ring A. These results are in contrast to those reported by others on the basis of in vitro studies with preparations of term placental tissue and indicate that progesterone formed by the human placenta at midterm is not utilized by this organ for the synthesis of C-19 and C-18 steroids. The data also indicate that a considerable amount of the 20α-dihydroprogesterone, which is known to be formed by the foetus from progesterone, is reconverted to progesterone when it returns to the placenta.

INCREASED VOLUNTARY INTAKE OF NaCl SOLUTION IN POTASSIUM DEPRIVED RATS. William D. Blake and Amin N. Jurf.* Univ. Maryland, Sch. of Med., Baltimore.

Richter showed many years ago that sodium-depleted rats voluntarily increased NaCl solution intake. Asked here is whether increased Na intake is specific to Na depletion or are there other equally effective stimuli. Rats were allowed to self-select NaCl and/or KCl solution from separate bottles (no water available). Under control diet conditions some rats were biased to favor KCl over NaCl by adding quinine to the NaCl or sucrose to the KCl. Rats were then given only water to drink and separated into three groups: (1) those remaining on the control diet, (2) those placed on a low K diet, and (3) those placed on a low Na diet. After two weeks on these diets rats were again offered the same NaCl-KCl solution-pair previously given. Rats which had been on low K diet, when offered quinine-NaCl and/or KCl, showed a significant increase in NaCl intake and decrease in KCl intake compared to rats remaining on control diet. Rats on low Na diet increased NaCl intake but less than rats on low K diet and the difference was not significant. A unitary hypothesis would implicate either intracellular cation concentration or some function of body fluid volume as the stimulus to NaCl drinking. Otherwise, Na and K deprivations stimulate Na intake by different mechanisms. (Supported by NIH Grant AM 06159).

THE WATER PERMEABILITY OF ERYTHROCYTES. Ronald M. Blum* and Robert E. Forster. Graduate Group on Molecular Biology and Department of Physiology, Division of Graduate Medicine, University of Pennsylvania.

The water exchanges of human erythrocytes were reinvestigated using a stopped flow rapid reaction apparatus. After a cell suspension was suddenly mixed with a solution of differing osmolarity, changes in its light transmission, either polychromatic or monochromatic (lambda=640 mμ), were used as a measure of average changes in cellular volume. Certain transmission artifacts were experienced during the first two hundred milliseconds, which probably result from the transition of the cells from the flowing to the stationary state. This problem was minimized by altering the flow pattern in the observation tube, increasing the concentration of cells in the suspension, and when necessary comparing with a control experiment. The water permeability of the red cells of three normal subjects at 26 C was calculated from the initial slope of the curve of volume as a function of time. During endosmosis the permeability averaged 0.24 cm^4/osmols x seconds which agrees well with the reports in the literature. However, during exosmosis the permeability averaged 0.41 cm^4/osmols x seconds. These results appeared unrelated to the absolute value of the initial osmotic gradient from 0.06 to 0.30 osmols. The implications of these results in terms of the different chemical properties of water in contact with the red cell membrane at the intracellular and extracellular interfaces will be discussed.

Regional Resistance Changes to Bilateral Carotid Artery Occlusion. Robert F. Bond* and Harold D. Green, Bowman Gray School of Medicine, Winston-Salem, North Carolina.

Four simultaneous blood flows were recorded in dogs by use of two model 322 dual channel electromagnetic flowmeters manufactured by Carolina Medical Electronics, Inc. Flows were recorded from the ascending aorta, cranial mesenteric artery, left renal artery and an artery feeding skeletal muscle. The ascending aorta was approached surgically through the third intercostal space. This wound was sutured and the pneumothorax reduced following the placement of the electromagnetic probe. The cranial mesenteric and left renal arteries were exposed through a retroperitoneal approach. In some experiments the skeletal muscle artery used was the caudal femoral artery while in others the omocervical artery was chosen. Arterial blood pressure was recorded through a cannula introduced into the brachial artery and directed into the arch of the aorta. Both pulsatile and mean flows were studied before, during and after bilateral carotid occlusion. Preliminary studies indicated that, although arterial blood pressure increased and cardiac output remained unchanged, pulsatile flow patterns in the mesenteric and renal arteries suggested a low resistance system and mirrored the aortic blood pressure. Pulsatile flow through the skeletal muscle was similar to but more oscillatory than in the ascending aorta indicating a higher resistance to flow. These oscillations were reduced, mean flow increased and systolic flow sharply increased in all beds and all responses to carotid occlusion were abolished by pretreatment with dibenzyline. Pulsus alternans was frequently observed during bilateral carotid occlusion. (Supported by USPH Grants 487, 5392, North Carolina and Forsyth County Heart Association).

HIGH SPEED CINEMATOGRAPHIC STUDIES OF THE MICROCIRCULATION IN THE HUMAN SUBJECT. Ted P. Bond*, M. Mason Guest, Thomas D. Kirksey* and John R. Derrick*. Departments of Physiology and Surgery, University of Texas Medical Branch, Galveston, Texas.

Cinematographic studies of the microcirculation in the omentum of human patients have been made during abdominal surgery. The omentum, mounted on a vertical mechanical stage, was transilluminated. A 50 x water immersion or a 10 x dry objective was employed with no other refracting systems between the objective and the film. Vessels were photographed at film speeds from 24 (normal speed) up to 3200 frames per second. The size of the vessels under observation has ranged from 8 to 100 microns. Sterility of optical equipment was achieved through gas autoclaving and appropriate drapery. Bacteriological cultures of the optical and photographic equipment have been negative and to date no infectious problems have been encountered. In arterioles and venules the red cells were generally oriented with their equatorial axes approximately parallel to the long axis of the vessel. Flow within vessels with a diameter greater than 15μ appeared to involve a central cylinder, made up of plasma and cells, which moved as a unit. Little or no difference in velocity could be observed between cells in the center of the vessel compared to more peripheral cells; thus the shear stress appears to be limited to the annulus, composed of plasma only and nearest to the vessel wall. In capillaries erythrocytes were converted from biconcave disks to hollow paraboloids (thimble like configuration). This change in shape permits movement through capillaries with diameters less than the equatorial diameter of the erythrocyte and it may also profoundly influence the diffusion of the respiratory gases to and from the tissues. These phenomena and the techniques utilized will be demonstrated in a cinematic projection.
(Supported in part by grant HE 09631 from the USPHS.)

METABOLIC AND THERMAL RESPONSES OF MAN DURING EXPOSURE TO He-O_2 AND AIR GASEOUS MIXTURES. R.W. Bowers, D.K. Mathews, and E.L. Fox, (Intr. by Charles W. Smith), Dept. of Physiology, The Ohio State University, Columbus, Ohio.

The effects of breathing and/or being surrounded by 79% He-21% O_2 and air on O_2 consumption ($\dot{V}_{O2}$), heart rate, mean skin temperature (MST), rectal temperature (RT), and mean body temperature (MBT) in a comfortable enviroment of 85°F and 35% relative humidity was studied in resting men during a two hour period. The conditions included: (1) air breathing, air surrounding (air:air); (2) He-O_2 breathing, air surrounding (he:air); (3) air breathing, He surrounding (air:He); and (4) He breathing, He surrounding (He:He). $\dot{V}_{O2}$ was found to be unaltered by the three experimental conditions when compared with the air:air environment. RT and HR were not affected. The 6F° difference between environmental and skin temperatures was great enough to cause a more pronounced drop in MST in He surrounding experiments ($p<0.01$). During the second hour there was a definite separation between air and He environments for MBT ($p<0.01$). This latter effect was due mainly to the contribution of the MST component in the equation for MBT. Two-hour exposures to He-O_2 environments at a comfortable temperature show no serious metabolic or thermal alterations in man.

THE EFFECT OF DECREASING THE FORCE OF ATRIAL CONTRACTION ON CARDIAC OUTPUT. Daniel L. Boyd and John F. Williams, Jr. (intr. by W. J. Daly) Dept. of Medicine, Indiana University School of Medicine and V. A. Hospital, Indianapolis, Indiana

Many studies have been performed concerning the effect of abolishing atrial contraction or of altering the timing of atrial systole on the cardiac output. However, there is little information concerning the effect of a moderate decrease in the force of a properly timed atrial contraction. That this may be of importance is apparent in view of the recent demonstration that mechanical, nervous and humoral factors normally exist which can alter atrial contractile force. Right atrial contractile force was measured in 22 experiments in 10 open-chested dogs using a lightweight, sensitive strain gauge arch. Atrial contractile force was decreased by electrical stimulation of the distal end of the severed right vagus nerve. Stimulation was of such magnitude that no discernible change occurred in right ventricular contractile force measured with a Walton-Brodie strain gauge arch. Heart rate was maintained constant by electrical stimulation of the right atrium. Pulmonary artery blood flow was measured with an electromagnetic flow meter. Heart rate averaged 170 ± 24 (SD) beats/min. During vagal stimulation atrial contractile force decreased in each experiment by an average of 47 ± 15% of the control. However, pulmonary artery blood flow which averaged 1.75 ± 0.74 L./min. during the control period fell by an average of only 0.10 ± 0.10 L./min. during vagal stimulation, decreasing in 19 of 22 experiments. It is concluded that decreases in right atrial contractile force of this degree have only a small effect on right ventricular output. Furthermore, this study suggests that those factors which have been demonstrated previously to result in a decrease in the force of atrial contraction probably have little influence on the cardiac output by their atrial effect alone.

STATIC VOLUME-PRESSURE RELATIONS IN LUNGS OF RATS EXPOSED TO 100 PERCENT OXYGEN. Gerald A. Brooksby and Robert W. Staley (intr. by H. A. Leon). National Aeronautics and Space Administration, Biotechnology Div., Ames Research Center, Moffett Field, Calif.

The toxic response of the lung to elevated oxygen pressures has long been recognized. In the rat this response is characterized acutely by edema and congestion and chronically by atelectasis, thickening of the interalveolar septa and emphysema. This study correlates these histological changes with static pulmonary mechanics in Sprague Dawley rats exposed continuously to 100 percent oxygen for up to 28 days at pressures of 250, 450, 600 and 760 mm Hg. Rats were sacrificed at weekly intervals during the exposure and surfactant activity and pressure-volume loops were obtained by inflating the excised lungs with air and saline. When compared with controls, no decrease in surfactant activity was observed in any of the oxygen-exposed animals. No change was observed in the pressure-volume characteristics of rat lungs exposed to 100 percent oxygen at 250 or 450 mm Hg for up to 28 days. A decrease in compliance ($P < 0.05$) was observed in all the rats exposed for 1, 2, 3 and 4 weeks to 100 percent oxygen at 600 mm Hg. On 100 percent O_2 at 760 mm Hg, rats exhibited decreased compliance after 1 and 2 weeks, but showed an increase in compliance after 3 and 4 weeks and a marked increase in the expansion index $\left(\frac{\text{Lung vol. at 5 cm } H_2O - V_D}{\text{Lung vol. max.} - V_D}\right)$ indicating "hyperinflation" of these lungs. The changes are compatible with the histological picture.

CARDIAC SYMPATHETIC PATHWAYS BLOCKED BY ATROPINE BUT NOT BY HEXAMETHONIUM. A.M. Brown (intr. by J.H. Comroe, Jr.). Cardiovasc. Res. Inst., Univ. of Calif. San Fran. Med. Ctr., San Francisco, Calif.*

The cardiac sympathetic nerves contain B fibres that run without synapse through both the stellate and caudal cervical ganglia. In dogs and cats anesthetized with either pentobarbital or chloralose-urethane, these fibres were selectively excited by stimulating the thoracic sympathetic trunk and simultaneously blocking the ganglia using 0.25% nicotine applied locally and/or hexamethonium (C_6) (10 mg/kg i.v., repeated as necessary). Presence or recurrence of ganglionic discharge was detected by continuously monitoring the activity of post ganglionic cardiac sympathetic nerves. Stimulation of these B fibres always increased both mean blood pressure and pulse pressure; an increase in heart rate occurred less often. No discharge arising from either stellate or caudal cervical ganglion was observed. The response occurred after a delay of 4-10 sec. It was prevented by the prior administration of propranolol (0.5 mg/kg i.v.) or atropine sulfate in doses as low as 0.01 mg/kg i.v. Such doses often caused a further fall in blood pressure. The doses of C_6 completely inhibited the response to vagal stimulation. It is concluded that these B fibres have synapses outside the paravertebral ganglia with cells that release catecholamines. Synaptic transmission was blocked by atropine but not by C_6. (USPHS grants HE-5251, HE-06285)

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ELECTRICAL RESPONSE OF THE PLANARIAN EYECUP IN DIFFERENT STATES OF LIGHT ADAPTATION. H. Mack Brown and T. E. Ogden. VA Hospital, Depts. of Neurology and Physiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

The slow potential (Ocellar Potential - OP) evoked from the planarian ocellus by a strobe flash (5000 Lux) was recorded with conventional microelectrode techniques. The amplitude of the OP was examined under 3 conditions of adaptation. (1) Paired identical flashes with interflash intervals of 2-60 secs. The response to the second flash increased as a simple exponential function of time in the dark (interflash interval). (2) Test flashes were presented during steady background illumination of varying intensity. The amplitude of the OP varied linearly with the logarithm of background illuminance. (3) The ocellus was allowed to dark adapt for 1 min. Successive flashes of light were presented at 2 sec. intervals; this progressively light adapted the eye. The first flash in the series elicited the maximal response. The response to the second flash was about 30% of the maximum. Subsequent responses increased by approximately equal increments during the next 6 flashes, after which a steady state was maintained. The first two experiments suggest that the amplitude of the OP is proportional to the amount of pigment present in the photosensitive cells of the ocellus. Results of the third experiment cannot be explained by photoregeneration; also, the structure of the planarian eye precludes the possibility of neuronal interaction. Therefore, these results must reflect the limiting characteristics of the cell membrane involved in the generation of the OP.

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THE EFFECTS OF ATMOSPHERES RICH IN OXYGEN ON OXIDATIVE PHOSPHORYLATION BY LIVER MITOCHONDRIA. Harold E. Brown*, Clinton E. Robinson* and Frode Ulvedal. Technology Incorporated, San Antonio, Texas, and the USAF School of Aerospace Medicine, Brooks AFB, Texas.

Male Rhesus (Mucacca mulatta) monkeys were exposed to an atmosphere of 99+% oxygen at a total pressure of 380 mm Hg. Two experiments were conducted with animals being exposed to the experimental atmosphere for 21 days and 9 days, respectively. Two animals were sacrificed on days 7, 14, and 21 in the first test and on days 1, 3, 6, and 9 in the second. Animals were sacrificed on days 14, 21, and 29 following removal of the test environment in the first experiment to evaluate the phosphorus incorporation/oxygen uptake (P/O) ratios during a post-experimental period. Liver mitochondria were isolated and P/O ratios determined, utilizing α-ketoglutarate as the substrate. P/O ratios were reduced from the normal of 3.74 to less than 2.0 following 6-7 days of exposure and remained depressed throughout the period of elevated O_2. Following return to normal air, P/O ratios were restored to control values. In order to evaluate this effect further, in vitro studies were performed to determine the effect of different gaseous environments on P/O ratios in rat mitochondria. Mitochondria, isolated as above, were gassed for 20 minutes with warmed, humidified O_2, 50% O_2/50% N_2, 20% O_2/80% N_2 and room air. P/O ratios were depressed in both groups with elevated O_2 percentages. In both the in vivo and in vitro studies, the P/O ratio reduction was due to an inhibition of phosphorus incorporation, the oxygen uptake being essentially unchanged. This appears to be due to an uncoupling phenomenon, possibly different from the classical chemical inhibition of oxidative phosphorylation.

POTENTIAL DEPENDENCE OF THROMBUS INDUCTION AT BLOOD-PLATINUM INTERFACES IN LIVING DOG ARTERIES. J.C. Brown*, S.M. Lavelle* & P.N. Sawyer. The Vascular Surgical Service of the Depts. of Surgery & Surgical Research, State University of New York, Downstate Medical Center, Brooklyn, N.Y. and the Dept. of Experimental Medicine, University College, Galway, Ireland. Supported in part by grant in aid HE 07371-04 from the National Institutes of Health, Bethesda, Md.

Electrical thrombosis is well documented. However, electrochemical blood cell precipitation has only recently been shown to occur at a critical electrode-blood interface potential approximating +0.4 volt NHE in vitro (Sawyer, P.N., Brattain, W.H. and Boddy, P.J., Proc.Nat.Acad.Sci. 51:428, 1964; Sawyer, P.N., Wu, K.T., Wesolowski, S.A., Brattain, W.H. and Boddy, P.J., Proc.Nat.Acad.Sci. 53:294, 1965). Experimental techniques were developed for maintaining constant interfacial potentials between platinum electrodes and flowing blood in arteries of living dogs. Thrombosis on these interfaces at potentials between $\pm$ 1 volt NHE was evaluated. Electrodes more positive than +0.3 $\pm$ 0.1 volt NHE with respect to blood produced thrombosis while those more negative did not. These results suggest that intravascular thrombosis occurs at the same interfacial potential as cell precipitation in vitro as well as the existence of a critical potential in the generation of intravascular thrombosis.

INTRACELLULAR RECORDING OF RAPID LIGHT-EVOKED RESPONSES FROM PIGMENT EPITHELIUM CELLS OF THE FROG EYE. Kenneth T. Brown and J. Michael Crawford*. Univ. Calif. Med. Center, San Francisco, California.

An intense light flash evokes a sequence of three electrical responses from the isolated pigment epithelium-choroid complex of the toad or frog eye. The first two responses are very rapid, and seem comparable to the early receptor potential of retinal photoreceptors. After removing the retina from the frog eye, the pigment epithelium cells are at the surface of the preparation. Thus the first membrane penetrated is that of the pigment epithelium cell, and intracellular recordings from these cells may be positively identified. Such recordings, obtained with micropipette electrodes, show that the pigment epithelium cells are photosensitive and are the primary generators of light-evoked responses of this preparation. Both of the rapid responses invert in polarity across the front membrane of the pigment cell. Also the second response, but not the first, declines as the membrane potential decreases due to damage by the electrode. These results strongly indicate that the second response, and perhaps the first one as well, represent early stages of activity in an excitable membrane. In a photosensitive cell these responses are triggered by the action of light upon a photopigment. The responses of pigment epithelium cells are little affected by light adaptation, and appear to be mediated by melanin. All three responses have spectral response curves which are quite flat, approximating to the absorption spectrum of melanin. Also this sequence of responses is readily elicited from the whole eyes of pigmented rats, while superficially similar responses from albino rat eyes appear due to a residual early receptor potential which remains after strong light adaptation. (Supported by USPHS Grant No. B-1903).

LUTEOTROPIC RESPONSE TO REPEATED ADMINISTRATION OF PROLACTIN IN TWO INBRED MOUSE STRAINS. Henry C. Browning (intr. by Anna N. Taylor). U.Texas, Dental Branch, Houston, Texas.

The formation of corpora lutea in bilateral intraocular ovarian isografts in male BALB/c and Strong A mice was induced by administration of 5 ug of luteinizing hormone (NIH, bovine). Functional hyperemia of these corpora was then produced by daily doses of 40 ug of prolactin (NIH, ovine) for 10 days in BALB/c, or of 10 ug for 3 days in Strong A mice. The mean duration of this hyperemia was 8.2 $\pm$ 0.47 and 3.3 $\pm$ 0.21 days in the two strains, respectively. The same treatment was repeated one month later. The hyperemic response fell to 4.1 $\pm$ 0.22 days in BALB/c mice but did not change significantly in Strong A mice either then or on two further repetitions at monthly intervals. Presumably, there is a difference in the immune response to ovine prolactin in the two mouse strains.

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DMSO PERMEATION THROUGH SINGLE AND MULTI-LAYERED MEMBRANES. Wilton Bunch* (Intr. by C. Edwards). Department of Physiology, University of Minnesota, Minneapolis, Minnesota.

Dimethylsulfoxide (DMSO) has received much attention recently because of its reported ability to protect cells from freezing and to alter the permeability of biological membranes. The washout of injected, labeled DMSO from single muscle fibers of the barnacle has been studied. The time course was approximately exponential; the internal concentration was reduced by 50% in about 5 minutes. Calculations based on the diffusion equation suggest that the cell membrane exerted a significant retarding effect on the penetration of DMSO. The washouts of urea, glycerol and aspirin, which were slower than DMSO, were unchanged by its injection. The permeability coefficients for DMSO and urea were calculated, using the diffusion coefficients measured in 5% agar; the values were $9.06 \pm .73 \times 10^{-5}$cm/sec for DMSO, and $1.5 + .02 \times 10^{-5}$cm/sec for urea. The effects of DMSO on the potential difference and the urea flux across the frog skin have also been examined. The flux of urea was increased by 250 mM DMSO; the membrane potential was abolished. A solution of 1 molar DMSO increased the flux still further. Removal of the DMSO was followed by a partial recovery of the membrane potential. The data suggest that although DMSO penetrates the cell wall more rapidly than other nonelectrolytes of similar size, it does not act as a carrier for other molecules. In multi-layered membranes it does increase the flux of other molecules, possibly by increasing the intercellular shunts. (Aided by NIH Grant NB-02712.)

BLOOD OXYGEN CAPACITY STUDIES IN SOME VERTEBRATES. Jack D. Burke, Department of Anatomy, Medical College of Virginia, Richmond, Virginia.

The Roughton and Scholander microgasometric syringe method with Grant's modification was used to determine total blood oxygen capacity in some vertebrates. These animals were representatives of various classes and included fishes, frogs, turtles, birds and mammals. There was a statistically significant relation between BOC and body weight for both intraspecific and interspecific specimens studies in each class. (Supported by USPHS Grants, 3807 and 8774.)

PHYSIOLOGIC EVIDENCE FOR SPATIAL DISTRIBUTION OF GROUP Ia AFFERENT TERMINALS ON MOTONEURON SURFACE. R.E.Burke*(intro. by P.G.Nelson) Spinal Cord Sec., LNP, NINDB, NIH, Bethesda, Md.

Evidence has been presented (Physiologist 8:125, 1965; Science 151:1088, 1966) that a class of miniature excitatory post-synaptic potentials (mEPSPs) recorded intracellularly in cat extensor motoneurons during muscle stretch can be related directly to activity in single group Ia afferent fibers on the basis of a predictable rhythmic pattern of occurrence. The waveforms of mEPSPs arising from a particular group Ia fiber (i.e. within a given rhythmic set) show little variation in shape, but there is a considerable range in waveform duration and shape among mEPSPs arising from activity in different fibers (i.e. from different sets). The minimum duration has been found with mEPSPs apparently originating from single synaptic endings ("quantal mEPSPs") which rise to peak in 0.25 msec and decay to 1/e of peak amplitude ("decay time") in about 1.0 msec. From this minimum a spectrum of waveforms for different sets of rhythmic mEPSPs is seen, to maximum durations of up to 2.5 msec time to peak and decay times of 8 to 9 msec. Analysis of apparently non-rhythmic mEPSPs resolvable in stretch-evoked synaptic activity shows the same spectrum in time to peak and decay time measurements. It is inferred that the wide range in mEPSP waveforms observed results from variations in the locus of the active group Ia synaptic endings on the motoneuron surface, a significant proportion of which appear to terminate on dendritic regions at considerable electrotonic distances from the cell soma.

NEW OBSERVATIONS ON THE NATURE OF THE HYPOTHALAMIC HORMONE TRF. R. Burgus*, R. N. Stillwell*, J. A. McCloskey*, D. N. Ward*, E. Sakiz* and R. Guillemin. Baylor University College of Medicine and M. D. Anderson Hospital, Texas Medical Center, Houston, Texas.

TRF from 500,000 sheep hypothalami was purified by gel filtration on Sephadex G-25 of a 2 N acetic acid extract of acetone powder, chromatography on carboxymethyl Sephadex C-50, repeated filtration on Sephadex G-25, column partition chromatography in the system butanol-pyridine-acetic acid, adsorption on charcoal (Norit A) eluting with ethanol (15,000 TRF units/mg), and TLC on cellulose in acetone-water 2-1. Upon rechromatography in various TLC systems, the material with TRF activity gives a single, ninhydrin negative, Pauly positive spot, which is neutral to slightly basic in electrophoresis at 6.4, 2.9 and 8.5. Amino acid analysis of 6 N HCl hydrolyzates (24 hours or 72 hours, 110°C) shows ≤ 5-8% amino acid by weight. Moreover, treatment with the proteinases pepsin, trypsin, pronase, carboxypeptidases A & B or leucineaminopeptidase does not reduce biological activity. The purified material has no absorption max. in the visible and shows only end-absorption in u.v. When the purified material is treated with 0.1 HCl at room T a ninhydrin-, Pauly-positive material can be extracted from the neutralized solution by methylene chloride; TRF activity remains in the aqueous phase. Infrared studies of TRF treated in this manner show good evidence for carboxylate functional group(s) and indicate a number of hydroxyl or amino groups. Gas chromatography (50-250°C, 1% SE-30, deactivated support) of the highest purity TRF gave no significant peaks either untreated or with material treated under conditions giving trimethylsilyl-, pivalyl- or methyl-derivatives.

MOTONEURON RESPONSES TO HYPOTHALAMIC AND AMYGDALOID STIMULATION. *Kenneth Campbell**, *Koichi Ishikawa** and *Douglas Stuart*. University of California, Davis, California.

In 20 unanesthetized cats, the firing patterns of L_7 and S_1 flexor and extensor motoneurons and gamma motoneurons were analyzed during electrical stimulation of various hypothalamic and amygdaloid sites. Posterior hypothalamic stimulation revealed that: 1) all motoneuron responses were similar for contralateral and ipsilateral stimulation; 2) in contrast to our previous work on lightly anesthetized preparations (*Amer. J. Phys. Med.*, In press), decelerated responses of extensor alpha motoneurons were evoked almost as frequently as accelerated responses. Acceleration was the predominant effect for flexor alpha motoneurons and gamma motoneurons; 3) alpha motoneurons with smaller amplitude potentials were more responsive to stimulation than those with larger amplitude potentials. Preoptic, anterior hypothalamic and amygdaloid stimulation proved far less effective than posterior hypothalamic stimulation in altering motoneuron discharge. No consistent relationship could be developed between the site of and rate of stimulation in any of these structures and the direction of effect (i.e. toward acceleration or deceleration) exerted on extensor motoneuron discharges. Amygdaloid stimulation revealed many instances wherein the direction of effect exerted on motoneuron discharge was opposite to posterior hypothalamic stimulation. In general, motoneurons were more responsive to stimulation of the lateral nucleus and the medial nucleus of the medial group than to stimulation of other regions of the amygdala. (Supported in part by USPHS Grants NB 05199 and FR 05457.)

EMBRYONIC KIDNEY AFTER MATERNAL UNILATERAL NEPHRECTOMY. Ugo Carpentieri* and Wiktor W. Nowinski. Biochemical Research Division, Dept. of Surgery, Texas Univ. School of Med., Galveston, Texas.

After unilateral nephrectomy, mitotic index in the remaining kidney increases, reaching a maximum on the second day (Rollason, 1949). Ogawa and Nowinski (1958) found a mitosis-stimulating substance in the serum of operated rats, which was present at the described stages. On the other hand, Morpurgo (1920), using the technique of parabiosis showed that if a kidney of one partner is removed, the remaining kidneys of both partners undergo a compensatory hypertrophy. In view of these findings, authors decided to investigate whether these humoral factors act upon embryonic kidney, that is, whether after unilateral nephrectomy of the mother rat the mitosis-stimulating substance and that responsible for the hypertrophy, pass through the placenta. For this purpose, a group of young pregnant females were nephrectomized two days before delivery and mitotic index in the kidneys of newborn rats was calculated. In a second group of animals, unilateral nephrectomy was performed on females at 7-9 days of pregnancy and the weights of kidneys of newborn rats were compared to those of rats born from normal females. In both these groups no evidence was found that the substances pass through placenta, although the mothers showed positive results.

VASCULAR TISSUE CA^{++} AND POSSIBLE INVOLVEMENT IN SUPERSENSITIVITY. Oliver Carrier, Jr. and S. Shibata* Dept. of Pharmacology, Univ. Miss. Med. Ctr., Jackson, Miss.

Following reserpine pretreatment of an animal the calcium content of vascular tissue falls. In dog femoral artery from control of 7.50+0.63 to 3.88+0.33 mEq/kg dry tissue ($P<0.01$) after 0.1 mg/kg reserpine per day for 2 days; in rat aortas 24 hours after 5 mg/kg reserpine from 9.43+0.44 to 7.39+0.38 mEq/kg dry tissue ($P<0.001$); in young rabbit (1 kg) aortas 24 hours after 4 mg/kg reserpine from 6.20+0.37 to 2.64+0.44 mEq/kg dry tissue ($P<0.01$). In older rabbits (2 kg) no significant change could be produced. Aortic strips from both groups of rabbits were tested for supersensitivity following reserpine. None could be demonstrated in the group of older rabbits with 10^{-10} to 10^{-5}M epinephrine or norepinephrine, however, in the aortic strips from the younger rabbits significant ($P<0.01$) supersensitivity was obtained at 10^{-10} to 10^{-6}M norepinephrine. It is suggested that calcium is involved in supersensitivity following reserpine. This could be due to an increased pool of ionized calcium resulting in loss of the ion by diffusion and a concomitant increase in membrane permeability and excitability.

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COMPARISON OF IN VIVO EFFECTS ON THE CANINE FIBRINOLYTIC ENZYME SYSTEM OF TRANS-AMCHA FED AT VARYING DOSE LEVELS. E. Celander* and D. R. Celander. Col. Osteopath. Med. & Surg., Des Moines, Iowa.

Trans-aminomethylcyclohexane carboxylic acid (AMCHA), a potent inhibitor, both of activators of profibrinolysin as well as of fibrinolysin itself, has been studied in the dog for effects on various components of the fibrinolytic system. Among the factors studied were urokinase, urinary proactivator, fibrinogen, euglobulin lytic activity, plasma proactivator, antifibrinolysin and antiurokinase. All samples were dialyzed to remove AMCHA before analysis. Lee-White clotting time was also determined. AMCHA was provided in 4 equal doses daily at levels of 55, 110 and 220 mg/kg/day for up to 24 days. Five to eight control samples were obtained from each animal prior to feeding AMCHA. In addition, three control animals were examined for changes in the fibrinolytic components which might be related to reactions to repeated blood sampling. Consistent changes were not seen in any of the factors studied with the possible exception of occasional wide fluctuations in fibrinogen and decreases in plasma proactivator during AMCHA administration. The data obtained to date do not suggest that feedback mechanisms controlling the level of fibrinogen or of other factors studied are deranged by AMCHA. Lee-White clotting time remained normal throughout and the animals maintained excellent appetite and remained in good health. Blood was not found in either feces or urine during the course of the experiment. (Supported by NIH Grants AM-6285 and HE-7260.)

EFFECTS OF CHLOROMYCETIN, AND OF HYDROLYTIC ENZYMES ON PHOSPHATE UPTAKE IN THE FERTILIZED SEA URCHIN EGG. Edward L. Chambers. Univ. of Miami School of Med., Miami, Fla.

Phosphate uptake in the unfertilized egg of the sea urchin, Lytechinus variegatus, is virtually negligible. Following fertilization, after a lag phase of 5', uptake rate increases dramatically (100 fold) to reach, by 30', a constantly maintained value (accumulation phase). Fertilized eggs were suspended in 0.1-0.3% chloromycetin in sea water starting 5' and 60' after insemination. The rate of phosphate uptake was measured as μmP/ml eggs/minute, and compared to controls in normal sea water. When the eggs were exposed to chloromycetin during the lag phase, at first the rate of increase of uptake was slowed, following which (after 30') inhibition of uptake occurred. Immersion of eggs during the accumulation phase resulted in a progressively increasing inhibition, but this was much less for a given period of exposure than that observed for eggs exposed during the lag phase. The results indicate that the phosphate transport system is newly synthesized at fertilization (rather than preformed), and that both the origin as well as the continued functioning of the system are dependent on protein synthesis. In order to determine whether a surface located carrier-protein could be involved in the transport, after removing the fertilization membranes and hyaline layer material phosphate uptake was measured of the denuded eggs exposed for 60'-180' periods to 0.2% trypsin (2 x crystallyzed), 0.025% papain (with activators), 0.1% panprotease, and 0.05% lipase, at pH values of 8.0, 7.0, and 6.0. Full digestion of surface materials was indicated by the complete dissociation of the blastomeres but phosphate uptake was unaltered. (Supported by grants GM 08497 from U. S. P. H. S., GB 2893 from NSF and DRG-849 from Damon Runyon Memorial Fund.)

CARBOHYDRATE METABOLISM IN CONTRACTING DOG SKELETAL MUSCLE IN SITU. C. K. Chapler, * H. G. Welch, * and W. N. Stainsby, Dept. of Physiology, College of Medicine, University of Florida, Gainesville, Florida.

These experiments were designed to quantitate carbohydrate metabolism in contracting skeletal muscle. The venous outflow from the gastrocneminus-plantaris muscle group was isolated and measured at rest and during one hour of continuous twitch contractions. The twitches resulted from supra-maximal stimulation of the distal stump of the cut sciatic nerve. In each experiment only one twitch rate was studied; different experiments examined rates of 1-5 T/sec. From measurements of blood flow and arteriovenous differences uptake or production of oxygen, glucose, and lactate were determined. In another series of experiments muscle glycogen depletion was measured. In five experiments at 5 T/sec, after the contractions started: 1) The average oxygen uptake increased to a maximum in 10 minutes. Thereafter oxygen uptake decreased slowly to approximately 60% of the maximum rate by the end of contractions. 2) The average glucose uptake increased reaching maximum values in 20 minutes and then decreased to 60% of the maximum rate. 3) The average lactate production increased to a maximum in 10 minutes and then decreased to about zero by 30 minutes where it remained for the rest of the contraction period. The total oxygen uptake for the hour of contractions averaged 7300 µl/gm. For the same period, glucose uptake averaged 4000 µg/g and lactate production averaged 1200 µg/g. Glycogen depletion averaged 4000 µg/g. The data indicate that glucose uptake plus the glycogen breakdown minus the lactate production can account for about 60% of the oxygen uptake. Data at lower twitch rates were similar but quantitatively smaller. (Supported by N.I.H. Grant GM-06264).

AFFERENT NEUROGRAPHIC AND HISTOLOGIC CORRELATES OF CORTICAL SYNCHRONIZATION AND DESYNCHRONIZATION INDUCED BY CENTRAL VAGAL STIMULATION. M. H. Chase, Y. Nakamura,* C. D. Clemente and M. B. Sterman. Depts of Anatomy and Physiology and the Brain Research Institute, Univ. of California, Los Angeles, Calif.

In previous studies we have shown that cortical synchronization and desynchronization may be induced by central cervical vagal stimulation in the acute, immobilized cat preparation. By simultaneously recording the vagal neurographic record and the EEG patterns of response we were able to determine that synchronization was correlated with neurographic potentials having conduction velocities greater than 20M/sec., while desynchronization occurred in conjunction with a potential whose conduction velocity was approximately 15M/sec. These responses occurred at both high and low frequencies of stimulation, indicating that the differentiating factor was the fiber group activated, as reflected by its action potential, rather than the frequency of its activation. In order to determine which components of the neurographic record reflected activity along sensory fibers, a separate series of cats underwent unilateral supranodose transection two to four weeks prior to being placed in the recording paradigm. By the simultaneous excitation of both the intact and supranodose transected vagi with stimuli of equivalent magnitude, it was possible to identify those components of the standard neurographic record that reflect activity along sensory fibers, as these are the only ones which remain viable on the transected side. With the intact vagus thus serving as a control, we observed, on the transected side, those potentials which had been associated with both cortical patterns of response. Histologic comparisons of the intact and transected vagi were then carried out. By utilizing an analysis of fiber diameter as an index of conduction velocity we were able to confirm the neurographic observations. (Supported by MH 10083)

FATTY LIVER INDUCED IN THE INFANT RAT BY CHRONIC CO HYPOXIA. H. Chiodi and N.G. Bazan*. Dept. Physical Medicine & Rehabilitation, College of Physicians & Surgeons, Columbia University, New York, N.Y.

Chronic hypoxia, either in the mountains or in a low pressure chamber, has been shown to cause fatty liver degeneration in newborn rats but not in fetuses or in rats more than 8-10 days old. Liver lesions were associated with generalized trophic changes such as decreased body weight, growth retardation, etc., which in most cases produced death within two weeks from the onset of the hypoxia. In the present study, when rat litters one day old were exposed to a chronic CO hypoxia producing around 40 per cent blood carboxihemoglobin, a fatty liver degeneration similar to that induced by high altitude hypoxia was observed. Confirming previous studies, the hypoxic infant rats showed a highly significant increase of total lipids of the liver almost all in the triglycerides fraction, without significant changes of the FFA. Fatty livers showed microscopic lesions similar to those found in high altitude hypoxic animals. In the infant rats with liver lesions, plasma bilirubin, particularly the conjugated fraction, was significantly increased. If the mother alone was rendered chronically hypoxic by injecting CO intraperiotoneally, no liver lesion appeared in the infant rats she nursed.

VASCULAR RESPONSES TO AN AUTOMATICALLY CONTROLLED ARTIFICIAL HEART. Neal R. Cholvin, Howard H. Erickson*, Curran S. Swift*, and Phillip T. Pearson*, Biomedical Engineering Program, Iowa State University, Ames, Iowa.

This study seeks to investigate the short term responses of the remaining systemic and pulmonary vascular regulatory mechanisms in deventricularized experimental dogs maintained by two artificial ventricles. This acute preparation resembles a denervated intact heart preparation but has the differentiating feature that the cardiac "pump" is not influenced by hormones in the blood stream. The pneumatically-powered artificial ventricles are automatically regulated by using right and left ventricular input (atrial) pressures or left atrial pressure and venous oxyhemglobin concentration as feedback control parameters. The metabolic state of the preparation is maintained by adjusting circulating blood volume and blood pH. A number of perturbations of the animal:machine system are then induced and the system response monitored. Responses in the experiments to small perturbations in input pressures depend upon the reaction time of the artificial ventricle's control system. If the activation rate of the artificial device is rapid compared to vascular regulatory mechanisms in the animal, a sustained oscillatory pattern in blood pressure and flow results. Slow corrections by the physical system result in more stable responses in the animal's vasculature, ranging from diminishing oscillations to heavily damped changes in flows and mean pressures. Control of one ventricle using atrial pressure as the feedback parameter and of the other ventricle using oxyhemglobin concentration results in longer duration compensatory changes in flow rates. This type of response might be expected since blood biochemical changes are more indirectly related to flow rates than are pressures.

THE RELATIONSHIP OF METABOLISM TO VASOACTIVITY OF ISOPROTERENOL AND PROPRANOLOL. C. C. Chou*, G. E. Camm*, J. B. Scott and F. J. Haddy. Dept. of Physiology, Univ. of Okla. Med. Ctr., Oklahoma City, Okla.

The mechanism by which isoproterenol (I) dilates blood vessels and propranolol (P) blocks isoproterenol is not well understood. It is conceivable that the mechanism is related at least in part to effects on local tissue metabolism. This study inquires into this possibility. Collateral-free naturally perfused and constantly pump-perfused dog hindlimbs were treated as follows: control (C_1), i.a. infusion of I at 2 μg/min (I_1), control (C_2), i.a. infusion of P (P_1), P + I (I_2) and control (P_2). In each step, arterial and venous CO_2 or O_2, venous pH, perfusion pressure or blood flow were determined and CO_2 production (CO_2 pr.) or O_2 consumption calculated. The mean values of CO_2 pr. and blood flow or vascular resistance (mm Hg/ml/min) were:

		C_1	I_1	C_2	P_1	I_2	P_2
Natural	Bl. flow ml/min	112	218*	127*	103*	114	105
Flow	CO_2 pr. ml/min	4.27	5.59*	3.85*	3.53*	3.47	3.41
Constant	Vas. Resistance	1.13	0.56*	1.20*	1.40*	1.40	1.42
Flow	CO_2 pr. ml/min	2.50	3.35*	2.55*	1.74	1.79	1.74

*Change from preceding value is significant at p value less than 0.05

Thus, I decreased resistance and increased CO_2 pr. and P blocked both effects. Venous pH did not change. O_2 consumption was not altered by I infusion during constant flow and, in preliminary experiments, during natural flow. In the pump-perfused preparation, acetylcholine (1 μg/min) decreased vascular resistance but failed to alter CO_2 pr. or O_2 consumption. This study suggests that the vascular effect of isoproterenol and the blocking effect of propranolol on isoproterenol may well be, at least in part, secondary to metabolic effects on surrounding tissue.

HEART ACTION POTENTIAL: CONVERSION OF SPIKE TO PLATEAU. Leon Churney and Hisashi Ohshima*. Department of Physiology, Louisiana State University, School of Medicine, New Orleans, Louisiana.

The untreated, excised ventricle of the Amphiuma or Necturus heart fires plateau-shaped action potentials (APs) of long duration. Immediately after burning, crushing, cutting, pressure, pricking, or localized injections near the recording microelectrode of isosmotic solutions of KCl or $MgCl_2$, or of a 0.5% solution of ceepryn chloride in Ringer's, short duration, nerve-like spikes are recordable. These generally lack overshoot and their downstroke is convex to the time line. Spikes are converted spontaneously with time to the larger plateaus. In several instances the transformation was facilitated by increasing the stimulus intensity or duration, or by changing the stimulus polarity. The course of the conversion is generally smooth, except at the peak where notching often occurs. Superposition of the falling limbs of the APs in a given series shows that, once a plateau appears, phase 3 is coincident in all APs. This is interpreted to mean that basically the duration of the AP is determined by phase 2, or perhaps by interaction of phases 0-2. Isosmotic $CaCl_2$ solution inhibits the spontaneous transformation of spike to plateau, whereas Ca-free Ringer or isosmotic Na_2 oxalate solutions facilitate conversion. Immersion of living atrial bundles in Ca-free Ringer's solution plus 0.05% EDTA for 1/2 hr - a period much longer than that required for the effects on the AP to become apparent - does not result in a noticeable dissociation into individual fibers. Surprisingly, restoring or replacing the Ringer's solution prolongs, and perhaps even initiates, the appearance of bizarre complexes. In view of the acknowledged role of Ca ions in the healing process, it is difficult to understand how healing is implicated in the spontaneous conversion with time of the spike to the plateau.

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SUPPRESSION OF THE AUGMENTED ACID AND PEPSIN SECRETORY RESPONSE TO 2-DEOXY-D-GLUCOSE BY HYPOTHALAMIC LESIONS PRODUCING HYPERPHAGIA. E. Cirpili* and P. T. Ridley. Dept. of Physiol. The George Washington University School of Medicine, Washington, D. C.

Interdigestive acid and pepsin secretion and the response to 2-deoxy-D-glucose (2-DG) were determined in rats with chronic gastric fistulae following the production of hypothalamic hyperphagia with bilateral ventromedial lesions. Hyperphagic rats maintained on restricted food intake showed a significant increase in interdigestive acid and pepsin secretion when compared with a group of normal animals. The response to 2-DG in control and sham-operated animals was a highly significant increase in both acid and pepsin output, but no significant elevation of gastric secretion was elicited in the hyperphagic animals. Interdigestive gastric hypersecretion and suppression of the 2-DG response also was seen in a group of rats which were tested before and after hypothalamic lesions producing hyperphagia. Histological examination of the brains of the above hyperphagic animals confirmed bilateral destruction of the ventromedial nuclei. Earlier findings have shown suppression of acid and pepsin secretion in hyperphagic rats during insulin hypoglycemia. These studies offer a second line of evidence associating the ventromedial nuclei with the acid and pepsin secretory responses which occur during hypoglycemia or interference with glucose metabolism. (Supported by U.S.P.H.S. Grant 5-SO1-FR-5359-05).

COMPUTER CONTROL SYSTEM FOR MEASURING TRANSIENT CONDUCTANCE CHANGES IN FROG SKIN IN RESPONSE TO STEP CHANGES IN TEMPERATURE. J.S.Clark and R. M.Gardner (intr. by H.R.Warner), Dept. of Biophysics & Bioeng., Univ. of Utah, Salt Lake City, Utah. Supported by a grant from the Utah Ht. Assoc.

The temperature dependence of Na^+ and K^+ conductances in frog skin contains information bearing directly on the magnitudes of activation energies associated with the diffusion barriers to these ions and should, therefore, be useful for gaining insight into the nature of their conduction processes. Recent temperature studies have shown that the magnitudes of temperature sensitive conductive elements of frog skin membranes have a pronounced time dependence after the onset of a step temperature change. The time constant of this variation, being of the order of a few seconds, is long compared to the temperature equilibrium time constant of the frog skin. Conductivity values occurring immediately after temperature equilibrium measure the primary effects of temperature on physical-chemical parameters of the membrane while the later time variation of such data seems indicative of secondary changes occurring in the membrane while adjusting to a new equilibrium. The present technique utilizes a digital computer with its analog-to-digital and digital-to-analog capability for both control and data reduction. Consistent step temperature changes are produced by rapid changes of bathing solutions of different temperatures under computer control. Conductive and capacitive measurements are made by analyzing trans-membrane potential changes in response to trans-membrane current changes which are under computer control. The dynamic range of the voltage recording amplifiers is increased by a factor of 50 with no loss in sensitivity by using the computer to send feedback potentials after analyzing each data sample. Sampling capability is in excess of 10KC. The experiment is completely automatic during data sampling. Data is outputed on digital tape for a permanent record and is immediately available for computer analysis.

EFFECT OF MASKING ON THE SECOND PEAK ("N_2") OF THE CLICK ACTION POTENTIAL. A. C. Coats (intr. by P. Kellaway). Baylor Univ. Coll. of Med., Houston, Tex.

"Click" action potentials, recorded from cats with round window and auditory nerve electrodes, were "masked" (their amplitudes depressed) with either pure-tone or white-noise stimuli. It was observed that low frequencies (below about 3,000 cps) produce relatively greater N_2 depression, and high frequencies produce relatively greater N_1 depression. White noise depresses N_1 and N_2 about equally. These observations seem to show that N_2 originates from more apical portions of the basilar membrane than N_1. In cochlear models, Tonndorf has observed that the "traveling-bulge" response to an impulsive stimulus resembles a train of waves rather than a single wave. The envelope of each successive half-wave reaches a maximum at a progressively more apical location. If each successive half-wave is considered a separate stimulus, it is not surprising that the click action potential consists of more than one peak (an "N_3" is not infrequently observed), with the maximum of each succeeding peak coming from a more apical location.

EFFECT OF CO PRODUCTION, DISTRIBUTION AND METABOLISM ON BLOOD [COHB] R.F. Coburn* and K. Luomanmäki* (Introd. by R.E. Forster) Dept. of Physiology, Grad. Div., School of Medicine, Univ. of Pa., Phila., Pa.

We have previously (J. Clin. Invest. 44:1899, 1965) studied the relationships of CO production and excretion, and blood [COHb] and body CO stores. We had assumed that CO is not metabolized and that its partition between blood and extravascular tissues is constant. In the present experiments we introduced $C^{14}O$ into the blood of 34 dogs, anesthetized with iv pentobarbital, and 2 normal men, and studied (a) the distribution of the isotope and the effect of changes in arterial PO_2 and pH; (b) the rate of metabolism of $C^{14}O$ to $C^{14}O_2$ ($\dot{V}met$); and (c) the rate of change of blood [COHb] and the body CO stores. The experimental subjects breathed in a closed system thereby preventing excretion of CO via the lungs. In 11 dogs $C^{14}O$ was distributed with an average of 77.1% ± SD 7.4% in blood and the remainder in extravascular CO pools. This partition remained constant with changes in arterial PO_2 from 35 to 500 mm Hg and in pH from 7.28 to 7.50, and with increases in blood [COHb] from 0.8 to over 50% saturation; therefore shifts between different CO pools did not influence blood [COHb] during these experiments. $\dot{V}met$ averaged 0.20%/hr ± SD 0.18%/hr of total $C^{14}O$ administered in 19 dogs, and 0.11 and 0.16%/hr in two human subjects and was shown to be a first order reaction. Body CO stores increased at an average rate of 0.21 ml/hr ±SD 0.09 ml/hr in 26 dogs with initial blood [COHb] less than 0.8%. $\dot{V}met$ is less than 5% of the rate of CO production at normal [COHb] but increases as blood [COHb] increases and therefore is of significance as a determinant of [COHb]. At normal [COHb] measured rate of increase in body CO appears to be very close to the rate of endogenous CO production.

THE UTILIZATION RATE OF A SUBSTRATE (α-KETOGLUTARATE) BY THE DOG KIDNEY IN RELATIONSHIP TO NET SODIUM REABSORPTIVE RATE. Julius J. Cohen, University of Rochester, Rochester, N. Y.

The linear relationship between the rates of net renal tubular reabsorption of sodium and the renal utilization of oxygen ($\dot{Q}_{O_2}$) has been interpreted to indicate that most of the energy available to the kidney is used to transport Na^+. In previous studies we have shown that exogenous (infused) α-ketoglutarate (α-KG) is avidly utilized by the dog kidney without changing renal $\dot{Q}_{O_2}$. The rate of renal α-KG utilization ($\dot{Q}_{\alpha\text{-KG}}$) is high enough to account for all of the $\dot{Q}_{O_2}$ if complete oxidation of the α-KG is assumed. This high $\dot{Q}_{\alpha\text{-KG}}$ occurs by displacing the endogenous substrates of renal metabolism such as glutamine and free fatty acids. In order to determine whether $\dot{Q}_{\alpha\text{-KG}}$ is also related to net Na^+ reabsorption, the filtered load of Na^+ was reduced by partial ureteral occlusion. The simultaneous control rates of maximal $\dot{Q}_{\alpha\text{-KG}}$ and net reabsorption of Na^+ were determined in one kidney in hydrated mongrel dogs under α-chloralose anesthesia. Observations of $\dot{Q}_{\alpha\text{-KG}}$ and net Na^+ reabsorption were then made during a steady state at an increased ureteral pressure. In contrast to the reported decreased $\dot{Q}_{O_2}$, no decrease in, or in many instances, a rise in $\dot{Q}_{\alpha\text{-KG}}$ was observed when net Na^+ reabsorption fell. These observations indicate that renal $\dot{Q}_{O_2}$ alone may not accurately reflect the changes in free energy made available for renal work. Substrate utilization rate and pattern may provide more complete information concerning the energy available for renal work. (Supported by USPHS Grant A03602 and the Life Insurance Medical Research Fund).

EFFECTS OF ETHANOL ADMINISTRATION ON THE PEROXIDATION OF LIVER LIPIDS. M. Comporti* and N. R. Di Luzio, Dept. of Physiology & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tennessee.

Previous studies from this laboratory have demonstrated that antioxidant administration prevented the ethanol-induced fatty liver and hyperlipemia, as well as the carbon tetrachloride-induced fatty liver, necrosis and toxicity. *In vitro* experiments demonstrated enhanced lipid peroxidation in ethanol-treated rats which was effectively inhibited by antioxidant administration. Comporti *et al.* demonstrated that CCl_4 *in vivo* and *in vitro* increased lipid peroxidation. These studies suggested that peroxidation of lipids was a fundamental factor in the pathogenesis of certain types of chemical-induced liver injury. To further validate this hypothesis, the peroxidation of liver lipids was measured by the formation of malonaldehyde by liver homogenates, prepared 1 to 24 hr. after oral administration of ethanol or glucose. Lipid peroxidation was significantly enhanced as early as 1 hr. after ethanol and persisted for 12 hr. Enhanced peroxidation occurred prior to triglyceride accumulation. Normal peroxidation values were observed 24 hr. after oral administration of ethanol, at which time an 8 fold increase occurred in liver triglyceride. The addition of ethanol *in vitro* to normal liver homogenates also enhanced peroxidation of lipids. These studies further demonstrate that enhanced lipoperoxide formation is possibly a fundamental factor in the pathogenesis of hepatic injury. (Supported by USPHS Grant AM-08084.)

RENAL TUBULAR TRANSFER OF SODIUM, POTASSIUM, AND WATER IN ADRENALECTOMIZED RATS. Marshall A. Cortney (intr. by C.A.M. Hogben). Dept. of Physiology and Biophysics, Univ. of Iowa, Iowa City, Iowa.

Adrenalectomized (adrex) and control rats were infused with 10% mannitol in 0.9% saline at 0.2 ml/min. The urine flows of the two groups were similar, 0.08 and 0.097 ml/(min X 100g body wt). The inulin clearances of the adrex rats averaged 0.4 and those of the controls 0.8 ml/(min X 100g body wt). Fractional water reabsorption did not differ for the two groups until the middle portion of the distal convolution, but was lower in the more distal portions of the nephrons of adrex rats. TF/P inulin ratios averaged 1.8 at the end of the proximal convolution and 2.5 at the beginning of the distal tubule. Na F/P ratios were similar throughout the tubules of both groups; 0.8 at the end of the proximal convolution, 0.35 at the beginning of the distal tubule, and 0.4 in the urine. Fractional reabsorption of Na was similar for both groups until the middle portion of the distal convolution, but was lower in the later portions of the distal tubule of the adrex rats. Thus, the similar urine flows resulted from a reduced reabsorption of sodium in the distal portions of the nephrons in adrex rats. K F/P ratios declined similarly for both groups along the proximal convolution, but were 0.5 and 0.2 respectively in the adrex and control rats at the beginning of the distal tubule, and 1.8 and 4.0 in the urine. There was similar fractional reabsorption of K for both groups along the proximal convolution, but at least 20% of the filtered K was present in the early distal tubule of the adrex rats while as little as 7% was present at that site in the controls. K was secreted into the distal portions of the nephrons of both groups, but less was secreted by the adrex rats.

EFFECT OF EXERCISE ON THE DISTRIBUTION OF DYE TRANSIT TIMES THROUGH THE SYSTEMIC CIRCULATION. C.M.Coulam*, H.W.Marshall* and H.R.Warner. Dept. of Biophysics & Bioeng., Univ. of Utah, L.D.S.Hosp. and Holy Cross Hosp., Salt Lake City, Utah. Supported by grants from NIH Nos. HE 04664 and FR 00012.

A method has been developed for computing the distribution of blood transit times (transfer function) from indicator dilution curves recorded from upstream and downstream circulatory sites. The method employs a Fourier series transformation of the upstream and downstream curves and yields a time-domain transfer function which is independent of recirculating dye particles. Teflon catheters were introduced via percutaneous technique in anesthetized mongrel dogs several days prior to the study and were positioned in the pulmonary artery and renal vein (downstream sites). Immediately prior to the study teflon catheters were placed in the aorta (upstream site) and left ventricle (indicator injection site) via a cut-down procedure on the carotid arteries using local anesthesia and sterile technique. Transfer functions calculated between the aorta and pulmonary artery (systemic circuit) during the resting state showed a distribution pattern consisting of an initial large, narrowly dispersed peak (renal system) followed by a smaller, more widely dispersed wash-out curve (peripheral system). During exercise the dispersion pattern became much more narrow as transit times around the peripheral circuit approached those of the renal system. Post-exercise dispersion patterns gradually returned to those of the resting state (one hour) as peripheral pathway transit times lengthened although cardiac output returned to normal within two minutes.

MYOCARDIAL METABOLISM DURING ACETOACETATE INFUSION. C.M. Cowan*, S. Gudbjarnason and R.J. Bing. Wayne State Univ. School of Medicine, Detroit, Michigan.

Myocardial metabolism during acetoacetate (AcAc) infusion (one hour) was studied in 25 dogs by determination of coronary arteriovenous blood differences of AcAc, beta-hydroxybutyrate (BHB), lactate, pyruvate, glucose, and oxygen. Myocardial biopsies taken before and after infusion in 18 experiments were analyzed for glycogen and free fatty acids (FFA). AcAc was extracted in increasing amounts by the heart at arterial AcAc concentrations (concs) up to 100 mg/100 ml of blood(mg%). Up to 43% of AcAc was reduced to BHB. Arterial BHB concs up to 30 mg% resulted in increasing myocardial BHB extraction, but at higher arterial BHB concs there was diminished myocardial BHB extraction. At arterial BHB concs over 35 mg% there was myocardial release of BHB. At low arterial AcAc concs there occurrred an increase in arterial lactate conc and an increase in myocardial lactate extraction. Arterial AcAc conc over 75 mg% were associated with myocardial release of lactate. Glucose and pyruvate did not contribute significantly to myocardial metabolism during ketosis. Myocardial tissue FFA decreased 63% during ketosis, while tissue glycogen decreased 27%. Glycogen decrease was greatest at low myocardial AcAc extraction levels. A total of 100% of the myocardial oxygen extraction ratio could be accounted for by AcAc, BHB, and lactate metabolism. It is concluded that AcAc is readily metabolized by the heart at arterial levels up to 100 mg%. At arterial AcAc elevations above 55 mg% there is myocardial BHB release, and at arterial AcAc elevations above 80 mg% there is myocardial lactate release.

RENAL SERVO-CONTROL OF ARTERIAL BLOOD PRESSURE. M. P. Crawford*, T. Q. Richardson, and A. C. Guyton. (intr. by W. A. Neely) Dept. of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Mississippi

A modified technique for studying the development and regression phases of Goldblatt hypertension has been presented. A cylindrical clamp with an enclosed balloon was placed around the left renal artery. The right kidney was removed. After complete recovery from the surgery, air pressure in the balloon was increased as a slow "ramp" function over a period of several weeks. As the balloon was inflated, it pressed the renal artery against the wall of the clamp, and the arterial pressure rose in step with the pressure in the balloon. The plasma concentration of sodium chloride and heart rate showed a significant transient decrease as the pressure increased, which suggests that the plasma concentration of salt per se is not important to the development of Goldblatt hypertension. Heart rate decreased markedly during early development of the hypertension, which was attributed to pressoreceptor buffering. After mean arterial pressures averaging 147 mm Hg had been reached in four dogs, the balloon pressure was reduced suddenly to zero, and the average pressure fell to 99 mm Hg within 3 days, most of the decrease coming the first day. (Supported by NIH and AHA grants)

THE COMPOSITION OF THE EXTRAPALLIAL FLUID OF MERCENARIA MERCENARIA. M. A. Crenshaw (intro. by J. T. Irving) Forsyth Dental Center, Boston, Massachusetts.

The molluscan shell is formed from the thin layer of extrapallial fluid which is enclosed between the mantle and the inner shell surface. Analyses of this fluid were carried out to determine if its composition offered any clues about its special function. Samples were obtained with a catheter glued into a hole drilled through the shell. The major inorganic components were in Donnan equilibrium with sea water except for Ca and CO_2. The soluble Ca was 1.4 times and the CO_2 twice that of sea water. The pH of the extrapallial fluid was 7.3-7.4 as compared to 7.9-8.0 of sea water. The inorganic composition of blood was very similar to extrapallial fluid, but the composition of mantle fluid was closer to that of sea water. The concentration of non-dialyzable material was greatest in blood, intermediate in extrapallial fluid, and lowest in mantle fluid. The same decreasing order of protein concentration was found. Precipitation of aragonite was observed when extrapallial fluid samples were exposed to air, but no Ca salt was precipitated from blood or mantle fluid. This difference appears to be due to the reduction of Ca activity in blood and mantle fluid by the organic binding of Ca.

UNIT ACTIVITY IN THE LATERAL RETICULAR NUCLEUS. E. C. Crichlow (intr. by C. B. Casas), Dept. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle.

Brodal has reported that cells of the parvicellular portion of the lateral reticular nucleus (LRN) receive spinal afferents only from the ipsilateral half of the body and are devoid of inputs from supraspinal structures. Cells of LRN responsive to ipsilateral forepaw (IFP) stimulation were studied with 3M. KCl filled micropipettes in chloralose anesthetized cats. Of 79 cells, 11 responded only to IFP stimulation (Class I cells), 12 responded to IFP plus one other paw (Class II cells), 23 responded to IFP and two other paws (Class III cells) and 33 responded to all paws (Class IV cells). The mean initial spike latency to IFP stimulation of Class I cells was 23.5 $\pm$ 4.39 (S.E.) msec, of Class II cells 27.9 $\pm$ 3.22 (S.E.) msec, of Class III cells 31.9 $\pm$ 1.97 (S.E.) msec and of Class IV cells 28.9 $\pm$ 1.79 (S.E.) msec. Stimulation of ipsilateral motor cortex activated cells responsive to peripheral stimulation. The distribution of the mean initial spike latencies to cortical stimulation suggests activation via a cortico-reticular pathway incorporating at least one synapse. With cortical stimulation as the conditioning stimulus and peripheral stimulation as the test stimulus, inhibition of the test response was evident with C-T intervals up to 400 msec. Reversal of the order of stimulation produced no similar effect.

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THE TERMINATION OF PRIMARY AFFERENT FIBERS OF CAROTID SINUS AND DEPRESSOR NERVES IN CAT BRAINSTEM. Wayne E. Crill* and Donald J. Reis, Cornell University Medical College, New York, New York.

The distribution of carotid sinus nerve (CSN) and depressor nerve (DN) terminals in the brainstem were identified in cats anesthetized with chloralose and immobilized with Flaxidil by the method of antidromic activation (Wall). The lower brainstem was systematically explored with stimulating microelectrodes while recording from CSN and DN simultaneously or singly. The evoked responses recorded distally in the nerves followed stimulation in the brain at frequencies up to 800 c/s and were relatively resistant to anoxia and barbiturates proving a presynaptic origin in CSN and DN fibers. Positive loci were defined as points where the threshold current dropped to the lowest level (< 10 μamp). The extent of each point on the vertical stereotaxic plane averaged 316μ. In accord with anatomical data, both CSN and DN were excited ipsilaterally from points in the solitary tract and nucleus extending from 2.5 mm anterior and 4 mm posterior to the obex with considerable overlap. In addition many points were located in the medial reticular formation (MRF) and cuneate nucleus. CSN terminals predominated in MRF while DN alone was excited from the cuneate. Stimulation at positive loci always resulted in a fall of blood pressure and bradycardia but only above the threshold for action potentials. With increasing stimulus current, the size of the action potential and the fall of BP and heart rate increased. Stimuli supramaximal for the action potential often converted a depressor to a pressor response. (Supported by NIH grants NB-04876 and NB-05064.)

MATHEMATICAL DETERMINATION OF THE OPTIMAL HEMATOCRIT. Jack W. Crowell and Elvin E. Smith. Department of Physiology & Biophysics, University of Mississippi Medical Center, Jackson, Mississippi

Animals subjected to simulated high altitudes or severe hemorrhage tolerate these conditions best if their oxygen transport system is working at maximum capacity. One factor of importance is the hematocrit ratio and that hematocrit ratio associated with maximal transport of oxygen is defined as the optimal hematocrit ratio. This may be determined mathematically by multiplying the oxygen content equation (O_2 = mH) times Poiseuille's equation modified by an equation for viscosity in terms of hematocrit so that

$$F = \frac{\pi PR^4}{8lv_p e^{kH}} .$$

By differentiating and equating the derivative to zero, one obtains

$$H_o = \frac{1}{k} .$$

Thus the optimal hematocrit is inversely proportional to the coefficient of hematocrit in the relation of viscosity to hematocrit,

$$v = v_p e^{kH}$$

and optimal transport of oxygen occurs when the blood viscosity is 2.718 times the viscosity of plasma.

UNEVEN FILLING AND EMPTYING OF THE LUNG DEMONSTRATED BY CARDIOGENIC OSCILLATIONS. J. C. Cruz*, A. J. Olszowka*, and H. Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

During expiration each cardiac movement causes a disproportionate mixing of the upper and lower lung gases, giving rise to "cardiogenic" oscillations. In the upright man the alveolar O_2 tension is higher in the apex than in the base of the lung, while the reverse is true for CO_2 and N_2 tensions. Thus the oxygen oscillations are 180° out of phase with those of CO_2 and nitrogen. Using oxygen as a convenient marker we can determine whether a given inhaled gas has a higher concentration in the upper or lower part of the lung. According to the diagram of Milic-Emili and associates (J. Appl. Physiol. 21: 767, 1966), if argon is inhaled at the beginning of inspiration (after a complete expiration) the argon tension will be much higher in the upper lobe. On the other hand, if inhaled at the end of inspiration, the Ar should be more concentrated in the lower lobe. This was demonstrated experimentally. In the former case the Ar oscillations were in phase with the O_2 oscillations and 180° out of phase with those for N_2 and CO_2. In the latter case Ar and O_2 oscillations were out of phase; however, those for Ar and CO_2 were in phase. Similar results were achieved between the right and left lung in the lateral decubitus position. These experiments suggest that cardiogenic oscillations serve not only as useful indications of the regional differences in gas composition but also serve to demonstrate regional differences in lung filling. (Supported by the U.S. Public Health Service and the U. S. Air Force.)

INFLUENCE OF THE RATE OF SWEATING ON THE INHIBITORY DOSE OF ATROPINE. E. G. Cummings and F. N. Craig. Research Laboratories, US Army Edgewood Arsenal, Edgewood Arsenal, Maryland.

Before the injection of atropine, sweating in resting men, measured by continual weighing, increased with environmental temperature from 2 g/min at 35° to 13 g/min at 52°C. Atropine sulfate was infused intravenously at rates between 0.01 and 0.10 mg/min after rapid intravenous injections of from 0 to 0.5 mg. Higher rates of infusion were required to inhibit sweating at 52° than at 35°C. The accumulated dose (y) in micrograms/kg required to inhibit sweating by one half increased with the control rate of sweating (x) in $g/m^2/min$ according to the equation $y = (2.6 \pm 0.3) + (0.76 \pm 0.15)\ x$. The rapid recovery after the end of the infusion and the failure of the inhibition to progress as the dose accumulated at slow infusion rates suggested that the effect of atropine was being opposed by an added stimulus generated by the increase in skin temperature during the period of reduced sweating. The theory of a surmountable antagonism between atropine and endogeneous acetylcholine at receptor sites on the sweat glands appears to explain the results.

INTESTINAL VASCULAR RESISTANCE AS AFFECTED BY THE BIPHASIC RESPONSE OF SMOOTH MUSCLE TO THE POTASSIUM ION. J. M. Dabney, J. B. Scott and C. C. Chou*. Univ. of Okla. Med. Ctr. Oklahoma City, Okla.

The potassium ion affects the contractile state of both intestinal and vascular smooth muscle. The question arises whether the effect on intestinal muscle influences vascular resistance. To elucidate this question, isosmotic KCl was infused locally at 0.1 to 1.0 ml/min while resistance and wall tension were studied in a naturally perfused or in a pump perfused segment of the ileum. Venous outflow and lumen pressure were measured during natural perfusion. Ileal compliance and perfusion pressure were measured during constant flow. The results are shown below:

Effect of KCl on blood flow and lumen pressure

Infusion rate ml/min	0.0	0.1	0.2	0.5	1.0	0.0
Flow gm/gm tissue/min	0.28	0.29	0.33	0.34	0.18	0.28
Lumen pressure mm Hg	13	12	10	15	28	18

Effect of KCl on compliance and resistance

Infusion rate ml/min		0.1	0.5	1.0
Compliance	Control	1.00	1.34	1.27
	Experiment	1.06	1.65	1.10
Resistance	Control	7.96	8.97	8.98
	Experiment	7.62	6.29	12.88

Potassium has a biphasic action on ileal wall tension. This effect parallels the expected response of intestinal vasculature alone. It is proposed that K^+ affects vessel caliber by direct action on vascular muscle and indirectly by affecting ileal wall tension and that these effects are additive.

THE EFFECTS OF ACUTE HEAT STRESS IN MAN. A. DAMATO, S.LAU, J. HAFT (INTR.BY T. REGAN). USPHS HOSPITAL, STATEN ISLAND, NEW YORK.

THE EFFECTS OF ACUTE HEAT STRESS ON THE CARDIOVASCULAR SYSTEM OF 15 NORMAL UNACCLIMATIZED MALE SUBJECTS (MEAN AGE 32) WAS DETERMINED USING RIGHT HEART CATHETERIZATION. OXYGEN CONSUMPTION, CARDIAC OUTPUT, ARTERIOVENOUS OXYGEN DIFFERENCES AND HEART RATE WERE COMPARED FOR SUPINE REST AND EXERCISE AT A TEMPERATURE OF 78°F. AND AT EACH OF THE FOLLOWING 3 TEMPERATURES: 100°F, 115°F, 125°F. FIVE SUBJECTS WERE USED FOR EACH OF THE THREE COMPARISONS. RELATIVE HUMIDITY WAS MAINTAINED AT 42%. ALL SUBJECTS HAD AN INCREASE IN HEART RATE UPON EXPOSURE TO A HOT ENVIRONMENT. AT COMPARABLE OXYGEN CONSUMPTIONS FOR BOTH REST AND EXERCISE THERE WAS NO SIGNIFICANT DIFFERENCES IN CARDIAC OUTPUT AT 100°F AND 115°F WHEN COMPARED TO 78°F. HOWEVER, AT COMPARABLE OXYGEN CONSUMPTIONS A SIGNIFICANT INCREASE IN CARDIAC OUTPUT OCCURRED AT 125°F AT REST AND EXERCISE. ACCOMPANYING THESE INCREASES IN CARDIAC OUTPUT WERE INVERSE CHANGES IN A-V OXYGEN DIFFERENCES.

MECHANISM OF ACTION OF CHOLECYSTOKININ IN THE DOG. Ivan E. Danhof. University of Texas Southwestern Medical School, Dallas, Texas.

Motility of the four portions of the duodenum and upper jejunum (balloons in situ) and response of the gallbladder (cannulation of the common duct via the sphincter of Oddi after ligation of the hepatic duct) were studied in dogs given cholecystokinin (Cecekin-Vitrum-0.30-0.35 unit/kg) by systemic vein. Doses below this level either failed to stimulate the gallbladder or resulted in submaximal motor activity. Doses from 0.35-1.0 unit/kg gave essentially similar responses. Transient increases (lasting 1-2 mins) in motility of the second and third portions of the duodenum were observed after a 20-25 sec delay following injection. More sustained (6-8 mins) motility in the first portion of the duodenum was subsequently initiated after a 50-60 sec delay post-injection. The fourth portion of the duodenum and upper jejunum failed to respond with increased motility. Gallbladder motor responses were indicated by changes in color, character, and rate of bile collected from the cannula. CCK injection after infiltration with a 1% or 2% procaine solution of the common duct or transection of the duct resulted in similar duodenal motility patterns, but the gallbladder showed only a minimal, transient, and incomplete emptying response. After transection of the duodenum into constituent anatomic parts, CCK injection was followed by reduced and sequentially reversed motility in the first and second duodenal portions, the third portion failing to respond with increased activity. Removal of the second portion of the duodenum abrogates the motor response of the gallbladder to CCK almost entirely. The data suggest that gallbladder motor response to CCK is mediated by stimulation of the duodenal pacemaker and requires intact ductal innervation to effectively empty the viscus. (Supported by NIH grant AM-4841-04).

LOCAL EFFECTS OF GRADED HYPOXEMIA ON RESISTANCE TO BLOOD FLOW THROUGH THE INTACT DOG LIMB, KIDNEY AND HEART. R. Daugherty*, J. Scott, F. Haddy. Depts. of Physiol. and Med. Univ. Okla. Med. Ctr., Okla. City, Okla.

In the present study the effect of graded hypoxemia on resistance to flow through the limb, kidney and coronary beds was studied by passing the dog's femoral arterial blood through an isolated lung and perfusing it into the right brachial, left renal or left coronary artery at a constant rate. Systemic arterial pressure, brachial (P_{BA}mmHg), renal (P_{RA}mmHg) or coronary ($P_C$mmHg) perfusion pressure, and left ventricular contractile force (F % control), and P_{O_2} (mmHg), O_2 content (Vol %) and pH of the perfusing blood were measured during sequential ventilation of the isolated lung with 20,10,5,2.5,0 and 20% O_2 in N_2 and 5% CO_2.

	N	% O_2 in Ventilatory Mixture					
		20%	10%	5%	2.5%	0%	20%
P_{BA}	9	103	112	108	-	87*	138
P_{O_2}		105	56	32	-	8	104
Vol %		17.1	16.0	13.3	-	1.8	16.4
P_{RA}	10	114	120	112	102	122	123
P_{O_2}		105	53	30	17	5	108
Vol %		15.7	14.3	12.0	6.8	0.9	14.5
P_C	16	110	113	102	78*	63*	103
F		100	98	94	79*	31*	89
P_{O_2}		114	59	34	21	9	109
Vol %		15.6	14.6	12.0	7.0	1.3	15.5

*P = <0.01 relative to control.

Perfusate pH remained constant. Thus a reduction in perfusate P_{O_2} over the normal A-V difference produced no measurable change in limb, renal or coronary vascular resistance or contractile force. Further reduction in P_{O_2} (<30 mmHg) decreased limb and coronary resistance as well as contractile force but had no regular effect on renal resistance.

INTERNEURONAL CELL LOSS AND AMINO ACID CONCENTRATION IN CAT SPINAL CORD. R. A. Davidoff*, L. T. Graham, Jr.*, R. P. Shank*, R. Werman and M. H. Aprison, The Institute of Psychiatric Research, Indiana Univ. Med. Center and V. A. Hospital, Indianapolis, Indiana.

Recent evidence from our laboratory has shown that glycine (Life Sci. 4:1075, 1965) and GABA (Physiologist 8:103, 1965) have the distribution expected of postsynaptic inhibitory agents, glutamate of the monosynaptic excitatory agent (Fed. Proc. 24:462, 1965) and aspartate (in prep.) of a polysynaptic excitatory agent. Since inhibition and polysynaptic excitation involve interneurons in the spinal gray matter, interneuronal cell loss should be correlated with a lowered concentration of transmitter agents involved in the above processes. Occlusion of the thoracic aorta for 15-60 min produced damage to the lumbar spinal cord, manifested by neurological deficit and interneuronal cell loss (22-66%). Following survival for 11-35 days, measurement of 5 amino acids in the L7 segment revealed: glycine decreased in gray and to lesser extent in white matter; glutamate and aspartate decreased in dorsal gray and to lesser extent in ventral gray; GABA decreased in ventral white matter and increased in ventral gray; and glutamine was without consistent changes. These data, in conjunction with physiological studies, suggest the following possible roles: glycine as a postsynaptic inhibitory transmitter, aspartate as a transmitter released from excitatory interneurons, glutamate as the transmitter released from dorsal root fiber terminals as well as one released from excitatory interneurons. Supported by grants from USPHS and Schweppe Fnd.

EXCITATORY AND INHIBITORY PHENOMENA IN THE RAT DORSAL COLUMN NUCLEI. Neil Davidson (intr. by Kiyomi Koizumi). Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y.

Data from present experiments have confirmed previous findings that stimulation of the sensori-motor cortex produces a prolonged depression of post-synaptic activity in the dorsal column nuclei of the rat anesthetized with chloralose. The period of depression corresponds in onset and duration to a period of increased excitability in primary afferent terminals. This is determined by the antidromic excitability testing technique whereby afferent terminals in the nucleus are stimulated and their excitability estimated from the size of the antidromic response recorded in a peripheral nerve. Cortical stimulation also evokes a short latency, low amplitude response in the dorsal column nuclei which, because of its brief latency, is thought to be activity in the terminals of the corticofugal pathway. This response is succeeded by a slow, negative potential or, when a finer recording electrode is employed, by slow, irregular spike activity. These latter two corticofugal effects have much the same latency and duration of action as have the depression of synaptic activity and the increase in primary afferent terminal excitability. (Supported by Public Health Service Grants # (NB-00847-11) and (5 T1 GM 968-03))

VASCULAR RESPONSES OF DOG PAW PAD AND WEB. D. L. Davis. Medical College of Georgia, Augusta, Georgia.

Simultaneous recordings were made of opacity changes of dog paw digital pad and web along with small vessel pressures and flows. Opacity changes were recorded with Cadmium Sulfide photoconductive cells. Small vessel pressures and flows were recorded with the plastic catheter loop technique. Both opacity recordings and small vessel pressure and flow responses exhibited appreciable variations in successive experimental preparations, and to such procedures as sympathetic stimulation and to occlusion of either arterial inflow or venous outflow. At low frequency sympathetic stimulations pad opacities were increased along with the digital artery pressure, while web opacities were decreased. At high frequency stimulations pad opacities were initially increased and web opacities were decreased. Both opacities then decreased during the later part of the stimulation period. During recovery both opacities were markedly increased. Occlusion of arterial inflow produced a decrease in both opacities. The vasculature of the pad appeared to react purely passively to the arterial occlusion, while that of the web appeared to exhibit an overshoot during recovery. Venous occlusion produced marked increases in both pad and web opacities. During the occlusion period the pad opacity plateaued, whereas the web opacity continued to increase. During recovery the pad opacity returned to the control level rapidly, that of the web returned very slowly. The data indicate that the vasculature of the pad and web exhibit significant differences in response to the stimuli studied. These differences may explain the previously reported increases in digital artery flow in response to low frequency sympathetic stimulation. (Supported by a grant from the USPHS).

EFFECTS OF CALCIUM ON THE ACTION POTENTIAL OF PURKINJE FIBERS. L.D. Davis and J.V. Temte (intr. by Q.R. Murphy) Dept. of Physiol. Univ. of Wis. Madison, Wis.

The effects of variation in calcium concentration on the action potential of Purkinje fibers isolated from the dog heart was studied. The preparations were driven at a constant rate (95/min.) which allowed detection of changes in contour of the action potential. Action potentials recorded during perfusion with Tyrode solution containing 2.7 mmoles/L. $CaCl_2$ were compared with those recorded during subsequent perfusion with solution containing 0.675 (¼X), 1.35 (½X), 5.4 (2X) or 10.8 (4X) mmoles/L. $CaCl_2$. In ¼X or ½X solution duration of the action potential increased mainly due to a decrease in slope of phase 2 and a later onset of phase 3. In both 2X and 4X solution repolarization was speeded mainly by an earlier onset of phase 3. Slope of phase 2 increased in 2X but not in 4X solution. The rate of diastolic depolarization increased significantly in both 2X (92%, $P<.001$) and 4X (350%, $P<.001$) solutions. The rate of the calcium-induced diastolic depolarization was dependent on stimulus rate, being faster at higher rates (125/min.) than at slower rates (45/min.). This finding satisfactorily explains the difference in results between these experiments and those of Weidmann (J. Physiol. 129: 568, 1955) where heart rate was not held constant during calcium treatment. The results of the present study show that calcium affects repolarization of Purkinje fibers in a qualitatively similar manner to that described for fibers of the atrium and ventricle (Am. J. Physiol. 186: 317, 1956). (Supported by grants from the Wisconsin Heart Association and the USPHS No. 5T1HE5375.)

DESOXYCORTICOSTERONE SECRETION IN CHRONIC EXPERIMENTAL HEART FAILURE IN THE DOG. James O. Davis, Stuart S. Howards*, Fred S. Wright* and C. I. Johnston*. Dept. of Physiol., Univ. of Missouri School of Med., Columbia, Mo., and the Natl. Heart Inst., Bethesda, Md.

Experiments were undertaken to determine the contribution of desoxycorticosterone (DOC) to the increased mineralocorticoid activity in heart failure. Chronic experimental heart failure occurred secondary to induced tricuspid insufficiency and pulmonic stenosis. Adrenal vein plasma was analyzed for DOC, aldosterone and corticosterone by the double isotope derivative assay method. H^3/C^{14} ratios for DOC were constant after 3 chromatographies and recoveries of DOC added to plasma ranged from 65 to 118% (av. 88%). Simultaneous measurements of DOC, corticosterone and aldosterone revealed secretion rates of .18, 1.50, and .020 μg/min respectively for 8 normal dogs and .18, 1.33, and .097 μg/min for 5 dogs with heart failure. The 5-fold increase in aldosterone secretion was significant at the 5% level. Because of earlier evidence for increased activity of the renin-angiotensin system in experimental heart failure, the effect of angiotensin on DOC secretion was studied. In acute experiments, intravenous infusion of angiotensin into normal dogs increased DOC secretion. Secretion of DOC is also under control of ACTH so the possibility must be considered that DOC secretion is maintained at the normal level in heart failure by the negative corticosteroid feedback mechanism. This mechanism has been reported to maintain a normal or only slightly elevated rate of corticosterone secretion in sodium-depleted dogs (Am. J. Physiol. 208: 655, 1965).

EFFECT OF RUBY LASER RADIATION ON POTENTIAL DIFFERENCE AND SHORT CIRCUIT CURRENT OF THE FROG CORNEA. T. L. Davis, US Army Medical Research Laboratory, Fort Knox, Kentucky, (Intro. by W. A. Brodsky, University of Louisville School of Medicine)

The isolated frog cornea (Rana Catesbeiana) maintains a potential difference of 23.3 mv (15.0 - 34.0) and a short circuit current of 12.5 μa (7.5 - 22.0). These corneas actively transport only chloride ions. (from the endothelial to the epithelial side). The corneas were lased with a ruby laser (wavelength - 6934A). Incident energy densities averaged 27 joules/cm^2. There was a large transient increase in the short circuit current and a transient decrease in the potential difference. Steady state short circuit currents one hour post lasing averaged 17.6% (6.0 - 42.0) higher than control levels. These steady state increases in short circuit current appear to be cumulative with repeated lasing of the same cornea. Control experiments in which the temperature of corneal bathing solutions was raised from 25°C to 45°C showed a linear decrease in both short circuit current and potential difference. Lowering of the temperature showed a linear recovery to 60% of control values. The effects from lasing appear to be of a different nature from those due to an increase in the temperature of the bathing solutions.

DISSIMILARITIES IN OPTIC NEURON RESPONSE TO LIGHT AND X-RAY STIMULATION. W. W. Dawson. Dept. Ophthal. and Center for Neurobiological Sciences, Univ. Fla.

Visual responses are produced easily by X-ray stimuli. As the result of electroretinogram investigation this transducer process has been assumed identical with the process of visible light excitation. Single and multi-unit preparations of the optic nerve of *Limulus polyphemus* respond to X-irradiation of the lateral eye. In this animal threshold for afferent output has been demonstrated at $\sim 8 \times 10^{-5}$ rads for 50 KVP X-ray. Data are presented on density spectrum of normal and X-irradiated rod outer limbs in suspension, excitability of eyes treated pharmacologically to eliminate the inhibitory influences of the retrol-retinal nerve plexus and on responsiveness of eyes during adaptation to physiologically "equated" X and light irradiation. The results exhibit distinct dissimilarities for X-ray and light elicited bleaching and excitation. It may be premature to assign identical transducer processes for X-ray and light visual responses. (Supported by U.S. Army Medical R & D Contract DA-49-193-MD-2733.)

PROLONGED HYPOXIA ON VASCULAR SMOOTH MUSCLE. Reed L. Detar* and David F. Bohr. Dept. of Physiol., Univ. of Mich., Ann Arbor, Mich.

In experiments involving acute exposure of isolated helical strips of rabbit aorta to various oxygen pressures, a direct relationship between pO_2 and tension development in response to epinephrine has been seen. At $pO_2 < 1$ mmHg, epinephrine in concentrations up to 5×10^{-8} produces only small tension development, 10-30% of that occurring at 100 mmHg. The current study characterizes the dependence of contraction and relaxation on pO_2 after prolonged exposure to hypoxic conditions. During prolonged hypoxia (36 hrs) the response to epinephrine (5×10^{-8}) increases to 50-80% of that obtained before hypoxia. The effects of increased pO_2 on the response to epinephrine early and late in the hypoxic period were examined. During the early stages of hypoxia (< 12 hrs) an increase in pO_2 produces an initial relaxation followed by a gradual recovery of contraction to values equal to or above those observed at < 1 mmHg. An increase in pO_2 later in the hypoxic period (> 12 hrs) causes relaxation with little or no recovery. These results suggest 1) that a metabolic pathway capable of producing energy available for contraction is facilitated by the prolonged period of hypoxia, and 2) that this same metabolic pathway can be inhibited by oxygen or that oxygen provides a means for supplying additional energy for relaxation. Supported by a grant from the National Institutes of Health, HE-03756.

XENON^{133}MYOCARDIAL BLOOD FLOW DETERMINATION-A SIMPLE NEW BALLOON TECHNIQUE. R. H. Dietzman*, E. D. Nordberg*, and R. C. Lillehei. Univ. of Minn. Med. School, Minneapolis, Minn.

The clearance of Xenon^{133} from heart muscle following its selective injection into the coronary artery has been correlated with myocardial blood flow by others. The technique of delivery has been modified with the use of a special cannula with an attached balloon. After the aorta is occluded above the orfices of the coronary arteries by inflation of the balloon, Xenon^{133} is flushed into the coronary circulation. The clearance of Xenon^{133} from the heart muscle was determined by a scintillation counter, and the myocardial blood flow calculated from the wash-out curve. This technique simplifies the performance of myocardial blood flow determinations in the intact dog and retains the speed and accuracy of the selective technique. Eighteen dogs were studied. The myocardial blood flow as determined by the selective technique in 8 dogs ranged from 110 - 195 cc./100 gm./min. The standard deviation of the determinations within the dogs, and under controlled conditions of blood pressure and cardiac output, was 9 cc./100 gm./min. Using the balloon technique in 5 dogs, the corresponding figures are 100 - 160 cc./100 gm./min. with a standard deviation of 7 cc./100 gm./min. Nearly simultaneous myocardial blood flows were determined in 5 dogs by the two techniques. The average flows as determined by the two techniques were similar ($p = .09$). Determination of myocardial blood flow yields reproducible and comparable results by either technique.

MECHANISMS OF THE TACHYCARDIA CAUSED BY ATROPINE IN CONSCIOUS DOGS. David E. Donald, Shlomo L. Samueloff* and David Ferguson*
Mayo Clinic, Rochester, Minn.

Atropine (0.2 mg/kg) was given intravenously to normal, trained conscious dogs before and after thoracic sympathectomy, treatment with reserpine (0.1 mg/kg daily for 5 days), and treatment with propranolol (1 mg/kg), singly or in combination. Cardiac acceleration resulted in all cases, with an average maximum of 220 beats per minute and a decline from the fifth minute to 170 beats per minute by the thirtieth minute. The response was not potentiated by neostigmine bromide but was absent after cervical vagotomy or treatment with hexamethonium bromide (5.0 mg/kg). The acceleration in heart rate was accompanied by minor increases in cardiac output and in systemic blood pressure. Stimulation of the vagus nerve in the anesthetized, atropinized dog resulted in an increase in heart rate characterized by delay in onset and by persistence after stimulation had ceased. The increase in rate was still obtained after beta-adrenergic blockade but was abolished by hexamethonium bromide. The response was not potentiated by neostigmine bromide or by cocaine hydrochloride. The administration of acetylcholine to isolated blood-perfused hearts resulted in an increase in contractility, which was abolished by beta-adrenergic blockade. It is proposed that the tachycardia seen in the conscious dog after atropine use is not adrenergic in nature but results from a central stimulant action of atropine, impulses passing via the vagus nerves to some cardiac structure which pharmacologically behaves like a ganglion. The postganglionic mechanism is unknown.

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INTERHEMISPHERIC TRANSFER OF CONDITIONED REFLEXES ESTABLISHED TO ELECTRICAL STIMULATION OF NEOCORTEX. Robert W. Doty, Center for Brain Research, University of Rochester, Rochester, New York 14627.

Eleven macaques were trained to press one lever upon electrical stimulation at one cerebral locus or with one stimulus frequency, and another lever upon stimulation elsewhere or with a different frequency. Test stimuli at novel loci were then interspersed between presentations of the usual stimuli. Responses to test stimuli were neither rewarded nor punished. Following training to stimulation of area striata as one locus, 6 of 7 intact macaques, and one with corpus callosum sectioned, unhesitantly gave the same response to test stimulation at other striate loci in either hemisphere. Furthermore, even without callosal connections, differential responding to location or frequency (2 vs 10/sec) of stimuli applied to area striata appeared without training when the corresponding points in the opposite hemisphere were stimulated. Following training to stimulation of prefrontal cortex in 3 intact macaques no consistent lever-pressing was obtained upon stimulation of contralateral homotopic areas. In 2 macaques still living with section of anterior commissure intended in addition to that of corpus callosum no form of interhemispheric transfer could be obtained for either area striata or prefrontal cortex, although intrahemispheric generalization in area striata was excellent. One of the latter animals used either hand in efforts to capture a "fly" hallucinated upon stimulation of area 18. It thus seems possible a) that intercerebral communication of electrically elicited inherent responses can proceed without rostral commissural systems, b) that such transfer of learned responses may require the anterior commissure when the corpus callosum is lacking and c) that the cortical visual system differs from prefrontal cortex in ability to make such transfers.

CIRCULATORY DYNAMICS DURING PREGNANCY. Ben H. Douglas*, J. C. Harlan*, H. G. Langford, and T. Q. Richardson, Depts. Medicine and Physiology, Univ. Miss. Med. Ctr., Jackson, Mississippi

The circulatory system of a pregnant animal functions differently from that of a nonpregnant animal. In an attempt to more clearly define the dynamic conditions under which the pregnant system operates, the mean circulatory pressure (MCP) was measured in 10 dogs which were in the third trimester of pregnancy. Ten nonpregnant dogs served as controls. Briefly, the MCP was measured by fibrillating the heart and quickly pumping blood from the arterial to the venous system until the pressures reached equilibrium. This equilibrated pressure is a reasonable representation of the mean pressure in the circulatory system under normal, dynamic condition. It is important, for previous studies in this laboratory have shown that MCP is a major factor influencing venous return and cardiac output.

The MCP of the nonpregnant dogs was 7.0 mmHg $\pm$ 0.2 SEM while the MCP of the pregnant dogs was 9.4 mmHg $\pm$ 0.3 SEM. The most common factors known to increase the MCP above the normal are increased blood volume, increased interstitial fluid volume, and increased sympathetic tone. The MCP in the pregnant dogs was 2.4 mmHg greater than in the controls. Under acute conditions this can increase the cardiac output as much as 30%. It is possible that an increased blood volume in pregnant animals produces an elevated MCP which maintains an elevated cardiac output.

(Supported by Grants from NIH).

LOW URINE SALT CONCENTRATIONS IN SALT LOADED GULLS. Donald S. Douglas. Department of Biological Sciences, The George Washington University, Washington, D. C. 20006.

Analysis of urine samples collected from unanesthethized herring gulls indicates that cloacal salt reabsorption is not the cause of low salt concentrations observed in the urine of salt loaded gulls. The results suggest that when gulls are subjected to salt loads their kidneys respond by reabsorbing Na or Cl. Small fitted cannulae were used to collect urine as it came from the ureters, thus insuring that there was no opportunity for the cloacal mucosa to act upon the urine. Salt loads were administered as i.v. infusions of either 8% or 20% NaCl at rates of about 0.1 ml/min/kg. There were usually transient increases in urine salt concentrations during and immediately following loading to levels as high as 400 meq/l. This was followed by sharp declines within 2 or 3 collecting periods (about 30 minutes each) to concentrations as low as 10 meq/l. Total salt loads were on the order of 20-30 meq/kg bird. Such loads were at least twice that sufficient to induce the nasal gland to secrete a hypertonic solution at rates of 0.3 ml/min and Cl concentrations of 800 meq/l. In some birds inulin clearances were measured before and after salt loading. The results have failed to reveal consistent changes in glomerular filtration as a consequence of salt loading. For example, one bird showed a decrease in GFR from an average of 4.6 ml/min/kg (Range: 4.5 - 4.7) before loading to an average of 4.2 ml/min/kg (Range: 3.2 - 5.6) after loading. The maximum GFR was seen 60 minutes after loading was completed, while the minimum occurred about 120 minutes after loading.

INTERACTION OF PERIPHERAL AND CENTRAL INPUT IN THE CHIEF SENSORY TRIGEMINAL NUCLEUS OF THE CAT. **R. Dubner, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland.**

The response characteristics of single cells in the chief sensory trigeminal nucleus were studied in cats anesthetized with chloralose or nembutal. Peripheral receptive fields in the oro-facial region were located with natural stimuli, stimulated electrically, and the cellular responses interacted with peripheral input (light flash or auditory click) and central input (cerebral cortex and thalamic stimulation). Precise electrode localization was determined histologically with the aid of a dye-marking technique. All cells studied had restricted excitatory fields and were activated by hair movement, light touch, or pressure. Approximately thirty percent of the cells exhibited antidromic responses to stimulation of the arcuate nucleus of the thalamus. The responses of sixty-five percent of the cells were modified by cortical stimulation (somatosensory areas I and II); corticofugal inhibitory effects predominated and were maximal at 40-80 msec with a duration of 150-300 msec. Over thirty-five percent of the cells also exhibited excitatory and/or inhibitory responses to light flash or auditory click stimulation. All cells were located in or alongside the chief sensory nucleus, at the level of the motor trigeminal nucleus. The data indicate that considerable modification of somatosensory input can occur at this first central relay nucleus in the trigeminal system.

NITROGEN EXCRETION IN THE FRESH WATER PULMONATE SNAIL LYMNAEA STAGNALIS APPRESSA (SAY). Frederick G. Duerr (Spon. by W. O. Read). Univ. South Dakota, Vermillion, S. D. 57069.

Aliquots of the ambient medium (25 ml water containing 1,000 units penicillin G/ml in which snails reared under constant laboratory conditions (16 hr photoperiod and 25°C) were placed for 24 hr. were analyzed for ammonia, urea, uric acid, amino acids, soluble protein, & total Kjeldahl-N. In none of the samples taken from 33 experimental animals could any trace of excreted amino acids, soluble protein, or uric acid be detected. In 11 of the samples, traces of ammonia, urea, of Kjeldahl-N could be detected. The other 22 samples were N-free. The sensitivity of the tests was such that one can state that in most of the cases less than 50 µg of N was excreted/24 hr. by a single snail If one assumes that 50% of the metabolism of the snail is concerned with nitrogen catabolism, then one can theoretically calculate that a 1 1/2 g L. stag., respiring at a rate of 300 µl O_2/hr (Duerr 1965 Am. Zool 5) would excrete 4,000 µg N/25 hr. The experimental evidence indicates that L.stag. excretes very infrequently, if at all, and suggests that uric acid is stored within the tissues of the snail. This suggestion is supported by the fact that L. stag. tissue has been shown to contain uric acid, but not xanthine or guanine (Duerr 1965 Ann. R. Am. Mal. U.). A similar experiment without penicillin G was conducted on a group of 34 lab-raised L. stag.. Results comparable to that obtained by DeLaunay (1931 Biol. Rev. 6) and considered by many to be indicative of snail excretion in general were obtained. It is suggested that the ammonia and urea, reported by earlier workers to comprise a major portion of the nitrogenous excretion in L. stag. are artifacts produced by bacterial decomposition of the fecal strings present in a collection of ambient medium.

VENTILATORY RESPONSE TO STEP INCREASES OF INSPIRED CARBON DIOXIDE DURING REST AND EXERCISE. R. E. Dutton, V. Lopez-Majano* and V. Chernick*. The Johns Hopkins University, Baltimore, Maryland

Craig (J. Appl. Physiol. 7:467, 1955) has proposed that there is an interaction between the carbon dioxide and "exercise" stimuli to ventilation when CO_2 is breathed during exercise. In order to extend Craig's observations obtained under steady-state conditions to higher CO_2 concentrations, we have measured the ventilatory responses to step increases of inspired CO_2 by administering successive increments of 2% CO_2 every 90 seconds until an inspired CO_2 concentration of 10% was reached at rest, during mild exercise, and during moderate exercise. Above a P_{ACO_2} of 50 mm Hg, the ventilatory response curves during exercise approached the resting response curve obtained by this method. At a P_{ACO_2} of 70 mm Hg, the ventilation in all three conditions was nearly the same in the six normal subjects tested. Mean ventilation at this level was 95 L/min. It is suggested that at high P_{ACO_2} the respiratory control mechanism increasingly suppresses its response to stimuli related to exercise to a point where they are ineffective in increasing ventilation above that resulting from chemical changes alone. (Supported by US Public Health Service Grant HE09405.)

HORMONAL FACTORS IN CYSTIC FIBROSIS (C.F.) B.R. Dworkin* and R.S. Mendelsohn* (intr. by H. Necheles). Michael Reese Hospital and Medical Center, Chicago, Ill.

Because it has been reported that there is approximately a 2:1 increase in male to female survival in post-puberty C.F. patients, effects of female sex hormones were tested on viscosity of secretions; dogs' salivary secretion was used as test object. The viscosity of canine salivary secretions is greatly increased by administration of progesterone, while estrogen has a similar but considerably less pronounced effect. It was however, demonstrated that the increased salivary viscosity of a progesterone treated animal could be rapidly diminished to the pre-treatment level by the administration of estrogen. We are currently studying the variation in viscosity of salivary secretions in three female post-puberty C.F. patients. The relationship between salivary viscosity and endogenous estrogen and progesterone levels was investigated in these patients. In clinical trials Quinestrol appeared to be useful for the reduction of viscosity of secretions.

Supported by a grant from the John A. Hartford Foundation.

PULMONARY MECHANICS AND MORPHOLOGY FIVE DAYS AFTER PULMONARY ARTERY OCCLUSION. L. Henry Edmunds, Jr. and Gary L. Huber, (intr. by M.P. Spencer), Virginia Mason Research Center and Depts. of Biological Structure and Anesthesiology, Univ. of Washington, Seattle, Wash.

The relationship between morphologic changes, alveolar surface phenomena and quasi-static volume pressure (V-P) characteristics was studied in 18 dogs 5 days after pulmonary artery occlusion (PAO). The right or left main PA was occluded by surgical ligature or balloon catheter. Helium quasi-static V-P relationships were studied on vacuum degassed excised lungs in a humidified isolette at 37°C. (5 dogs). Saline V-P relationships were measured after gas studies. In 5 dogs the stability ratio (SR) of alveolar bubbles expressed from a sponge forcep biopsy were measured prior to fixation for light microscopy. In 5 dogs the minimal surface tension (γ) of extracts of 3.0 gm. of minced lung was determined on a Wilhemy balance. Sponge forcep biopsies of inflated lung were fixed in 1.33% s-collidine buffered osmium tetroxide and embedded in Epon 812 for electron microscopy. After PAO, gas and saline V-P diagrams showed decreased maximum inflation volume, but no change in pulmonary static recoil. Both normal and focal hemorrhagic atelectatic areas were present. Areas of normal lung were confirmed by light and electron microscopy, but areas of hemorrhagic atelectasis showed perivascular congestion and hemorrhage, intra-alveolar hemorrhage, swelling of alveolar septae, occasional necrosis of alveolar cells, and alterations in lamellated bodies. SR of normal appearing biopsies averaged 91%, whereas SR of biopsies with necrotic alveoli averaged 51%. SR of hemorrhagic but viable lung varied considerably but averaged 78%. The (γ) of lung extracts averaged 20.2 dynes/cm. Five days after PAO, focal hemorrhagic atelectasis is present, but areas of morphologically and mechanically normal lung remain.

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SEROTONIN AS AN INHIBITORY TRANSMITTER IN THE AMYGDALA.[1] E. Eidelberg, L. Deza* and G. P. Goldstein. Barrow Neurological Institute, Phoenix, Arizona.

The induction of increased brain levels of serotonin results in decreased cell firing in basolateral amygdaloid neurons, both in acute experiments with single-unit recording methods and in "tonic activity" measurements in chronic preparations (cats). Increases in catecholamine levels produce the reverse effect, although less consistently. Fluorescence histochemical studies, using the method of Hillarp et al., show the presence of numberous pericellular structures in the cat amygdala and hippocampal pyramidal cells, which have the distribution and size of axosomatic boutons terminaux. They fluoresce at 570 mμ (activ. at 365 mμ) and they are nearly undetectable after reserpinization. It is postulated that they are axosomatic synapses containing serotonin. The electrophysiological data indicates that they are predominantly or exclusively inhibitory.

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THE TIME INTERVAL TO PEAK VELOCITY OF PRESSURE AND FORCE CHANGES IN THE HEART. W.E.Elzinga* and W.D.Collings, Dept. of Physiol., Michigan State University, East Lansing.

The first derivative of intraventricular pressure pulses (dp/dt) is important in evaluating myocardial contractility. Particular interest has been given to an increase or decrease of the max. dp/dt developed during systole. There are few studies on the relative role of pressure and/or time variations in altering max. dp/dt.

The measurement of the time interval between the onset of systole and the development of max. dp/dt (TIp) is difficult because of the uncertainty of the onset of mechanical systole. In this study this difficulty has been partly overcome by using the peak of the ECG R-wave as a reference point for time measurements. Data in the form of pressure by indwelling needle and force by implantable transducer were obtained in situ on the right heart of nembutalized dogs. Pressure (P) values were read at the point of max. dp/dt on ventricular pressure tracings. Epinephrine (2.5, 5 & 10 ug, i.v.) caused the TIp to vary inversely with the dose, whereas P increased. During inhalation of chloroform, TIp increased and P decreased. Ouabain (.4-.6 mg., i.v.) had no effect on TIp and only slightly increased P.

When ventricular pressure data were compared to force data the time interval between the onset of systole and the max. df/dt (TIf) changed in a manner similar to the pressure data. It is suggested that a separate analysis of each variable in the first derivative would contribute to studies on myocardial contractility. (NASA grant NsG516)

DIFFERENCE BETWEEN DOGS AND CATS IN EFFECT OF LARGE DOSE OF GASTRIN ON GASTRIC SECRETION. Sverre Emås * and Morton I. Grossman. Veterans Adm. Center, Los Angeles, Calif.

A near maximal dose of histamine (0.08 mg dihydrochloride per kg body weight per hour) was given continuously intravenously for 5 hours to conscious dogs and cats with gastric fistulas (vagally innervated). After 2 hours, a large dose of gastrin (extract derived from 3.2 g wet hog antral mucosa per kg body weight) was given as a rapid intravenous shot. No side-effects were observed following the injection of gastrin. In 4 dogs the injection of gastrin reduced histamine-induced secretion of acid by 81%; inhibition was maximal in the first 15-min period and secretion returned to preinjection level in 1 hour. In 4 cats the injection of gastrin increased histamine-induced secretion of acid, reaching a maximum of 178% of preinjection level in the second 15-min period; secretion remained elevated for more than 2 hours. This level was higher than the maximal rate of secretion of acid attainable with either histamine or gastrin alone. Despite the marked difference in its effect on secretion of acid, the large dose of gastrin produced stimulation of secretion of pepsin in both dogs (800%) and cats (340%). Rapid intravenous injection of a large dose of gastrin produced inhibition of histamine-induced secretion of acid in dogs and stimulation of secretion of acid in cats but caused stimulation of secretion of pepsin in both species.

EFFECT OF BRADYKININ INFUSION ON VENOUS RETURN. Thomas E. Emerson, Jr., Depts. of Physiol. & Surgery, Okla. Univ. Med. Sch., Okla. City, Okla.

Transient and steady-state effects of 5 min bradykinin infusion (10 µg/min) on venous return to the heart and other circulatory parameters were studied in 28 dogs anesthetized with nembutal. Venous return was measured with a cylinder and stopwatch from the cannulated venae cavae; blood was returned to the right atrium with a Sigmamotor pump. Cardiac inflow was a) varied according to venous return by adjusting the inflow pump and b) was maintained constant. Other parameters were recorded. Preparations employed were a) intact, b) intact dibenzylinized, c)heart-lung by-passed, & d) abdominal eviscerated dogs. Bradykinin infusion resulted in an immediate increase of venous return in all preparations (intact dog, maximum mean increase = 104 & 216 cc/min with flow constant and variable, respectively). Coincident with this was a fall of systemic arterial pressure and vascular resistance. All parameters tended to return towards control by the 5th min of infusion. Mean venous reservoir blood volume increased a maximum of 83 ml in constant flow studies, indicating the amount of blood moved centrally during bradykinin infusion. Most of this increase occurred during the first 60 sec of infusion. Bradykinin caused a fall of pulmonary vascular resistance in variable flow tests which was due mainly to passive dilation. Heart rate did not change appreciably. Removing the cardiopulmonary system or abdominal viscera, or blockage of the sympathico-adrenal system did not alter the directional responses, however, the magnitude of venous return increase was lessened in each. These data show that bradykinin causes a large increase of venous return to the heart. This is due, at least in part, to translocation of blood from the heart and arterial segment to the venous segment subsequent to a fall of peripheral vascular resistance and arterial transmural pressure.(NIH Grant HE 10259-01).

INDEPENDENT TERMINATION SITES OF THE LEMNISCAL AND THE SPINOTHALAMIC AFFERENTS IN THE RAT THALAMUS. R. Emmers* and K. Crandall* (Spon.: Dr. J. V. Taggart). Department of Physiology, College of Physicians and Surgeons, Columbia University, New York City.

The course of the somesthetic afferents to the rat thalamus were traced by the following method. A stereotaxically oriented semi-micro recording electrode was directed to reach a site in SI of the thalamus and portions of the animal's body were stimulated by an electromagnetically activated tactile stimulator to identify the peripheral projection field for the particular thalamic site. Following this maneuver, a semi-micropipette was used to ablate a portion of the medulla or some funiculi of the spinal cord by negative pressure aspiration. This abolished the response at the recording site. Now, a similar response evoked by stimulation of the very same peripheral field was found in thalamic SII and additional ablation of some other funiculi of the spinal cord was performed to abolish the response. The recording sites and the lesions of the spinal cord were reconstructed from histological material. - Results indicated that afferents which terminate in SI ascend to the medulla, then cross to reach the thalamic site contralaterally with respect to its peripheral projection field. Consequently, these afferents belong to the lemniscal pathway. Afferents which terminate in SII were found to cross in the spinal cord near the entry of the particular sensory roots, then ascend along the ventrolateral funiculi to the thalamus. Consequently, they belong to the spinothalamic pathway. An uncrossed multisynaptic pathway was found also to terminate in SII. These results together with previous findings (Anat. Rec. 151:346, 1965) establish the fact that SI and SII are the nuclear areas for separate relay and termination of the lemniscal and the spinothalamic systems. (Aided by grant NB-03266 from NINDB)

CARBONIC ANHYDRASE DIFFUSION OF CO_2 IN WHOLE BLOOD. T. Enns, G.B. Sham*, and S. Anderson*, Physiol. Res. Lab., Scripps Inst. of Ocean., U.C.S.D., La Jolla, California.

Carbonic anhydrase increases the diffusion rate of CO_2 through aqueous solutions. Measurement of $^{14}CO_2$ diffusion through whole unstirred blood of rabbits also shows an increase of transport rate over that measured in aqueous solutions of equal pH. When the red cells are lysed by freezing, an even greater transport increase is obtained. Both facilitations are stopped by addition of acetazoleamide. From these data it can be calculated that CO_2 diffusion through whole blood is facilitated within the red cells by carbonic anhydrase, but similar CO_2 diffusion facilitation is not appreciable in the plasma. It also follows that within the mean transit time of the CO_2, approximately one minute, there was no appreciable exchange of bicarbonate ions in the red cells with bicarbonate ions in the plasma.

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PROPERTIES OF NEURONS OF RABBIT SUPERIOR CERVICAL GANGLION. S. D. Erulkar and J. K. Woodward*. Univ. of Penna., Philadelphia, Pa.

Responses to preganglionic nerve stimulation have been recorded from neurons in the superior cervical ganglion of anesthetized rabbits by means of extra- and intracellularly placed microelectrodes. Resting membrane potentials of 60-105 mV and spike potentials from 65-105 mV were measured. Spike potentials were generated usually from depolarizing potentials of 20-30 mV, but in some neurons, depolarizing potentials of only 5-10 mV were sufficient for spike generation. Spontaneous firing at rates varying from 5/sec to 1 every 3 seconds were recorded from different units. With the cathode of the stimulating electrodes placed on the preganglionic nerve 2.5 cm from the ganglion, response latencies ranging from 4-40 msec were recorded, with a peak distribution at 7-8 msec. The majority of the neurons responded to preganglionic nerve stimulation with two spikes, but these were separated by intervals of at least 7 msec. The latencies of these two spike potentials could be correlated with the time course of the slow potential waves recorded from the postganglionic nerve. For a few cells, reduction in stimulus intensity resulted in the failure of generation of the initial spike potential, even though the later spike potential was still elicited. Hyperpolarizing potentials were seen associated with spike discharge only, but could last for over 100 msec. For four cells, currents passed through the recording electrode elicited spike firing at rheobasic strengths of 1.8-3.7 x 10^{-10}A, and in these cases total neuron time constants of 2.5-5 msec were measured.

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DETERIORATION OF THE CONNECTIVE TISSUE OF THE GRAAFIAN FOLLICLE AS OVULATION APPROACHES. Lawrence Espey* and Paul Rondell. Physiology Department. University of Michigan. Ann Arbor.

There is increasing evidence which suggests that normal ovulation requires physiological decomposition of the connective tissue within the wall of the Graafian follicle. Tissue from porcine ovaries was used to examine this idea. Strips were cut from three groups of ovarian follicles estimated to be about 20 (stage I), 5 (stage II), and 1 (stage III) hours prior to rupture. The 2 X 20 mm sections of tissue were inserted into a typical muscle-tension recording chamber. The collagenous connective tissue of the thecae and tunica was evaluated by recording the tension developed when the strips of follicle wall were subjected to stretching, acid, and heat. The follicle sections were gradually stretched 2 mm (a 10% increase in original length) over a 15 min interval. The tension increased by 6.8 gms in stage (I), 3.1 gms in stage (II), and only 1.0 gm in stage (III) follicles. After 5 min of acid treatment (HCl, pH 2.0) the contraction of follicular collagen resulted in tension increases of 1.7 gms (I), 1.5 gms (II), and 1.4 gms (III). When the follicle sections were heated to 70°C the tension increased by 2.1 gms (I), 1.6 gms (II), and 1.9 gms (III). It is concluded that, as rupture approaches, the collagenous connective tissue of the follicle wall deteriorates and becomes more labile to dissociation when subjected to force (such as the intrafollicular pressure). The nature of the decomposition does not cause any appreciable reduction in the acid or heat contractility characteristic of the individual collagen fibrils.

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THE INFLUENCE OF HEPARIN ON INTRAVASCULAR PHAGOCYTOSIS. James P. Filkins and N. R. Di Luzio, Dept. of Physiology & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tennessee.

The function of the reticuloendothelial system in selectively removing certain colloidal and particulate materials from the vascular system is well recognized; however, factors which regulate the discriminatory nature and govern the rate of phagocytosis are undefined. Recently, heparin has been demonstrated to play a determinant role in *in vitro* phagocytosis by the isolated perfused rat liver and incubated liver slices. The present study was undertaken to determine the *in vivo* effects of heparin on the intravascular phagocytosis of colloidal carbon (C11/1431a, Pelikan) and a radio-iodinated "RE test lipid emulsion." Low doses of heparin to male rats (12.5 and 25 U/100g) significantly depressed intravascular removal of colloidal carbon in saline. Increasing the dose of heparin (50, 100, 1000, and 2500 U/100g) produced a transient depression in carbon removal which was succeeded by accelerated clearance. Heparin (100 U) injected during the course of a carbon clearance test promptly enhanced the clearance of gelatinized carbon, but impaired the removal of colloidal carbon diluted in saline. Heparin pretreatment (2500 U/100g) augmented intravascular phagocytosis of a gelatinized preparation of the "RE test lipid emulsion." These findings indicate that heparin may play a role in the interaction of gelatinized particles with a plasma opsonic system; furthermore, opsonins may provide the discriminatory mechanism while heparin governs the rate of intravascular phagocytosis. (Supported by the AEC.)

SYMPATHICO-ADRENOMEDULLARY (SAM) ACTIVITY IN DOGS DURING ACUTE HEAT EXPOSURE. Vincent Fiorica*, P. F. Iampietro, E. A. Higgins* and R. Moses*. Civil Aeromedical Institute, Office of Aviation Medicine, Federal Aviation Agency, Oklahoma City, Oklahoma 73125.

Whereas acidosis induced by hypercapnia is a potent stimulator of the sympathico-adrenomedullary (SAM) system in the dog, alkalosis (hypocapnia) is associated with a suppression of SAM activity. The present study tests the response of the SAM system to a metabolic stress when a respiratory alkalosis is simultaneously induced. Thirty dogs, in groups of five, were exposed to 70, 100, 105, 110, 115 and 120°F. Relative humidity at each condition was maintained at 50%. Continuous measurements of respiratory rate (f) and rectal temperature (T_r) were made. Arterial blood samples, taken at regular intervals during heat exposure, were analyzed for pH, P_{CO_2} and total catecholamines. Characteristic responses of T_r and f were obtained. A stable thermal equilibrium was achieved only in dogs exposed to heat conditions of 100 and 105°F. All dogs, however, evidenced polypnea (panting) and a respiratory alkalosis. At the end of the exposure period, pH was elevated above 7.60 in all dogs and P_{CO_2} depressed below 15 mm Hg. Plasma catecholamine levels were uninfluenced by these conditions and control levels were maintained within ±0.2 μg/L. These data suggest that the activity of the SAM system may be pH dependent and that the response of the system to exogenous stimuli may be modulated by the acid-base characteristics of blood at that time.

COLLAGEN AND ELASTIN COMPOSITION OF ARTERIES IN HYPERTENSIVE DOGS. Grace M. Fischer*, Ela I. Mata* and Josep G. Llaurado. Bockus Res. Inst. of Univ. of Pa., 19th and Lombard Sts., Philadelphia, Pa. 19146.

The effects of hypertension on connective tissue composition of arteries were studied in nine hypertensive dogs (kidney cellophane wrapping). Previously in normal dogs (Fed. Proc. 25:571, 1966) the collagen to elastin ratio (C/E), used as an index of biochemical stiffness, was found to be significantly different for arteries (carotid and renal) which are pathways to blood pressure sensors as compared with those leading to regulated beds. Since it is known that in hypertension arteries become "stiffer", the question may arise as to whether the connective tissue, in the form of an increased C/E over normal, plays a role in this increased stiffness. Arterial sites chosen for biochemical analysis were coronary, ascending aorta, carotid, abdominal aorta, proximal cranial mesenteric, distal cranial mesenteric, branches of cranial mesenteric, renal and femoral. Results were compared with those for similar sites in normal dogs. In no vessel did the C/E increase. On the contrary, in the femoral, renal and branches of mesenteric arteries the C/E was significantly lower (t test). It should be noted that the femoral and mesenteric arteries represent functional beds; thus increased distensibility would allow increased lability of function. The increased distensibility of the renal artery suggests the disruption of some signal transmitting properties of this artery to kidney baroreceptors. In conclusion, hypertension does not appear to "stiffen" the artery by altering its relative collagen and elastin composition. By implication, the relationship of hypertension and smooth muscle action is accentuated. (Supported by grants USPH HE 07762 and N-ONR 551 (54)).

COMPONENT VARIABILITIES OF PHOTICALLY EVOKED POTENTIALS DURING TRACE CONDITIONING. Donovan E. Fleming. VA Hospital, Phoenix, Arizona.

It has been observed that early and late wave components of evoked cortical potentials (EVPs) have differential rates of amplitude diminution or enhancement with habituation and conditioning (Key, Nature, 207:441, 1965; Klingberg and Grastyán, Acta Physiol. Hung., 23:115, 1963). Presently, to detail further the modifications of EVP components accompanying the conditioning process, several components were studied longitudinally via a trace conditioning procedure. From electrodes implanted over the visual cortex of cats, EVPs were recorded following habituation, during an extended series of conditioning trials, and following extinction. The US was a shock to the right hind leg presented 1 sec following a brief photic CS. Conventionally amplified EVPs were summed in groups of 10 by a Mnemotron Model 400B CAT. Consistent EVP components in the first 150 msec of the response were identified, peak delay (latency) and amplitude values of each determined, and component variabilities computed. A series of 5-8 positive-negative deflections were regularly identified. The presence of a few components, however, was dependent upon conditioning stage, e.g., a series of late waves occurring between 45-60 msec, initially present following habituation, disappeared during early conditioning, emerging with augmented amplitude as conditioning progressed. The early components were present during all conditioning stages. These, in addition to several late waves, increased in amplitude during early conditioning, then subsequently decreased as conditioning was prolonged. Such amplitude decrements were not of sufficient magnitude to reach pre-conditioning levels. Peak delay and amplitude variabilities of early components were generally lower than those of the late waves. The longitudinal analysis of EVP components reveals several contingencies which can be related to the stage of CR acquisition.

HYPERTHERMIA, DEHYDRATION, AND OXYGEN CONSUMPTION DURING EXERCISE IN A FOOTBALL UNIFORM. E.L. Fox, D.K. Mathews, and D.E. Tanzi (intr. by E.A. Hitchcock). The Ohio State University, Columbus.

Nine male subjects were exercised for 30 mins on a level treadmill at 6mph followed by a 30 min recovery period dressed in 1) shorts only; 2) a football uniform; and 3) shorts plus a back pack weighing the same as the uniform (6.2 kgs). Variables measured were 1) rectal temp (Tr) recorded every min of exercise and recovery; 2) five skin temps (Ts), thigh, stomach, upper back, forehead, and shoulder, recorded every 5mins of exercise and recovery; 3) heart rate (HR) recorded every 5mins of exercise and recovery by telemetry; 4) oxygen consumption (VO_2) and pulmonary ventilation (VE) by open circuit spirometry measured every 5th min of exercise and the last 5mins of recovery; and 5) weight loss (primarily sweat) measured by pre-exercise and post-recovery body weight difference. Environmental conditions for all tests were a temp of 25.6±1.2°C and a relative humidity of 33.0±6%. Results indicate that the elevation in Tr due to the weight of the uniform was 0.3°C ($P<.01$) greater than that caused by the exercise in shorts and resulted in 23% ($P<.02$) more sweating. The reduction in evaporative surface area resulting from wearing the uniform raised Tr an additional 0.3°C ($P<.005$) and increased sweating 64% ($P<.005$) over that caused by the weight of the uniform. Ts were elevated by as much as 5° to 7°C in the uniform compared to the controls. VO_2, VE and HR were elevated by both the pack and uniform tests, but VO_2 was highest in the pack test and VE and HR highest in the uniform test.

TECHNIQUE FOR TELEMETRY OF BLOOD PRESSURE AND MULTIPLE REGIONAL BLOOD FLOWS DURING EXERCISE Dean Franklin, W. S. Kemper*, & R.L. Van Citters Scripps Clinic Research Foundation, La Jolla, Cal. & U. of Washington, Seattle

The regional vascular responses of violently exercising sled dogs were monitored by a multi-channel telemetry system capable of measuring and telemetering aortic blood pressure and phasic blood flow through 3 vessels simultaneously. The output of a chronically implanted miniature blood pressure gage was converted to a 14.5 KHz FM signal. Outputs of 3 chronically implanted Doppler ultrasonic flowmeter transducers (ascending aorta, terminal abdominal aorta, renal and mesenteric arteries) were converted to 5KHz, 40KHz, and 70KHz FM signals. The four FM signals were summed and the composite modulated the frequency of a 260 MHz telemetry transmitter; the resulting signal was radiated from an antenna mounted on the sled. This signal was received at the remotely located recording station and discriminators were used to separate out the frequency components and reproduce the pressure and flow wave forms. The telemetry package was carried in a saddle on the dog. Owing to ambient temperatures (-40°C) Ni-Cad batteries were required; these were carried aboard the sled and a power line run to the dog via the harness. The system was used to record the cardiovascular responses of sled dogs to violent outdoor exercise in terms of rate, pressure, multiple regional flows and regional vascular resistance. Supported by USPH, AHA, the Arctic Aeromed Lab, and Washington State Heart Association.

H^3OH, Na^{22} and Cl^{36} fluxes of the short-circuited pigeon crop mucosa. William L. Frantz, Department of Physiology, Michigan State University, East Lansing.

Pigeon crop(mucosa)devoid of muscle and serosal layers are perfused by bird Ringer solutions buffered at pH 7.8. Temperature (38°C), surface area (2.54 cm^2), chamber volume (3.5 ml) and stirring rate are constant. To equilibrated fluids bathing either the mucosal or serosal surface measured volumes of H^3OH and Na^{22} or H^3OH and Cl^{36} are added. At designated intervals 20 µl samples of perfusant from the opposite chambers are counted in a liquid scintillation spectrometer (Nuclear Chicago Mark I). Tritiated water equilibrates between the mucosal to serosal surface with a 53 minute half-time when Na^{22} is actively transported (0.323 µeq cm^{-2} hr^{-1}.) Tritiated water exposed to the inactive mucosa equilibrates in fluid bathing the serosal surface with a 100 minute half-time. The same rate is measured when the tracer is introduced into the chamber bathing the serosal surface whether or not the membrane is actively transporting sodium. The fluxes of Na^{22} and Cl^{36} relative to the slow deterioration of the membrane are too slow to describe in half-time values. Cl^{36} has a slightly higher flux rate than Na^{22} but does not equilibrate with non-labeled chloride in the membrane or the opposite perfusing volume with a diffusion dependent time course.

(Supported in part by NSF Grant GB 3293)

LACTATE, PYRUVATE, AND PYRIDINE NUCLEOTIDES IN HYPERTHERMIC RATS' LIVER. D.W. Frascella* and H.M. Frankel. Dept. of Physiology and Biochemistry, Rutgers University, New Brunswick, New Jersey.

Experiments were conducted to assess the oxidative state of rat liver during hyperthermia by measuring liver tissue lactate (L), pyruvate (P), and pyridine nucleotides (NAD, NADH, NADP, NADPH). The rat liver was removed following cervical dislocation and frozen by immersion in liquid nitrogen. Compared to a control group (T_r 38°C) liver L, NAD, NADP, and NADPH were increased in rats with T_r 42°C. In rats with a T_r of 44°C, L was greater than, NAD and NADP were similar to, and NADPH was less than values observed at 42°C. P and NADH did not appear to change in a regular fashion with increasing temperature. Tissue L/P and NAD/NADH ratios increased with increasing T_r. These changes indicate that when whole body temperature is increased during acute hyperthermic stress, oxidative metabolic patterns of liver cells are altered.

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THE EFFECT OF HEMICHOLINIUM NO. 3 (Hc-3) ON AMPHIBIAN NERVE.
Donald T. Frazier, Department of Physiology, University of New Mexico School of Medicine, Albuquerque, New Mexico.

The effect of Hc-3 on the amplitude of action potentials recorded from partially stripped frog sciatic nerves has been studied. Stimulation and recordings were carried out in nerve chambers to which various concentrations of Hc-3 could be added (10^{-3}-10^{-5}M). The stimulating pulse was a square wave, supermaximal for all fibers and delivered to the nerve at various frequencies (0,10,30 cps). When compared to a control Ringer's solution, Hc-3 was found to markedly depress the amplitude of the action potential with the effect being both concentration and frequency dependent. Choline, when added in varying concentrations (10^{-3}-10^{-5}M) to the Hc-3 solution, reduced the effect of Hc-3 in a manner suggestive of competitive interactions. Choline at 10 times the Hc-3 concentration maintained the response of the nerve within control limits. Based on the concept that Hc-3 interferes with cholinergic transmission, these data could be interpreted as indicating the involvement of acetylcholine in nerve conduction. If, however, as the current hypothesis suggests, Hc-3 exerts its effect by competing with the transport of choline, one cannot exclude the possibility that cations other than choline are similarly affected.

NERVOUS CONTROL OF SECRETION OF MUCUS FROM GASTRIC ANTRUM AND CORPUS.
M. H. F. FRIEDMAN, FRIEDRICH C. LUFT*, M. TANSY*, AND ROBERT MACKOWIAK*
DEPARTMENT OF PHYSIOLOGY, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

Parameters of stimulation governing vagal and splanchnic control of secretion of gastric mucus were studied in dogs under chloralose-urethane anesthesia. Without interrupting either innervation or blood supply the stomach was partitioned into separate antrum and corpus chambers by a special dual-lumen septum cannula. Heart rate, blood pressure, respiration, gastric blood flow and ileal motility were monitored during the experiment. Peripheral vagus stimulation with low voltage, low frequency, and moderate current drain evoked mucous secretions from both antrum and corpus which were blocked by atropine. Secretion from the corpus was lighter, less viscid and had higher nitrogen concentration. Peripheral splanchnic stimulation with currents of similar characteristics produced secretion of mucus only from antrum which was not blocked by atropine. Afferent fibers for mucous secretion, especially from glands of the antrum, were found in the vagus trunks. Mucous secretion on central vagus stimulation was evoked only when stimulus intensity was such as to produce overt peripheral "sympathetic-type" responses even following adrenalectomy. The role on mucous secretion of afferent fibers in sympathetic trunks remains uncertain.

EFFECTS OF HIPPOCAMPAL STIMULATION ON SINGLE UNIT ACTIVITY IN THE AMYGDALA. Robert R. Fulp* and John A. Gergen. Bowman Gray School of Medicine, Winston-Salem, N.C.

The effects of anterior and posterior ventral hippocampal stimulation on single unit activity in the amygdala have been studied by use of etched steel microelectrodes in the cerveau isole squirrel monkey (Saimiri sciureus). Data have been analyzed with post-stimulus time histograms. The results are taken from a sample of 35 units recorded in 12 animals; of this population 16(46%) are considered affected by stimulus frequencies between 0.25-30/sec. For purposes of the present analysis the amygdala has been divided into corticomedial (12 units, 10 affected) and the basolateral (23 units, 6 affected) groups. Anterior hippocampal stimulation appears to be more effective than posterior stimulation in altering unit firing pattern (9/14 versus 10/34). The most common pattern of response (9/35) is inhibition not followed by any post-inhibition rebound. From posterior hippocampal stimulation latencies of onset of inhibition range from 10-40 msec (mode 20 msec) with duration from 40-175 msec (mode 80 msec). With anterior hippocampal stimulation latencies for inhibition range from 20-75 msec (mode 40 msec) with duration of 10-100 msec (mode 20 msec). One unit in the nucleus intercalatus demonstrates short latency recruitment (20 msec) followed by inhibition. Six units show only general inhibition of firing at faster frequencies of stimulation without a specific pattern being apparent in the post-stimulus time histogram. Results suggest that the ventral hippocampus has a predominantly inhibitory effect on unit activity in the amygdala. Differences found between effects of posterior and anterior stimulation remain unclear but may imply some localization of function in the interrelationship between hippocampal formation and amygdala. (Supported by USPHS NB3992)

DYNAMIC AORTIC DIAMETER MEASUREMENTS UNDER VARYING MEAN PRESSURE LEVELS. R.M.Gardner (intr. by H.R.Warner), Dept. of Biophysics & Bioeng., Univ. of Utah, Salt Lake City, Utah. Supported by a grant from NIH #FR 00012.

A roentgen ray fluoroscopy system connected through an image-amplifier image-orthicon television system has been used to measure internal aortic diameter in vivo. The diameter measurement is accomplished by injecting a radiopaque dye (Renovist) into either the left ventricle or ascending aorta. Then by recording the resulting angiogram on video tape and using a special electronic computation system, aortic diameter values can be calculated 60 times per second. From these measurements and aortic pressure which is recorded simultaneously on the data track of the video tape, elastic properties of the aorta is calculated. As a check of the static and dynamic response of the video technique simultaneous measurements of diameter were performed on dogs using a strain gage caliper (Patel JAP, 1963). Correlation between the two methods was 0.9 or greater in most cases with the caliper values systematically higher than the video by 1.6mm which is of the order of two wall thicknesses. It was not possible to measure pulsatile wall thickness variations since the resolution limit of the video system is 0.4mm. Experiments performed on animals with drug induced hypertension resulted in a marked increase in modulus of elasticity (i.e., the vessel became much less distensible with a rise in mean pressure). The method has been used on dogs and humans to calculate elastic characteristics of both the ascending and descending aorta and their variation with mean pressure.

ELECTROLYTE CHANGES IN HYPERTENSIVE PREGNANT RATS. Lyndle Garrett*, Ben H. Douglas*, and Oliver Carrier, Jr., Univ. of Miss. Medical Center, Jackson, Miss.

Previous studies in our laboratory have shown that uninephrectomized rats become hypertensive, have severe proteimuria, and show excessive weight gain, when they receive desoxycorticosterone acetate (DCA) and NaCl. In an attempt to correlate these changes with changes in tissue electrolyte content, the aortas of the following groups of animals were analyzed for percent H_2O, Na^+ and K^+ mEq/kg dry weight: Group I (11 normal females and 10 normal males). Group II (11 DCA-NaCl hypertensive nonpregnant females and 10 DCA-Na Cl hypertensive pregnant females). The following values were obtained: Group I controls. (females H_2O-65.5±1.4%; 226.8±12.7 Na^+; 129.0±8.6 K^+), (males H_2O-65.0±1.5%;222.0± 6.7 Na^+; 114.0±3.2 K^+). Group II Hypertensive females (nonpregnant - H_2O-65.2±2.7%; 295.0±8.6 Na^+; 133.0±5.2 K^+) (pregnant-H_2O-67.7±1.3%; 305.0±25.0 Na^+; 155.0±7.3 K^+). The Na^+ content rose significantly in the hypertensive pregnant and hypertensive nonpregnant females above control level ($P < 0.01$); however, there was no significant difference between the two hypertensive groups. The K^+ increased in the hypertensive pregnant animals ($P < 0.05$). The K^+ content in the nonpregnant females did not rise. It is suggested that hypertension in pregnant rats and nonpregnant rats is due in both cases to an alteration in the intra-extra cellular electrolyte ratios. (Supported by USPHS grants Nos. HE 09192-02 and HE 09391-01.)

POLARITY OF VAGUS STIMULATION AND ESOPHAGEAL CONTRACTIONS. A. Geisel*, P. Lott, Jr.*, and H. Necheles. Michael Reese Hospital and Medical Center, Chicago, Ill.

The effect of stimulation of the vagus nerves on esophageal motility was studied in dogs. Bundles of open tip tubes were used and motility was registered on a Dynograph. Stimulation of the vagi in the neck was performed with a Grass stimulator, using unipolar square wave pulses. Polarity of the stimulating electrodes was important. In most instances, reversal of current was followed by no or by low contractions and this could be repeated many times. These observations cannot be explained by anodal inhibition because while polarity 1 (positive electrode above negative electrode) was more effective in one dog, polarity 2 (electrodes reversed) was more effective in another dog. Furthermore, in the same dog the response to change of polarity may cause a remarkable change in the response to stimulation of one vagus and no change to stimulation of the other one. Stimulation of the right and left vagal trunks did not produce similar esophageal contractions, although responses of each vagus gave consistent and reproducible results with each polarity of stimulus. Frequently, stimulation caused a drop in blood pressure, but no correlation was found between changes in blood pressure and response of the esophagus to stimulation.

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ELECTRICAL CHANGES IN DENERVATED SKELETAL MUSCLE DURING ANAPHYLACTIC REACTION. E. Gijón*, X. García*, S.H. Bryant and J. del Castillo, Dept. Pharmacol., Sch. Med., San Juan, P.R. 00905

Strips of chronically denervated diaphragm from sensitized guinea-pigs contract in presence of low concentrations of homologous antigen (Alonso-deFlorida et al. Brit. J. Pharmacol. 25: 610 (1965). The same phenomenon occurs in denervated frog sartorious at 38°C (Gijón & Alonso-deFlorida, Unpub.). The electrical events accompanying this reaction have been studied, in both preparations, with intracellular microelectrodes. Antigenic albumins applied to discrete points of the surface of sensitized fibers with an electrically controlled microtap (O.D. of tip about 10 μ) caused depolarizations of up to 30 mV. Latencies as short as 200 msec could be obtained. Crossed-reactions between human serum albumin and ovalbumin were observed and repeated application of antigen to the same spot resulted in desensitization. Antigenic albumins had no effect on either innervated or non-sensitized denervated muscle fibers. Histamine and acetylcholine given with the microtap depolarized denervated fibers with same latencies as those following application of antigens. Innervated fibers were insensitive to histamine and only their end-plate region responded to acetylcholine. The results support a membrane site for antigen-antibody reaction. (Supported by USPHS Grants 1-S01-FR-05419, NB-03178 and NB-05235).

EFFECT OF CHANGES IN PULMONARY ARTERIAL, PULMONARY VENOUS, AND ALVEOLAR PRESSURES ON DIFFUSING CAPACITY IN DOGS. J.R. Gillespie,* J.H. Burgess,* P.D. Graf,* and J.A. Nadel. Cardiovasc. Res. Inst., Univ. Calif. San Francisco Med. Ctr., San Francisco, Calif.

We used the single-breath carbon monoxide diffusing capacity (D_{LCO}) to study the pulmonary capillary blood volume with different pulmonary artery, pulmonary venous, and alveolar pressures. In 8 anesthetized, paralyzed, artificially ventilated, supine dogs, we collected alveolar gas samples from each lung using a Lategola tracheal divider. Temporary left pulmonary artery occlusion with a balloon catheter increased D_{LCO} of the right lung (mean, +21% ±7.6), increased mean pulmonary artery pressure (mean, +5.5 mm Hg ±0.1), but did not change pulmonary venous pressure significantly. Left pulmonary artery occlusion decreased D_{LCO} in the left lung (mean, -41% ±3.5). During left pulmonary artery occlusion, stepwise inflation of a balloon catheter in the ascending aorta increased the pulmonary venous pressure and increased the D_{LCO} of the left lung linearly (mean change in D_{LCO}, +0.34 ml of CO ±0.03/min/mm Hg for each mm Hg increase of pulmonary venous pressure over alveolar pressure) up to the highest difference obtained (28 mm Hg; or 15 mm Hg above the top of the lung). We suggest that a decrease in inflow pressure decreases pulmonary capillary blood volume when the outflow pressure is constant; when inflow pressure is zero, capillary blood volume changes linearly with the difference between venous and alveolar pressures. (Supported by USPHS grant HE-06285. J.H.B. is an R.S. McLaughlin Fellow.)

COMPARATIVE "IN VIVO" DIALYSANCES FROM FOUR DIALYZERS. H. Earl Ginn, Billy J. Matter, John M. Leonard, and Wm. W. Lacy (intr. by Charles R. Park). Vanderbilt Univ. Hosp., Nashville, Tenn.

Dialysance measurements for urea, creatinine, phosphate, uric acid, and α-amino nitrogen were performed on chron-a-coil, twin-coil, 1-M^{2}Kiil, and 2-M^{2}Klung dialyzers at blood flow rates of 50-300 ml/min. Dialysate temperature was maintained at 39.5 -40°C. Dialysate flow rates were 18-20 L/min. with Kolff type, and 500 ml/min. with Kiil and Klung dialyzers. The subjects were patients undergoing intermittent hemodialysis for chronic uremia. Mean dialysance to D max. ratios were as follows:

	Urea	Cr.	PO_4	U.A.	α-AN.
Chron-a-coil	.51	.30	.21	.23	.28
Twin-coil	.64	.35	.28	.30	.36
Kiil	.67	.41	.42	.38	.45
Klung	.79	.67	.65	.58	.65

At all blood flow rates the Klung dialyzer had significantly higher dialysance determinations for all five chemicals measured. The priming volume, however, was lowest with the Klung Kidney. Interest was focused on the high rates of α-amino nitrogen cleared by the dialyzers. Column chromatography failed to demonstrate significant preferential dialysis of individual amino acids. Eight patients developed low serum α-amino nitrogen concentrations while on a low protein intake (20-30 Gm per day) for short periods. Consideration should be given for this loss of amino acids in patients undergoing long-term intermittent dialysis.

EXCHANGE OF MAGNESIUM BETWEEN BLOOD, BRAIN AND CSF. Ginsburg, S.*, Graziani, L.*, Escriva, A.*, and Katzman, R. Albert Einstein College of Medicine, New York, N.Y.

In the peripheral nervous system magnesium plays an important role in neural transmission. Less is known, however, of the effects of Mg on the central nervous system. CSF Mg concentration is greater than serum. Profound elevation of serum Mg concentration causes little change in CSF Mg. Acute experiments were done in anesthetized cats to determine Mg exchange between blood, brain and CSF. The ventriculo-cisternal system was continually perfused with artificial CSF in which the Mg concentration was varied from 0 - 12 mg%. Tracer amounts of Mg^{28} were used in the artificial CSF to determine efflux coefficients and were given intravenously to determine influx coefficients. Serum Mg concentrations were raised by injections of 4% $MgSO_4$. Efflux coefficients averaged .032 ± .011 ml of CSF/min cleared of Mg. Although variation in efflux coefficients was found, no correlation to changes in CSF or serum Mg concentrations could be made. After 2 hours of perfusion, 7.5% of the total isotope perfused was recovered from the brain. Following intravenous Mg^{28}, brain specific activity averaged only 4.6% of serum specific activity after 4 hours. Hence, an influx coefficient of isotope from serum could be measured and was .024 ± .007 ml of serum/min cleared of Mg. This was not affected by altering CSF Mg concentrations. When serum Mg concentration was raised, lower influx coefficient values were obtained. Preliminary work indicates that the chief source of Mg entering the CSF is from serum and less from brain. It is concluded that within the concentration limits in these experiments Mg may be cleared from CSF by passive diffusion. Serum Mg enters CSF by a concentration dependent process which in view of the existing gradient may represent active transport.

CARDIAC EDEMA AND K^+ LOSS IN THE ISOLATED PERFUSED GUINEA PIG HEART. John M. Ginski. University of Tennessee School of Basic Medical Sciences, Memphis, Tennessee

Progressive development of edema in the isolated guinea pig heart perfused for intervals of 15, 30, 60, 90 and 120 minutes, was studied. The ventricular dry solid weight, related to total body weight, did not change during these time intervals. Comparison of dry-wet ratios indicated a marked edema developed by 15 minutes, decreasing from 19.14% ± 0.77 to 16.57% ± 1.14. During the time intervals studied further edema did not occur. The initial edema formation could be retarded by addition of homologous erythrocytes to the modified Ringer-Locke solution used and was related to the total number of erythrocytes perfused through the heart/gram of ventricular wet weight. In the non-perfused guinea pig heart the ventricular electrolyte concentrations, expressed in meq/Kg wet weight for Na^+ is 60.0 ± 3.7; K^+, 89.9 ± 4.7; Mg^{++}, 29.6 ± 1.5 and Ca^{++}, 3.6 ± 0.5. Comparison of the non-perfused heart to those perfused for 120 minutes showed marked changes: Na^+ was elevated by 60% and Ca^{++} by 133%; K^+ was decreased by 34% and Mg^{++} by 29%. The degree of these changes appeared to be related to the rate of coronary flow. The loss of K^+ was modified by the addition of erythrocytes. Plotting K^+ concentration against total erythrocytes perfused produces a sigmoid-like curve with inflection points approximating 5 x 10^9 RBC/g ventricle/2 hr and 25 x 10^9 RBC/g ventricle/2 hr. This data suggests that by using a relatively low concentration of erythrocytes, edema formation and loss of K^+ can be prevented in this preparation. (Supported in part by USPHS HE 07674 and Tenn. Heart EC2.39 A63.742.)

The Carotid Baroreceptor Cardioinhibitory Reflex in the Cat. K. H. Ginzel (intr. by Earl Eldred), Riker Laboratories, Northridge, Cal.

The role of the cardioinhibitory center and of efferent vagal fibers in reflexes arising from baro- and chemoreceptors is still controversial. Experiments were designed to study reflexes mediated through the vagi, without interference from anesthesia and sympathetic outflows of supraspinal origin. In cats the spinal cord was divided at C1 under ether anesthesia. The vagi were left intact constituting the only nervous connections between the head and the body of the animal. Injection through the lingual artery into the carotid sinus of nicotine, sebacylcholine and potassium cyanide, stimulation of the carotid sinus nerve (10-100/sec), and increases in pressure in the isolated perfused sinus region all produced bradycardia and hypotension which were dependent on the intactness of the carotid sinus nerve and both vagi. Perfusion of the carotid sinus at constant pressure with hypoxic and hypercapnic blood known to excite chemoreceptors, had no influence on heart rate or systemic blood pressure. Thus, it appears that the fall in heart rate and blood pressure elicited by the above measures was due to activation of fibers ascending from baroreceptors to the cardioinhibitory center. Moderate doses of pentobarbital or chloralose, or light anesthesia with ether or Metofane reduced or abolished these responses but did not abolish reflex bradycardia and hypotension elicited by phenyldiguanide or veratridine injected intravenously. Similar results were obtained in decerebrate preparations in which the sympathetic outflow was left intact. It is concluded that a substantial portion of the baroreceptor reflex in the cat is mediated via the efferent vagus nerves; this reflex is centrally blocked by anesthesia and has, therefore, escaped observation in the past.

I. NORMAL MAN AND CHRONIC HYPERCAPNIA: METABOLIC ASPECTS

H. Glatte, G. J. Motsay, (intr. by B. E. Welch)
USAF School of Aerospace Medicine, Brooks AFB, Texas

Seven normal volunteers were exposed for five days to an environment of 21 mm Hg CO_2 (3%) at a total pressure of 700 mm Hg. Oxygen partial pressure was adjusted to provide normal alveolar levels. The five-day experimental period was bracketed by two five-day control periods. Subjects ate a constant liquid diet of known make-up. Metabolic measurements included daily serum and urine electrolytes, total CO_2, and arterial (capillary ear blood) pH and P_{CO_2}. End tidal air samples were collected daily for alveolar P_{O_2} and P_{CO_2}. Throughout the study, daily urinary 24-hour hydrogen ion excretion was measured (NH_4^+ + titratable acidity - HCO_3^-). All subjects tolerated the experimental atmosphere for five days with no undue problems. Symptomatology was limited to awareness of increased rate and depth of breathing and mild frontal headaches. Arterial and alveolar P_{CO_2}'s increased 3-4 mm Hg in the experimental atmosphere with an initial decrease in arterial pH from controls of 7.40 down to 7.37 by the first day. Arterial pH returned to control levels by the third to fourth day of exposure. A small but significant increase was noted in serum total CO_2 commensurate with a 2-3 mEq/l drop in plasma chloride levels. No definite chloruresis was seen. No increase was noted in NH_4^+, titratable acidity or net 24-hour H^+ excretion during the experimental period. The 24-hour H^+ excretion decreased in the follow-up control period. From the foregoing, it was concluded that endogenous buffers and respiratory mechanisms were adequate to compensate the respiratory acidosis as no increase was noted in renal acid excretion.

EFFECT OF GAS DENSITY ON THE WORK OF BREATHING. S.C.Glauser, E.M.Glauser and B.F.Rusy (intr. by E.M.Greisheimer) Temple Univ School of Med. Phila. Pa

The effect of gas density on the work of breathing may become important as man begins to live at great depths under the sea. At these depths it becomes necessary for him to breathe gaseous mixtures of densities much greater than air at one atmosphere, even if the main components are helium and oxygen. As the density increases, the Reynolds Number increases and finally the flow changes from predominantly laminar to turbulent flow. With turbulent flow the work of breathing becomes dependent on the density of the gas breathed. To simulate this situation, SF_6-O_2 mixtures can be breathed as they have a density 6 times that of air and 49 times that of helium. The work of breathing was measured by the increased O_2 consumption with the increase in minute volume in a rested supine subject. The change in minute volume was effected by increasing the CO_2 in the inspired gas to 7%. O_2 consumption was determined by measuring the inspired volume and O_2 concentration and the expired volume and O_2 concentration. All O_2 concentration were determined by Scholander analysis. It was found that at minute volume of 45 l/min, the difference in O_2 consumption between breathing air and breathing SF_6-O_2 mixtures was 173 ml O_2/min. This minute volume corresponds with a ventilatory response that would be evoked by mild to moderate work. Thus it can be seen that the cross over point where as much or more extra O_2 is metabolized by the work of breathing as is inhaled has not been reached in spite of very dense gases and extremely turbulent flow.

SITES OF SPECIFIC SENSORY AND COMMISSURAL SYNAPTIC ARRAYS ON CORTICAL PYRAMIDS. A. Globus and A. B. Scheibel (intr. by J. D. Schlag). Dept. of Anatomy, University of California, Los Angeles, Calif.

Precise sites of termination of corticipetal afferents can be determined by using the Golgi method to visualize areas of dendrite spine loss one month following surgical interruption of selected tracts. Using this technique we have been able to delimit terminal locations of the geniculo-calcarine and commissural (corpus callosal) afferents upon visual cortex in rabbits. Experiments with 50 unilateral enucleations, 5 posterior callosum sections, and a group of appropriate controls produced the following results. Experimental cortices in animals with enucleation showed reduction in spine counts (35%) along the apical dendrites. Spine populations were not reduced elsewhere. Animals with sectioned callosums had a reduction in spine counts (50%) limited to oblique branches of the apical dendrites. This is in accordance with morphological observations that the specific afferent arbors rise through the cortex perpendicular to the pia and parallel to the apical dendrites while corpus callosal afferent twigs ascend obliquely through the cortex, parallel to the oblique branches of the apical dendrite. We conclude that 1. specific afferent synapses are effected along the apical dendrite, 2. callosal afferents synapse along oblique branches, and 3. these findings suggest a spatially organized afferent array on cortical neurons similar to that demonstrated in hippocampal pyramids and spinal motor neurons. (Supported by NB 01063.)

STRUCTURAL SPECIFICITY OF LUNG LECITHINS DURING FETAL DEVELOPMENT. L. Gluck, R.A. Landowne and M.V. Kulovich (intr. by C.D. Cook) Yale Univ. Sch. of Med., New Haven, Conn.

Studies of phospholipid biosynthesis in developing mammalian lungs (Gluck et al, Abst. Am. Ped. Soc., J.Pediat., 1966) have shown that purified lecithin from the lung of the young rabbit fetus is not surface active (normal surface activity of fetal lung extract appears at 28 days gestation) while that of the term fetus or the adult is. The fatty acid components of these lecithins change with maturation toward a higher proportion of saturated fatty acids. However, these findings do not indicate any fundamental structural differences in lecithins between early and late fetuses or adults. It is important to know if there is, with maturation, preferential esterification of the saturated fatty acids on either the α- or the β-carbon of lecithin. Accordingly, purified lecithins from lungs of rabbit fetuses between 21 and 31 days (term) and from adult lungs were treated with phospholipase A (Naja naja venom), cleaving the fatty acids from the β-carbon. These fatty acids and those from the α-carbon of the resultant lysolecithin were analyzed separately by gas liquid chromatography with the following representative results:

Carbon		21 day	23 day	27 day	Adult
α	% sat. fatty acids	46.3	50.3	82.3	78.7
	% unsat. fatty acids	53.7	49.7	17.8	21.3
β	% sat. fatty acids	42.5	40.4	36.8	37.7
	% unsat. fatty acids	57.5	59.6	63.1	62.3

The composition of the individual fatty acids on the two carbons in the young fetus are essentially identical. In late gestation and in the adult, however, there is specific esterification of saturated fatty acids on the alpha carbon, the most abundant one being palmitic (C_{16}) acid.

RESPONSE OF NEURONS OF THE SUPERIOR OLIVARY COMPLEX OF THE DOG TO DICHOTIC STIMULI. Jay M. Goldberg and Paul B. Brown (intr. by D. J. Ingle). Dept. of Physiol., Univ. Of Chicago, Chicago, Ill.

It has proved difficult to obtain data on the discharge properties of cells of the medial superior olivary nucleus (MSO) of the cat, partly because, as in most species, the nucleus consists of a thin ribbon of cells. Microelectrode studies are somewhat easier in the dog because the ribbon is folded into a relatively thick U-shaped structure. Two kinds of cells are commonly encountered in the MSO and neighboring regions. EE cells are activated by tones delivered to either ear; EI cells discharge when tones are presented to one ear (usually the contralateral ear) and are inhibited by stimulation of the other ear. EE cells are sensitive to changes in the average intensity of tones delivered simultaneously to the two ears, but are relatively insensitive to interaural intensity differences. EI cells, in contrast, are quite sensitive to interaural intensity differences. Hence, the discharge of EE cells may be a function of the intensity of high frequency tones, independent of angular displacement from the midline, whereas EI cells may be involved in the representation of such displacements. Cells of both types are affected by phase differences of low-frequency tones presented dichotically. The results indicate that discharge would be a maximum when a binaural stimulus of low frequency was opposite one ear, intermediate when the stimulus was located in the median plane, and minimum when the stimulus was opposite the other ear. Some cells were noted for which a tone presented to one ear was inhibitory, but was distinctly facilitatory when presented simultaneously with certain tones to the other ear. (Supported by Grants NB-05237 and NB-01427 from the Natl. Inst. of Health.)

MEASUREMENT OF DNA IN INTESTINAL FLUIDS. Dale P. J. Goldsmith, University of Nebraska College of Medicine, Omaha, Nebraska.

Experiments were carried out to find a specific and quantitative assay for DNA in intestinal fluids. Nucleoproteins in canine jejunal secretions were precipitated with cold TCA by the method of Croft and Lubran (Biochem. J. 95 612, 1965). Nucleic acids were extracted from the precipitates with hot TCA and assayed for DNA either by the method of Ceriotti (Miller et al, Proc. Soc. Exp. Biol. Med. 106 270, 1961) or the method of Dische as modified by Croft and Lubran (loc. cit.). Alternatively, the nucleoproteins were extracted with hot KOH, from which DNA and proteins were precipitated with acid. The DNA in this precipitate was extracted into hot perchloric acid and determined spectrophotometrically in the ultraviolet region. In a series of assays on the same sample of intestinal fluid, the following values for DNA were obtained by the three methods (numbers in parentheses indicate number of determinations): Ceriotti (4) 2533 μg, SE 117; Dische (8) 2634 μg, SE 49; U.V. (4) 2873 μg, SE 93. In another set of experiments a sample of secretion was divided into several equal portions, half of which were treated with 1000 μg pure DNA each. The nucleoproteins and nucleic acids in each portion were precipitated with TCA and the precipitates assayed for DNA as described above. The percent of added DNA recovered in two or four trials with each method was: Ceriotti, 76 and 100%; Dische, 100, 97, 83 and 114%; U.V. 61 and 99%. Each method thus appears to measure DNA reasonably well, although the Dische method is the best. The similarity of results in the three procedures suggests a high degree of specificity of each method for DNA, and a lack of interference by extraneous substances.

THE EFFECT OF VENTROMEDIAL TEGMENTAL LESIONS ON THE DISPOSITION OF DOPAMINE-H^3 IN THE MONKEY. M. Goldstein, B. Anagnoste, W. S. Owen and A. F. Battista (intr. by A. Janoff). N.Y.U. Medical Center, Depts. of Psychiatry and Neurosurgery. New York, N.Y. 10016

To elucidate the factors which cause the decrease of catecholamine content in the striatum following ventromedial tegmental lesions in monkeys, the storage and metabolism of dopamine-H^3 in the caudate nucleus of these animals were investigated. Two to six months after lesion production, the animals were injected with dopamine-H^3 (50 μc, 5 μg) into both lateral ventricles of the brain by a stereotaxic technique. Three hours after administration of the labeled dopamine the animals were killed and the caudate nucleus from the lesion side and the intact side were dissected and labeled amines were isolated by previously described procedures. In all three experiments the accumulation of dopamine-H^3 in the caudate nucleus on the lesion side was decreased by approximately 90%, while 3-methoxydopamine accumulated to a greater extent on the lesion side than on the intact side. The concentration of the newly formed norepinephrine-H^3 was 40-60% lower on the lesion side as compared with the norepinephrine-H^3 levels on the intact side. These results demonstrate that the ventromedial tegmental lesion primarilly affects the storage of dopamine in the ipsilateral caudate nucleus and support the idea that these lesions might produce a degeneration of dopamine neurons. (Supported by grants from P.H.S. MH-02717, NB-04257 and by N.S.F. GB-3176).

ORGAN PERFUSION WITH FLUOROCARBON FLUID. Frank Gollan and Leland C. Clark, Jr., VA Hospital, University of Miami School of Medicine, Coral Gables, Fla., and Medical College of Alabama, Birmingham, Ala.

The solubility and diffusibility of gases are much higher in organic fluids than in water. A synthetic fluorocarbon fluid (FX-80, 3M Company, St. Paul, Minn.) dissolves considerably more oxygen than whole blood. Since this fluid is inert and nontoxic, mice, rats, cats and pups can use it as a respiratory medium at atmospheric pressure for many hours. On returning to air the fluorocarbon fluid evaporates from the lungs and the animals survive. (L. C. Clark and F. Gollan. Science, in press). In this series of experiments isolated rat hearts were perfused alternately with oxygenated diluted blood and fluorocarbon fluid for one hour. The rat hearts continued to contract vigorously when perfused with oxygenated fluorocarbon fluid at room temperature. This fluid has a viscosity of 0.8 centistokes and a density of 1.77 and the perfusion pressure can be lowered to about one third of that of blood to obtain the same flow. In washing out the organic fluid with blood, the perfusion pressure has to be raised again to achieve adequate flow and contractility. The perfusion of isolated organs with such a water immiscible, nonpolar fluid containing no ions may lend itself to a study of intermediary metabolism.

MECHANISMS OF ANESTHESIA: NITROUS OXIDE INHIBITION OF SODIUM TRANSPORT. SHELDON F. GOTTLIEB AND STEPHEN V. SAVRAN*. DEPTS. OF PHYSIOLOGY AND ANESTHESIOLOGY, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

Bags made of inverted frog (Rana pipiens) skin were filled with 0.4 strength oxygenated Ringer's solution and exposed in a pressure chamber to nitrogen or nitrous oxide with a small concentration of oxygen. Changes in sodium ion concentration were measured after 20 to 22 hours of experiment. With increasing concentrations of nitrous oxide in the range of 100 to 200 psig inhibition of sodium transport increases. The sodium transport inhibition was shown not to be due to pressure per se since 175 psig nitrogen did not measurably inhibit. Experiments using the short circuit technique indicate that inhibition of sodium transport induced by nitrous oxide is reversible. The sodium transport inhibition paralleled previously reported effects of nitrous oxide-induced depression of nerve excitability (Carpenter, F., Am. J. Physiol. 178, 505, 1954: Gottlieb, S. F. and Weatherly, J. M., Am. J. Physiol. 208, 407, 1965). It is postulated that alterations in ion transport may be part of the basic mechanism which produces anesthesia.

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CORRELATION OF GASTRIC MOTILITY AND SECRETION WITH A VAGAL STIMULANT (2-DG) AND WITH HISTAMINE IN THE FISTULA DOG. G. R. Grahame*, J. M. Garrett*, D. Godwin* and B. I. Hirschowitz. Dept. of Med., Div. of Gastroenterology, Univ. of Ala. Med. Ctr., Birmingham, Alabama.

Antral motility was recorded continuously from a 2 x 2 cm water filled balloon inserted 1 cm beyond the gastric cannula. H^+ and pepsin were measured in consecutive 15 minute samples of gastric juice. In 6 studies in 5 dogs following a one-hour basal period, 2-DG (100 mg/kg) was infused IV for 30 minutes and observations continued for 2 hrs. In the basal hour, mean secretion was 8 ml (0.4 mEq H^+) and Type II motor activity was present 13% (av.) of the time. Nine minutes (av.) after starting 2-DG, rhythmic Type II contractions (5/min.) began and were found in 72.8% (53, 53, 93, 79 & 84 resp.) of the succeeding hour during which time all the dogs showed marked stimulation of secretion (127 ml, 16.2 mEq H^+). Both motility and secretion continued to the end of the 2 hours of observation. Atropine (0.08 mg/kg) intravenously stopped motility in 15 secs. and prevented motility and secretion when given before 2-DG. In each of 3 dogs, after 60 min. without stimulation, (H^+ = 0, motility = 26%), histamine (6.5, .12, 25 and 50 µg base/kg/hr) was infused IV for 2 hrs. Although a graded response of H^+ secretion up to maximum was obtained, no definite increase or decrease of motility compared to basal motility was observed. Likewise in 2-DG stimulated dogs the maximal dose of histamine (50 µg base/kg/hr^{-1}) had no consistent effect on motility. Thus 2-DG results in vagal stimulation of electrolytes, pepsin and motility whereas histamine acts only on electrolyte secretion. (NIH Support).

RECIPROCAL TIME-VASCULAR VOLUME-AND CONDUCTANCE IN VASCULAR BEDS. H. D. Green, C. E. Rapela, C. I. Porciuncula,[x] R. Carter,[x] and T. Hosick.[x] Bowman Gray School of Medicine, Winston-Salem, N. C.

Flow ($\dot{Q}$) may be calculated: (1) from the area under the indicator concentration curve using a slug injection, or (2) from the plateau height using a continuous injection of an indicator. Mean transit time ($\bar{T}$) may be computed by: (a) integration of the indicator curve obtained by (1) which then gives a curve that is similar to the curve obtained by (2); (b) computing the area to left and above the integral curve; and (c) dividing the latter area by the plateau height of the integral curve. Vascular volume (capacity) is $Q = \dot{Q} \cdot \bar{T}$. Conductance (1/resistance) is $C = \dot{Q}/P$, where P is effective perfusion pressure. Reciprocal time (proportional to mean velocity) is $\bar{T}^{-1} = C \cdot P/Q = \dot{Q}/Q$. These equations demonstrate that if vascular capacity remains constant, reciprocal time and mean velocity decrease in proportion to flow; if volume decreases in proportion to flow, reciprocal time remains constant; and if volume increases as flow decreases reciprocal time decreases. According to these equations, an increasing value of $\bar{T}^{-1}$ in the presence of an increasing flow indicates that volume is either decreasing or increasing less rapidly than flow; or, if flow is decreasing, that volume is decreasing more rapidly than flow. Reverse relationships are indicated by a decreasing value of $\bar{T}^{-1}$. (Supported by PHS grants 5 T1 HE 5392 and HE 00487, and a grant from NCHA.)

PHYSIOLOGY OF MOLLUSCAN VISCERAL NON-STRIATED MUSCLE: THE GUT OF THE CHITON, PONEROPLAX ALBIDA. M. J. Greenberg, G. Burnstock, A.G. Willis, and Susan Kirby (intr. by H. Lipner). Dept. of Zoology, University of Melbourne, Australia.

Two anatomically distinguishable regions of the chiton gut were studied: posterior intestine (P.I.) and rectum. Histological observations were made; the rectal innervation is the denser of the two areas. The electrophysiology of the gut was studied by the sucrose gap technique. The P.I. resembles vertebrate "unitary" smooth muscle: it is spontaneously active with a low resting potential; slow waves, unassociated with tension changes, are common; spikes, or trains of spikes, sometimes appear on the crests of slow waves and are associated with contraction. Responses to intramural nerve stimulation seem to include both excitatory and inhibitory components; rebound excitation follows recovery from inhibitory nerve stimulation. Direct muscle stimulation is possible only with long duration pulses. Rectum electrophysiology was like that of vertebrate "multiunit" smooth muscle; it is usually not spontaneously active; resting potential is high, and there are no slow waves. Short pulse intramural stimulation produces junction potentials which facilitate with repetitive stimulation leading to spikes and contraction; procaine and cinchocaine block reversibly these electrical and mechanical responses. The pharmacology of the P.I. and the rectum are similar. Acetylcholine (ACh), catecholamines, and 5-hydroxytryptamine (5HT), depending on dose, either depress or excite gut mechanical activity. 5HT depression of the rectum is more marked than that of the P.I. Benzoquinonium inhibits ACh, but not 5HT. Methysergide blocks 5HT. In spite of differences in detail, the chiton gut control mechanism is probably similar to that of other molluscan visceral muscles. (Supported by NIH Grant HE09283, and by the NSF).

FURTHER STUDIES ON THE RENAL EXTRATUBULAR ACTION OF VASOPRESSIN*
Edward H. Grinnell*, Jeno Kramar and Willard M. Duff*. Creighton Medical School, Omaha, Nebraska.

Antidiuresis was formerly believed to be the result of an exclusive tubular effect of vasopressin. Previous observations of creatinine excretion in alcoholized hydrated rats indicated a typical biphasic change during vasopressin induced antidiuresis: decrease followed by increase. This observation suggesting an extratubular factor in the renal response has been further analysed. (1) The possibility of the biphasic change in the creatinine excretion being simply the reflection of a "dead-space" phenomenon in the injection type of experiments was ruled out by statistical means and by the demonstration of similar changes during vasopressin infusion. (2) Observation of inulin clearance in the rat and dog showed evidence that the glomerular filtration rate is, indeed, influenced by vasopressin. (3) Similar changes in inulin clearance found in trained unanesthesized dogs ruled out anesthesia as an interfering factor. (4) Studies on the renal arteries of anesthesized dogs demonstrated decreased blood flow during antidiuresis.

These data obtained from both direct and indirect measurements in rats and dogs justify the conclusion that in these two animal species vasopressin has a definite vascular effect which, to our knowledge, has heretofore not been fully appreciated.

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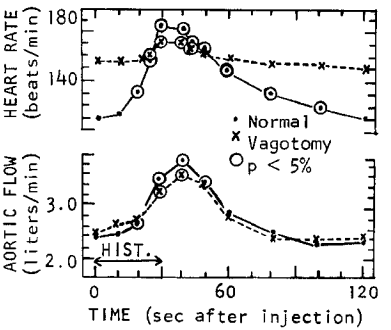
ROLE OF THE VAGI IN THE UNANESTHETIZED DOG'S RESPONSE TO A HISTAMINE-INDUCED HYPOTENSION. H. A. Griscom* and R. S. Shepard. Dept. of Physiol. and Pharmacol., Wayne State Univ. Sch. of Med., Detroit, Mich.

Histamine (2-4 μg/kg, iv) was infused into 5 dogs with implanted electromagnetic flowmeter probes and into 7 without probe implants before and 1 day after bilateral cervical vagosympathotomy. In the animals without the probe implant histamine produced a reduction in arterial pressure both before (-29±4.9 mm Hg) and after (-35±5.8 mm Hg) vagotomy. These dogs also responded to the histamine with an increase in heart rate before vagotomy (+51±9.2/min) that was greater than their increase after vagotomy (+19±5.3/min). In the animals with the probe implant (see figure) histamine produced comparable changes in pressure and heart rate, and an increase in aortic flow. Prior to vagotomy the increase in flow was associated with no significant change in stroke volume (-1.9±1.2 ml), but after vagotomy histamine produced a significant increase (+3.6±0.38 ml) in stroke volume. We conclude that the vagi perform an important role in increasing aortic flow in response to histamine. In the absence of the vagi the dog becomes more dependent upon stroke volume changes to increase the aortic flow.



(Supported by NIH grant NB-03022 and HE-07678)

THE ANTIUROKINASE OF PLASMA AND SERUM. M. Mason Guest, Ted P. Bond* and Paul H. Muehlke*. University of Texas Medical Branch, Galveston, Texas.

Plasma contains large quantities of antifibrinolysins (antiplasmins) which obscure effects of inhibitors of activation in conventional assays. Since profibrinolysin (plasminogen) and fibrinolysin (plasmin) are adsorbed onto fibrin and antifibrinolysins are not absorbed, separation of the activated fibrinolytic enzyme from antifibrinolysins is possible. To assay inhibitors of profibrinolysin activation (antiurokinase), appropriately diluted plasma (or serum) is incubated at 37° for 10 minutes with urokinase in phosphate buffer at pH 6.4. After cooling to 0°, fibrinogen followed by thrombin is added. The fibrin is wound onto a roughened blue glass rod, washed in pH 6.4 phosphate buffer and transferred into pH 7.7 phosphate buffer at 37°. Determined visually, the end point is complete lysis of the fibrin. Blanks (urokinase without incubation with plasma) lyse in 15 minutes. A unit has been established. Evidence has been obtained that the concentration of antiurokinase in plasma is a major determinant of whether or not fibrinolytic activity develops during and following thrombus formation. Based upon the results of preliminary experiments it appears that intravascular clots would not persist in the absence of the inhibitor of fibrinolytic activation. The implications of these findings with reference to heart disease and stroke will be briefly discussed.

(Supported by USPHS grants HE 06238 and HE 09911.)

THE EFFECT OF ENDOTOXIN SHOCK ON PLASMA ZINC CONCENTRATIONS. Bobby J. Gunter*, Lura A. Solomon*, Lerner B. Hinshaw, and Carl A. Nau*, Inst. of Envir. Health; Department of PM&PH, University of Oklahoma Medical Center, and Veterans Administration Hospital, Oklahoma City, Oklahoma.

Acidosis and hemoconcentration have been consistent findings in irreversible endotoxin shock. An enzyme, carbonic anhydrase, identified as a zinc protein complex and present only in red blood cells, is responsible for carbon dioxide transport in blood. It was thought to be of interest to determine if changes in plasma zinc concentrations were correlated with alterations in certain parameters associated with the deleterious effects of endotoxin. Plasma zinc was measured by atomic absorption spectrophotometry. Adult mongrel dogs were intravenously anesthetized with sodium pentobarbital, 30 mg/kg body weight. E. coli endotoxin (Difco) 0.4 mg/kg (LD_{80}), was intravenously injected in experimental animals. Control animals received no endotoxin. Results show that plasma zinc decreased from a mean of 73 ug/100 ml to 52 ug/100 ml the first 24 hours after endotoxin administration. The mean recovery value reached 71 ug/100 ml in the animals surviving endotoxin injection. Plasma zinc concentration decreased with an increase in hematocrit in endotoxin perfusion experiments. Zinc concentrations in control animals remained relatively constant. It is postulated that zinc shifts from plasma to red blood cells or diffuses into intracellular spaces during endotoxin shock.

(Partially supported by USPHS grant HE 09381).

REPRODUCIBILITY OF CIRCADIAN TEMPERATURE RHYTHM IN THE RAT KEPT IN CONTINUOUS LIGHT OF $\sqrt{}$ 30 LUX INTENSITY. Franz Halberg, Walter Nelson*, Walter Runge*, Grover Pitts, Dale Smith*, John Tremor*, Thomas M. Edwards*, Pierre Hahn*, George Cook*, Paul Sebesta* and Otto Schmitt. Univ. of Minnesota, Minneapolis; Univ. of Virginia, Charlottesville; and Ames Research Center, NASA, Moffett Field, California.

Intraperitoneal temperature telemetered as a frequency modulated (American Electronic Labs.) or pulse-code modulated (Franklin Institute) signal from separate groups of mature female rats ($N \geq 6$) was recorded at $\Delta t < 1$ h for spans of $\geqslant 1$ week. From a least squares spectrum (Acta Endocrin. Suppl. 103, 1965) of each individual series, period, τ, and amplitude, C, estimates were obtained, averaged for each group and standard errors computed. For inbred Sprague-Dawley rats kept at 24 ± 1°C ambient temperature in continuous light (LL) of $\approx$ 500, $\approx$ 50 or $\approx$ 5 lux, average τ's were 25.36 ± .05; 25.20 ± .05 and 24.91 ± .05 and C's, in °C, were .39 ± .03; .33 ± .02 and .51 ± .02, respectively. With increasing light intensity in LL the circadian τ lengthened ($P < .01$) but the circadian C was smaller than that in LD. For female inbred Fischer rats in LL $\approx$ 30 lux, τ = 25.34 ± .05 and C = .61 ± .03. For CFE rats (Carworth Farms) in LL $\approx$ 3 lux, τ = 25.28 ± .20 and C = .45 ± .02. For 4 groups of CFE's in LL $\approx$ 30 lux, on solid (Chow) or chemically defined liquid diets, τ's were 25.38 ± .09; 25.45 ± .07; 25.57 ± .08 and 25.38 ± .08, while C's were .31 ± .02; .26 ± 04; .26 ± .04 and .36 ± .05, respectively. For CFE rats in a prototype biosatellite in LL $\approx$ 30 lux, on liquid diet, τ = 25.33 ± .07; C = .61 ± .04. Thus, for several replicate groups of rats from several stocks kept in LL $\approx$ 30 or $\approx$ 50 lux, objective group τ estimates different from the lunar or solar day were reproducibly found in studies preparatory to a biosatellite survey of circadian and other temperature rhythms.

SENSORY THALAMUS IN HEDGEHOG. W. Hall*, R. P. Erickson, J. A. Jane*, M. Snyder* and I. T. Diamond, Department of Psychology, Duke University, Durham, North Carolina.

The dorsal thalamus in the hedgehog is poorly differentiated and GM, GL, VP and Po often coalesce without clear boundaries. This organization would appear to provide a good chance to test our idea that the exquisite sensitivity of single thalamus neurons to a restricted range of stimuli may be an achievement of a secondary stage of mammalian evolution. Accordingly we explored the sensory thalamus with microelectrodes, in the presence of clicks, light flashes and electrical and mechanical stimuli applied to the body. In 13 hedgehogs deeply anesthetized with pentobarbital 87 thalamic neurons were found to be responsive. If we place all units located in doubtful or borderline zones in the catchall class Po, then the following results were obtained: all 9 units found in GL responded only to light; 17 out of 27 units in GM responded only to auditory stimuli and 7 of the remaining 10 responded to both somesthetic and auditory stimuli. In VP, 17 out of 29 units had restricted receptive fields while 12 units had widespread receptive fields, or were responsive to clicks, or both. The responses of many units which could be evoked only by stimuli of one modality were blocked by stimuli in a second modality. The convergence of input upon single neurons may represent a primitive level of organization but this is not necessarily the opposite of complex. We conclude, using the criterion of convergence, that the hedgehog thalamus is more primitive than the opposum which in turn is more primitive than the cat. (Supported by PHS grant MH4849 and NSF grant GB2087.)

Biological Effects of Possible Spacecraft Atmospheres: Exposure of Rabbits to Helium, Neon, Nitrogen, Argon and Oxygen by
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Union Carbide Corp., Linde Div. Research Lab., Tonawanda, N. Y.

Practical experience has shown that for short space flights a low pressure pure oxygen atmosphere is acceptable; for longer flights a two-gas atmosphere will be desirable. Our experiments were designed to aid in the selection of the best inert gas diluent. Rabbits were exposed at room temperature in a closed environmental system designed to remove contaminants while conserving inert gas, and to maintain a P_{O_2} of 180 mm Hg, a total pressure of 760 mm Hg, and 50% relative humidity. Seven-day exposures were made with helium, neon, nitrogen or argon as diluents; an additional run was made at a total pressure of 192 mm Hg with only oxygen and water vapor present. A comprehensive biochemical, physiological and hematological surveillance was carried out, for two weeks before the exposure and for four days following it. Oxygen and food consumption, relative to air controls, was increased in helium-exposed animals and reduced in argon-exposed animals; neon and nitrogen caused no differences. No gross changes were observed in biochemical and hematological parameters, but animals exposed to helium showed a slight decrease in hemoglobin, hematocrit and red cell count; and possibly an increased 24 hour Fe^{59} uptake on emerging from the chamber. Only those animals exposed to the low pressure pure oxygen environment lost weight. (Supported by Contract AF 41(609) 2711)

DETECTION AND QUANTITATION OF SUB-CLINICAL CONGESTIVE HEART FAILURE IN DOGS.
Robert L. Hamlin, C. Roger Smith, James N. Ross*. The Ohio State University, Columbus, Ohio.

This study was designed to evaluate the time-sequence for excretion of an oral sodium load administered for five consecutive days following five days of either a low sodium diet or starvation to aged dogs with a high predisposition for congestive heart failure or to dogs with known spontaneously occurring congenital or acquired heart defects. Intake of low Na consisted of fewer than 2 m.Eq. and high Na of over 100 m.Eq. Na/dog/day. Healthy dogs excreted the entire Na load within 12 hours after ingestion. Dogs with severe clinical signs of congestive heart failure excreted less than 15% of the Na load. Aged dogs with mitral insufficiency or asymptomatic dogs with even the mildest heart worm infestation excreted their Na load but took 24 to 72 hours to reach maximal rate of excretion. Impaired ability to excrete a salt load appears to be a sensitive indicator of cardiac disease, and the severity of both impairment and heart disease correlates well. This research is supported, in part, by USPH, NHI, HE-09884-01.

FUMARATE REDUCTASE ACTIVITY IN MARINE BIVALVE MOLLUSKS. C. S. Hammen and Susan C. Lum (intr. by J. Walter Wilson) Univ. of Rhode Island, Kingston, R. I.

Tissue homogenates of six species of lamellibranchs were examined for ability to catalyze fumarate reduction (FR) while oxidizing reduced riboflavin phosphate. These homogenates were also assayed for succinate dehydrogenase activity (SD), measuring phenazine methosulfate and iodonitrotetrazolium reduction photometrically. The ratio of activities, SD/FR, which is the ratio of forward and reverse reactions in the citric acid cycle, has been shown to decrease as organisms become more anaerobic. If it is assumed that the range of values for facultative anaerobes is about 0.1 to 3.0, then Tagelus plebius (6.4) and Donax variabilis (4.6) are predominantly aerobic, Solemya velum (3.0) and Mercenaria mercenaria (2.4) are less aerobic, and Modiolus demissus (0.28) and Crassostrea virginica (0.08) are facultative anaerobes well adapted to oxygen deficiency. These results are closely correlated with habitat and activity. Tagelus and Donax, although quite different in size, are both vigorous burrowers and are rarely seen without siphons extended. At the other extreme lie Modiolus and Crassostrea, which are sessile and often close the valves tightly for hours when exposed at low tide. The oyster had the greatest FR and the least SD, but the high pumping rates and high oxygen consumption observed in this species indicate not a tendency toward obligate anaerobiosis, but rather an extraordinary ability to shift from one form of metabolism to another.

PRESSURE-VOLUME CURVES OF THE GREATER AND LESSER CIRCUITS, Harlan, J. C.* B. H. Douglas,*and T. Q. Richardson. Dept. of Physiology, University of Mississippi Medical Center, Jackson, Mississippi.

The effect of suddenly changing blood volume on greater circuit pressure (GCP) and lesser circuit pressure (LCP) has been studied in mongrel dogs. Approximately one week before measuring GCP and LCP, the dogs were anesthetized with sodium pentobarbital, and a silastic loop was placed around the aorta and pulmonary artery through the fourth intercostal space. One end of the loop was tied to an anterior rib, and the other end was placed subcutaneously in the animal's back. Also, a catheter was placed into the left atrium with the distal end placed subcutaneously. When the dogs had recovered from surgery, they were anesthetized with sodium pentobarbital and catheters for measuring pressures placed into (1) pulmonary artery, (2) right atrium, and (3) aorta. A pump used to transfer blood from a reservoir and from the arterial to the venous system was connected to the dogs by catheters in the left femoral artery and right femoral vein. The loop and left atrial catheter were brought to the exterior through a small incision. All pressures were monitored with Statham pressure transducers and recorded with a Grass polygraph recorder. GCP and LCP were measured following infusion of a desired quantity of blood by fibrillating the heart and tightening the silastic loop. Blood was pumped from the aorta into the inferior vena cava until the arterial and venous pressures equilibrated. The equilibrated pressure in the aorta and vena cava, and the equilibrated pressure in the left atrium and pulmonary arterial is the LCP. These preliminary studies indicate that a 19% increase in blood volume causes the GCP to rise from 6.2 mm Hg up to 14 and LCP increased from 9.8 mm Hg up to 18 mm Hg.

Supported by NIH grants.

CHRONICALLY IMPLANTED EPICARDIAL ELECTRODES IN MAN. P.D. Harris,* D.H. Singer* and J.R. Malm* (spon. by P. Gerst). Depts. of Surgery and Pharmacology, Col. of Physicians & Surgeons, Columbia U., New York,N.Y.

Conventional ECG's often do not permit a precise interpretation of the complex arrhythmias seen after cardiac surgery. Data from animal experiments indicate that analysis of local electrograms from selected parts of the heart could provide a more logical approach to the interpretation and treatment of these arrhythmias. These data further show that fine teflon-coated, stainless steel wires of .0007" diameter could be implanted on the heart, left in place for up to six weeks, and withdrawn by gentle traction through the closed chest wall without evidence of cardiac impairment. The wires could be used for recording and stimulating at low current strengths throughout this period. This technique therefore seemed applicable to man. Similar wires have since been implanted epicardially onto selected atrial and ventricular sites in ten patients during cardiac surgery. Records of local electrograms greatly facilitated interpretation of AV dissociation and of ectopic rhythms, particularly the distinction between supraventricular and ventricular rhythms. In some instances, His bundle rhythms were found to be associated with the absence of atrial electrical and mechanical activity. Atrial or ventricular stimulation by a battery pacemaker permitted regulation of cardiac rate and suppression of ectopic rhythms. Removal after 1 - 7 days took place without incident. Preliminary studies also indicate that the method is suitable for investigation of cardiac electrical activity in man, as well as for diagnostic and therapeutic purposes.

THE CIRCULATORY RESPONSE TO BRADYKININ DURING HYPOXIA AND AFTER AUTONOMIC NERVOUS BLOCKADE. D.C.Harrison, W.L.Henry, B.Paaso, and H.A.Miller. (Intr. by R.H.Maffley) Dept. of Medicine, Stanford Med.Sch.

In order to determine the effects of hypoxia and the role of the autonomic nervous system on the circulatory response to bradykinin, aortic pressure (AoP), heart rate (HR), right ventricular contractile force (CF), left ventricular pressure (LVP), aortic blood flow (CO), and femoral flow (FF), were measured continuously in 11 open chest dogs while breathing air and 8% oxygen, and after blockade of the autonomic neural receptors. Arterial pH, pCO_2 and pO_2 were measured frequently, and systemic vascular resistance (SVR) and hind limb vascular resistance (HVR) were computed. While breathing air (mean pO_2=98 mmHg) 0.5 μg/Kg bradykinin given IV produced decreases of 42% in AoP, 54% in SVR, and 55% in HVR, and a 56% increase in CO. During hypoxia (mean pO=40 mmHg) there was a decrease of 43% in AoP, 65% in SVR, and 45% in HVR, and a 36% increase in CO. Blockade of the autonomic nervous system was accomplished with atropine 0.25 mg/Kg, phenoxybenzamine 2 to 5 mg/Kg and MJ 1999 0.5 to 3.0 mg/Kg and was confirmed by challenges with acetylcholine, isoproterenol, and synephrine, before and after total block. After blockade, bradykinin produced decreases of 48% in AoP, 60% in SVR, and 54% in HVR, and 42% increase in CO. Changes in HR and CF produced by bradykinin were small during all conditions studied. These studies show that bradykinin acts by direct vasodilatation and this action is not altered by hypoxia. Further, its circulatory effects are apparently not mediated via the autonomic nervous system. (Supported by NIH Grant 09058-02)

METABOLISM OF Mn^{54} AND OTHER CATIONS IN THE FRESH-WATER CLAM. Florence L. Harrison (intr. by G. D. Potter). Bio-Medical Research Division, Lawrence Radiation Lab., University of California, Livermore, California.

The accumulation and distribution of specific cations has been followed in the fresh-water clam Anadonta nuttalliana Lea. The clams were maintained in artificial pond water in an aquarium system designed to maintain the concentration of any given ion at a specified level. With Mn^{54} it was found that manganese was removed from the water against steep concentration gradients. In animals exposed to Mn^{54} for five weeks (manganese level, 0.1 ppm), the radioactivity increased steadily. When the water was replaced with nonradioactive pond water, the activity in the body was decreased by 33% after 10 days and by 36% after 120 days. Uptake and loss were followed simultaneously in 15 parts of the body. The main site of Mn^{54} was a tissue located near the attachment of gills to mantle. After the uptake period it contained about 50% of the Mn^{54} while representing only 2% of body wet weight; stable manganese concentrations as high as 3% of dry weight were found. In this tissue the intracellular Mn^{54} was located primarily in 1-to-2 micron granules. Ca^{45}, Zn^{65}, and Co^{60} also accumulated in this tissue; Eu^{155}, Fe^{55}, Sc^{46} and Cr^{51} did not. The activity of the latter ions was high in the digestive system. (Work supported by Div. of Biol. and Med., U.S. Atomic Energy Commission.)

EFFECTS OF CARBON DIOXIDE ON BRAIN TEMPERATURES IN THE MONKEY. J.N. Hayward, Dept. Anatomy, U.C.L.A. and V.A. Hospital, Long Beach, California.

Experiments were performed on adult female rhesus monkeys to determine the relationship between the carbon dioxide induced changes in cerebral blood flow and regional brain temperatures. Thermocouples were implanted chronically in various parts of the brain and in the arterial blood at the arch of the aorta. In awake moving monkeys breathing normally, brain-blood temperature differences of 0.2-0.6C were present for long periods of time (Ref. P.S.E.B.M. 121:547, 1966). When these animals were lightly anesthetized, immobilized and artificially ventilated, it was necessary to keep the end-expired carbon dioxide level between 4 and 5% in order to maintain the normal brain-blood thermal gradients. If the end-expired carbon dioxide level was lowered below 2% by hyperventilation there was an increase in all of the brain temperatures. If the end-expired carbon dioxide was raised to 8% there was a corresponding decrease in all of the brain-blood thermal gradients. These cerebral thermal changes began 1 minute after inhalation of carbon dioxide, reaching a maximum change after 5 minutes and showing marked local differences in the degree of cooling. Since it is known that inhalation of 8% carbon dioxide causes an abrupt increase in cerebral blood flow it must be concluded that the cooling of the brain during hypercapnia was the result of increased removal of brain heat by the blood. The local differences in the brain response to carbon dioxidesuggest that this thermal approach might provide a method for study of regional cerebral blood flow in the chronic animal.

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BIOLOGICAL CHARACTERIZATION OF AVIAN INSULIN

R. L. Hazelwood, J. R. Kimmel and G. H. Pollock (intr. by W. J. Schindler) University of Houston and Kansas University School of Medicine.

Efforts were made to establish the potency and the biological characteristics of avian insulin by comparing it with crystalline beef, pork and sheep preparations in in vitro and in vivo systems.

Crystalline insulin was prepared from frozen chicken pancreas by methods reported earlier. (Fed. Proc. 25:761, 1966). In comparison with equivalent amounts (weight) of mammalian insulin the avian hormone is equally effective in promoting glucose uptake in the isolated rat diaphragm, is more effective in producing hypoglycemia with concomitant hepatic glycogenesis in birds, and 25% less effective than beef hormone in producing hypoglycemia and hepatic glycogenesis in rats. Bovine insulin injected into normal chickens is considerably less (30%) effective in altering these parameters than when the avian hormone is injected in equivalent amounts. Thus, the data indicate that the "avian resistance" to mammalian insulin may be an indication of inhibitory avian plasma factor(s). In vitro studies employing incubations of homologous and heterologous sera and insulin mixtures support this suggestion.

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ROLE OF EARLY EXPERIENCE IN DETERMINING THE BLOOD PRESSURE RESPONSE TO SOCIAL STRESS. Henry, J.P. and Stephens, P.,* Dept. Physiology, U.S.C. School of Medicine, Los Angeles, California.

Scotch has ascribed a role to social stress in the pathogenesis of hypertension in man (Am.J.Pub.Hlth.53:1205, 1963). Christian describes changes in the glomerular mesangium in animals under social pressure (Prog.Horm.Res. 21:530, 1965). We (J.Geront. 20:239, 1965) have described the lifelong normotension (126±12 mmHg) of sibling CBA mice separated for sex and living with minimal competition in standard 11x5 x5" boxes. Six such boxes were connected into a circle by 1" tubing. In each of two experiments 25 males and 25 females were placed in the circles. All were 120 days old having lived in isolation in 1 pt. jars from age 10 days. One further experiment used a likesized group the majority of which had been "socialized" by breeding in situ in the circle. Competition of varying intensity developed among the males in all "circles" and with it sustained pressure elevations which persisted despite ether anaesthesia, i.e., 154±8 mmHg (control) and 149±7 mmHg (ether). Supported by NASA Grant No. N_8G-433.

		Blood Pressure mmHg			Adrenal	Body
		0-3 mo.	3-6 mo.	6-9 mo.	mg.	Wt.Gm.
Early social deprivation I	♂	150	163	189	5.5	25.9
	♀	144	144	150	5.1	28.6
Early social deprivation II	♂	153	164	160	5.4	29.0
	♀	145	144	145	6.9	26.4
Early social adjustment	♂	144	143	138	4.3	32.0
	♀	131	138	130	6.0	26.1
Isolated in jars: no social stress	♂	128	130	132	3.2	33.2
	♀	124	125	124	5.1	30.2
Normal sibling controls in standard boxes	♂	127	127	129	3.6	31.4
	♀	120	124	125	4.9	27.4

BLOOD FLOW RATES THROUGH SEVERAL ADIPOSE TISSUE DEPOTS OF UNANESTHETIZED RATS. J. Alan Herd and H. Maurice Goodman. Harvard Medical School, Boston, Massachusetts

Blood flow rates through interscapular, mesenteric, retroperitoneal, epididymal, and inguinal adipose tissue were determined in fed Holtzman rats weighing 200 g. Measurements made during the day when animals were sleeping were compared with those made during the evening when the animals were active and feeding. The method involved I.V. injection of tritium-labelled D.D.T. and measurement of radioactivity in arterial blood of rats sacrificed at 15 min intervals after injection and in adipose tissue of rats sacrificed 3 hr after injection. The animals were restrained initially for I.V. injection, freed into their cages for the 3 hr period in which D.D.T.-^{3}H accumulated in their adipose tissue, and anesthetized ultimately for blood and tissue sampling. During the day, the rates of blood flow were 0.27 ml/min per g of wet tissue in interscapular brown fat, 0.16 ml/min in mesenteric fat, 0.15 ml/min in retroperitoneal fat, 0.10 ml/min in epididymal fat, and 0.10 ml/min in inguinal fat (n=12.) Expressed as ml/min per g of fat-free tissue, these values averaged about 0.5 ml/min, about the same as the rate of hepatic blood flow. During the evening, rates of blood flow through all depots were about 50% greater than during the day.

STEADY-STATE AND TRANSIENT RESPONSES OF VENTRICULAR OUTPUT TO VARIED AFTER-LOAD PRESSURE. Caleb Herndon*, Kiichi Sagawa, and Tsuneaki Sugimoto*. Univ. of Miss. Medical Center, Jackson, Mississippi

A recent study by the author on steady-state left ventricular output against a wide range of mean aortic pressure (after-load) in open-chest, isolated canine heart preparations revealed that, when left atrial pressure (pre-load) was set and controlled at relatively low levels (3 to 5 mm Hg) ventricular output remained almost constant over mAP ranging from 30 to 150 mm Hg, whereas, it indicated steady and increasingly marked decrease over a similar aortic pressure range when LAP was maintained at higher levels (8 to 15 mm Hg). Thus the effect of after-loading pressure on ventricular output was dependent upon pre-loading conditions. Epinephrine was found to extend the steady-state characteristic curve toward higher mAP ranges. In a separate series of experiments, transient response characteristics of ventricular output to changing after-load pressure was investigated by varying mAP sinusoidally with a fixed amplitude ($\pm$ 30 mm Hg) and several frequencies (0.5, 1, 2, 4, and 8 cycles/min.) around three mAP levels (60, 120, and 150 mm Hg). Considering the above stated influence of pre-loading conditions, the frequency response run was repeated with two different LAP levels (5 and 10 mm Hg approx.) in individual animals. If one regards variation of after-loading pressure as input to the contracting ventricle and alteration of cardiac output as its output, the system exhibits the property of first order differential element (or a high pass filter). The time constant of the system (T in kTs/1 + Ts) was found a function of mAP. Elevation of mAP rendered the time constant larger at any LAP. At higher LAP's, however, this effect of AP on T was clearer.
(Supported by USPHS Grant HE 09644.)

SLEEP PATTERNS IN HYPOTHYROID PATIENTS. G. Heuser, A. Kales, A. Jacobson, M. J. Paulson, J. R. Zweizig, R. D. Walter and J. D. Kales. (intr. by D. H. Solomon). Depts. of Medicine, Psychiatry, Anatomy, the Brain Research Institute and the Neuro-endocrine Clinic, Univ. of California, Los Angeles, Calif.

Hypothyroid patients often show sleepiness and behavioral abnormalities. A detailed study of their sleep patterns, correlated with behavior, has not previously been reported. We investigated this relationship in 7 ambulatory hypothyroid patients. It was possible to study 4 of these before (with PBIs of 1.2, 1.9, 2.8, 2.9 respectively) and after therapy with dessicated thyroid. Each of these 4 subjects was studied for 3 consecutive nights in either phase (hypo- and euthyroid) of the project to allow for adaptation and base line sleep measurements. EEG, submental EMG and eye movements were continuously monitored with standard scalp and facial electrodes. In 3 of the subjects there was no significant difference in sleep patterns before and after treatment: Absolute and percentage time spent in rapid eye movement (REM) and non-REM sleep (stages 2,3,4) were similar and in agreement with findings reported for normal adults. The fourth subject, who was clinically the most severely hypothyroid, showed almost no slow wave sleep (stages 3 and 4) prior to treatment, with a significant increase when euthyroid. In all patients, the time from lights-out till sleep onset and first REM period was not significantly different in the hypothyroid state. Psychological tests revealed a consistent personality pattern before and after therapy. However, there was more emotional lability, increased anxiety and somatization and less organized cognitive functioning in the hypothyroid state. In conclusion, sleep patterns in patients whose hypothyroidism is moderately severe, are not significantly different from those in the euthyroid state or in normal adults. (Supported in part by USPHS Grant no. MH 10083.)

TWO COMPONENTS OF PRESSURE-VOLUME HYSTERESIS IN CAT LUNG. Jacob Hildebrandt (intr. by A. C. Brown). Dept. of Physiol. and Biophys., Univ. of Wash., Seattle, Washington.

Previously we reported (Physiologist 8:193, 1965) that the mechanical properties of lung tissue, as determined by forcing the lung volume sinusoidally in a plethysmograph, were in several respects consistent with a viscoelastic model. The present paper reports the results of testing the model by forcing the volume of excised cat lungs in a square wave pattern. In a linear system, the pressure transients following step changes in volume can be used to derive a model of the system, and thus to predict the pressure response to other input waveforms, such as sines or triangles. In the case of the lung, however, it was found that, even for small perturbations of 2-5% volume change, only the magnitude of the sinusoidal pressure response could be predicted quantitatively, whereas the experimental phase angle was roughly twice the size predicted by the step response. By comparing experimental steady-state sinusoidal responses to those predicted from an analysis of viscoelastic stress relaxation following sudden lung expansions or compressions, it can be concluded that some energy-dissipating process in addition to relaxation is involved. This process is not time or rate dependent, but position dependent, and could be termed static tissue hysteresis to distinguish it from viscoelastic, or dynamic tissue hysteresis. An extension of the small-signal analysis into the large-signal nonlinear region (up to 40 ml tidal volumes, or 20% volume change) with the aid of a computer-simulated nonlinear viscoelastic model confirmed that here, too, 1/3 to 1/2 of the energy losses were of the static hysteretic type, and 1/2 to 2/3 were of the viscoelastic or dynamic hysteretic type. (Supported by Training Grant PHS T1-GM-739-08 from the National Institutes of Health.)

ADAPTATION OF CENTRAL RESPIRATORY NEURONS. Judith R. Hildebrandt (intr. by A. C. Young). Dept. of Physiol. and Biophys., Univ. of Wash. Seattle, Washington.

The adaptive properties of central respiratory neurons can be studied by comparing the natural firing pattern with the intracellularly recorded slow potential underlying the action potentials. However, the validity of this method depends on the extent to which the measured slow potential--usually taken as the firing level--reflects either the threshold potential or the average synaptic potential. In many cases, because the nature of the measured slow potential is hard to determine, it is desirable to use a constant, known input to the cell in the form of an intracellularly applied pulse of depolarizing current. One electrode was used for both intracellular recording and stimulating inspiratory and expiratory neurons in the medulla of the cat. The types of responses of respiratory neurons included 1) a non-adapting discharge with a steady frequency, 2) a very rapidly adapting response with a single action potential or a pair of action potentials and 3) a less rapidly adapting response in which the frequency was high initially and declined progressively. Respiratory neurons which gave either of the latter two responses to constant depolarizing current pulses were those cells whose natural discharge pattern was adapting, that is, cells whose frequency of firing declined progressively even though the depolarization underlying the discharge was maintained or increased throughout the discharge. Cells which gave the first type of response to constant depolarizing current pulses and thus were considered non- or very slowly adapting had a natural discharge pattern which appeared to be wholly determined by the synaptic input to the cell. It is therefore suggested that adaptation normally limits the discharge of most of the central respiratory neurons. (Supported by PHS T1-GM-260-07.)

ROLE OF THE SYMPATHOADRENAL SYSTEM IN THE RENAL RESPONSE TO ENDOTOXIN IN THE PRIMATE. Lerner B. Hinshaw, Dale A. Reins*, Lura A. Solomon*, Vincent Fiorica*, and R. T. Brantley*. V.A. Hospital; Depts. of Physiology and Surgery, Univ. of Okla. Med. Ctr. and Civil Aeromedical Institute, Oklahoma City, Oklahoma.

The purpose of the present study was to correlate the activity of the sympathoadrenal system with the hemodynamic response of the primate kidney to endotoxin. Twenty-one Sooty Mangabey and Rhesus monkeys were anesthetized and the left kidney of each animal was exposed through a retroperitoneal approach. Renal venous blood was drained into a reservoir for blood flow measurement. Blood was continuously returned from the kidney to the femoral vein by means of a Sigmamotor pump. Plasma catecholamines were determined by a fluorometric trihydroxyindole procedure. Monkeys were divided into three groups: controls (no endotoxin); innervated or denervated kidneys (with E. coli endotoxin administered intravenously at a dosage of 4-10 mg/kg body weight). Monkeys not given endotoxin showed relatively constant renal hemodynamic parameters for two hours. In monkeys administered endotoxin, mean renal artery pressure decreased from 118 to 49 mm Hg, blood flow fell from 4.6 to 1.6 cc/min/gm and mean renal vascular resistance increased. Catecholamine concentrations increased in controls from 1.3 to 2.5 and in experimentals from 1.6 to 2.2 micrograms per liter of plasma. Results from injections of phentolamine corroborated the relative absence of elevated catecholamines in the blood of shocked animals. Renal denervation depressed the degree of renal vasoconstriction after endotoxin. It is suggested that the renal vasoconstriction is not due to circulating catecholamines, but occurs partially as a result of sympathetic stimulation. Renal autoregulation, if normally present, was obliterated in shock. (supported by USPHS grant HE-09381)

CONTINUED STUDIES OF THE TROPHIC FUNCTION OF RENAL NERVES. Elliott Lee HIX, Department of Pharmacology, Kirksville College of Osteopathy & Surgery, Kirksville, Missouri.

Surgical denervation of the kidney in day-old puppies arrests morphological and functional development of the organ (Hix, Fed. Proc. 21, 1962). This early dependence of the kidney upon its innervation is most apparent during the first 10 days of postnatal life, i.e. denervation of the kidney in animals older than 10 days produces no marked inhibition of growth or function. This observation suggested that physiologic maturity (secretory and/or impulse transmission) of renal nerves may determine the apparent calendar-age-related kidney response to denervation. To examine this thesis, as well as the probable contribution of non-neural renotrophic factors, the Norepinephrine (NE) and RNA levels in denervated and control kidneys were determined at 2-3 day intervals for 21 days postsurgically. Denervated kidneys showed a consistent 0.7 ug. NE/gm. wet wt. between 1 and 21 days after surgery. The contralateral control kidneys showed the same tissue content of NE for 7-11 days, but after 11 days the NE increased steadily to 1.8 ug. at 21 days. This relationship between postnatal age and NE content of the kidney appeared to correspond well with that postnatal age when denervation fails to arrest or stunt kidney development. Bulk kidney RNA increased in denervated kidneys 21 days after surgery 100% over that of the control kidneys. A greater RNA content (mg./gm. wet wt.) was observed in all denervated kidneys regardless of the morphologic changes denervation produced. Sephadex column chromatography indicated extracted kidney RNA was not degraded, thus the increased RNA produced by denervation was real and not apparent. (Supported by NIH Grant AM0-1761-06 and the American Osteopathic Association)

RELATIONSHIPS BETWEEN LEFT VENTRICULAR VOLUMES AND HEART WEIGHT, BODY WEIGHT & BODY SURFACE IN MAMMALS. J. P. Holt, E. A. Rhode*, and H. Kines*. Heart Research Lab., Dept. Med., Univ. of Louisville, and Univ. of Calif., Sch. of Vet. Med., Davis, Calif.

Left ventricular end-diastolic, EDV, end-systolic, ESV, and stroke volume, S, were measured by the indicator-dilution technique in the control state in anesthetized rabbits, swine, dogs, horses and cattle, whose heart weights, HW, varied 800 fold. HW, expressed as % of body weight, varied from 0.14 (rabbit) to 0.89 (dog), and the relationship between EDV and body weight showed considerable variation. In contrast there was a good relationship between EDV and HW. The following relationships were found in which either one standard deviation was less than $\pm$ 7% or the correlation coefficient, r, was better than 0.986: $EDV = 1.75\ ESV = 0.62\ HW^{0.94}$; $S = 0.43\ EDV = 0.26\ HW^{0.94}$; $CO = 139\ EDV^{0.72} = 97\ HW^{0.68} = 0.04\ BS^{1.18}$. CO is cardiac output; BS is body surface; dimensions are: ml, ml/min., gm, and cm^2. The relationship between rate, R, and HW was: $R = 361\ HW^{-0.26}$ with an r value of -0.95. Constant values for the various species were found for the ratio of L. ventricular muscle wall-thickness to the internal radius of the EDV considered to be a sphere (0.35 $\pm$ 16% SD), and for stroke-work/gm of HW (0.27 $\pm$ 18% SD gm-meter); while CO/gm of HW varied 8 fold and the rate varied 5 fold. It is concluded that the L. ventricle of all mammals is geometrically constructed and functions on the basis of one pattern. EDV, ESV and stroke volumes are functions of heart weight, and cardiac output is appropriately adjusted to the particular metabolic rate and body surface nearly entirely by means of heart rate.

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ADRENOCORTICAL RESPONSE TO SIMULATED HIGH ALTITUDE AND TO OXYGEN AT HIGH PRESSURE. R. T. Houlihan, R. E. Weiner*, and J. Zavodni*. Department of Zoology, Pennsylvania State University.

This study was initiated to investigate the adrenocortical response of rats to simulated high altitude or low oxygen tension and to high oxygen pressure. Animals were maintained in an air environment at 305 mm Hg and 745 mm Hg, absolute pressure and in an oxygen environment at 750 mm Hg absolute. The corticosterone content of plasma and 3 hours adrenal gland incubates was determined at one, two and seven days for the animals in the air environment and at one and two days in the oxygen environment. The steroid was identified by chromatography and fluorescent spectral analysis; and quantitated with sulfuric acid fluoroscence. The results of this study show that in the simulated high altitude there is an initial rise in plasma corticosterone for two days followed by a severe decline at seven days. The corticosterone produced by excised adrenal glands on a ugm per mg wet weight basis declined throughout this study. In oxygen at high pressure no appreciable response was detectable at one day but the plasma corticosterone level at two days had increased significantly. It appears that in these extreme environments the adrenal gland plays a role in the debilitation of the animal. (Supported by NIH grant AM 6323 and NONR contract NR102-654.)

EFFECT OF TEMPERATURE ON ACID-BASE BALANCE IN THE BULLFROG. Barbara J. Howell, Pierre Bouverot*, and Hermann Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Arterial blood samples from indwelling catheters in unanesthetized bullfrogs (R. catesbeiana) display changes in pH which vary inversely with temperature. Before sampling, animals were maintained for at least 3 days at temperatures of 5, 20, and 30°C. Blood was collected directly into heparinized capillary tubes. By the Astrup method samples were equilibrated with various CO_2 tensions for calculating the arterial P_{CO_2} and HCO_3^- (mM/L). Repeated samples could be obtained in the same animal for as long as 3 weeks. The steady state values are shown below.

	5°	20°	30°
pH	8.14	7.84	7.69
P_{CO_2}	8	16	22
HCO_3^-	46	34	26

These pH values (and similar values from other cold-blooded vertebrates) suggest that the difference between the pH of the blood and the pH of water at neutrality (pN) is a constant for this temperature range. Since pN = .5 pKw, the acid-base balance appears to be related to the ionization constant of water as it changes with temperature.

VENTILATORY EFFECTS OF PROGESTERONE IN ACUTE METABOLIC ACIDOSIS AND ALKALOSIS WITH REFERENCE TO THE CHANGES IN CSF., Chin-Tang Huang*, and Harold A. Lyons. Downstate Medical Center, S.U.N.Y., Brooklyn.

Progesterone was investigated for its effect on ventilation during acute metabolic states of acidosis and alkalosis. Changes in ventilation, arterial blood gases, pH and CSF were examined. These parameters were also examined during the breathing of CO_2. Slopes of CO_2 response, $\dot{V}E/PaCO_2$ were respectively 0.65, control; 0.98, progesterone; 0.33, $NaHCO_3$; 0.49, $NaHCO_3$ + prog.; 0.76, NH_4Cl; and 0.82, NH_4Cl + prog. Similar changes of CSF slopes were seen. No changes in pH_{csf} were observed following administration of progesterone. During CO_2 breathing pH_{csf} decreased 0.046 units and pCO_{2csf} rose 6.2 mm Hg, relatively less than respective arterial blood changes of 0.090 units and 11.6 mm Hg. These changes were unaltered after administration of progesterone. A paradoxical shift of pH between blood and CSF was observed in acute metabolic acidosis and alkalosis, similar to previous reports (Robin, Bradley and Mitchell). This alteration was unaffected by progesterone although the ventilatory response was present. The data indicated that progesterone stimulates and increases the sensitivity of the respiratory CO_2 drive, but is mediated in some effector site other than medullary chemoreceptors. (Supported by NIH Grant 5T1-HE-5485-04)

THE ROLE OF THE FOLDS OF HOBOKEN IN THE POST-NATAL CLOSURE OF THE HUMAN UMBILICAL VESSELS. Trevor Hughes (intr. by M.B.McIlroy). Cardiovasc. Res. Inst., Univ. Cal. Med. Ctr., San Francisco, Calif.; Cook County Hosp., and Hoektoen Res. Inst., Chicago, Ill.

The folds of Hoboken are transverse invaginations of the full thickness of the outer part of the umbilical arteries and vein—their function is unknown. In the present study they were examined by direct observation and cinephotography during and after delivery, by histology, and by the preparation of cleared specimens which show the progressive stages of constriction of the vessels. The pressures developed by the contraction of these vessels were also measured. The folds are not present on delivery but form within 30 sec by contraction of the circular muscle. There are usually 2-3/cm along the artery and 1 or less/cm along the vein. The nodes between the folds are still distended with fetal blood and empty over a 2-3 min period, squeezing the blood out of the cord. It is possible that the folds play an important role in the closure and emptying of the vessels after birth. The formation of the folds rapidly decreases the lumen of the vessels in these areas without displacing a large volume of blood. Presumably the narrowing of the lumen of the arteries increases the resistance to flow of blood to the placenta. The apices of adjacent folds then form fixed points which alter the direction of the force of contraction of the longitudinal muscle now arched over the blood in the nodes. It is thus at an increased mechanical advantage to assist the circular muscle to express the blood from the nodes. The pressure developed by a 15-cm segment of artery, isolated between clamps, varies up to 150 mm Hg; by the vein up to 50 mm Hg. These pressures decrease linearly as the vessels empty. (Supp. by USPHS grant HE-5251, HE-06285.)

PRESSURE PROFILE IN A SOFT-WALLED TUBE. Y. Hukushima* and S. Rodbard. City of Hope Medical Center, Duarte, California.

Since the blood flows through soft vessels enclosed in a positive extravascular pressure P_E, we have analyzed the pressure profile in soft-walled vessels in model experiments. Intravascular pressure P_I was recorded by direct writer. A catheter withdrawn at a constant rate from an arterial reservoir (P_A = 100 cm H_2O) to the venous pressure P_V downstream from a soft rubber tube exhibited a negligible pressure drop; pressure energy was converted to kinetic energy with minimal losses. The vessel was then enclosed in a capsule in which P_E could be controlled. When P_E = 70 cm H_2O and P_V = 0, the vessel was partially collapsed and in recurrent oscillation. Pressure fell steadily as the tip was withdrawn until, at the downstream segment, a sharp fall to P_V was observed; effluent velocity was minimal. Elevations of P_V resulted in a progressively reduced perfusion pressure (P_A - P_V). Oscillation amplitude and conductance (flow rate/pressure drop) increased slightly as P_V approached P_E. Oscillations were minor upstream, and marked downstream. When $P_V > P_E$, the vessel was fully distended and flow was laminar with minimal energy losses. Essentially similar data were obtained with P_V = 0, and P_E was varied. The results show that when $P_E = P_I$, stream energy is expended in recurrent collapse of the soft-walled vessel. These results do not support the concept that a "waterfall" or "sluice" controls flow rate. Instead, the energy losses are found to be associated with vascular collapse and the reduced cross section area of the vessel, and the recurrent vibrations. This behavior controls conductance and blood flow. Aided by HE08721, NHI, USPHS.

EFFECTS OF HIGH ENVIRONMENTAL TEMPERATURE ON THE BILIARY SECRETION OF EXOGENOUS AND ENDOGENOUS L-THYROXINE. Max O. Hutchins (Intr. by S. N. Kolmen). University of Texas Dental Branch., Houston, Tex.

90 day old male rats were exposed to an environmental temperature of 34°C 2°C for three weeks. At the end of the treatment period calculations were made of the percent exogenous I^{131}-T_4 excreted into the bile, biliary clearance of endogenous I^{131}-labeled thyroid hormones, body weights and food consumption. All data were compared to that from rats kept at room temperature during the treatment period. In heat exposed rats there was a significant decrease in bile flow and biliary clearance of endogenous I^{131}-labeled thyroid hormones but not in the percent of exogenous I^{131}-T_4 excreted into the bile during a 6 hour collection period. Chromatographic analysis revealed no difference among the hepatic metabolites of exogenous I^{131}-T_4 found in the bile of the treated groups. The reduction in biliary clearance of endogenous I^{131} seen in heat exposed rats was believed to be due in part to a reduction in bile volume, however, when heat exposed rats were given a choleretic, sodium dehydrocholate (Decholin, Ames Co.), during a collection of bile, bile flow became equal to that of normal controls but not to that of controls given Decholin. No change was seen in the biliary clearance of exogenous I^{131}-T_4 in Decholin treated, heat exposed rats. It is concluded that heat exposed rats excrete less endogenous T_4 via the bile than controls, but not I^{131}-T_4 given intravenously. This decrease in hepatic secretion of I^{131}-labeled thyroid hormones is not due to the observed reduction in bile flow in heat exposed rats.

A MATHEMATICAL MODEL OF RENAL AUTOREGULATORY ADJUSTMENTS. P. M. Hutchins*, F. L. Thurstone*, H. D. Green, and H. E. Schmid, Jr., Bowman Gray School of Medicine, Winston-Salem, North Carolina.

A model was constructed utilizing the transient and steady-state characteristics of a typical renal autoregulatory response pattern. The equation for this model is $T_A = \frac{c}{r^3} + P_o r - v\frac{dr}{dt} - m\frac{d^2r}{dt^2}$ where: T_A is the tension per unit length in the afferent arteriolar wall, r is the radius of the afferent arteriole, and c, P_o, v and m are constants. Typical autoregulatory patterns were obtained by presenting step changes in arterial pressure to the kidneys of three dogs exhibiting different degrees of vascular tone. The same step changes in pressure, represented by voltages, were used to force an analog computer simulation of the model. The patterns generated by the computer compared favorably with those observed in the experimental animals. It was found that the only constant that changed significantly during step changes in pressure was v. At present, this model sheds no light as to whether this adjustment in caliber of the renal afferent arteriole with changes in arterial pressure is mediated within the vascular smooth muscle or through some extra-vascular path. It is suggested that in seeking a mechanism of action for this phenomenon, one might find relationships existing between certain factors concerned with autoregulation which summate to give a system equation similar to that described for the model. (Supported by PHS grants GM 1044 and GM 32,046).

	Perfusion Pressure	
tone	step increase	step decrease
high	910	1820
medium	470	1630
low	420	2450
units of v are mm Hg/μ^2 · sec.		

EFFECT OF INTERMITTENT BRIEF INHALATIONS OF 3.5 to 5% CO ON THE DIFFUSING CAPACITY OF THE LUNGS OF HUMANS. R.W. Hyde, R. Rynes*, M. Marin*, and G. Carson*, (intro. by S.Y. Botelho) Dept. of Physiology, Grad. Div. and Dept. of Med., School of Med., Univ. of Pa., Phila., Pa.

We measured the single breath CO diffusing capacity ($D_{L_{CO}}$), at an alveolar P_{O_2} of approximately 120 mm Hg, by inspiring 0.4% CO and 21% O_2 before and at various intervals after 2 brief exposures (single breath held for 6 sec) to a high concentration of CO (3.5 to 5%). In 5 subjects the average control value for $D_{L_{CO}}$ = 35 ml/min/mm Hg. After breathing room air for 30 to 60 minutes following the two single breath exposures to a high concentration of CO, $D_{L_{CO}}$ was found to be 26 ml/min/mm Hg (percentage change -19% to -38%). Two hours after the two brief exposures to the high concentration of CO, the average value for $D_{L_{CO}}$ was 31 ml/min/mm Hg (range: -5% to -21% of control levels). In order to exclude the possibility that the fall in $D_{L_{CO}}$ resulted from errors in the estimate of equilibrated pulmonary intracapillary P_{CO} (P_{cCO}), which is required to calculate $D_{L_{CO}}$, the following additional experiments were carried out: A) P_{cCO} was measured by the 2 minute breath holding method and compared to measurements derived from the carboxyhemoglobin level in the venous blood. P_{cCO} by the two methods agreed within 10%. B) One subject breathed 95% O_2 and 5% CO_2 for a period immediately preceeding the measurement of $D_{L_{CO}}$ at 30-60 minutes after the brief exposure to the high concentration of CO. In this subject the average P_{cCO} was less than 4% of alveolar P_{CO} and thus the P_{cCO} had little effect on the calculated value of $D_{L_{CO}}$. Nevertheless $D_{L_{CO}}$ still fell 21% after exposure to 3.5-5% CO. We conclude that errors in the measurement of P_{cCO} cannot explain the observed decrease in $D_{L_{CO}}$. A likely explanation for the fall in $D_{L_{CO}}$ is that the high concentration of CO has a toxic effect on the pulmonary tissue.

EFFECT OF ORALLY ADMINISTERED PROTEOLYTIC ENZYMES ON CARBON TETRACHLORIDE INDUCED GRANULOMA POUCH. Irving Innerfield* and Herman Cohen, Dept. of Biochem., Grad. School, Fairleigh Dickinson Univ., Teaneck, N. J., and Princeton Labs., Princeton, N. J.

Two host responses developed in rats 24 hours after carbon tetrachloride injections subcutaneously: (1) tense, ballooned-out granulomas; (2) dense leucocytic invasion, edema and necrosis of cutaneous muscle. These responses were inhibited, or significantly modified, in rats receiving streptokinase-plasminogen, trypsin or large doses of urethane orally, or hydrocortisone parenterally. Epsilon aminocaproic acid blocked the anti-inflammatory and granuloma-inhibiting effects of trypsin or streptokinase-plasminogen, but not of urethane. Papain, bromelain, chymotrypsin, Asperkinase and phenylbutazone were inactive.

The important implications of the data are: (1) that orally administered trypsin or streptokinase-plasminogen is active in modifying the inflammatory response to carbon tetrachloride, and (2) that the action of these substances is related to their enzymatic activity.

SPINAL REFLEX RESPONSES TO HYPOTHALAMIC STIMULATION. *Koichi Ishikawa**, *Kenneth Campbell** and *Douglas Stuart*. University of California, Davis, California.

In 23 lightly anesthetized cats, L_7 and S_1 mono- and polysynaptic responses to repetitive (0.4/sec) stimulation of branches of the sciatic nerve were summated with a computer of average transients before, during and after three types of hypothalamic stimulation. In the first case, repetitive stimulation was employed wherein a 120 msec train of 500 p/sec, 0.1 msec duration pulses was repeated each 600 msec. For triceps surae reflexes, this produced a consistent suppression of the amplitude of the monosynaptic response and less certain suppression of polysynaptic responses. For lateral peroneal nerve reflexes, it produced enhanced monosynaptic and possibly polysynaptic responses. In the second case, restricted to triceps surae reflexes, repetitive stimuli were again employed using a 12 msec duration repetitive train of the same parameters delivered at 20, 30 and 50 msec intervals. At the 20 and 50 msec intervals suppressed mono- and polysynaptic responses were evident, but at the 30 msec interval both responses were enhanced. Finally, stimuli were employed wherein an 8 pulse train of hypothalamic shocks at 500 p/sec frequency and 0.1 msec duration preceded the peripheral nerve shock by intervals from 10 to 100 msecs. In this case, both monosynaptic and polysynaptic triceps surae reflexes displayed a peak of enhancement near 15 msecs and a peak of reduction near 40 msecs with a return to control amplitude at the 100 msec interval.
(Supported in part by USPHS Grants NB 05199 and FR 05457.)

TURNOVER AND OXIDATION OF FFA IN MEN AND IN DOGS. B. Issekutz, Jr., W. Bortz,* P. Paul* and A. Wroldsen.* Div. of Research, Lankenau Hosp., Philadelphia, Pa.

Palmitate-1-C^{14} was infused i. v. at a constant rate for 3-8 hours into obese (100-150 kg), nonobese (65-85 kg) subjects and into unanesthetized dogs (10-27 kg) with indwelling arterial and venous catheters. O_2 uptake and CO_2 output were measured. Specific activity (SA) of CO_2 and of plasma FFA were determined. There was a straight line correlation between plasma FFA and turnover rate of FFA in men as well as in dogs. The same FFA level represents a higher turnover rate in men than in dogs, and it seems to represent a higher rate in obese than in nonobese. Also, when the turnover rate was related to the basal metabolic rate and expressed as μEq/Cal, the order of magnitude was: obese > nonobese > dogs. The assymptotic value of CO_2 SA was approached more slowly in men than in dogs. Depending on the plasma FFA level, 40-70 percent of the exhaled CO_2 derived from the direct oxidation of FFA. Values calculated from the isotopic data agreed well with the total CO_2 output derived from fat oxidation as it was estimated from urinary nitrogen output and nonprotein RQ. In this respect there was no marked difference between obese and nonobese subjects. Conclusion: the plasma concentration of FFA is an index of the rates of turnover and oxidation of FFA, and the turnover rate is higher in obese than in nonobese persons.
(Supported by NIH Grant No. AM-08887.)

REMOVAL OF CHOLESTEROL AND OTHER LIPIDS FROM HUMAN ATHEROMATOUS ARTERIES BY DILUTE HYDROGEN PEROXIDE. B. E. Jay and J. W. Finney (intr. by J. G. Bishop). Baylor Univ. Grad. Div. at the College of Dentistry, Dallas, Texas.

Dilute solutions of hydrogen peroxide have been infused intra-arterially in patients as a method of increasing the amount of available oxygen in a regional system. Some patients in whom this procedure has been used for prolonged periods of time have undergone postmortem examination. Aortas were taken at that time and divided into two segments, below and above the catheter tip (infused and noninfused). These segments were analyzed chemically and histologically and showed a 20-50 per cent reduction in total lipids and subintimal lipid deposits. In vitro studies have been carried out using atheromatous human aortas procured at autopsy, minced, and incubated for various periods of time with dilute hydrogen peroxide at 37°C. The supernatant fluid was analyzed for cholesterol, cholesterol esters, free fatty acids, triglycerides, and phospholipids. Time-rate studies have been done and all studies controlled. Total serum lipids have been evaluated quantitatively and qualitatively before and after the intra-arterial infusion of hydrogen peroxide in patients.

VAGUS REGENERATION IN DOGS. N.C. Jefferson, A. Geisel*, A. Doi*, and H. Necheles. Michael Reese Hospital and Medical Center, Chicago, Ill.

Some investigators maintain that proper vagotomy is not followed by regeneration of the vagus nerves and that depression of gastric acid secretion persists practically indefinitely. In our experience and in that of various authors, apparently complete vagotomy with subsequent negative insulin tests can be followed eventually by increasing gastric acid secretion, recurrence of ulcer, and perforation and hemorrhage. Regeneration can occur in most nerves, the recent data of Guth on rapid regeneration of the vagus nerve in the cat are good proof for that. We have performed vagotomies in dogs above the diaphragm, with excision of at least 2 cm of all branches and ligatures around the stump. A year or more later, the vagus nerves were stimulated in the neck and gastric motility was recorded. In a number of animals, vagus stimulation was followed by gastric contractions and careful dissection of the site of the section of the vagus nerves and histologic studies demonstrated the formation of connecting branches between the sectioned ends of the nerves. Slides demonstrate gastric motility and regrowth of nerves between them and abundant fibers below the sections. We conclude that in the dog anatomic and functional regeneration of the vagus nerve can occur. We believe that the same may happen in man, as attested by our own experience and by observations reported by others.

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STORAGE OF CARBON DIOXIDE IN THE EXERCISING DOG BREATHING 5% CARBON DIOXIDE IN AIR. Donald B. Jennings (Intr. by V. C. Abrahams), Department of Physiology, Queen's University, Kingston, Ontario, Canada.

Repeated studies were carried out in four fasting dogs prepared with chronic tracheostomies for placement of endotracheal tubes and carotid loops for arterial blood sampling. Oxygen consumption and the ratio of CO_2 production to oxygen consumption (R) were determined at 5-10 minute intervals over periods up to 1 1/2 hours while the animals walked at 1 mph on a treadmill. In 7 experiments the dogs breathed room air throughout; in 12 experiments the inspired gas mixture was changed to 5% CO_2 in air after 30 minutes of exercise. In the latter series, arterial CO_2 tension and content were measured in one study on each animal. The mean R was 0.76 during continuous exercise on room air; was significantly decreased to 0.60 at the 5 minute period of breathing 5% CO_2; and had returned to control levels by 10 minutes of breathing 5% CO_2. The calculated storage of CO_2 was 2.15 ml./kg./mm.Hg. $PaCO_2$. This amount is somewhat greater than that reported for the resting anaesthetized dog breathing 5% CO_2, but is less than the amount of CO_2 storage one might anticipate on the basis of the CO_2 dissociation curve for dog skeletal muscle. The differences may be explained on the distribution of blood flow to muscle.

(Supported by the Ontario Heart Foundation)

SWEATING RESPONSES OF MALES AND FEMALES AT REST IN WARM BATHS.
Becky Johnson*, B. A. Hertig, David Gifford* and F. Sargent, II.
Department of Physiology and Biophysics, and Physical Environment Unit, University of Illinois, Urbana, Illinois.

Difference in sweat rates between men and women is not significant in dry heat, while in humid heat the difference is significant (Morimoto et al., submitted to J. Appl. Physiol.). Brown and Sargent (Arch. Environ. Health, 11:442, 1965) have reported that in humid heat females develop hidromeiosis (decrement in rate of thermally induced sweating) more readily and to a greater extent than do males. We have extended these observations by immersing four male and four female unacclimated subjects in the bath, after the technique of Hertig et al. (J. Appl. Physiol. 16:647, 1961). Differences were observed in sweating response between the sexes, particularly (a) threshold skin temperature for sweating at rest: males av. 35.6°C (range 35.1-35.9), females av. 36.4 (range 36.0-36.8); (b) total sweating for two hour exposures at 0.6°C above threshold: males 164 g/m^2, females 133 g/m^2; and (c) time course of hidromeiosis: males 1st hr sweat 117 g/m^2, 2nd hr sweat 59 g/m^2, females 79 and 62 g/m^2 respectively. The temporal and quantitative sex differences in hidromeiosis are most likely related to sensitivity to the effect of skin wetness, these differences being greatest in the saturated conditions of the bath. Supported in part by Grant GB-4374 from the National Science Foundation.

CONTROL OF ADRENAL STERIOD SECRETION IN A PRIMITIVE MAMMAL, THE AMERICAN OPOSSUM, DIDELPHIS VIRGINIANA. C. I. Johnston*, James O. Davis, Fred S. Wright*, Stuart S. Howards*, and Phyllis M. Hartroft*. Dept. of Physiol., Univ. of Missouri School of Med., Columbia, Mo., the Natl. Heart Inst., Bethesda, Md., and the Washington Univ. School of Med., St. Louis, Mo.

A study was undertaken of the factors influencing adrenocortical steroid secretion in a primitive mammal, the American opossum. Adrenal venous blood was obtained by cannulating the left renal vein, into which the left adrenal vein drains, and by tying the renal vessels distally at the renal hilus. Opossums were given 2 mg dexamethasone i.m. to suppress pituitary ACTH release. Infusion of mammalian ACTH produced a significant increase in aldosterone, corticosterone (B) and cortisol (F) secretion. Infusion of a kidney extract prepared by the renin method of Haas et al. (Arch. Biochem. Biophys. 48: 256, 1954) resulted in a significant elevation in blood pressure as well as an increase in aldosterone, corticosterone and cortisol secretion rates. When the renin was infused into hypophysectomized opossums, increases in steriod secretion also occurred though to a lesser degree for B and F. The rise in adrenal steriods in response to the stress of laparotomy did not occur in opossums which received dexamethasone or in those which were hypophysectomized. Control rates of secretion of the steroids were the same in the dexamethasone treated group and the hypophysectomized group. Sodium depletion by a low sodium diet and administration of a mercurial diuretic produced a significant increase in the granulation of renal juxtaglomerular cells. The responses to ACTH and the "renin" preparation observed in the opossum are similar to the findings in the dog and frog. The renin-angiotensin system participates in the physiological response to sodium depletion and in the control of aldosterone secretion in the opossum.

SODIUM AND POTASSIUM EXCRETION PATTERNS DURING THE ESTROUS CYCLE IN THE DOG. Helen Johnston* and H. E. Schmid, Jr., Bowman Gray Sch. of Med., Winston-Salem, N. C.

The rate of excretion of Na and K was determined over 8 hr. periods of urine collections following an ad libitum ingestion of a single meal per day of commercial dog food (Na content-0.17, K content-.20 meq/gm). Mongrel dogs and pure-stock beagles were studied before, during and after estrus. The stages of the estrous cycle were determined by changes in vulva size, amount, consistency and color of the vaginal fluid, and microscopic analysis of vaginal smears. During metestrus I and early metestrus II, the average rate of excretion of Na for 3 dogs was found to change from a normal pattern of 55.6% of the total 24 hr. excretion in the 1st 8 hr. period, 30.5% in the 2nd, and 13.8% in the 3rd to a new pattern of 46%-1st, 33.6%-2nd, and 20.2%-3rd. The rate of excretion for K changed from 52.4% in the 1st, 34.7%-2nd, and 12.8%-3rd to 47.1%-1st, 38.6%-2nd, and 14.3%-3rd. Associated with this change there was a 66% increase in food intake. Preliminary studies indicate that the changes in the rate of Na and K excretion were secondary to the increased food intake. The pattern of excretion rates during proestrus, estrus, and metestrus was similar to that seen during metestrus and did not change significantly throughout these periods in a dog placed on a high constant food intake. The changes in excretion rate were reproduced in dogs placed alternately on high and low food intakes. It therefore appears that the changes in the rate of excretion of Na and K seen during metestrus may be related to the increase in food intake. It still remains to be determined whether these changes were caused by a primary hormone effect on electrolyte-balance controlling mechanisms or on altered dietary habits. Supported by grants from NIH, GM-1044 and HE-05948.

METABOLIC ADAPTATION OF RATS TO A HIGH OXYGEN-LOW PRESSURE ENVIRONMENT. John Patrick Jordan, J. B. Allred and A. D. Bond (intr. by W. O. Fenn), Oklahoma City University, Oklahoma City, Oklahoma.

The effects of prolonged exposure to a space cabin environment (O_2 at 5.2 psia) on the metabolism of rats were studied. Control animals were housed in an identical chamber in which the gas phase was air at 1 atm. Throughout 12 weeks of continuous exposure to the test environment, body and tissue weights did not differ significantly between the two groups of animals except for a greater heart weight in the experimental animals. However, using tissue composition and C^{14}-turnover rate data obtained from injection of acetate-1-C^{14} at varying times prior to sacrifice, several parameters suggest adaptation. The rate of $C^{14}O_2$ expiration, coenzyme A concentration in brain, liver and kidney as well as hematocrit values and hemoglobin concentration decreased after 4 weeks of exposure but essentially returned to control values after 12 weeks of exposure. Tissue cholesterol concentrations were increased in the 4 week exposed animals and tended to return to normal values after 12 weeks of exposure. C^{14}-turnover rate data showed greater differences between the two groups of animals after 4 weeks than after 12 weeks. However, not all metabolic parameters returned to control values, e.g. C^{14}-turnover rates of liver lipid and tissue carbohydrate were greater in experimental rats after 12 weeks but the turnover rate of heart cholesterol was less. Steady state analyses of tissues and carcass indicate an increase in carbohydrate and a decrease in lipid, particularly the saponifiable fraction, with prolonged exposure. We conclude that adaptation to the environment involves a change in the importance of certain metabolic pathways. (Supported by NASA Grant NsG-300)

The Effect of Some Chelating Agents on Myosin A. George Kaldor and Long Kuo*, Dept. Physiol. and Biophys., Woman's Med. Coll. of Pa., Phila., Pa.

ChelCD (1-2-diaminocyclohexane tetraacetic acid) in 5.0 mM concentration at pH 7.5, in the presence of 0.1 M KCl caused a 2 fold increase in the ATPase activity of Myosin A. This activation was reversed by 2.0 - 3.0 mM Mg, by 2.0 - 3.0 mM Mg-ChelCD complex or by 2.0 - 3.0 mM Ca-ChelCD complex almost equally well. About 5.0 mM Ca-EGTA /ethylene glycol - bis (aminoethylether) tetraacetic acid/ complex or 5.0 mM Mg-EDTA (ethylene diamine tetraacetic acid) complex and more than 5.0 mM Ca^{++} were needed to inhibit the ChelCD activation. Similarly, the well known Myosin A Ca^{++} ATPase stimulating effect of 5.0 mM-EDTA was reversed by 2.0 mM Mg^{++}, by 5.0 mM Mg-EDTA complex, by 5.0 mM Mg-ChelCD complex or by 5.0 mM Ca-EGTA complex. Our results showed that some metal-chelate complexes may inhibit the ATPase activating effect of the chelating agent. By addition of 5.0 mM of the various metal-chelate complexes to a mixture containing 5.0 mM chelating agent, the concentration of the free metal did not increase significantly (Average less than 10^{-7} M). At pH 6.25 the NH_4^+ activated (0.3M NH_4^+) Myosin A ATPase was not inhibited by EGTA (up to 5.0 mM), but about 50% inhibition was caused by 5.0 mM Ca^{++}. The addition of 5.0 mM EGTA to the 5.0 mM Ca^{++} inhibited mixture doubled the inhibition. In this case the Ca-EGTA complex was more inhibitory than the free Ca^{++}. Therefore, these results would seem to indicate that some chelating agents and their metal complexes may have also a direct effect on the Myosin A enzyme over and above their metal binding ability. Supported by NIH Grant NB 06517.

ELECTROPHYSIOLOGICAL CORRELATES OF SLEEP AND DREAMING IN ASTHMATIC SUBJECTS. A. Kales, G. F. Bajor, A. Jacobson, G. N. Beall, T. Wilson, G. Heuser and G. Zaid (intr. by J. P. Segundo). Depts. of Psychiatry, Anatomy and Medicine, Univ. of California, Los Angeles, and VA Center, Los Angeles, Calif.

There have been no previous studies of nocturnal asthmatic attacks with all-night EEG recording. The present study was designed to correlate asthmatic episodes with stages of sleep including rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. Asthmatics with a history of nocturnal episodes were studied nightly in the sleep lab from approximately 10-11 P.M. to 6 A.M. They were monitored continuously with EEG, submental EMG and eye movements recorded from scalp and facial electrodes respectively. In addition respiration was recorded by conductive rubber pneumograph. The subjects were instructed to signal the investigator if they awakened, were short of breath and needed to use their inhaler. Eight asthmatics were studied for 17 subject nights. There were 33 asthmatic episodes in which the subjects awakened and signaled. The stages of sleep preceding such episodes were both REM and NREM (stages 2,3,4). Nine of the asthmatic episodes occurred out of REM sleep, five after lengthy REM periods and four after a few minutes of REM sleep. Of the 24 incidents occurring in NREM sleep, 15 arose out of Stage 2 sleep. However, in a number of those awakenings from a Stage 2 the breathing difficulty began while in Stage 3 or 4 sleep with gradual lightening to Stage 2 then awakening. The over-all incidence of episodes showed some preponderance during the last two hours of the night. We concluded that the occurrence of nocturnal asthmatic episodes is not related to a particular stage of sleep. (Supported in part by Public Health Service Grant No. MH-10083.)

DIFFERENTIAL RESPONSES OF SEQUENTIAL MICROVASCULAR ELEMENTS IN THE PERFUSED RAT MESENTERY. *Patricia R. Kane* and *Allen A. Rovick*. Department of Physiology, Loyola University Stritch School of Medicine and the Graduate School, Chicago, Illinois.

A microcinephotographic system was used to study fields which included either a precapillary vessel and a branch or a pre- and a postcapillary vessel. Dimensional changes were produced by step alterations in perfusion pressure or by introducing or removing a sinusoidal arterial pulse without changing the mean pressure. In 17 pulse pressure studies performed during observation of sequential precapillary vessels, the diameter change of the proximal vessel was opposite to that of the distal vessel in 70% of the cases. Step alterations in arterial pressure in the same fields produced opposite responses in the two vessels or the distal vessel showed no net change in 9 of 11 cases. The diameter change in the proximal vessel was in the same direction as the pressure change with one exception. In this case, both vessels decreased in size when the pressure was raised. When a pre- and a postcapillary vessel were simultaneously studied, pulse pressure changes produced opposite responses or no response in one of the two vessels in 75% and mean pressure changes in 78% of the cases. Since the pressure gradient was unaltered when pulse pressure was changed, any dimensional shift in the proximal vessel should produce a parallel pressure change in more distal vessels. Opposite dimensional changes of distal vessels are therefore presumptive evidence of an active response. Extrapolating to the effects of alteration in mean pressure, it is suggested that the response of small pre- and postcapillary vessels to step pressure stimuli is active. *(Supported by NIH Grant HE 08682 and USPHS Fellowship 5F1 GM-17,888.)*

CALIBRATION OF RADIOGRAMS FOR THE CALCULATION OF PERIPHERAL BLOOD FLOW[1] Albert F. Kelso and Alexandra A. Townsend, Department of Physiology, Chicago College of Osteopathy, Chicago, Illinois.

The purpose of this report is to indicate a method for calibrating radiograms which will improve the reliability of the estimated blood flow for a region of the peripheral circulation. Peripheral blood flow is calculated as the fraction of the cardiac output which is distributed to the region being studied. The fraction is estimated from the ratio of the radioactivity recorded in simultaneous radiograms of a region of peripheral circulation and the heart during the first passage of a radioactive tagged bolus of blood through the circulation. We noted a systematic error for the calculated coronary, renal and hepatic blood flows obtained by this method and attributed the error to the variations in the distance of the detector probes from the monitored blood volume. The systematic error was reduced by recalibrating the radiogram using a correction factor obtained by a graphic method. In a graph of the detector field the location of the peripheral circulation being monitored was plotted, and the sensitivity calibration was corrected by the inverse square of the mean distance of the monitored blood volume from the center of the crystal detector. The fraction of the cardiac output perfusing the kidney or liver estimated from the recalibrated radiograms was in closer agreement with simultaneously measured flows obtained with an electromagnetic flow meter. Calibration of the radiogram to obtain records of radioactivity which are in close correspondance to the specific activity of the monitored blood volume improves the estimate made of peripheral blood flow by the radiographic method.

[1]Assisted by grants from the American Osteopathic Association

AORTIC PRESSURE PULSES PRODUCED BY CONTROLLED FLOW INPUT. J.E. Kendrick. Dept. of Physiol., School of Medicine, Univ. of Wisconsin.

Pulsatile pressures in the abdominal aorta of totally perfused dogs have been studied. Stroke volume and rate of the perfusion pump were constant and continuously adjustable. The output flow curve of the pump was nearly constant and of a rectified sine waveform. Pulsatile pressures measured from the renal and inferior mesenteric arteries were subjected to Fourier analysis. As the pulse traveled over the aortic segment (approx. 10 cm) between the measuring sites it was increased in size. This peaking is largely due to amplification of the moduli of the 1st and 2nd harmonics of pressure. Higher harmonics were generally attenuated.

Increasing pump frequency (stroke volume constant) from 1.76 to 3.70 cycles/second tended to cause an increase in all harmonics studied (1-4) except the second. Increasing pump frequency with a concomitant decrease in stroke volume such that pump output remained constant generally caused a non-uniform decrease in all harmonics. Decreasing stroke volume (frequency constant) generally decreased the amplitudes of all harmonics. Phase velocity data suggests that this value is almost independent of stroke volume or pump output in the physiological range and inversely related to pump frequency. Group velocity of the pulse varied in an inconsistent manner with pump frequency. (Support: U.S.P.H.S. HE04098 and Wis. Heart Assoc.)

ACUTE CHANGES IN LUNG MECHANICS FOLLOWING AIR EMBOLI IN DOGS. M.A. Khan*, S. Suetsugu*, I. Alkalay*, A. Platthy*, and M. Stein. Rhode Island Hospital and Brown University, Providence, Rhode Island.

Intravenous injections of air (.25-1.0 ml/kg) in anesthetized dogs produced significant alterations in lung mechanics. Decreases in lung compliance (C_L), and increases in total lung flow resistance (R_L), respiratory rate (R.R.), and arterial-alveolar CO_2 tension difference ($a\text{-}APCO_2$) were observed. These changes occurred immediately after the air injection and lasted one to ten minutes. Blood platelet counts performed before and immediately after the release of air emboli revealed no change. Heparinization of animals prior to air embolization abolished completely the increases in R_L, decreases in C_L, as well as the alterations in R.R., but not in $a\text{-}APCO_2$. In three thrombocytopenic animals, air emboli also failed to produce changes in lung mechanics. Postmortem examinations of the animals revealed varying sized air bubbles in the right ventricle and/or pulmonary arteries. Neither gross nor microscopic evidence of pulmonary edema was present. The mechanism of the alterations in R_L and C_L is not clear, but it is probable that the observed changes are not due to the physical presence of the air emboli alone. Previously, we have shown that the release of massive stasis thrombi to the lungs of dogs resulted in similar rapid changes in lung mechanics due to serotonin release from platelets. The present study suggests that the alterations in R_L and C_L following air embolism also may be related to thrombin-induced release of 5-HT from circulating blood platelets. (Supported by Grant No. HE-10017 from NIH.)

MUCOCILIARY CLEARANCE OF PARTICLES FROM BULLFROG LUNGS. Kaye H. Kilburn and Ronald Mitchell. Duke Univ. Med. Center and Durham Vets. Admin. Hosp., Durham, N.C.

Clearance of inhaled particles from alveoli to the ciliomucus escalator was studied in the lungs of six living 350-500 g bullfrogs (Rana catesbiana). Both bullfrog lungs are attached to ducts which branch from a short common airway off the glottis. Each is analagous to an alveolar duct, large alveolar sac and alveoli in mammalian lungs. The clearance of india ink was observed microscopically and recorded by colored cine photography in lungs turned inside out by pushing the distal tip through the dilated glottis. They were partly inflated and kept moist. Particles placed onto alveolar fluid were moved by beating ciliated tufts, lung inflation which simulated breathing and vascular pulsations onto narrow ciliated ridges. Mucus was transported by cilia on helical ridges of increasing width to a single 1-2mm wide longitudinal ridge which moved mucus to the glottis for removal into the esophagus. Transport was 1.5-3.5 cm/min on small to large ridges. Access to the ridges was slower and depended upon retraction of sticky mucus by movement of ridges during breathing and pulling of the mucus blanket by ciliary beating. Clearance of particles from alveoli to alveolar ducts in the bullfrog may be analagous to mucociliary clearance from alveoli to respiratory bronchioles in mammalian lungs. Drying, mechanical damage, ultraviolet light and cigarette smoke reduced clearance in frog lungs. Acetylcysteine had no effect.

Relationship of Dietary Intake to Water Requirements for Exhaustive Running in Rats. M.A. Kilmore, J. McCormick, L.M. Breslouf (intr. by C.M. Blatteis) Nutr. Br., Food Div., U.S. Army Natick Labs., Natick, Mass.

One advantage of a high fat diet may be its ability to yield more metabolic water and thus reduce the need for exogenous water. The present study was undertaken to determine if this has any practical implications for an exercising animal. Male, 50 day old, Long Evans rats were divided into five groups of 24 animals and fed the following diets for four weeks: Group 1, 2% fat and 67% CHO; Group 2, 30% fat and 39% CHO; Group 3, 69% fat and no CHO; Group 4, same as group 1 plus 50% water in agar gel; Group 5, same as group 3 plus 50% water in agar gel. Proteins, minerals, fiber, and vitamins were constant (31%) in all diets. Water was given ad libitum. The animals were then run on a treadmill, held at a 12° grade, at 19.2 m/min., increased hourly by 3.2 m/min., until exhausted. Food was withdrawn from all the rats 18 hours before running. One half of the rats in each group were deprived of water 96 hours prior to this test. The average exhaustive running times of the rats with free access to water in groups 1-5 were 101, 118, 126, 63, and 133 minutes, respectively. The animals without water in groups 1-3 ran 58, 78, and 68 minutes less, respectively, but those in groups 4-5 ran only 6 and 30 minutes less than those which received ad libitum water. These results suggest that (1) exogenous water is an important requirement for prolonging running time in rats, (2) water added to the diet in the form of agar gel partially fulfills the exogenous water requirements of exercising rats, and (3) a high fat diet does not obviate the need for exogenous water even though more endogenous water may be provided.

NON-UNIFORM DISTRIBUTION OF CORONARY BLOOD FLOW IN SYSTOLE. Edward S. Kirk (intr. by C. Ladd Prosser). Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

The observation that a redistribution of myocardial blood flow occurs at the onset of cardiac arrest (Kirk, E.S. & C.R. Honig, Am. J. Physiol. 207: 661, 1964) suggests that coronary arterial flow during systole is not uniformly distributed to the myocardium. This idea was tested by measuring the effect of occlusion of coronary inflow during diastole on the distribution of tissue blood flows. The left coronary arteries of anesthetized dogs were cannulated and perfused at constant flow. A solenoid clamp on the perfusion tubing was activated by a pulse generator triggered from the ECG. Controlled delay and duration permitted the solenoid to occlude coronary inflow throughout diastole thereby restricting inflow to the period of systole. The clearance of depots of Na^{24}-saline localized to either the deep (endocardial) or superficial (epicardial) regions of the myocardium showed an immediate change when diastolic occlusion was initiated: tissue blood flow in the superficial regions apparently increasing at the expense of the deep flows. I conclude that coronary blood flow during systole is perferentially distributed to the superficial regions of the myocardium. The observed transmural gradient of vascular resistance during systole corresponds to the gradient of intramyocardial pressures during systole. Since in the unanesthetized dog a sizeable and often variable proportion of the total coronary flow takes place during systole (e.g., Gregg, D. E. et al. Circulation Res. 16: 102, 1965) it appears that the coronary blood flow is often undergoing redistributions between the layers on the myocardial wall.

HEMODYNAMIC CHANGES IN RIGHT AND LEFT HEART BYPASS WITH ARTIFICIAL VENTRICLES. M.Klain*, W.E.Stewart*, K.H.Leitz*, C.L.Sarin*, Y.Nose*, and W.J.Kolff. Cleveland Clinic Foundation, Cleveland, Ohio.

To clarify changes produced in the circulation with the use of artificial hearts 20 two hour right or left heart bypasses were performed on sheep. Blood was drained from the right or left atrium and pumped to pulmonary artery or aorta by a Silastic artificial ventricle pneumatically driven by an NASA driving system which simulated natural pressures. Transfer to the artificial ventricle was immediate, thereafter the output increased slowly. The chest was closed and the sheep placed in a near normal position on its chest. Right heart pumping led to an immediate increase of pulmonary artery pressure and decreased blood oxygenation. Left atrial pressure tended to increase. Both improved with time, but not to normal levels. Increased pumping volume with the artificial right ventricle produced a tachycardia and higher systolic peaks in the carotid artery. Left heart bypass was tolerated better than right heart bypass. Changes in the pulmonary circulation were usually temporary. However, pulmonary hypertension also occured with the onset of pumping. In right heart pumping more severe damage of the lung occured, especially when left atrial pressure exceeded 15 mm Hg. Pooling of blood somewhere in the body led to insufficient venous return in some experiments. Oxygenation and pooling improved by turning the animal over on its chest. Results indicate that (1) transition from natural to artificial right ventricle leads to pulmonary hypertension even at low flow rates, (2) left heart bypass also leads to reactive changes in pulmonary circulation but less. Artificial heart experiments are suggested to study regulatory feedbacks in the circulatory system. Use of the NASA computerized system which can generate various pressure waves and flow patterns allows evaluation of parameters important for feedbacks.

EFFECT OF PREMATURE SYSTOLES ON RHYTHMICITY OF AUTOMATIC CELLS. H.O. Klein,* D.H. Singer,* and P.F. Cranefield. Col. of Physicians & Surgeons, Columbia University, New York, N.Y.

The belief that post-extrasystolic alterations in atrial and ventricular activity (P-P and R-R intervals) reflect corresponding alterations in rhythmicity of pacemaker cells of the sinoatrial node (SAN) and His-Purkinje system is based on analyses of surface records of electrical activity. This premise was tested by random introduction of atrial premature systoles (APS) in isolated rabbit right atria. Transmembrane potentials and bipolar surface electrograms were recorded from SAN and atrium. Alterations in SAN and atrial activity depended on the prematurity of the APS: 1) the earliest APS did not discharge the SAN. SAN and P-P intervals were unchanged; 2) the earliest APS which discharged SAN produced a shortening of the returning SAN cycle. P-P intervals were however usually prolonged because of markedly increased atrium to sinus and sinoatrial conduction times; 3) late APS lengthened both SAN and P-P cycles; conduction time was unchanged; returning P-P intervals were frequently "fully-compensatory." APS in the presence of acetylcholine produced similar alterations; the "critical" zone during which APS resulted in shortened returning cycles was longer than in controls. These results are contrary to the belief that altered P-P intervals following APS reflect similar changes in SAN since long P-P intervals occurred with shortened SAN cycles and fully compensatory pauses were seen despite premature SAN discharge. The discrepancy between SAN and atrial cycles was due to slowing of conduction from atrium to sinus and from sinus back to atrium. Preliminary experiments on dog Purkinje fibers resulted in a similar pattern of responses. This would explain the shortening of the returning cycle seen after ventricular premature systoles in complete heart block. (Supported in part by USPHS research grant HE08508-03.)

ELECTROENCEPHALOGRAPHIC-BEHAVIORAL DISSOCIATIONS DURING ANIMAL HYPNOSIS. W. R. Klemm, College of Vet. Med., Iowa State Univ., Ames. (Present address: Dept. Biol., Texas A&M Univ.)

Generally, there is a correlation between brain electrical activity patterns and behavior. However, a few important exceptions are known, and this report is of another exception.

Cortical and subcortical activity in hypnotized rabbits was of the "arousal" type during the initial stages of hypnosis; although, behaviorally, hypnosis appeared to be a state of "sedation". Moreover, on 8 occasions in 6 rabbits transient episodes of electrographic seizures occurred during hypnosis without interrupting the tonic immobility. To confirm this observation, tests were conducted with several seizure-inducing drugs. Whether the drugs were injected before or during hypnosis, the motor component of the seizures was abolished by hypnosis, yet epileptiform EEG activity persisted during the apparent behavioral sedation.

This functional disconnection of motor activity may have mechanisms in common with the several other known dissociation states. These results emphasize the need for better understanding of the various degrees of functional dichotomy in sensory and motor systems.

MEASUREMENT OF TRACE AMOUNTS OF INERT GASES IN BLOOD BY GAS CHROMATOGRAPHY. F. J. Klocke and R. A. Klocke (intr. by D. G. Greene). State Univ. of N. Y. at Bflo. School of Med., Buffalo, N. Y. and Walter Reed Army Inst. of Research, Washington, D. C.

Although the physical properties of biologically inert gases make them uniquely suitable for a variety of physiological studies, the use of nonradioactive gases has been limited by the sensitivities of available methods for quantitating trace amounts of the gases in blood. The present study describes a thermal conductivity gas chromatograph which appears to be 1-2 orders of magnitude more sensitive than conventional systems. The unit employs a sealed thermistor microdetector and 1/8" O.D. packed columns and is designed to minimize "noise" caused by fluctuations of temperature, carrier flow and detector current. The detector is commercially available, powered by mercury reference cells and suitable for use with carrier gases other than helium (including O_2). The detector, columns and flow control system are housed in a constant temperature water bath instead of the usual air ovens, and the bath is operated 2-3°C. above ambient. Sample gases are introduced into the carrier stream after having been extracted in a modified Van Slyke apparatus and compressed in a small sampling loop, according to the technic of Farhi, et al. (J. Appl. Physiol. 18:97-106, 1963). CO_2 and water vapor absorbents are included in the tubing connecting the sampling loop to the chromatograph sample inlet. In studies employing 2.0 ml blood samples, the following limits of detection have been achieved: He, 2×10^{-6} ml; H_2, 2×10^{-6} ml; Ne, 1×10^{-6} ml; N_2, 1×10^{-6} ml; A, 8×10^{-7} ml; CH_4, 1×10^{-6} ml; SF_6, 2×10^{-7} ml. These values correspond to detector sensitivities of between 10^{-7} and 10^{-8} ml/sec and 10^{-10} and 10^{-11} g/sec.

EFFECT OF CHRONIC ETHANOL ADMINISTRATION ON THE RESPONSE OF THE DOG TO SERIAL HEMORRHAGE. David H. Knott and James D. Beard (intr. by G. B. Spurr). Univ. of Tennessee Medical Units, Memphis, Tennessee.

A hemorrhage technique utilizing the bleeding volume was employed on weekly basis (6 weeks) in 10 control dogs and in 10 dogs receiving daily doses of alcohol (4 g/kg body weight in a 33% v/v solution) via gastric tube during the six-week experimental hemorrhage period. The hemorrhage procedure has been described previously by the authors (New Eng. J. Med. 269:292-295, 1963). Plasma volume (T-1824) was measured prior to and at 2 hours after each hemorrhage; respective blood volumes were calculated using the large vessel hematocrit. Mean arterial pressure and heart rate (EKG) were monitored prior to and for 2 hours subsequent to bleeding. Plasma and erythrocyte concentrations of Na^+, K^+ and Cl^-, hematocrit, hemoglobin, red and white cell counts and reticulocytes were measured prior to each hemorrhage. Blood glucose was determined prior to and at 15 min and 2 hours after bleeding. All 10 dogs survived the six weekly hemorrhages; however, only 1 animal from the ethanol-treated group survived. The mean survival time of the nonsurvivors was 19 days. Prehemorrhage blood volumes were slightly higher in the alcohol dogs because of a larger plasma volume. Failure of the erythrocyte K^+ concentration to increase in addition to an attenuated reticulocyte response in the alcohol dogs suggest that ethanol impaired the hematopoietic compensation to repeated hemorrhage. A progressively more profound post-hemorrhage hyperglycemia in the alcohol-treated animals indicates that the severity of the stress was greater in this group. The chronic ingestion of ethanol markedly impaired the ability of the dog to withstand repeated hemorrhages. (Supported in part by Tenn. Heart Assoc. and the State of Tennessee, Department of Mental Health, Division on Alcoholism.)

RESPONSE OF THYROPARATHYROIDECTOMIZED RATS TO INDUCED HYPERCALCEMIA. Leon Kraintz and F. W. Kraintz*. University of British Columbia, Vancouver, B. C., Canada.

It has previously been shown that the thyroparathyroidectomized rat (TPTX) fed Purina Chow has significantly higher plasma calcium than the parathyroidectomized rat (PTX) 10 days after surgery. In addition, studies of the recovery from induced hypercalcemia in TPTX, PTX, and thyroidectomized rats bearing parathyroid transplants have shown that the thyroid rather than the parathyroid is responsible for combating hypercalcemia. (Talmage et al., Endocrinol. 76: 103, 1965). The studies reported here show the time course of the response to hypercalcemia in intact and TPTX young male rats 5 days after surgery. Both groups of rats were given calcium gluconate (5 mg Ca/100 gm B. W. i. p.). Microcalcium determinations were done at 30 minute intervals on tail blood plasma during the 4 hour post injection period. The plasma calcium increment above the pre-injection values at the end of 1/2 hour and for the remaining 4 hours is consistently greater in the TPTX rat. The intact rat recovers from the hypercalcemia in 2 1/2 hours and, in addition, shows a significant hypocalcemia below pre-injection levels at 3 hours. These results confirm a delayed recovery from induced hypercalcemia in the absence of the thyroid and parathyroids and also demonstrate that hypercalcemia in the intact rat is followed by a hypocalcemia which is evidence for the secretion of the plasma calcium lowering factor, thyrocalcitonin, in response to the induced hypercalcemia.

CENTRAL CIRCULATORY RESPONSES BEFORE AND AFTER ACCLIMATIZATION TO WORK IN DRY HEAT. K. K. Kraning II, L. B. Rowell, T. O. Evans* and J. W. Kennedy*. University of Washington School of Medicine, Seattle, Wash.

Recent work from this laboratory (in press) showed that tachycardia induced by short periods of graded work plus external heat stress were not attended by increased cardiac output (CO) but by decreased central blood volume (CBV) and stroke volume (SV) when compared to 78 F control values. Present experiments were designed to determine whether amelioration of circulatory strain during acclimatization results mainly from (a) reversal of peripheral displacement of vascular volume attending initial heat exposure or (b) from changes in CO attending reduction in cutaneous blood flow. In 7 normal young men CO, CBV and SV were determined from multiple, serial, right atrial injections of indocyanine green with proximal aortic sampling and blood pressure (BP) measurement. Measurements were made during prolonged (40-70 min) exercise (0% grade, 3.5 mph) on day 1 and day 11 (70 min) of daily exposure at 120 $\pm$ 2 F dry bulb and 80 $\pm$ 3 F wet bulb. On day 1 all men showed progressive increase in CO with time (1.5 to 4 L/min [6 men], 10 L/min [1 man]) while CBV, SV and BP were nearly constant -- even at exhaustion. So far 3 men after acclimatization showed the expected decrements in heart rate (29 bpm), rectal (1.4 C) and skin temperatures (1.6 C). $\dot{V}o_2$ was unchanged while sweat loss increased. CO and aortic BP were unaffected by acclimatization (2 men); CBV increased 80 ml in one and was unchanged in the second. SV increased 14 and 27 ml (2 men). In contrast a third man showed a large decrease in CO (average 6 L/min), SV (28 ml), CBV (550 ml) and mean BP (13 mmHg). Therefore, circulatory responses to acclimatization demonstrated to varying degrees both hypothesized mechanisms.

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EFFECT OF LUNG VOLUME ON MICROHOLES MADE IN ALVEOLAR WALLS. K.Kuno* and N.C. Staub. Cardiovasc. Res. Inst. and Dept. of Physiol., Univ. of Cal. San Fran. Med. Ctr., San Francisco, Calif.

Many pathologists believe alveolar wall fenestrations are the earliest lesions of emphysema. Among the factors that might prevent healing is the effect of alveolar tissue elasticity and surface tension on the size of the holes during breathing. In freshly isolated lobes of cat lungs, we have made rows of fenestrations using 50-μ diameter, electrolytically sharpened tungsten needles. After rapidly freezing the lobe with liquid propane, the tissues are freeze-dried and the holes located and measured in 300-μ, cleared sections. Maximum length-width dimensions of holes made and frozen at a given lung volume during deflation from transpulmonary pressure (P_{TP}) = 30 cm H_2O decrease linearly as volume decreases. The holes at full volume average 42.5 μ diameter. Holes made at P_{TP} = 7 cm H_2O (35% volume) during the third inflation with air, then inflated and deflated and frozen immediately have larger diameters at larger volumes. There is no hysteresis with volume. The average diameter at P_{TP} = 30 cm H_2O is 35.5 μ. Fenestra diameter follows the cube root of volume almost exactly between 25-100% volume. Below 25% volume (P_{TP} = 1 cm H_2O on deflation) we do not find any open holes. This sudden effect may relate to the folding up of the alveolar walls as volume decreases below the point where elastic tissue tension becomes zero. The data indicate that alveolar fenestrations do change size with breathing as a simple function of lung volume. (Supported in part by USPHS grant HE-06285.)

SYNCHRONIZED ACTIVITY IN A NEUROSECRETORY CELL CLUSTER IN APLYSIA. I. Kupfermann,* E. Kandel, and R. Coggeshall.* New York Univ. Sch. of Med., New York, N.Y. and Harvard Med. School, Boston, Mass.

The nervous system of Aplysia californica contains two clusters of cells each located in a "bag" within the connective tissue at the junction of the pleuro-abdominal connectives with the abdominal ganglion. Each cluster of "bag cells" contains many small neurons whose size (10-50μ) and number (100-800) are functions of the age of the animal. In adult animals, these cells send many granule filled processes into the connective tissue sheath, and fulfill the morphological criteria for neurosecretory cells. In the isolated abdominal ganglion the cells are silent but generate spikes when stimulated with an intracellular microelectrode. Responses to connective stimulation were highly labile. Single shocks produced no responses but stimulus trains led to the activation of an excitatory interneuron which produced repetitive firing of the bag cells, lasting several sec. to 10 min. Continued stimulation of a connective rapidly led to a response decrement, lasting from several minutes to over an hour. Simultaneous recordings from 2 cells at a time revealed that all bag cells on the same side always fired synchronously. Current injected into one bag cell never affected another bag cell, indicating that the cells were not electrically coupled. Bag cells on opposite sides sometimes also showed a tendency for synchronization. These findings suggest (1) that the several hundred bag cells on each side constitute a homogeneous population innervated and synchronized by a single interneuron, (2) the bag cell interneuron on each side is affected by input from the connectives and from the other bag cell interneuron. (supported by NIH MH 12155-01 and NSF GB-3595).

PRESSURES IN THE PULMONARY CIRCULATION OF THE RAT. George H. Kydd, U.S. Naval Air Development Center, Johnsville, Warminster, Pa.

In connection with other work underway at our laboratory, pressures in the right ventricle and pulmonary artery have been measured in mature Charles River rats (CD) by catherization of the jugular vein under urethane anesthesia. In addition, aortic pressure was measured from a T tube in the lower thoracic aorta and EKG was obtained from chest electrodes. These pressures were recorded in response to the breathing of oxygen or air and to increase in intratracheal pressure which was measured from a special cannula. The heart rate was stable in spite of the various procedures and in general was 5-6 beats/second. The maximum and minimum respiratory variation for systolic (SR) and dyastolic (DR) pressures on the right side, and the aortic systolic (SL) were arranged. Breathing air, SR ranged up to 80 mm Hg with a mean of 39.6 mm Hg and DR was as low as -28 mm Hg with a mean of -7.2 mm Hg. For the right mean pressure (RMP) a special equation was used since dyastolic pressure was frequently negative: RMP = 1/2 (Systolic max. - Dyastolic max.) + 1/2 (Dyastolic max. - Dyastolic min.). While breathing air RMP was 27.7 and on oxygen it was 25.2 mm Hg. The aortic mean pressure (AMP) in air was 94.0 and on oxygen it was 101.1 mm Hg. During increased intratracheal pressure, the aortic pressure fell typically, however, right ventricular and pulmonary arterial pressure tended to remain constant. This maintenance of a constant SR indicates that the ventricular volume is maintained and if the decrease in AMP is correctly linked to a decreased cardiac output, it means that the right ventricle is less efficient in emptying itself, a condition similar to failure. The resistance against which the ventricle works is generated by the increased intratracheal pressure, raising the question as to source of the resistance in the lungs.

EVIDENCE FOR NEUROLOGIC CONTROL SYSTEM OF URETERAL PERISTALSIS. Peregrina Labay, Saul Boyarsky,* Carl Gerber and Norman Kirshner. Duke University Medical Center, Durham, N. C.

Specific fluorescence assay of canine and human ureteral musculature shows endogenous catecholamine content of 0.2-0.3 μg/gr of tissue, a concentration similar to that of the bladder, but significantly higher than that of skeletal muscle. The noradrenaline can be depleted completely by reserpine therapy. Uptake of radioactive noradrenaline by the ureter approaches that by the heart. These data provide specific biochemical tests for the presence of sympathetic nervous endings in the ureter. In vitro, in modified Locke's solution, dog ureter responded to noradrenaline, 20-40 μg/cc, with increased peristaltic frequency for 1-10 minutes. We have succeeded in demonstrating that noradrenaline in doses of 50-80 μg/kg i.v. increases ureteral peristaltic frequency and amplitude. Previous demonstrations have failed because of inadequate dosage. By continuous infusion the dosage is as low as 10 μg/kg/min. i.v. Intraortic administration is effective at doses of 2-6 μg/kg/min. Adrenal compression further supports the conclusion that the ureter contains adrenergic receptors; it is followed by increase in ureteral peristaltic rate. These experiments provide biochemical, physiologic and pharmacologic evidence for the presence of a sympathetic nervous control system in a myogenically functioning organ.

A TECHNIQUE FOR THE ON-LINE MEASUREMENT OF THE INCIDENT AND REFLECTED COMPONENTS OF PRESSURE IN A HYDRODYNAMIC SYSTEM. Gerald F. Lackey*, Fredrick L. Thurstone*, and George S. Malindzak, Jr. Bowman Gray School of Medicine, Winston-Salem, N. C.

The incident and reflected components of pressure at a given point in a hydrodynamic system can be measured simultaneously, independent of the complexity of the wave form of the pulse, when the characteristic impedance of the vessel is known. A mathematical model has been developed that permits the separation of the incident and reflected components from instantaneous pressure and flow measurements at a single point in a system consisting of a rubber tube with saline as the fluid. Pressure and flow were measured using a special cannulating flow transducer with self-contained pressure taps. Fourier transforms of pressure and flow permit spectral analysis of single pulses in the model system and determination of the characteristic impedance of the system. These studies indicate the usefulness of this technique in the analysis of certain properties of the cardiovascular system and could prove a valuable diagnostic tool in evaluating cardiovascular disease.
(Supported by PHS Grant HE 5392).

VENTILATORY DRIVE OF CAROTID BODIES IN RESPONSE TO CO_2 IN THE DOG. S. Lahiri*, F.F. Kao and S.S. Mei*. Dept. of Physiol., State University of New York, Downstate Medical Center, Brooklyn, New York.

The ventilatory drive of the carotid bodies to CO_2 was investigated in anesthetized dogs in which the sites of these chemoreceptors on both sides were completely isolated from their own circulation and perfused by blood from the respective common carotid arteries of a donor dog under anesthesia. Ventilation, alveolar P_{CO_2}, femoral arterial blood pressure and heart rate were monitored continuously, and the arterial P_{CO_2}, P_{O_2} and pH were determined in spot samples in steady state. In one part of this cross circulation experiment, both dogs were given O_2 to breathe, and to this an appropriate amount of CO_2 was added to bring their arterial P_{CO_2} to the same level. Then holding this P_{CO_2} constant in the recipient dogs, the donor dog was given CO_2 to inspire at different levels in O_2. The ventilatory response defined the CO_2 response of the carotid bodies at a given level of central and aortic body response to CO_2. Similar experiments at other levels of P_{CO_2} in the recipient dog were repeated to obtain a family of these lines. The $\dot{V}$-P_{CO_2} points where both dogs had the same arterial P_{CO_2} defined the total response (peripheral + central) of the recipient dog to CO_2. Out of nine pairs of these preparations we made so far, a variable but definite contribution of the carotid chemoreceptors to the ventilatory response of the recipient dog to CO_2 was obtained. Supported in part by grants from N.I.H. H-4032 C13, and H.R.C. of New York City U-1490.

NORMAL CANINE VENTRICULAR BASE AND APEX FIBER SIZE. Michael M. Laks* and H.J.C. Swan. Cedars-Sinai Medical Center, Los Angeles, California

The purpose of these experiments was to determine myocardiac fiber size at the base and apex of the normal dog heart as a preliminary to the study of induced ventricular hypertrophy. Sections of trabeculae carnae were taken from the 1 cm. cut of the bases (free wall) and from the last 1 cm. cut at the apices (free wall) of right and left ventricles. In order to obtain the least distortion the fresh myocardium was fixed in osmium tetroxide, imbedded in Epon 812, and cross sections made at ½ micron. The following measurements were made from light microphotographs: minimal diameter (D_{min}), maximal diameter (D_{max}), and total surface area by planemetry (A). If one assumes that the muscle fiber is a right circular cylinder, the minimal diameter of any ellipse produced by a plane cut through the center of that cylinder is the diameter of the circle. If all fiber sizes were similar, a coefficient of variation between minimal diameter as indicated above would be zero. The coefficients of variability were as follows: D_{min} = 22%, D_{max} = 24%, and A = 30%. For normal dog hearts, D_{min} (microns/m^2) of the R.V. base = 20 ± 3.5 significantly exceeded ($P \Rightarrow 0.005$) R.V. apex 17 ± 3.4. The mean diameter of L.V. base was 17 ± 3.5 and exceeded D_{min} L.V. apex 15 ± 3.4. In the normal dog heart the fiber diameter of the R.V. base exceeds that of the apex and of the L.V.

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HYPERTENSION PRODUCED BY ANTI-RAT PLACENTAL ANTIBODY. Herbert G. Langford, Ben H. Douglas,* and Roger B. Arhelger*. Departments of Medicine and Pathology, Univ. of Mississippi Medical Center, Jackson, Mississippi.

Current concepts of preeclampsia assign a central role to the placenta. In an attempt to injure the placenta, 15 rats were immunized with rat placenta in Freund's adjustment. Fifteen nonpregnant rats were also immunized and served as controls. Mild blood pressure elevation not increased by pregnancy and proteinuria developed in both groups. In further studies pregnant and nonpregnant rats were given 0.5 ml rabbit anti-rat placenta serum I.V. (RARPS). Control rats were given normal rabbit serum. Pregnant rats receiving RARPS developed significantly more hypertension by the 5th day than the nonpregnant rats, and control rats blood pressure did not change. The response to rabbit anti-rat kidney serum (RARKS) was then compared with the response to RARPS. Blood pressure of RARPS serum injected pregnant rats was 159 ± 5, nonpregnant rats 126 ± 4, control pregnant rats 123 ± 3. However, pregnancy did not affect the blood pressure response of rats given RARKS (Pregnant 131 ± 3, nonpregnant 135 ± 2, control pregnant 123 ± 3).

We conclude that rabbit anti-rat placenta serum produces more hypertension in pregnant than nonpregnant rats, a difference not produced by anti-kidney serum.

(Supported by Grants from NIH).

CHANGES IN THE LIPID COMPOSITION OF THE ORGANS OF THE CHITON, KATHARINA TUNICATA, IN RESPONSE TO GAMETOGENESIS AND STARVATION. J. M. Lawrence (intr. by R. V. Talmage). University of South Florida, Tampa.

The total lipid, neutral lipid, and polar lipid content of the digestive gland, gonads, foot, and mantle of the chiton, Katharina tunicata, were determined during gametogenesis and starvation. The total lipid was extracted with chloroform and methanol, and the neutral lipid and polar lipid fractions separated on silicic acid columns. High levels of neutral lipid were associated with high percentages of total lipid in the foot, mantle and digestive gland in the early stages of gametogenesis. In late stages of gametogenesis, lower levels of neutral lipid and total lipid were found in these organs. Animals starved during this period had comparable low levels. The testis contained low levels of total lipid and neutral lipid while the ovary contained high levels regardless of the reproductive or nutritional condition of the animal. Neutral lipid from non-gonadal organs appear to be utilized during gametogenesis and/or starvation.

EFFECT OF TEMPERATURE AND SPECIES ON KINETICS OF $CO + O_2Hb \rightarrow COHb + O_2$ IN RED CELLS, W. H. Lawson, Jr. (intr. by L. W. Eichna) Downstate Med. Ctr., Brooklyn, N. Y.

The rate CO combines with oxygenated intact red cells and hemoglobin solution was measured in vitro as a function of temperature with a stop flow rapid reaction apparatus. Measurements were made between 7 and 41C with blood diluted 1:50 in isotonic buffer from 3 each of humans, dogs, and cats. Mean initial rates for red cells (θ) at 37C, initial PO_2 75 mmHg, and pH 8.7 for the respective species were .67, .91, and .54 ml/(ml x min x mmHg) corrected to a blood hgb. concentration of 15 grm. % and initial CO less than 3% of the O_2 concentration. We confirmed the results of Roughton and Forster that varying pH from 8.7 to 7.2 has no effect on θ in the presence of insignificant amounts of reduced hemoglobin. There was a linear relation between log rate and reciprocal of the absolute temp., and calculated "activation energies" were 11.3, 12.9, and 10.6 kcal./mole in the respective species, agreeing within either 10 or 20% of that predicted for red cells from hemoglobin solution rates whose energies of activation were greater at 19.6, 19.1, and 19.8. Red cells offer about 57% of the resistance to CO diffusion in the normothermic dog lung (Dco) inspiring 21% O_2 (J. Appl. Physiol. 21:365, 66), and at 25C the 56% reduction in θ from 37C should result in a 43% reduction in Dco. A 59% reduction in Dco was measured by Otis and Jude in the dog at 25C (Am. J. Physiol. 188: 355, 57), suggesting that nearly all the reduction in Dco in moderate hypothermia can be accounted for by the reduction in θ .

ACTIVE NEURAL MEMBRANE FACING A LIMITED EXTRACELLULAR SPACE: A COMPUTER SIMULATION. Robert Lebovitz.* (intr. by B.M. Wenzel). Dept. of Physiology and Brain Research Institute, UCLA

A computer simulation of active neural membrane facing a restricted extracellular volume has been developed to explore the neurophysiological consequences of the close intermembrane spacing found in the CNS. The neural membrane is described by the Hodgkin-Huxley equations while the structure opposite to the discharging membrane, a functional composite of neural and glial membrane, is treated in terms of its role as a contributor to significant fluctuations in the external ionic concentrations. The dynamics of the system (active neural membrane)-(aqueous space)-(boundary membrane) indicates that, due to such transient shifts in ionic gradients, the behavior of the neural membrane departs qualitatively as well as quantitatively from that of active membrane that faces an extended external space. In addition to depolarizing afterpotentials, the simulated active membrane displays more elaborate boundary dependent behavior such as repetitive firing, burst responses, and large (30-40 millivolt) cumulative depolarizations. This activity occurs in response to a single, brief suprathreshold pulse when the intermembrane space is small (100-150 Å). At larger separations (150-250 Å) the recent history of the active membrane and/or the boundary membranes becomes the significant determinant of these responses. The theoretical observations are compared with published intracellular records obtained particularly from closely spaced hippocampal units and are discussed as possibly reflecting a mechanism for nonsynaptic modulation of unit activity. (Supported by USPHS grants 5 TI GM 448-06, 5 TI MH 6415-10, NB-02501, and FR-3.)

BLOOD GAS TRANSPORT AND RESPIRATORY PATTERNS IN SELECTED AMPHIBIANS. C. Lenfant & K. Johansen. Inst. of Resp. Physiol. Firland Sanatorium and Depts. of Physiol. & Zoology, Univ. of Wn., Seattle, Wn.

In order to evaluate some of the respiratory adaptations concomitant to the transition from water breathing to air breathing 3 amphibians were studied: the aquatic Necturus maculosus which possesses external gills & a poorly developed lung, Amphiuma tridactylum which has no gills but remains in water all the time depending on pulmonary breathing, and the Bullfrog, Rana catesbeiana, which is more terrestrial & uses pulmonary respiration. Respectively for Necturus, Amphiuma & Bullfrog the oxygen capacity was 6.3, 7.6, & 8 vol %; the affinity for O_2, or P_{50} at the physiological P_{CO_2}, was 14, 27 & 39 mm Hg; the Bohr effect or $\log \Delta P_{50}/\Delta pH$ was -.131, -.205, & -.288; the CO_2 combining power at the physiological P_{CO_2} was 21, 32 & 31 vol % & the buffering capacity, or $\Delta HCO_3/\Delta pH$, was -8., -9., & -16. mM/L/pH. The respiratory behavior of these animals at 20°C was studied by in vivo blood gas measurements. P_{aO_2} & P_{aCO_2} of Necturus kept in water were 35 & 4.4 mm Hg respectively. When removed from water the exchange of blood gases was greatly impaired in spite of frequent air breathing. In free-breathing Amphiuma P_{aO_2} was 81 and P_{aCO_2} 6 mm Hg. When prevented from air breathing P_{O_2} decreased and P_{CO_2} increased slowly suggesting that the animal uses its skin to exchange gases with water fairly effectively. In Bullfrog P_{aO_2} was 95 & P_{aCO_2} 8 mm Hg. When the animal was immersed P_{O_2} decreased & P_{CO_2} increased rapidly suggesting the absence of an efficient skin respiration. These findings are regarded as expressing adaptive changes to meet an increased O_2 availability of the external medium, & an elevated internal P_{CO_2} in the transition from aquatic to aerial respiration.

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MYOCARDIAL AMINO ACID UPTAKE, IN VITRO. Eugene A. Lentini, Dept. of Physiology, Medical College of Virginia, Richmond, Va.

Investigations relating the glucose uptake of trabecula carneae to the developed tension (Physiologist 5:174:1962) led to studies designed to determine the uptake of amino acids by this same preparation. The amino acids initially selected were lysine, methionine, arginine, and leucine. These were selected due to their positive inotropic effect on the trabecula when glucose was present in the Ringer's perfusion solution.

The muscle preparation was placed under a total resting tension of one gram and stimulated at a frequency of 1/sec. The oscillographic recording of the isometric developed tension was achieved by using a strain gage transducer. The amino acid uptake was calculated from differences in the amino acid concentration of the bathing fluid during the experimental periods.

It was noted that only 6 of 35 preparations revealed an amino acid uptake. Of the amino acids tested as substrates, lysine was more consistently utilized by heart muscle as compared to the other amino acids. Uptakes of glucogenic amino acids as glycine and alanine were not evident. Only 2 of 8 additional preparations showed an uptake of glucosamine when present as the only substrate. Changes in the developed tension did not relate to changes in the amino acid concentration of the bathing medium.

The data suggest not only that the amino acid uptake by trabeculae carneae does not occur to the same extent as the glucose uptake but also is inadequate for maintenance of the developed tension.

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DISTRIBUTION OF NEURONAL MEMBRANE POTENTIAL. H. Levitan,* D.H. Perkel,* J.P. Segundo, and G.P. Moore. Dept. of Anatomy and Physiology and Brain Research Inst., UCLA and the RAND Corp., Santa Monica, Calif.

The integrative properties of single nerve cells are intimately associated with the dynamic properties of the membrane potential. Subthreshold fluctuations in potential were measured and described by membrane potential histograms under a variety of input conditions. The membrane potential histogram estimates the probability density function of the membrane potential; the area under this curve between any two values of potential estimates the fraction of time during which the potential lies between these values. Intracellular recordings were made with potassium chloride or citrate microelectrodes from neurons in the visceral ganglion of Aplysia californica. Synaptic input to these cells was provided either by the "spontaneous" activity of other cells or by electrical stimulation of the connectives. When necessary a hyperpolarizing current was applied in order to supress spike production. Comparisons were made between membrane potential densities under non-stimulated conditions and during stimulation in which variations were made in parameters, such as: (i) mean stimulation rate, (ii) evoked PSP amplitude, (iii) PSP sign, i.e., excitatory or inhibitory, (iv) membrane potential resting level without synaptic input, (v) source of synaptic input to the cell, when several connectives provided synaptic input, and (vi) PSP arrival statistics, e.g., regular or Poisson-like. Computation of histograms and related quantities (mean, standard deviation, etc.), performed by digital computer, showed that membrane potential profiles vary characteristically with these parameters. The importance of the membrane potential distribution lies in its correlation with interspike interval statistics and with input-output transmission probabilities. (Supported by NIH and USAF Project RAND)

LEARNED BEHAVIORAL DISCRIMINATION OF FOOD OBJECTS BY APLYSIA CALIFORNICA. Marvin E. Lickey and Robert W. Berry (intr. by Felix Strumwasser). California Institute of Technology, Pasadena, California.

Many physiological studies of the Aplysia central nervous system have recently appeared. In contrast, relatively little attention has been directed toward the behavior of this marine gastropod. The present experiments demonstrate what we believe to be a learned behavioral discrimination between two different food objects. The procedure is as follows: A 24 hour feeding rhythm is first established by allowing the animal to eat the seaweed Ulva, the natural food, for a fixed three hour period each day for at least five days. Two days prior to the onset of the discrimination training trials the food portion is reduced to 0.5% of the animal's body weight in order to establish a deprivation state. During training the animal is offered either Ulva or a glass rod on alternating trials for a total of twenty discrimination trials each day. Initially, the animal will seize and try to ingest the glass rod nearly as often as it ingests the Ulva. After five to ten days of training the animal refuses to seize the glass rod and withdraws the mouth parts from all contact on 90 to 100% of all glass rod trials. This discriminative behavior can persist for at least nine days in the absence of practice. It can be abolished by about three days of counter training in which Ulva and the glass rod are offered simultaneously.

In view of the many advantages of the Aplysia central nervous system for neurophysiological studies, these results suggest that Aplysia may provide favorable material for the study of neural mechanisms of learning.

Autoregulation of Adipose Tissue in the Mouse. R. A. Liebelt and L. A. Vismara (intr. by V. Critchlow). Baylor Univ. Coll. of Med., Houston, Texas.

Previous studies suggested that individual fat depots in mice are functionally integrated into the total body mass of adipose tissue (Ann. N. Y. Acad. Sci. 131:559, 1965). The present study attempted to extend these observations by transplanting isogeneic grafts of adipose tissue to intact hosts or those having had gonadal fat depots (GFO) surgically removed. A total of 62 inbred males and females of the DBA/2 and (BALB/c X Ce)F1 hybrid strains were divided into 4 groups at 3-4 months of age: Group I-sham-operated; Group II-partial incision of right GFO but not removed; Group III-right GFO removed; and Group IV-both GFO's removed. All animals had an isogeneic graft of G. F. O. of comparable size placed either free in the peritoneal cavity or sutured to liver. Animals were killed at 2, 4, 6 and 9 months following transplantation. Gross and histological criteria were used to classify grafts as: reject, poor, or good. Only 3/18 grafts were rated as good in Group I as compared to 4/15 in Group II, 8/14 in Group III and 13/14 in Group IV. Castration of additional animals assigned to similar groups gave comparable results. Grafts of inguinal fat organ were also more successful in hosts lacking both GFOs. Thus, the successful transplantation of specific amounts of isogeneic adipose tissue can be enhanced by surgical removal of GFO, that is, creating a deficit in total adipose tissue mass. These data are consistent with the suggestion that the anatomically dispersed fat depots are functionally integrated by autoregulatory mechanisms.

DICHOPTIC INTERACTIONS OF LATERAL GENICULATE NEURONS OF CATS TO CONTRA- AND IPSILATERAL EYE STIMULATION. D.F. Lindsley, M. Gollender* and K.-L. Chow. Stanford Univ. Med. School, Stanford, California.

In "semi-chronic" cats 14 of 62 lateral geniculate (LGD) neurons examined showed dichoptic interaction, i.e. the response of the unit to stimulation of the contralateral eye by a light spot alone was modified when paired with a flash to the ipsilateral eye, even though the flash itself neither evoked a response nor changed the spontaneous activity of the unit. Also 2 other units showed a labile, binocular interaction. Initially, these 2 units did not respond to a flash to the ipsilateral eye, though they did respond to spot stimulation of the contralateral eye. After several minutes of pairing the spot and the flash, the flash alone began to elicit a response from the unit. It should be noted that in the 46 neurons that did not show either a dichoptic or binocular interaction the response of the units to pairing of the spot and flash was exactly the same as the response to spot alone. Dichoptic interactions were not found in any single class of LGD neurons, as they occurred in both on and off cells about equally and were found in neurons in the middle of and the edge of layers A and B, though mainly in A. Interactions were of 3 general types: pattern, latency and pattern-latency. The spot-flash intervals which were effective in producing dichoptic interactions were limited, in general, to 25, 50 and 100 msec. Five of the 14 dichoptic units and the 2 binocular units developed a labile response following 2-3 min. of spot-flash pairing different from the response after 1 min. of pairing.

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EPINEPHRINE-LIKE ACTIVITY OF FILTRATES OF BACILLUS ANTHRACIS. H.S. Lipscomb, R.P. Williams, H.R. Hill, K-C Chao, D. Hawkins, Jr., and J. Neuenschwander (intr. by J. Awapara). Baylor Univ. College of Medicine, Houston, Texas.

Crude filtrates of culture medium inoculated with the Vollum strain of Bacillus anthracis were studied in vivo and in vitro and found to possess an activity similar to that produced by l-epinephrine. In vivo, the pithed rat displays a striking rise in arterial blood pressure, the effect being primarily one of widened pulse pressure. This effect can be blocked selectively by drugs which affect α- and β-adrenergic receptor sites, and can be potentiated by cocaine. Filtrates of culture medium alone, or of E. coli, are without effect. Adrenalectomized, reserpine-treated animals, no longer responsive to tyramine, continue to show a response, indicating that the material is not active through secondary release of endogenous catecholamines, but, rather, through an intrinsic, epinephrine-like activity of the filtrate itself. In vitro, the material affects aorta-strip and guinea pig ileum in a fashion similar to that of epinephrine. The material did not make either in vivo or in vitro preparations more sensitive to subsequent doses of epinephrine, as has been described for classic endotoxins (Zweifach, et al, J. Exp. Med.: 104, 881 - 1956), nor did the material kill the assay animals at doses up to 0.8 grams; therefore, we conclude that the material is not the classic "endotoxin" of anthrax. Under investigation is the structural identification of the material and its possible role in the clinicopathologic picture of anthrax septicemia. The possibility exists that other bacterial septicemias may be associated with the production of similar substances. This represents the first report of a hormone-like activity in bacterial filtrates. (Supported by NIH Research Grants AM-04122, AI-1535, and GRS P-66-1)

BREATH-BY-BREATH CO_2 ELIMINATION BY ON-LINE SPECIAL PURPOSE ANALOG COMPUTER. J. A. Lipsky and Alfonso Angelone*. Department of Physiology, The Ohio State University, College of Medicine, Columbus, Ohio.

A special purpose on-line analog computer has been designed to rapidly and repetitively determine CO_2 elimination on a breath-by-breath basis. Input information consists of CO_2 concentration at the level of the lips and expired air volume, as determined by infrared analysis and pneumotachography, respectively. The basis of the computation utilizes the relationship $\dot{V}_{E_{CO_2}} = \int \text{Flow} \times F_{E_{CO_2}}\, dt$ which provides not only an estimation of CO_2 elimination per breath, but also a continuous indication of CO_2 elimination within a single expiration. The static accuracy of the system is better than 0.1% over an optimal input voltage range of 0.2 - 1.0 vdc. Under dynamic conditions, an excellent correlation exists ($r = 0.9941$) between the breath-by-breath technique and a standard collection technique. Data from 34 consecutive sets of measurements, encompassing CO_2 elimination rates ranging from 150 - 900 cc CO_2/minute, indicate an absolute mean difference of +1.5%. Breath-by-breath computations indicate that an oscillatory pattern of CO_2 output exists during steady-state respiration. Under these conditions, the difference between maximum and minimum levels of CO_2 output per breath may be in the order of 10 cc. The on-line analog computer provides a means of rapidly determining CO_2 output from a large number of breaths, and enables real time quantitation of CO_2 transients. (Supported by PHS Research Grant HE-0878-03 from the National Heart Institute, and the General Research Support Grant of the USPHS.)

ATPase ACTIVITY OF RETINAL ROD OUTER SEGMENTS. Richard N. Lolley (intr. by Wm. G. Clark). Neurochem. Labs, V. A. Hospital, Sepulveda, Calif.

Sensory perception is an organism's informational contact with its environment. In higher animals, specialized structures have developed which receive, convert and transmit sensory stimuli from the environment to the brain. Thus, retinal rod cells respond to light and the mechanism(s) for transduction appear to reside in the retinal rod outer segment (ROS). The participation of cation transport in ROS function has been suggested because isolated ROS preparations have shown significant Na-K activated ATPase activity. Homogenous preparations of frog ROS have been isolated by density gradient centrifugation at 50,000 x g for 90 min (4°C) in an isotonic gradient of Ficoll and 0.24 M Sucrose. Under these conditions the ROS are isopycnotic with 24-25% Ficoll-sucrose. These structurally intact ROS exhibit very little glucose metabolism: Malic dehydrogenase activity < 0.7 mM DPNH reduced/hr/gm protein. ROS hydrolyze ATP at a rate of 1.6 mM/hr/gm protein. The ATPase is Mg-dependent and its activity is unaffected by exogenously added sodium (58 mM) and potassium (5 mM). Oubain (0.1 mM) shows no significant inhibition. The ATPase activity is not influenced by continuous or flashing light. Slightly less homogenous ROS preparations (the fraction above the ROS layer) show 15-20% Na-K activation but these fractions contain numerous small unidentified fragments. These data strongly suggest that the ROS is lacking or very deficient in the Na-K activated ATPase system.

FAT INHIBITION OF GASTRIC SECRETION STIMULATED BY SHAM FEEDING AND INSULIN HYPOGLYCEMIA. James F. Long (Intr. by Robert S. Alexander), Albany Medical College, Albany, New York.

Olive oil, 1.25 ml/kgBW, was infused directly into the duodenum of 3 dogs prepared with gastric and duodenal fistulas and esophagostomies over a 40 min. period starting either 5 mins. before a 10 min. period of sham feeding (SF) or 15 mins. after IV injection of 1U/kg insulin (I). Acid and pepsin outputs collected every 30 mins. for 4 hrs. after stimulation in 9 SF and 9 I experiments were compared to 9 SF and 9 I experiments without fat, and to 9 trials with fat infusion without cephalic stimulation. The fall in blood sugar after I alone and after I plus fat were not different at any time period. Olive oil inhibited acid output initially, 55 and 50% for SF and I, respectively, during the first hr. after stimulation. This was followed by a rebound in acid output at 2 1/2 - 3 hrs. when outputs exceeded SF or I alone by 114 and 152%, respectively. Fat infusion alone produced delayed stimulation of acid and pepsin outputs. The stimulation occurred at the same time as the rebound occurred when fat was given with SF and I. The amount of acid secretion in response to the fat alone was equivalent to that which was secreted during the rebound period. The total amount of acid and pepsin secreted over the 4 hr. collection period was less for SF and I plus fat than for SF and I alone. Compared to previous results obtained with feeding stimulation in innervated pouch dogs, fat is not as effective an inhibitor of cephalic stimulation as it is feeding stimulation and the rebound is significantly greater with feeding stimulation than with SF or I.

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PLACENTAL EXCHANGE OF CARBON MONOXIDE IN SHEEP AT HYPERBARIC PRESSURES. L. D. Longo*, G. G. Power*, and R. E. Forster II (Introduced by C. J. Lambertsen). Dept. of Physiology, Graduate Division, and Dept. of Pharmacology, School of Medicine, University of Pennsylvania, Philadelphia, Pa.

In an attempt to determine the rate limiting factors in maternal-fetal gas exchange in the placenta, we measured the uptake of CO by the fetus in 6 pregnant ewes breathing 100% O_2 at total pressures up to 5 atmospheres absolute. In 3 ewes at about 3800 mm Hg total pressure, the average values of P_{O_2} were as follows: inspired, 3600 mm Hg; uterine artery, 3200 mm Hg; uterine vein, 1500 mm Hg; fetal umbilical vein, 700 mm Hg; and umbilical artery, 40 mm Hg. At this pressure the uterine arterio-venous difference averaged 4 ml/100 ml blood, while the fetal placental arterio-venous difference averaged 5 ml/100 ml blood. Over a period of 10 to 70 minutes following the introduction of 46 ml of CO into a closed rebreathing circuit to which the ewe was attached the fetal uptake of CO averaged 0.04 ml/min; the maternal-fetal CO partial pressure gradient 0.26 mm Hg; and the CO diffusing capacity ($D_{P_{CO}}$) 0.15 ml/(min x mm Hg), a value about 10% of that found at normal atmospheric pressure breathing air. The decrease in $D_{P_{CO}}$ at elevated levels of maternal blood P_{O_2} suggests that the reaction rates of CO with hemoglobin and the placental capillary blood volumes are important factors in limiting the placental exchange of CO. (This work supported in part by Grants HD 01860 and HE 08184.)

STEROIDS THAT MIMIC THE EFFECTS OF GONADOTROPINS ON THE OVARY AND UTERUS. Ardis J. Lostroh, Hormone Research Lab., Univ. of Calif. Berkeley.

Ovine gonadotropins, injected once daily subcutaneously for a period of 3 days, elicit characteristic responses in the ovary and uterus of the hypophysectomized rat. Follicle-stimulating hormone (FSH), 2 μg/day, induces antrum formation in developing follicles; interstitial cell-stimulating hormone (ICSH), 0.6 μg/day, effects repair of ovarian interstitial cells; the combination of FSH and ICSH stimulates mitotic activity among the granulosa cells of the follicle, follicular growth, and changes in the uterus associated with proestrus and estrus. Steroids (aqueous suspensions, 1 mg/day x 3 days), injected into Sprague-Dawley rats hypophysectomized at 28 days of age, had the following effects. 1) ICSH-like: pregnenolone, 17α-hydroxypregnenolone, progesterone, and 17α-hydroxyprogesterone each effected some repair of the interstitial tissue; 2) FSH-like: dehydroepiandrosterone stimulated the formation of small antra; 3) combination ICSH-FSH-like: both dehydroepiandrosterone and testosterone propionate effected significant increases in uterine weight; androstenedione was less active in this respect. Estrogen enhanced mitotic activity of the granulosa cells and stimulated the uterus. In the ovary of the rat, the Δ^5 pathway appears to be favored over the Δ^4 pathway. Sites for gonadotropin action compatible with these results will be proposed. (Supported in part by a grant from the U. S. Public Health Service, AM-6097).

EXTERNAL STIMULATION OF GASTRIC ANTRUM AND GASTRIC SECRETION. P. Lott, Jr*, T. Geisel*, N.C. Jefferson, and H. Necheles. Michael Reese Hospital and Medical Ctr. Chicago, Ill.

Liberation of gastrin from the gastric antrum has been achieved by direct stimulation of the antral mucosa, such as changes in pH, stimulation by food, stimulation of vagus nerves, physical stimulation and transplantation of the antrum into the colon. We wondered whether external stimulation of the antrum through the serosa would have similar effects and might give us clues to the mechanism of liberation of gastrin. Dogs were prepared with gastric cannulas or Heidenhain pouches. Two electrodes were attached to the serosa of the anterior and the posterior antrum and brought out in the neck. After the dogs had recovered, experiments were performed on basal secretion and secretion stimulated by food, insulin, or histamine. After basal secretion was collected, the antrum was stimulated for one hour through the electrodes by square wave pulses, followed by collection of basal secretion or of secretion stimulated by food, insulin or histamine. In a number of tests external stimulation of the antrum increased the volume and the acidity of gastric secretion considerably.

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THE EFFECT OF FEEDING ON DUODENAL BLOOD FLOW IN THE NON-ANESTHETIZED DOG. H. S. Loucks, R. B. Rich*, and K. J. Forman*, Department of Physiology, The George Washington University, School of Medicine, Washington, D.C.

Blood flow was recorded as velocity flow with an ultrasonic flowmeter. Using aseptic techniques the flowmeter transducer was implanted around the pancreatico-duodenal artery in two well-trained mongrel dogs. After recovery from surgery, blood velocity was recorded for sixty minutes under four different experimental situations: a) when the animals were 18-24 hours postprandial, b) when beef broth was introduced in the gastric antrum at time 0, c) when cream was placed in the gastric antrum at time 0, and d) when tap water was placed in the duodenum at time 0. The velocities at time 0 were similar in situations a, b, and c. A decrease in blood velocity of approximately 20% occured in the postprandial state. An increasing trend of approximately 20% during the sixty minutes occured for both the beef broth and the cream. With tap water in the duodenum, the blood velocity remained unchanged although it seemed to start at a lower level than in the previously described situations. Comparisons with intestinal motility are in progress utilizing a second flowmeter channel to monitor chyme flow.

(Supported by Grant NSF GB 3319)

ANALYSIS OF RIBOSOMAL PROTEIN BY POLYACRYLAMIDE GEL ELECTROPHORESIS. R. B. Low* and Ira G. Wool (intr. by Dwight J. Ingle). Univ. of Chicago, Chicago, Ill.

To determine if the genome(s) for ribosomal protein(s) is the same in all mammalian tissues the product of the genome was analyzed using high resolution polyacrylamide gel electrophoresis. Ribosomes were isolated from liver, kidney, myocardium and skeletal muscle of the rat; from reticulocytes of the rabbit; and from bacteria (E. coli). Ribosomal protein was extracted with 8M urea and 4M LiCl and analyzed by electrophoresis on acrylamide gels at pH 4.5 and pH 8.3. The gels were stained with Amido Schwartz and scanned with a Canalco Model F microdensitometer. Each of the ribosomal proteins from mammalian tissues yielded twenty-three bands when analyzed at pH 4.5 and densitometric tracings established that the patterns of the basic ribosomal proteins from the several tissues were identical. Protein from E. coli ribosomes gave, on electrophoresis, twenty-six bands and the pattern was different from that of mammalian ribosomal protein. No distinct band was found when protein from mammalian tissue was analyzed at pH 8.3 (acidic proteins). Ribosomal protein from E. coli gave seven or eight bands at pH 8.3. It is concluded that the same genome is responsible for the synthesis of ribosomal protein in all mammalian tissues and that a different genome directs the synthesis of ribosomal protein in bacteria.

DIMENSIONAL ADAPTATIONS OF LEFT VENTRICLE TO AORTIC CONSTRICTION.
D.M. MacCanon, J. Balfus*, D.W. Bruce*, and M. Worthen*. Division of Cardiovascular Research of The Chicago Medical School, Chicago, Ill.

Studies were made in open chest anesthetized dogs of the left ventricular responses to experimental obstruction of aortic outflow. Left ventricular pressure, dp/dt, wall tension, apical length and circumferential length changes were recorded. Normally both dimensions increased during isovolumetric contraction as the left ventricle became more spherical. Circumferential shortening normally dominated ejection. Aortic constriction increased both dimensions and gradually shifted shortening function to the apical portion. Tension curves became peaked and followed the pressure pattern. Further constriction produced extreme apical changes with little additional circumferential change. Removal of the pericardium enhanced circumferential dilatation and graduated the rather abrupt terminal failure characteristic of closed pericardium experiments. Supported by a grant from the Chicago and Illinois Heart Association.

A PLETHYSMOGRAPHIC TECHNIQUE FOR RECORDING
THE PHASIC VARIATIONS IN HUMAN VENOUS BLOOD FLOW
Ian F.S. Mackay, P. Van Loon* and J.T. Campos*
Dept. of Physiology, Medical School, San Juan, P.R.

The subject lies supine on a tilt-table approximately 10° to 20° head down. The forearm is flexed and so positioned that the zero level of venous pressure passes through the center of a forearm plethysmograph. The following records of changes in limb volume were made:-

A. The forearm volume changes due to phasic arterial input and phasic venous drainage.

B. The phasic arterial input volume alone(with a venous occluding cuff applied at 50 mm. Hg. pressure).

Record B. is subtracted from record A., from which is calculated the resting phasic venous volume changes. From the latter are calculated the phasic venous flow rates.

It was found there was a large forward flow related to ventricular contraction followed by a reduction in flow. These findings are in agreement with those of Brecher[1] and Muller[2], measured directly in dogs and human subjects.

1. Brecher, G.A. The Venous Return. 1956.
2. Muller, O. and Shillingford J. British Heart J. 17:163, 1955.

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CIRCULATORY EFFECTS OF CENTRAL VAGUS AND SPLANCHNIC NERVE STIMULATION. ROBERT MACKOWIAK*, DONALD STOCK*, JAMES TOWNSEND*, AND M.H.F. FRIEDMAN. DEPARTMENT OF PHYSIOLOGY, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

Experiments were performed on mongrel dogs and cats anesthetized with thiopental-chloralose-urethane. Vagus nerves were isolated and divided in the neck while splanchnic nerves were isolated just above the diaphgram and divided. Bipolar electrodes were attached to the cephalad portion of the nerve and surrounded with liquid petrolatum to isolate the stimulating current. Cardiac dynamics and peripheral hemodynamics were monitored.

In the dog central vagus stimulation with current of low intensity (1-2 milliamp, 3-5 volt, 1 millisec. pulse at 20 per sec) resulted in bradycardia and hypotension. Increased current strength to 10-20 volts produced tachycardia and elevated blood pressure which were unrelated to respiratory effects. Central vagus stimulation in the cat always produced bradycardia and hypotension with current intensity ranging from 1 to 20 volts.

Central splanchnic stimulation with low intensity current produced in the dog a pure fall in arterial blood pressure without effect on heart rate: this hypotension was unaffected by bilateral vagectomy or atropine. Currents of higher intensities (10-20 volts) produced both hypertension and tachycardia.

ELECTRICAL POTENTIALS AND ION CONCENTRATIONS ACROSS THE INTESTINE OF CRYPTOCHITON STELLERI. D. S. Mailman and A. L. Lawrence (intr. by J. W. Hudson). University of Houston, Houston, Texas.

The intestine of the mollusc Cryptochiton stelleri was studied from the viewpoint of mapping potentials and ion concentrating ability. Electrical potentials were determined by means of high impedance electrometer. Cl^- concentrations were determined by means of a Cotlove chloridometer and Na^+ and K^+ by flame photometry. Everted cannulated segments were studies by the method of Wilson and Crane. Invertebrate glucose Ringers bathed the segment on both sides. The anterior intestine (presphincter portion of the gut) was found to have a potential of the order of 0.5 mV (serosal negative). The posterior intestine (postsphincter portion of the gut) was found to have a potential of the order of 1.0 mV (serosal positive). Anoxia decreased the potentials to approximately one-half of their aerobic values. Readmission of oxygen increased the potentials approximately six-fold within one minute. Altering the temperature (5°-10°-15°-20°-25° C) indicated maximum potentials in the anterior gut at 15° C and posterior at 20°. Temperatures of 25° caused complete loss of potential. Considering the potentials and observed ion concentrations, sodium was actively transported out of the lumen at the beginning and end of the hind gut and potassium into the lumen in the anterior gut and out of the lumen in the posterior gut. Cl^- was largely passively distributed. Ion transport was considered to be at least partially electrogenic in nature.

Supported in part by NIH Biophysics training grant.

INFLUENCE OF ANGIOTENSIN II ON PLASMA CATECHOLAMINES BEFORE AND DURING INFUSION OF NOREPINEPHRINE. W. M. Manger, G. G. Nahas, K. G. Wakim, S. Dufton,* J. Manger.* Columbia Med. Ctr., New York and Mayo Clinic, Rochester, Minn.

An interplay between the sympathoadrenal system and angiotensin in renal hypertension has been suggested. We (Milhaud, Nahas, Manger) have demonstrated release of catecholamines (mainly epinephrine) from isolated perfused adrenals following administration of angiotensin. Experiments were designed to study effect of angiotensin on stored catecholamines in vivo. Under local anesthesia blood was obtained simultaneously from femoral artery and vein for quantitating catecholamines before and during norepinephrine infusion (2μg/Kg/min). Blood was obtained immediately before and 2 minutes after rapid intravenous angiotensin (.025 mg/10Kg) injection prior to norepinephrine infusion, again 50 and 60 minutes after starting the infusion and finally 2 minutes after another angiotensin injection. Angiotensin increased mean arterial pressure significantly but only a very slight increase in arterial plasma catecholamine concentration occurred before norepinephrine infusion. However, angiotensin injection during norepinephrine infusion caused a marked increase in arterial concentration of norepinephrine (from 29 to 52.2μg/L plasma) with usually only a small elevation of norepinephrine in the venous plasma. A slight increase in epinephrine occurred in both venous and arterial plasma. The mechanism whereby angiotensin liberates norepinephrine is uncertain. It is conceivable that angiotensin may partially displace norepinephrine from its storage sites. (Supported by W. M. Manger Res. Fndn., N. Y.)

RELATIONS BETWEEN THE DISTRIBUTION OF TENDON ORGANS AND MUSCLE SPINDLES IN THE CAT. E. Roger Marchand*, E. Shumpert*, E. Eldred and C. F. Bridgman*. Dept. of Anatomy, Univ. of California, Los Angeles, Calif.

The distribution of tendon organs (TOs) in the extensor digitorum brevis (EDB) and longus (EDL) muscles of the adult cat have been studied from serial histological sections stained by the Van Gieson technique. The TOs of the EDB, unlike those in other muscles of the cat, were found to attach solely along the tendonous slips of insertion; on both superficial and buried portions of the tendon.

A characteristic relation between TOs and spindles was found for 17 of the 37 TOs identified in one EDB muscle. The spindles took origin in the acute angle formed between the TO and its attached muscle fascicle on the one hand and the aponeurosis. TOs found in this relationship to spindles were longer, broader and contained more fascicles of collagenous fibers than TOs elsewhere having no close association to the spindles. This pattern was seen in some spindles in the EDB, EDL and gastrocnemius of the cat and in the EDL of the rat. Study is being extended to younger animals to determine the developmental significance of the relationship, and to the monkey to see if this is found in a higher species. (Supported in part by NSF grant GB 3159 and USPHS grant NB 03019.)

EFFECTS OF OXYTOCIN ANTAGONISTS ON THE ELECTRICAL AND MECHANICAL RESPONSE OF THE RAT UTERUS. J. M. Marshall and N. Taira*. Dept. of Pharmacology, Harvard Medical School, Boston, Mass.

At least three types of compounds antagonize the uterine response to oxytocin: 1) simple aliphatic substances containing free SH groups, of which thioglycollate (TG) is a prototype; 2) sulfhydryl blocking agents, e.g., N-ethylaleimide (NEM); 3) some analogues of oxytocin, e.g., 2-O-methyltyrosine oxytocin (Tyr-Me^2-O). The purpose of the present study was to determine whether the effects of these three representative antagonists are mediated by changes in the membrane potentials of the myometrial cells. Uterine strips were isolated from rats at term pregnancy. Membrane potentials were recorded with glass, KCl-filled micropipettes, and contractions with a mechanotransducer, RCA 5734. TG (5 mM) and Tyr-Me^2-O (10^{-7} M) inhibited the uterine response to oxytocin but not to acetylcholine, bradykinin or electrical stimulation. The inhibition was competitive, i.e., it could be surmounted by increasing the dose of oxytocin. It was accompanied by a suppression of action potential production but not by a change in level of the resting potential. NEM (1 mM) caused a non-specific, insurmountable antagonism to all stimulants. It abolished the production of action potentials but did not alter the level of the resting potential. Hence, these three antagonists of oxytocin may be classified as non-depolarizing blocking agents. (Supported by USPHS grant HE-05702.)

INFLUENCE OF THYMECTOMY ON RENAL EXCRETION OF SODIUM AND POTASSIUM IN THE RAT. Constance R. Martin and Siret D. Jaanus*. Dept. Biol. Sci., Hunter College, C.U.N.Y., Park Avenue, New York, N.Y.

Male hooded rats weighing 110-120 grams were subjected to thymectomy, sham thymectomy, thymectomy-adrenalectomy, sham thymectomy-adrenalectomy, adrenalectomy or no surgery, and housed 2 to a metabolism cage in a temperature and humidity controlled room. Drinking fluids (1% NaCl for adrenalectomized groups and 1% $NaHCO_3$ for all others) and powdered Purina Chow were given ad lib., and intakes were measured. Urine samples were collected at 2-4 day intervals and analyzed for Na and K by flame photometry. Thymectomized rats retained significantly more Na and K than did sham thymectomized or unoperated rats. Kidney and adrenal weights of thymectomized rats equalled those of unoperated rats drinking tap water, but kidneys and adrenals of sham thymectomized and unoperated rats on $NaHCO_3$ were markedly enlarged. No differences between sham thymectomized and unoperated (or between sham thymectomized-adrenalectomized and adrenalectomized) rats were observed. Thymectomized-adrenalectomized rats retained more Na than did sham-thymectomized-adrenalectomized rats, although all adrenalectomized rats excreted more Na than did corresponding groups with adrenal glands. The data suggest that the thymus gland influences electrolyte excretion in the Na loaded rat by a mechanism which is independent of mineralocorticoid function. (Supported by Grant # P-382, American Cancer Society.)

SURFACE BEHAVIOR OF INDIVIDUAL LIPIDS SIMILAR TO PULMONARY SURFACTANT. M. J. MASTRANGELO, W.P. GIORDANO AND R. P. JOHNSON (INTR. BY E. G. CUMMINGS) MEDICAL RSCH. LAB., EDGEWOOD ARSENAL, MD.

SURFACE FILMS OF AMPHIPATHIC NEUTRAL LIPIDS AND PHOSPHOLIPIDS, SIMILAR TO THOSE FOUND IN PULMONARY SURFACTANT, WERE CHARACTERIZED BY THEIR SURFACE BEHAVIOR, INCLUDING THAT UNDER HIGH SURFACE PRESSURE. TO ACHIEVE THIS END, EACH LIPID WAS STUDIED WITH RESPECT TO: EQUILIBRIUM POINT, HYSTERESIS, HYPERCOMPRESSIBILITY AND ISOTENSION POINT, THE LATTER TWO BEING NEWLY DEFINED PARAMETERS. SATURATED (STRAIGHT) HYDROCARBON CHAIN MOLECULES EXHIBITED MUCH LOWER ISOTENSION POINT SURFACE TENSIONS THAN THEIR RESPECTIVE UNSATURATED (BRANCHED) ANALOGS, WHEREAS THE REVERSE WAS TRUE FOR THE EQUILIBRIUM POINT SURFACE TENSIONS. SATURATED COMPOUNDS EXHIBITED CONSIDERABLY MORE HYPERCOMPRESSIBILITY THAN THEIR UNSATURATED ANALOGS. THE ORDERING OF LIMITING SURFACE TENSION AT HIGHEST COMPRESSION (ISOTENSION POINT) WAS NOT ASSOCIATED EXCLUSIVELY WITH OBVIOUS STERIC RELATIONS BUT RATHER SUBTLE AND UNDEFINED ELECTRONIC FACTORS WERE ALSO PARTICIPATING. THE SIGNIFICANTLY LOWEST SURFACE TENSIONS OBTAINED ON COMPRESSION WERE EXHIBITED BY DIPALMITOYL α LECITHIN, SPHINGOMYELIN, AND PALMITIC ACID. THE LATTER THUS DEMONSTRATES THAT LIPIDS OTHER THAN PHOSPHOLIPIDS CAN EXHIBIT SURFACE ACTIVITY SIMILAR TO PULMONARY SURFACTANT. DEVELOPMENT OF POST ISOTENSION POINT HYSTERESIS WAS LIMITED TO THE SATURATED CLASS OF MOLECULES TESTED.

THE RELATIONSHIP OF PHYSICAL FITNESS TO WORK TOLERANCE AT 12,500 FEET Donald K. Mathews* and Charles E. Billings. Depts. of Physical Educ. and Preventive Medicine, The Ohio State University, Columbus, Ohio

Is the physical fitness of young men living at 750 feet related to work tolerance during acclimatization at an altitude of 12,500 feet? Twenty-four subjects were grouped into three squads of equal physical fitness based on maximal oxygen consumption as determined during several five minute rides on a bicycle ergometer. One squad was placed on the standard interval training program (running), a second was placed on the standard Army conditioning program and the third served as a control squad. Each squad was trained for seven weeks. After retesting, the squads were taken to an altitude of 12,500 feet for three weeks. While at altitude, sub-maximal and maximal work studies were repeated at intervals.

The results indicate that: 1. The highly conditioned subject is able to perform more work at high altitude than the subject in poor condition, but the difference between the two is less than at 750 feet; 2. Stay at altitude improves work performance more in the poorly conditioned than in the well conditioned subject; 3. Maximum oxygen consumption at high altitude is more severely degraded in highly fit than in less fit subjects; 4. Symptoms of altitude sickness are as prevalent in highly fit as in unfit subjects.

MEMBRANE PROPERTIES OF CANINE SINGLE VENTRICULAR FIBERS STUDIED BY A METHOD OF CONCURRENT STIMULATION OF THESE FIBERS. Kojiro Matsuda and Akimitsu Kamiyama (intr. by C. McC. Brooks) Department of Physiology, Faculty of Medicine, University of Tokyo, Japan.

It was found that in order to observe the electrical behavior of single fibers of true ventricular muscle, the conventional method of using paired microelectrodes for recording and passing current was not applicable as in the case of Purkinje and atrial fibers. However, the electrical behavior of ventricular fibers could be studied if a number of fibers were subjected to polarization concurrently. Papillary muscle taken from the right ventricle of the dog heart was used. Current was passed simultaneously through the fibers of the sample at its basal cut end by use of a special separation device. Membrane potentials were recorded from the superficial fibers as close as possible to the separation diaphragm and at various distances therefrom. The electrotonic potentials induced were of measurable size and shape. The logarithms of potential size and half-time of rise showed a linear relationship to distance from the diaphragm. Membrane constants were estimated to be as follows: space constant = 1.26 mm; time constant = 2.0 msec; critical level of membrane potential = -65.4 mV. Judging from size of the electronic shift in membrane potential, the decrease in membrane impedance at the crest of the spike was less than 10% of its diastolic value in these true ventricular muscle fibers. (Supported by a grant from the Ministry of Education of Japan).

ELEVATION OF MEAN CIRCULATORY PRESSURE FOLLOWING EPINEPHRINE AND NOREPINEPHRINE INFUSION. R. E. McCaa*, B. H. Douglas*, and T. Q. Richardson. (intr. by M. D. Turner) Dept. of Physiology, Univ. Miss. Med. Center, Jackson, Mississippi

The effect of infusing epinephrine or norepinephrine on mean circulatory pressure (MCP) has been studied in ten dogs. Varying MCP levels were obtained by infusing epinephrine or norepinephrine to elevate the mean arterial pressure to different pressure levels in dogs anesthetized with 28 mg/kg sodium pentobarbital. After a desired mean arterial pressure level had been reached, the MCP was measured by (1) temporarily stopping the heart by fibrillation, (2) pumping blood from the aorta into the inferior vena cava to equilibrate the pressures in the circulatory system, (3) measuring the equilibrated pressure, which is the MCP, within 7 seconds after stopping the heart, and (4) defibrillating the heart. In these studies the mean arterial pressure was elevated in progressive steps up to a maximum of 286 mm Hg with norepinephrine and up to 247 mm Hg with epinephrine infusion. MCP was elevated in the five dogs infused with norepinephrine from the control of 7 mm Hg up to a maximum of 18 mm Hg. In five dogs infused with epinephrine the MCP rose from 7 mm Hg up to 25 mm Hg. Therefore, it is concluded that when mean arterial pressure is elevated by infusing epinephrine or norepinephrine, there is a greater increase in MCP in dogs infused with epinephrine. (Supported by NIH grants)

APPLICATION OF DIGITAL DATA INSTRUMENTATION TO SWEAT RECRUITMENT STUDIES. *Robert D. McCook* and *Robert D. Wurster**. Department of Physiology, Loyola University Stritch School of Medicine and the Graduate School, Chicago, Illinois.

The plethora of data derived from our experiments on the control of sweating necessitates the use of digital data gathering and computer analysis. This requires the reduction of data from plethysmographs, thermistors and hygrometers to an analog voltage. This analog is then digitalized and recorded on perforated paper tape. This technique has allowed a more extensive analysis of the effects of heat (60-65°C ambient) on either the upper or lower half of the body. Heat applied to the lower portion of the body leads to the previously reported recruitment pattern from inferior upward taking 15 minutes or longer from first appearance of sweat to full recruitment. Heating of the upper portion of the body (above the umbilicus), however, reduces this recruitment time (often to less than 1 minute) or causes reversed recruitment from superior to inferior. This is interpreted as further evidence of the essential role of skin temperature in temperature regulation. *(Supported by NIH Grant HE 08682 and GRSG 5 SO1 FR 05368.)*

EFFECT OF INERT GAS ON HIGH-PRESSURE OXYGEN TOXICITY IN RATS. D. McGavin*, R. K. Gupta*, P. M. Winter*, and E. H. Lanphier. Depts. of Physiol. and Pathol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Observations of Penrod and others suggest that presence of an inert gas in the alveoli during exposure to hyperbaric oxygen might prolong survival by delaying development of atelectasis. Groups of 14 - 16 rats (Holtzmann), 150 - 250 gm, were exposed to 3 atm partial pressure of O_2 in a high pressure chamber until death: Group I, 100% O_2 at 3 atm abs; II, 50% O_2 - 50% N_2 at 6 atm; III, 50% O_2 - 50% He at 6 atm. Convulsions occurred in almost all rats, showing no relationship to the gas breathed. Mean survival times: 100% O_2, 479 ± 88 min; N_2 - O_2, 520 ± 112; He - O_2, 493 ± 97 (differences not significant). All lungs showed patchy or generalized purplish to brown discoloration or deep reddening. In varying degree, all microscopic sections showed emphysematous dilatation and destruction, capillary congestion, moderate patchy atelectasis, and edema. Widening of interalveolar spaces with prominence of macrophages, and presence of a hyaline-like material at alveolar margins were common findings. In general, changes were more extensive in the rats exposed to 100% O_2. Presence of an inert gas during exposure to 3 atm of O_2 appeared to decrease the severity of atelectasis in rats but did not prolong survival. (Supported in part by ONR Contract Nonr 969(03).)

FORCE VELOCITY CURVES FROM VASCULAR SMOOTH MUSCLE. Thomas W. McIntyre (intr. by A.J. Brady). Cardiovasc. Res. Lab. and Dept. of Physiol., Univ. of Calif., Los Angeles, Calif.

Force velocity curves have been measured on an isolated segment of the ductus arteriosus of the fetal guinea pig. Afterloaded contractions yield force velocity curves that are similar in appearance to those obtained from striated preparations. However, quick release experiments show a distinct triphasic time course which has not been reported in other preparations. The quick release time course consists of an undamped displacement followed by a fast phase of shortening and then a slower prolonged shortening. The slow phase is identical to the afterloaded curve with a V_{max} of 0.01 l_o/sec. The fast phase has an extrapolated V_{max} of 0.1 l_o/sec., and is similar in shape to the slow phase. Both curves tend to fit the equation of Fenn and Marsh better than the Hill equation. The triphasic nature of the quick release time course can be explained in terms of the model proposed by A.F. Huxley (1957). If the overall contraction-reaction is:

$$A + M \underset{2}{\overset{1}{\rightleftharpoons}} AM + \text{Force}$$

(shortening).

In an afterload contraction rate 1 would dominate while in the quick release contraction rate 2 would dominate until the amount of AM in the combined state was appropriate to the load on the muscle at which time the steady state is reestablished and rate 1 dominates again.

MECHANISM OF EPINEPHRINE-INDUCED HYPERFIBRINOGENEMIA IN THE RAT. J. M. McKenzie, M. A. Johnson* and P. R. Fowler*. Pharmacology-Biochemistry Laboratory, Civil Aeromedical Institute, Federal Aviation Agency, Oklahoma City, Oklahoma 73125.

The increase in concentration of plasma fibrinogen which occurs 24 hr. after injections of EPINEPHRINE was prevented by prior treatment with ACTINOMYCIN-D. This indicates that EPINEPHRINE increases fibrinogen synthesis and is consistent with the report by Henriques, et al [Biochem. J. 66:222(1957)] that EPINEPHRINE accelerates the incorporation of glycine-C^{14} into fibrinogen. Hyperfibrinogenemia was not produced by injections of DEXAMETHASONE, CORTICOSTERONE, or ACTH; nor did DEXAMETHASONE alter the response to EPINEPHRINE. HISTAMINE caused a rise in fibrinogen concentration, but this response was probably due to a release of endogenous EPINEPHRINE rather than a more direct effect of HISTAMINE on fibrinogen production. This interpretation is supported by another experiment in which the antihistamine agent METHAPYRILENE failed to suppress the response to injected EPINEPHRINE. Thus, our results indicate that neither the pituitary-adrenal axis nor the release of HISTAMINE is an important factor in the increased synthesis of fibrinogen induced by EPINEPHRINE.

THE LINEA UTERI, A CONDUCTION PATHWAY IN RAT MYOMETRIUM. C. E. Melton and T. J. Saldivar*. Civil Aeromedical Institute, Office of Aviation Medicine, Federal Aviation Agency, Oklahoma City, Oklahoma 73125.

Electrical activity, as recorded with external electrodes, underlying uterine contractions is extremely complex because the geometry of the cell system allows impulses to travel in different directions at the same time. Much of the complexity can be eliminated by cutting the myometrium into narrow strips. Strips have different properties depending upon the part of the uterus from which they are taken, however. Strips of longitudinal muscle taken from the antimesometrial region conduct impulses faster, contract at a higher frequency, have a higher excitability, have larger action potentials, develop more tension, and show a different pattern of spike discharge than do strips taken from the mesometrial border. The antimesometrial strip traverses the cervix and connects both horns; it is visible to the naked eye in situ as a whitish translucent ridge and can be dissected easily from adjacent and underlying myometrium. For convenience, this strip is named the linea uteri (line or thread of the uterus). The linea uteri may be a prime conduction pathway in the myometrium from which activity spreads laterally to involve the rest of the myometrium. Action potentials entering other pathways could spread in both directions, cancelling or reinforcing pre-existing activity, enter new pathways or re-enter the original pathway. Such asynchronous and reverberating activity could account for the slow development and maintenance of tension. The linea uteri should prove useful as a standard myometrial preparation.

FLOW LIMITED DIFFUSION ACROSS THE SHEEP PLACENTA. Giacomo Meschia, Frederick C. Battaglia* and Paul D. Bruns*. University of Colorado Medical Center, Denver, Colorado.

Uterine and umbilical flows and transplacental diffusion of antipyrine and tritiated water have been measured simultaneously. The ratios, diffusion rate divided by the concentration difference between uterine and umbilical arteries, are equal and linear functions of the reciprocal of the sum of the reciprocals of the flows. These results seem to indicate that (a) the diffusion of antipyrine and tritiated water is 100% flow limited and (b) the placenta simulates the properties of a concurrent exchange system. (Supported in part by a Grant-in-Aid, N.I.H. Hd 00781.)

IN VIVO PHYSICAL PROPERTIES OF THE WALL OF SMALL ARTERIES. M. W. Meyer, Dept. of Physiol., Univ. of Minn., Mpls., Minn.

This study examined radial changes in small arteries by altering flow rate under in vivo conditions in which changes in length were previously found to be negligible. A section of vessel in the mesentery was freed for cinephotomicrography. A small cannula was inserted into a branch near the site of observation for measuring pressure. An electronic fiber optic system synchronized pressure with dimensions. Pressure levels were altered by clamping and restoring blood flow to a section of mesentery, perfusing at various levels at constant flow and then introducing a perturbation. Radius-pressure relationships revealed that during the run-off phase after clamping and stepwise lowering of pressure the radius did not change linearly with pressure. For a 20% decrease of total radius change, the percent of total pressure drop averaged about 66%. When the perturbation was introduced at flow rates yielding normal or higher pressures, control radii were smaller than those seen as the pressure returned to control. Under these conditions, pressure dropped below control for a short period. Change in radius lagged the change in pressure when the flow was restored or a perturbation introduced. Radii observed during incremental lowering of the pressure were larger for comparable pressures obtained by stepwise increasing the pressure. As pressure was increased above the normal level, vessels actually decreased in bore in some instances. Results suggest that the walls of these small arteries can respond actively to changes in distending force depending upon the initial conditions. (Supported by NIDR)

NEURAL CIRCUITS INVOLVED IN REACTION TIME PERFORMANCE IN PRIMATES. Josef M. Miller*, Mitchell Glickstein and William C. Stebbins*. Kresge Hearing Research Institute, Univ. of Michigan Med. School, Ann Arbor, Mich. and Regional Primate Research Center, Univ. of Washington Med. School, Seattle, Wash.

Monkeys with bipolar electrodes implanted in the lateral geniculate nucleus (LGN) and primary visual cortex were trained to release a key rapidly following onset of photic stimulation or direct electrical stimulation of the visual system. The behavioral situation was structured similar to the classical human visual reaction time experiment. Behavioral response latencies were stable and comparable to visual reaction time for human subjects. The effects of varying the intensity of peripheral and central stimulation on response latency were studied. Latency-intensity functions were approximately exponential with increases in average latency and variability of latency occurring at weaker intensities of stimulation. Behavioral latencies to photic stimulation were longer than to direct electrical stimulation of LGN or visual cortex. These latency differences were approximately equivalent to latencies of the visually evoked potentials reported for the LGN and visual cortex in unanesthetized monkeys. Extension of these techniques for the analysis of activity in the auditory system has resulted in findings similar to those observed in the visual system.

STUDIES ON THE ISOLATED P-III COMPONENT OF THE CAT ERG. R. F. Miller* and T. E. Ogden. Depts. of Neurology and Physiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

In cats anesthetized with pentobarbital, complete isolation of the P-III component of the ERG was obtained by a combination of mechanical clamping of the central retinal and ipsilateral carotid arteries. The behaviour of P-III during dark adaptation was studied in the intact eye preparation with intraretinal microelectrode recording techniques. Following the gradual injection of pentobarbital (30-40 mg) into the vitreous chamber, dark adaptation curves (amplitude vs. time in the dark) for P-III became anomalous. An early phase of P-III enhancement reached a maximum (200-400% of dark adapted amplitude) 5 seconds after the adapting light was turned off. This "off-rebound" phenomenon lasted about 15 seconds and was a function of the duration and intensity of the adapting light.

Since, in this preparation, only horizontal and receptor cells are functional, it was postulated that the effect of the nembutal might be to release normally masked synaptic input to the receptors. A well known hypothesis of P-III generation postulates active depolarization of the proximal receptor terminals. Thus hyperpolarization of these terminals should increase the amplitude of P-III by increasing the electrochemical gradient of its generator. This possibility was tested by the injection of additional pentobarbital (10-20 mg) into the vitreous chamber. This promptly abolished the P-III off-rebound, but had no effect on P-III amplitude. These results suggest that P-III off-rebound is not a photochemical effect, but is probably synaptically mediated.

(Supported by GRS Grant FR-05428 and USPHS Grant NB-04135)

CARDIOVASCULAR RESPONSES TO DEXTRAN-40 IN NORMAL AND SHOCK PATIENTS. P.A. Mohr*, J.S. Carey*, D.O. Monson* and W.C. Shoemaker. Dept. of Surgical Research, Hektoen Institute, Cook County Hospital, Chicago, Ill.

The time course of cardiovascular responses to volume loading were measured in 18 shock patients and 4 normal subjects. 500 ml. of 10% Dextran of M.W. 40,000 (D-40) were administered at the rate of 10 ml/min. and measurements were made at 10 min. intervals. The initial response in all patients was a rise in central venous pressure (CVP). This change was followed with increased cardiac output (CO), central blood volume (CBV), stroke volume, stroke work and cardiac work as well as decreased total peripheral resistance (TPR) and mean transit time. Mean arterial blood pressure (MBP) increased slightly and heart rate remained unchanged. Maximum changes occurred at 50 min. (500 ml. D-40) and were maintained at least one hour.

		D-40 Infusion					30 min. after Infusion
	Control	100 ml.	200 ml.	300 ml.	400 ml.	500 ml.	
C.O.	5.13	5.59	6.15	6.47	7.12	8.06	8.09
mBP	67	68	70	72	74	76	73
CVP	3.5	4.3	6.2	9.0	10.8	11.6	8.9
TPR	1088	991	862	832	767	677	695
CBV	1408	1488	1529	1539	1604	1781	1831

In normal subjects, infusion of D-40 resulted in qualitatively similar but less pronounced responses compared to the shock group. Maximum changes in normal subjects occurred at 40 min., and values approached control levels in one hour. The responses to D-40 were compared with the administration of whole blood, plasma, clinical dextran and saline in shock patients. The data suggest that the action of D-40, occurs as a result of increased plasma volume, improved peripheral blood flow and an increased venous return to the right heart.

CARDIOVASCULAR PATTERNS IN ACUTE HEMORRHAGIC SHOCK IN DOG AND MAN. D.O. Monson*, L.K. Kho*, R.H. Norton*, J.S. Carey* and W.C. Shoemaker. Dept. of Surgical Research, Hektoen Institute, Cook County Hospital, Chicago, Illinois.

Cardiovascular measurements were made in 10 patients in acute hemorrhagic shock not associated with surgical trauma or sepsis and compared with the sequence of events in hemorrhaged dogs. In progressive blood loss in dogs, initially CO decreased and total peripheral resistance (TPR) increased. Subsequently TPR and BP decreased and terminally CO increased. Initial observations in patients revealed two distinct categories: (a) 7 patients with low CO, high TPR, low stroke volume and low central blood volume and (b) 3 patients with high CO, low peripheral resistance, high stroke volume and high central blood volume. Nine patients survived; the remaining patient developed increased CO and decreased TPR before death. The responses to blood transfusion in both groups are summarized:

	HR	MAP	BP	CVP	CI	SI	CBV	TPR
7 Pts. Decreased cardiac output								
Control	105	61	88/45	1	2.18	23.7	862	1433
500 ml. blood	97	79	112/63	5	3.20	33.5	1047	1129
1 hr. later	96	78	115/62	3	3.29	34.9	1048	1106
3 Pts. Increased cardiac output								
Control	105	64	90/53	0	4.66	45.1	2136	646
500 ml. blood	104	89	121/71	2	6.47	64.8	2554	615
1 hr. later	102	74	110/58	1	5.65	54.9	2318	593

Oxygen consumption which was initially decreased in the low CO patients increased with both blood and low viscosity dextran. The high CO group initially had high O_2 consumption which was not appreciably changed by volume therapy. The data suggest that there is a definite sequence of cardiovascular events in both dogs and patients after blood loss.

BRADYKININ RELAXATION OF DUODENUM. Edward H. Montgomery and Donald C. Kroeger (Intr. by W. A. Spencer). University of Texas Dental Branch., Houston, Texas.

Bradykinin, a nonapeptide, causes a contraction of most smooth muscle in vitro; however, the rat duodenum is relaxed. The proximal portion of the duodenum exhibits relaxation whereas the more distal portions exhibit a biphasic response while the jejunum and ileum show only a contractile response to bradykinin. The relaxation response in the rat duodenal tissue is blocked by the combined adrenergic blocking agents, phenoxybenzamine and propranalol. Treatment of the duodenal preparations with reserpine, in vitro, also diminishes the relaxant response. After the relaxation is blocked, a contractile response to bradykinin is observed. It is concluded that bradykinin may be relaxing this tissue by an indirect mechanism of releasing bound catecholamines. If the bound catecholamines are depleted with reserpine or blocked by adrenergic blocking agents, then bradykinin has a direct contractile action on the duodenum.

STATISTICAL CORRELATES OF NEURONAL NETWORK STRUCTURE. G.P. Moore, D.H. Perkel*, H. Hegsted*, J.P. Segundo, H. Levitan*. Dept. of Physiology and Anatomy and Brain Research Institute, UCLA, Los Angeles, Calif. and the RAND Corporation, Santa Monica, Calif.

By means of simultaneous intracellular microelectrodes, the spontaneous activity of pairs of ganglion cells in the marine gastropod Aplysia was recorded permitting simultaneous observation of the synaptic input and spike output of both cells. The spike auto- and cross-correlation functions for both cells were computed. In certain regions of the visceral ganglion it is possible to find a number of cells which exhibit "common" (i.e. simultaneous) post-synaptic potentials elicited by other spontaneously active cells in the ganglion. The presence of common excitatory input gives rise to a high coincidence of firing in the two cells. When cells share a common excitatory input from a "pacemaker" i.e. regularly discharging source, this gives rise to periodicities in the auto- and cross-correlograms. In a few instances there has been some evidence of a closed, probably polysynaptic, recurrent loop affecting one or both cells; in this case periodicities of a somewhat different nature appear. Such observations provide a basis for the interpretation of correlation functions between cells whose input is not known, and thereby permit the experimenter, on the basis of observations of output, to make inferences concerning the nature, amplitude, and temporal distribution of an unobserved input. The physiological results have been corroborated and systematically extended through the use of digital computer models of interacting neurons.

EFFECT OF STRESS ON PLASMA LH ACTIVITY IN OVARIECTOMIZED RATS. **Ward W. Moore. Dept. Physiol., Ind. Univ. Med. Ctr., Indianapolis, Ind.**

The 1 hour-2 ovary ovarian ascorbic acid depletion (OAAD) assay for LH was used in a study on the effect of stress (0.2 ml of 10% formalin every 12 hours for 48 hours) on the plasma (2.0 ml) OAAD activity in the adult ovariectomized Holtzman rat. Experimental groups included combinations of ovariectomy (23 days post-operative), adrenalectomy (5 days post-operative), pretreatment with cortisol (60 mg/kg, IP, for 2 days), and stress. The stressful stimulus employed in this study decreased the OAAD activity in 2 ml of ovariectomized rat plasma from 12.3 ± 1.21% to 0.1 ± 0.81%. This decline in OAAD activity could be prevented by pretreatment with cortisol (13.7 ± 2.23%), whereas cortisol alone had no effect on the plasma OAAD activity (12.1 ± 1.46%). The plasma OAAD activity of the ovariectomized-adrenalectomized rat was decreased following stress from 12.6 ± 1.11% to 0.5 ± 1.50%. In the later preparation cortisol prevented the fall in OAAD activity induced by stress (11.6 ± 1.76%) and had no effect on the activity in the non-stressed rat (11.3 ± 1.47%). These data are consistent with the view that activation of the ACTH releasing mechanisms during stress is accompanied by an inhibition of the LH synthesis and/or release mechanisms. **(Supported in part by PHS grant NB-01296-08.)**

ARTERIAL SUPPLY TO THE BRAIN OF THE DOLPHIN, TURSIOPS TRUNCATUS. P.J. Morgane, W.L. McFarland* E.L. Nagel*, M. Viamonte*, and R.E. Galiano*. Communication Research Inst. and Univ. of Miami Med. School, Miami, Fla.

Roentgenographic and anatomical analyses of the blood supply to the brain of the bottlenose dolphin have been carried out. Two dolphins were intubated, anesthetized with a nitrous oxide-oxygen mixture, and respired on the Bird respirator. The spinal retial system was exposed by dorsal laminectomy, contrast media injected by a phase injector synchronized with the roentgenographic system, and serial roentgenographic analyses performed. The spinal retial complex was shown to be a massive vascular system completely investing the spinal dura. This system confluences into several branches, enters the cranial cavity through the foramen magnum, becomes intradural, and forks into finger-like projections to invest the brain about its temporo-basal aspect. These vascular limbs branch on the fronto-basal aspect of the brain and form the internal ophthalmic arterial retial system. Roentgenographic analyses showed the primary intracerebral arteries to fill from this basal retial complex. No vertebral or basilar arterial system was identified. Contrast media injected into the aorta filled the spinal retial system via the intercostal vessels but did not enter the cranial cavity, ending in the atrophied internal carotid vessels. Confirmation of the roentgenographic picture was obtained by injection of dyed vinylite into the spinal retial vessels followed by acid digestion leaving a vascular cast duplicating the features seen on X-ray examination. These studies indicate that the entire blood supply to the dolphin brain is via the spinal retial complex and distributes to the brain in a highly specialized pattern. Studies are in progress to determine the functional significance of this specialized retial system especially from the standpoint of its being a potential oxygen reservoir for the brain during diving. (Supported by Grants NB-03097, NIH and GB 4407, NSF.)

DEVIATION FROM COSINE LAW OF EXCITABILITY IN ISOLATED MUSCLE FIBERS. Louis A. Mulieri* and F. J. Sichel. Department of Physiology and Biophysics, Univ. of Vermont, Burlington, Vermont.

Previous work in our laboratory on sartorius of R. pipiens has indicated that besides the plasma membrane a second excitable structure possessing stimulus orientation sensitivity may be present within the muscle cell. The mode of detection involved observation of certain departures from the classical du Bois-Reymond "cosine law" of excitability when the muscles were stimulated by a homogeneous electric field oriented at various angles, θ, with respect to the long axis of the muscle. In order to interpret these departures it was felt that a reexamination of the applicability of the cosine law to muscle was desirable. A treatment of the problem using cable and superposition theory indicated that, unlike the case of nerve, the excitability of a single muscle fiber in a homogeneous field should vary as $(L \cos\theta + T \sin\theta)$. This predicted departure from cosine law behavior, even for almost transverse fields, is small enough to make a whole muscle preparation unsuitable for its detection. This is probably due to the distribution of fiber orientations, dimensions, and thresholds. Single fibers were dissected undamaged from the semitendinosus muscle and mounted between two glass isometric levers. Developed tension was converted to voltage (RCA 5734's) and displayed on an oscilloscope. The homogeneous stimulating field was varied in orientation by rotating the Ringer bath and electrodes. Only true twitch responses were studied. The $(L \cos\theta + T \sin\theta)$ relation fits the data quite well. (Supported by grants HE-00336 and 5-T1-GM-439, USPHS).

MYELOID HYPERACTIVITY IN MONKEYS INOCULATED WITH HUMAN LEUKEMIC BLOOD. J.S. Munroe (Intr. by W.F. Windle). Lenox Hill Hosp., and Inst. Rehab. Med., New York Univ. Med. Ctr.

Two steroid-conditioned yearling monkeys (M. speciosa) presented a picture of myeloid hyperactivity after single inoculations with blood from a chronic myelogenous leukemia patient. Blood and marrow from 14 control animals receiving normal human blood or chicken oncogenic viruses did not exhibit a myeloid hyperactivity picture. In the first monkey abnormal cells, including myelocytes, metamyelocytes, plasma cells and histocytes appeared in circulation 22 days after inoculation, increasing numerically during the next 18 days; nucleated cells reached 54,000 before death at 38 days. Sternal bone marrow showed marked hypercellularity compatible with the blood shift to the left. The second monkey exhibited a similar though less advanced picture before death 13 days after inoculation and the leucocyte alkaline phosphatase test score went from thirty before inoculation to zero 4 days before death. A third monkey (C. aethiops) receiving human leukemic blood showed no blood-picture alteration but the marrow was depressed in the myeloid and erythroid series. This is the first time a condition like that described has been seen after the passage of material from a human malignancy into a nonhuman primate. (Research grant CA 832-01VR from Natl. Cancer Inst.)

INTERNEURONS IN THE TEMPERATURE SENSITIVE PREOPTIC REGION. N. Murakami* D. Cunningham, J.A.J. Stolwijk and J. D. Hardy. John B. Pierce Foundation Laboratory, New Haven, Connecticut.

When firing rates of temperature sensitive units are plotted against hypothalamic temperature (34° - 40°C) a clear linear relationship is not obtained for some neurons. To study this response, animals were prepared with four implanted thermodes in a single line 4 mm right lateral, 3 mm on centers, with the most caudal thermode at 21 mm rostral. A thermistor was implanted 9 mm right lateral at coordinate 25.5 mm rostral. Thermocouples were introduced stereotaxically on the left at various locations and simultaneous temperature records obtained from thermistor and thermocouple as the temperature of the thermodes was cycled $\pm$ 4°C at various frequencies. Temperature attenuation and lags were measured at 12 locations and were compared with calculations made from heat flow theory. Experimental and theoretical results were in good agreement so that the temperature of a particular site could be estimated from its coordinates and the temperature record from the thermistor. About 100 neurons were observed and their firing rates plotted against the tissue temperature at their location. In most cases a good linear relationship was obtained even during marked thermal transients. However, in several cases neurons appeared to be responding to temperatures near the midline rather than their own location. These findings suggest that such temperature sensitive neurons may function as interneurons of the thermoregulatory pathway.

CENTRAL AND PERIPHERAL FACTORS IN BEHAVIORAL THERMOREGULATION IN THE RAT. D. Murgatroyd (Introduced by J. D. Hardy). John B. Pierce Foundation Laboratory, 290 Congress Avenue, New Haven, Connecticut.

One group of rats were exposed to ambient temperatures ranging from -4 to + 41°C for periods up to eight hours and allowed to bar press for radiant heat or cold air. Records were made of their hypothalamic temperature and bar press rate during these exposures. The animals' demands for heating or cooling depended on both hypothalamic and peripheral temperature. Internal temperature was maintained at pre-exposure (normal) levels, however, only with high levels of reinforcement per bar press. A second group of rats were studied under the same conditions. During each exposure their preoptic temperature was successively raised and lowered by perfusion with warm and cold water. Level of response depended on both central and peripheral inputs. Data appear to agree with the formulation that behavioral thermoregulation in the rat is a function of the product of the central and peripheral temperature displacements.

EFFECT OF HEMORRHAGE ON BLOOD VOLUME AND CARDIAC OUTPUT OF ALPHA ADRENERGIC RECEPTOR BLOCKED DOGS. S. Nagy (intr. by R. A. Huggins). Institute of Experimental Surgery, University Medical School, Szeged, Hungary.

In anesthetized dogs alpha adrenergic blockade was induced by 1 mg/kg phenoxybenzamine. Blood volume was measured as the sum of cell and plasma volumes with Cr^{51}-tagged cells and I^{131}-albumin. Cardiac output was determined with I^{131}-albumin. Oxygen content of arterial and mixed venous blood was determined manometrically. The animals were bled four times at hourly intervals. Measurements were performed before and after bleedings. Compared to untreated controls, blocked animals showed a larger reduction in cardiac output after hemorrhage and the amount of fluid and protein entering the circulation was less in them. In blocked animals with blood losses over 12 ml/kg there was a linear relationship between the amount of blood withdrawn and the decrease of cardiac output. The oxygen uptake of these animals was less than that of the controls. Alpha receptor blockade which is reported to be effective in preventing irreversibility in hemorrhagic shock affects adversely the compensatory response to acute hemorrhage.

NATURE OF SUPPRESSION OF THE TRIGEMINAL MONOSYNAPTIC REFLEX INDUCED BY STIMULATION OF THE CORTEX OF THE CAT. Y. Nakamura and L. J. Goldberg (intr. by C. D. Clemente). Department of Anatomy and the Brain Research Institute, University of California, Los Angeles, Calif.

Stimulation of the rostral portion of the anterior sylvian gyrus suppresses the monosynaptic reflex evoked by stimulation of the mesencephalic nucleus of V in the masseter nerve of the cat (Sauerland et al. 1966, Clemente and Sterman 1966). This work investigated in cerebellectomized flaxedilized cats (spinal cord sectioned at C_2) this suppression by recording intracellularly from masseter motoneurons with KCl- or K-citrate-filled micropipettes. The masseter motoneuron, identified by antidromic excitation, responded to stimulation of the mesencephalic nucleus of V with a monosynaptic EPSP which usually triggered a spike. Cortical stimulation induced prolonged hyperpolarization of masseter motoneurons. Monosynaptic and antidromic spikes were inhibited coincident with this hyperpolarizing potential. This potential was changed into a depolarizing one by intracellular Cl^- injection, suggesting that it was generated by an ionic mechanism similar to that for IPSP's in other nerve cells. These results show the participation of postsynaptic inhibition in cortical suppression of the trigeminal monosynaptic reflex. (Supported by MH 10083)

URINARY 3-HYDROXY-4-METHOXYMANDELIC ACID (VMA) EXCRETION DURING GRADED TREADMILL EXERCISE

Charles Neal, B.S., Carl Smith, M.D., Kurt Dubowski, Ph.D., and John Naughton, M.D.
(Introduced by Stewart Wolf, M.D.)
From the Department of Internal Medicine, University of Oklahoma Medical Center, Oklahoma City, Oklahoma

The relationship of the demands of muscular exercise to catecholamine excretion was explored in 19 men varying in age from 21 to 28, after 2½ hours of normal activity and after a second 2½ hour period, the first portion of which included graded treadmill exercise. Each subject was hydrated with 5.0 ml/kg water ingested immediately before and immediately after the work performance. The subjects performed the Balke physical working capacity test to determine their peak O_2 intake. Thereafter following a ten-minute rest period they worked at an energy expenditure which approximated 50% of their peak aerobic work capacity for 45 minutes. Respiratory gas exchange was determined every 15 minutes. Oxygen concentration was measured with a Beckman E-2 analyzer and CO_2 concentration determined with a Godart Capnograph. 3-Methoxy-4-Hydroxymandelic acid (VMA) concentrations were determined by the method of Sunderman et al. on the control and exercise urine specimens. The results revealed significant increases of the VMA excretion in all exercise specimens varying from 9.0 to 98 μg per hour. For each ml/min per kg increase in the average O_2 consumption there was an average increase in urine VMA of 5.5 μg which established a significant linear relationship ($p < 0.05$) between the level of energy expenditure and the amount of catecholamines secreted during work performance.

EFFECT OF BLOOD CO_2 TENSION ON THE PERFORMANCE OF THE HEART-LUNG PREPARATION. N. S. Nejad* and Eric Ogden, NASA, Ames Research Center, Moffett Field, California.

Acapnia and hypercapnia were induced in dog heart-lung preparations by ventilating the lungs with gas mixtures of 40% O_2, 0 to 10% CO_2, with the balance N_2. Continuous measurements of respiratory and blood gas as well as blood pH were made. Systemic and pulmonary flow were recorded with a Wilson flowmeter and a pulse field electromagnetic flowmeter, respectively. The preparations received continuous infusion of glucose (10 mg/min) and insulin (0.008 U/min). Performance of the heart was evaluated either by keeping the stroke work constant and comparing the changes in left atrial pressure or by keeping the atrial pressure constant and measuring the changes in stroke work. As the arterial CO_2 was increased stepwise from approximately 0 to 75 mm Hg the heart performance consistently declined. This occured even when arterial pH changes were prevented by the addition of alkali to the blood. When the CO_2 tension was subsequently reduced the performance improved. It was further observed that after a short period of "overshoot" in either direction the left atrial pressure would stabilize at a new level in approximately four minutes. This overshoot may be due to changes of intracellular and extracellular concentration of electrolytes and/or release of endogenous catecholamines.

EXOGENOUS HYPOPHYSIAL AND PLASMA GONADOTROPIN LEVELS IN MALE AND FEMALE RATS FOLLOWING DEAFFERENTATION OF THE MEDIAL BASAL REGION OF THE HYPOTHALAMUS. D. M. Nelson* and D. C. Johnson. Kansas University School of Medicine, Kansas City, Kansas.

Retrochiasmatic severance of anterior neural pathways to the medial basal hypothalamus (MBH) was performed steriotaxically with a small knife in normal post-pubertal rats. Sham-operated and non-operated groups served as controls in a 32-day study involving both sexes. Gonadotropin activity was determined on pooled samples of plasma and hypophyses:LH (OAAD) and FSH (HCG-Augmentation). Parameters studied in addition to gonadotropin determinations included weights of: testes, seminal vesicles, ventral prostates, ovaries, uterii, pituitary glands, and adrenals. A diestrous vaginal smear profile was exhibited by the majority of females (13 of 16) in the deafferentation group at the end of the study. Histological comparisons of ovaries were made. Difference of pituitary LH and FSH content resulting from treatment were more pronounced in females than males. Plasma LH levels did not differ significantly in either sex. Markedly lower pituitary weights resulted from deafferentation in both sexes. In males, marked reduction in ventral prostate and seminal vesicle weights resulted, but not testes, and in females, significant decreases in both ovarian and uterine weights followed deafferentation. Adrenal and body weights were unaffected by treatment. Hypophysial FSH content of control males was 9 times the level found in control females, whereas, this ratio had dropped to about 3 between deafferented animals. The data suggest that afferent pathways reaching the MBH via the anterior hypothalamus play an essential role in the endocrine control of reproduction.

EFFECTS OF OXYGEN ON ENZYMES OF TWO AGENTS OF THE CHLAMYDIA GROUP. E. M. Neptune, Jr., and E. Weiss. Naval Medical Research Institute, Bethesda, Maryland.

Pyruvic oxidase and α-ketoglutaric dehydrogenase (Biochem. J. 88, 31, 1963) were implicated as the site of specific lesions in the altered metabolism of rat brain exposed to 5 atmospheres (100%) of oxygen. These two enzymes were also studied in purified preparations of the microorganisms (Chlamydia) of trachoma and meningopneumonitis. These two organisms were selected because they convert pyruvate only to acetate and glutamate to α-ketoglutarate to succinate and there are no further reactions which might make difficult the interpretation of the results. Activities were determined in a gas phase of nitrogen, air or 100% oxygen at one atmosphere (absolute). The pyruvic oxidase activity from trachoma agent was maximum under N_2, less with air and least under O_2. Surprisingly, the reverse was found with the meningopneumonitis agent. Lipoate addition to the pyruvic oxidase system from trachoma agent produced a greater activity in all three gaseous environments, but the response was greatest under O_2. CO_2 from carbon-1 of glutamate by both bacterial sources was depressed to 90% in air and 75% in O_2 as compared to N_2. We assume that this most likely represents α-ketoglutaric dehydrogenase activity. These data validate earlier work on these enzymes from rat brain and denote the difference in susceptibility of pyruvic oxidase systems of different tissues and different species. The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large. From the Bureau of Medicine and Surgery, Navy Department.

I^{131} L-THYROXINE METABOLISM IN CARCINOGEN-TREATED RATS. W.C. Newman, Jr.* and R.C. Moon. Dept. of Physiology and Biophysics, Univ. of Tenn. Med. Units, Memphis, Tenn.

In addition to its remarkable ability to induce mammary cancer in experimental animals, 3-methylcholanthrene (MCA) is capable of affecting certain endocrine and metabolic functions. We have previously found that administration of MCA to rats depressed their thyroid function. In the present studies, the effect of MCA on urinary and fecal excretions of I^{131} was observed during daily administration of I^{131}-labeled Na L-thyroxine to rats. Excreta were collected from each rat at 2-day intervals, and the radioactivity of each sample was determined with a gamma-sensitive scintillation counter. Rats were considered to be in isotopic equilibrium when essentially all of the daily dose of I^{131} could be recovered in their urine and feces. At such time, control rats and rats receiving daily intragastric feedings of sesame oil excreted approximately 60% of the daily I^{131} dose as iodide in their urine. In contrast, rats which received daily intragastric feedings of 10 mg MCA in sesame oil excreted the major fraction of the daily administered dose of radioactivity in their feces, and only about 25% in their urine. Chromatographic-autoradiographic analysis of butanol extracts of feces from control and MCA-treated rats revealed only thyroxine-like iodine. As measured by both chemical and isotopic methods, the plasma protein-bound iodine concentration was reduced in MCA-treated rats. The effect of MCA on thyroxine metabolism was not mediated by altered food intake or altered fecal mass and probably resulted from accelerated loss of thyroxine in the feces rather than from a reduced rate of deiodination of thyroxine by peripheral tissues. (Supported by USPHS Grant CA 05105)

STEROL ACTIVATION OF SEXUAL REPRODUCTION AND GROWTH IN A FUNGUS. C. Norman* and I. W. Sizer. M.I.T., Cambridge, Mass.

Recent identification of certain sterols as initiators of sexuality, i.e., of sexual fruit-bodies in the fungus Phytophthora cactorum prompted us to investigate their basic mode of action. A concentration of 1×10^{-5} M β-sitosterol accelerated the growth rate of 4 mm mycelial discs cultured in a chemically defined glucose-asparagine liquid medium, and rapidly induced the development of sexual, and obligatory asexual fruit-bodies. In the absence of sterol, asexual reproduction only occurred after a relatively long period of slow vegetative growth. Our ability to control the appearance (differentiation) and the disappearance (dedifferentiation) of fruit-bodies by respectively lowering or raising the substrate level in the medium suggested that the substrate molecules were acting as main effectors in repressing or inducing the development of fruit-bodies, and that one of the principal actions of sterol is to increase the rate of substrate utilization. The increase in glutamic-aspartic transaminase activity observed 4 hrs after the initial addition of sterol to 5 day old cultures persisted for at least 72 hrs. The disappearance and reduction in staining intensity of protein bands separated by disc electrophoresis indicated the pronounced loss of soluble protein which occurred when fungi, with or without sterol, changed from the vegetative to the reproductive phase. Growth, differentiation and transaminase activity were all suppressed by inhibitors of protein and nucleic acid synthesis such as actinomycin D, puromycin, and actidione. Suppression, in the presence of sterol, was less severe and non-selective for sexual or asexual reproduction. The evidence suggests a multiple role for sterols, and favors the concept of the unity of action of sterol hormones on the molecular level in phylogenetically diverse organisms. One of us (C.N.) gratefully acknowledges the support of a PHS Special Fellowship (1-F3-GM-28, 145-01) from NIGMS.

GLUCOSE ABSORPTION DURING CHRONIC RESTRAINT. M.F. Nudd*, W. M.W. Yau*, and G.H. Gass. Endocrinologic Pharmacology Research Lab., Southern Illinois University, Carbondale, Illinois.

Control rats allowed the full 7280 cc. of a hanging wire cage were compared to animals restrained in adjustable cages in which the volume was calculated according to the formula: [body weight (gms.)] x 1.037 + 494 = cage volume in cc. These dimensions were found to immobilize the animal without mortality over the 25 week experimental period. Growth curves of the two groups show that the restrained rats do not grow as fast nor as large as the unrestrained. The relative rate of gastrointestinal absorption of dextrose was studied using serial peripheral plasma glucose determinations following a 400 mg. dextrose (or dextrose - C^{14}) test meal. Quantitative determination of absorption, accomplished by enzymatic and/or radioisotope analysis of the contents of the GI tract 45 minutes after the test meal, failed to show any significant differences in absorption. Animals in the fifth week of restraint which the in vivo studies showed to be representative of the minor differences between groups were used for in vitro studies. Incubation of intestinal segments in Krebs-Ringer-bicarbonate glucose medium (Crane and Wilson technique) was used for in vitro studies. The results from these studies confirmed those using in vivo techniques. (Supported by NASA Grant NGR-14-008-003.)

INCORPORATION OF LABELLED LEUCINE INTO PROTEIN OF VENTRAL ROOT AXONS FOLLOWING INJECTION INTO CAT SPINAL CORD SEGMENTS. S. Ochs, J. Johnson*, and M.-H. Ng*. Department of Physiology, University of Indiana Medical Center, Indianapolis, Indiana.

Small volumes of ^{3}H-leucine or ^{14}C-leucine were injected into the L7 and S1 segments of cat cords to expose the motoneuron somas to high levels of the precursor. After incorporation, axoplasmic flow carried the labelled material into the ventral roots. Activity measured in segments of the ventral roots showed changes in the proportion of activity in the distal segments with time after injection indicative of axoplasmic flow. Radioautography showed the intra-axonic locus of the radioactive material. The protein nature of the labelled substance was shown by homogenizing the ventral roots and differential centrifugation. Activity was found present in the "nuclear", "mitochondrial", and "ribosomal" fractions but was present in largest amount in the "soluble protein" fraction. A TCA precipitation of the soluble fraction showed a high level of activity. Upon hydrolysis and with paper chromatography, activity was found in the spot identified as leucine. A Dowex 50 column extraction of the soluble protein showed a low percentage of activity present as free leucine. Puromycin was injected into the cord and it inhibited the downflow of activity into the roots when a subsequent injection of ^{3}H-leucine was made. Downflow following ^{32}P was not inhibited by puromycin. The substance ^{3}H-cycloleucine injected into the cord did not move down into the ventral roots. These experiments with puromycin and cycloleucine indicate that unlike the products of normal protein synthesis, abnormal proteins or foreign substances in the soma do not gain entry to the axon. (Supported by NSF Grant GB 4385.)

OSCILLATORY POTENTIALS OF THE PIGEON ERG. Thomas E. Ogden. Depts. of Neurology and Physiology, Univ. of Utah College of Medicine, Salt Lake City, Utah.

The ERG of the pigeon has been investigated using intraretinal microelectrodes and a closed eye preparation. Equithesin (Jensen-Salsbery) anesthesia was used. Under these conditions, the oscillatory potentials of the ERG are not prominent. Soon after the injection of 0.2 cc 5% procaine into the vitreous chamber, prominent potential oscillations were recorded from the inner retinal layers during light stimulation. The major ERG components were unchanged. This phase of oscillatory wave enhancement was followed by phases of oscillatory wave depression, then b-wave depression, as the local anesthesia penetrated into deeper retinal layers.

It has been suggested that the intraretinal oscillatory waves represent summed synaptic potentials of the inner plexiform layer. The rhythmic nature of this light evoked discharge could be under the control of efferent fibers from the pigeon tectum which terminate in this layer. Thus the initial effect of the procaine may be to block the efferent fibers, releasing the oscillatory wave activity. This hypothesis was tested in animals with surgically interrupted optic tracts. Twenty-four hours after optic tract section prominent spontaneous oscillations were recorded from the inner retinal layers in the dark. This activity was blocked by light. Forty-eight, or more, hours after OT section, oscillatory waves were never seen before or after procaine application. These findings suggest that functional ganglion cell membrane is necessary for the generation of the oscillatory waves and lend some support to the above hypothesis.
(Supported by USPHS Grant NB-04135)

CONTINUOUS DISTRIBUTION OF LUNG VOLUME(V)TOTAL VENTILATION($\dot{V}$)AND BLOOD FLOW($\dot{Q}$)ANALYZED BY THE DISTRIBUTION FUNCTION OF N_2 CLEARANCE TIME CONSTANT(T). T.Okubo* & C.Lenfant. Inst. of Resp. Physiol. Firland Sanatorium & Depts. of Physiol. & Med., Univ. of Wn., Seattle, Wn.

During O_2 breathing, the decay of mixed expired N_2 concentration is usually represented by the sum of exponentials with discrete time constants. In the present report we represent the washout by a continuous distribution of time constants, utilizing Schwarzl and Staverman's 4th link of approximation (Physica 18:1952) to solve the inverse Laplace transform. This method was applied to the lung volume washout curve and to the arterial P_{O_2} increase curve in 12 normal subjects & 8 patients with diffuse obstructive pulmonary syndrome. In normal subjects the distribution of lung volume shows 2 peaks: a low peak corresponding to a small portion of V at the early part of the washout ($T_{\nu}.1$) and a higher peak corresponding to most of V and appearing later in the washout($T_{\nu}.6$). The distribution of ventilation reveals a large ventilation to the small portion of V and a relatively smaller $\dot{V}$ to the larger part of V. The distribution of $\dot{Q}$ almost coincides with the higher peak of the distribution of V. In diseased subjects 3 peaks are apparent in the lung volume distribution function. An early peak($T_{\nu}.1$)corresponds to a very small fraction of the lung volume. A large ventilation, but no blood flow coincides with this peak. Next comes a higher peak($T_{\nu}.3$) corresponding to a larger part of the lung volume. A relatively large $\dot{V}$ and most of the blood flow coincides with this peak. Later in the washout appears the highest peak corresponding to most of the lung volume ($T_{\nu}2.$). This part of the lung has a low ventilation and a low blood flow. The data indicates that the portion of the lung corresponding to the 2nd peak of the lung volume distribution contributes the most to the overall gas exchange in both normal and diseased subjects.

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DECREASES OF FORCED EXPIRATORY FLOW AFTER A BRONCHODILATOR AEROSOL. C. R. Olsen, F. C. Hale*, and M. Newman*. VA Center and UCLA Medical School, Los Angeles, Calif.

Maximal mid-expiratory flow (MMF) decreased in response to isoproterenol aerosol in 27 of 100 consecutive studies; in 7 there was no change. Possible mechanisms considered were fatigue, mucus raised into lumina of large airways, decrease of lung volume over which MMF was measured, and increased compressive narrowing of relaxed tracheae and bronchi. Fatigue and narrowing by mucus were not probable causes in most cases, since maximal expiratory flow, measured from the same forced expirations, increased in 27 of the 34. Total lung capacity (TLC) measured in 11 of these patients, did not change significantly after isoproterenol (avg. 7.74L before and 7.61L after) when airway conductance/thoracic gas volume increased from 0.08 to 0.10 cm^{-1} sec^{-1} ($P < 0.01$). Assuming no change of TLC, we could measure flows after isoproterenol over the same lung volumes as for the control MMF's (isovolume MMF). Isovolume MMF increased in 24 of the 34 who showed decreases of MMF. Isovolume MMF did not change in 2, and decreased in 8 studies. The 10 patients who failed to increase isovolume MMF had control MMF's of <40% predicted normal; only one of these 10 patients had bronchitis. Clinical data from these patients suggest that decreases of isovolume MMF occur when there is peripheral obstruction to expiratory flow (bullous emphysema and asthma). This decrease of isovolume MMF may represent increased compressibility of central airways (Am. Rev. Resp.Dis. 90:298, 1964) after inhaled isoproterenol.

PERITONEAL GAS EXCHANGE. W.W. Oppelt,*+ D.M. Travis, and K.A. Berdick*
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Equilibration of peritoneal gas pockets with blood should give information about tissue gas tensions without creating injurious subcutaneous gas pockets. Continuous perfusion of the peritoneal surfaces by O_2 might result in sufficient transfer of O_2 and CO_2 to aid patients in respiratory failure. Mongrel dogs, 18-20 kg. were anesthetized with pentobarbital, 14 ga needles or polyethylene catheters with multiple holes were introduced into the peritoneal cavity, and 2-3 L of various mixtures of air and O_2 were injected. Partial pressure (pp) of O_2 and CO_2 was monitored with infrared CO_2 meter and Pauling O_2 analyzer. CO_2 was found to equilibrate in about 2 hours, while O_2 equilibration had not occurred by 4 hours using either air or O_2. Peritoneal O_2 uptake was 1 ml/min using air, and 3 ml/min using O_2. Hypoxemia and hypercapnea induced by rebreathing 10% O_2-air mixture caused increased CO_2 and O_2 transfer rates between peritoneal cavity and blood, presumably related to visceral vasodilatation and more favorable gas pp gradients. Thus gas transfer between peritoneal cavity and blood seems to be related to absorbing surface area, peritoneal blood flow, and gradients of gas pp. In other anesthetized dogs various mixtures of air and O_2 were pumped into the peritoneal cavity through one catheter and exhausted through another. An estimated 3-5% of pulmonary gas exchange could be carried out through the peritoneum in the normal anesthetized dog, using O_2. Greater gas exchange should be accomplished by pharmacologic manipulations causing vasodilatation and conditions of more favorable gas pp gradients. Peritoneal gas perfusion might be useful in treatment of acute respiratory decompensation in emphysematous patients or in newborns with hyaline membrane disease. Supp: NIH GM 760-05

+Burroughs Wellcome Scholar in Clinical Pharmacology.

RESPONSE OF THE HUMAN UPPER EXTREMITY VASCULAR BED TO INTRABRACHIAL ARTERIAL INFUSIONS OF MAGNESIUM SULFATE AND HYPOTONIC SODIUM CHLORIDE SOLUTIONS. H.W.Overbeck*, R.M.Daugherty*, and F.J.Haddy. Depts. of Physiol. and Med.Univ. of Okla.Med.Ctr. and V.A.Hosp., Okla.City,Okla.

We have reported the development of an injector needle for intrabrachial arterial infusions, which improves mixing of substances with arterial blood without creating hemolysis (Clin.Res.13:95,1965). This needle allows accurate indicator-dilution calculation of regional blood flow in the dog and man (Physiologist 8:247, 1965), and also improves mixing of vasoactive substances with blood upstream to the arteriole. Such mixing is critical for valid measurement of vascular responses to vasoactive agents. Using this needle, we have measured upper extremity vascular responses to intrabrachial arterial infusions of magnesium sulfate solution and solutions of hypotonic sodium chloride (150 mOs./L. 8 ml./min.) in five normotensive men and three men with essential hypertension. The magnesium solution was isotonic (295 mOs./L.), being composed of 1 part of 10% magnesium sulfate plus 39 parts of isotonic sodium chloride solution. It was infused at 8 ml. per minute and increased calculated limb serum magnesium 0.64 to 1.60 mEq./L. Calculated limb plasma osmolarity decreased 8 to 42 mOs./L. during infusion of hypotonic sodium chloride solution. Magnesium sulfate solution decreased limb vascular resistance in seven of the eight subjects. Hypotonic sodium chloride solution increased limb vascular resistance in all eight subjects. These changes were statistically significant. With both agents there was apparently a positive correlation between initial level of resistance and magnitude of evoked change in resistance. There was no grossly apparent difference in response in the hypertensive group, although defects in arteriolar magnesium and/or water metabolism have been suggested to play a role in the genesis of essential hypertension.

ALTERATIONS IN CARDIAC SYNCHRONY AND CONTRACTILITY DURING INDUCED PULSUS ALTERNANS. *John B. Pace*, *Donald V. Priola* and *Walter C. Randall*. Department of Physiology, Loyola University Stritch School of Medicine, Chicago, Illinois.

Cardiac synchrony and contractility were studied during artificially induced pulsus alternans. Pressures were recorded separately from the four chambers of the heart and aorta, together with a standard limb lead of the ECG. Measurements were made of individual cycle parameters including: systolic and diastolic pressures, dP/dt, interval from beginning of the R-wave of the ECG to onset of ventricular pressure rise (R-RV and R-LV). With the onset of alternans the R-LV interval of the reduced contraction was consistently increased, while dP/dt was markedly decreased in proportion to the depression in systolic pressure. Lengthening of the R-LV interval was frequently disproportionate to the change in R-RV interval, thus significantly altering the apparent synchrony in contraction of the two ventricles. The P-R interval increased during alternans with the greatest increase occurring during the contraction of lesser magnitude. Alternans sometimes appeared in both ventricles simultaneously, while in other instances it was confined to only one ventricle. In some instances, it was observed in all four chambers. Depressed contractility occurred in situations in which ventricular and diastolic pressure became elevated, suggesting an alteration in the contractile nature of the myocardium. *(Supported by NIH Grant HE 08682.)*

INERT GAS LOSS AND VOLUME CHANGE IN AN ARTIFICIAL GILL SYSTEM. C. V. Paganelli, L. E. Farhi, and H. Rahn. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

An artificial gill for gas exchange in water has been designed in the form of a gas-filled chamber covered by a microporous, hydrophobic membrane which excludes liquid water but is permeable to gases dissolved in water (Fed. Proc. 25: 202, 1966). If such an artificial gill contains a collapsible element so that total pressure in the chamber is equal to ambient hydrostatic pressure in the water outside the chamber, loss of N_2 or other inert gas from the gill atmosphere will take place. This loss results from the fact that P_{N_2} in the chamber increases with depth, while water P_{N_2} is relatively constant at about 0.8 atm. Therefore the rate of N_2 loss will be proportional to depth. Chamber P_{N_2} at any depth is approximately equal to ambient pressure minus chamber P_{O_2}, which is fixed at about 0.1 atm by our experimental conditions. For example, at an equivalent depth of 4 atm abs, ΔP_{N_2} between chamber and water will be 3.1 atm. Since the N_2 permeability of our membrane is 225 ml (STP) $min^{-1} m^{-2}$ atm^{-1}, N_2 will be lost at an initial rate of nearly 700 ml $min^{-1} m^{-2}$. The kinetics of this loss and its importance to the functioning of artificial gills at depth will be discussed. (Supported in part by U. S. Air Force.)

IMPORTANCE OF HISTAMINE IN MEDIATING BRONCHOCONSTRICTION BY CIGARETTE SMOKE. Frank Palecek* and Domingo M. Aviado. Dept. of Pharmacology, Univ. of Penna. School of Med., Philadelphia, Pa.

The increase in lung resistance and fall in compliance following the inhalation of cigarette smoke are mediated by the release of histamine, as suggested by the following sets of observations: (a) In the anesthetized dog, the lung compliance and resistance were measured by the method of Mead and Whittenberger (1953). The inhalation of cigarette smoke, histamine solution in aerosol form and the intravenous injection of nicotine caused an increase in pulmonary resistance, which is blocked by atropine. The three forms of stimuli induce bronchoconstriction partly by stimulation of the vagus. (b) Blockade of histamine synthesis by administration of α-hydrazino-histidine abolished the bronchoconstrictor response to cigarette smoke in the dog. (c) In the anesthetized cat cigarette smoke, nicotine and histamine aerosol were followed by the same type of response as in the dog, though to a less extent. Pretreatment with α-hydrazino-histidine abolished not only the bronchoconstrictor response to smoke, but also to nicotine and intravenous histamine. (d) The anesthetized rabbit did not respond to all forms of stimuli. A pulmonary mechanism reactive to histamine, nicotine and cigarette smoke is absent in the rabbit. (Supported by a grant from the Council for Tobacco Research).

OXYHEMOGLOBIN DISSOCIATION CURVE IN MICE INFECTED WITH MALARIA. Mila Paleckova*, Frank Palecek* and Domingo M. Aviado. Dept. of Pharmacology, Univ. of Penna. School of Med., Philadelphia, Pa.

Mice inoculated with Plasmodium berghei die in about seven days of progressive parasitemia and anemia. The blood was collected from mice sacrificed on the fourth, fifth, sixth and seventh day after inoculation. The oxygen content and capacity of the collected blood were measured by the microtechnique of Laver, Murphy, Seifen and Radford (1965). Compared to blood from noninfected mice, the blood from the infected mice had the following characteristics: a) Reduction in blood pH associated with an increase in plasma levels of lactic acid. b) Reduction in oxygen content in the blood exposed to 37, 70 and 141 mm Hg P_{O2}. c) Decrease in hemoglobin content and in oxygen carrying capacity of the blood. d) A shift of the oxygen dissociation curve to the right. e) The hemolyzed blood from infected mice was more acidic than non-hemolyzed blood but the dissociation curve was shifted to the left. Although the changes in pH of the blood can adequately explain the shift in the dissociation curve, it is not possible to exclude an alteration in the properties of the hemoglobin brought about by the malarial parasites. (Supported by the Department of the Army under contract No. DA-49-193-MD-2755).

DEPOSITION OF AEROSOLS IN THE HUMAN RESPIRATORY TRACT AS INFLUENCED BY DEGREE OF LUNG INFLATION. E. D. Palmes, H. M. Marrero*, and B. Altshuler*, New York University Medical Center, New York, New York.

In recent work at this laboratory it was demonstrated that homogeneous aerosols in the size range approximately 0.1 to 1.0 microns diameter are deposited in the human respiratory tract during breath holding at a rate depending on the amount of aerosol present, i.e. the logarithm of the fraction aerosol-exhaled/aerosol-inhaled decreases linearly with time of breath holding from 0 to about 25 seconds. The slope of this curve depends on the effective size of the lumen of the intrapulmonary spaces. It was found in series of experiments on two subjects that this slope can be altered in the same subject and with the same aerosol by varying the degree of pulmonary inflation at the end inspiratory position. As expected, the rate of loss was lower at higher inflation but the degree of change is much greater than that predicted for uniform expansion of tubular or multi-spherical models. These considerations, therefore, appear to require non-uniform expansion of different portions of the respiratory tract in going from approximately 3/4 TLC to TLC. Supported by USPHS Grants OH-00057, ES-00014 and CA-06989.

RESPIRATORY GAS TRANSPORT BY BLOOD IN THE MONOTREMES-PLATYPUS AND ECHIDNA. J. T. Parer* and J. Metcalfe. University of Oregon Medical School, Portland, and Oregon Regional Primate Research Center, Beaverton, Oregon.

The platypus and echidna usually regulate their body temperatures at about 31° C and have low resting rates of O_2 consumption. The O_2 capacity of the blood of each is approximately 22 vol%. The O_2 tensions necessary for 50% saturation of hemoglobin with O_2 at 31° C and pH 7.40 are 27 and 21 mm Hg for the platypus and echidna, respectively. In 3 unanesthetized echidnas with indwelling catheters, the average resting O_2 consumption was 3 ml/kg/min, and cardiac output 59 ml/kg/min. The rabbit, of similar body weight, has values about 4 times greater for each of these two functions. The O_2 tension in mixed venous blood of echidnas averaged 26 mm Hg in contrast to values near 40 mm Hg in rabbits and other animals with body temperatures normally around 38° C. In echidnas, the resting cardiac output does not appear to be regulated to maintain the same $P\bar{v}_{O_2}$ as in 38°-homotherms, a difference probably related to the difference in body temperature and O_2 consumption. In unanesthetized echidnas, arterial O_2 tension averaged 64 mm Hg, and CO_2 tension 55 mm Hg. In this species, ventilation does not appear to be regulated to maintain an alveolar P_{CO_2} of 40 mm Hg, a difference probably related to the burrowing habitat. (Supported by Medical Research Foundation of Oregon, Training Grant #5 T1 HE 5499 from the National Heart Institute, and the National Heart Foundation of Australia, Tasmanian Division.)

STUDIES OF PARATHYROID INFLUENCE ON THE INCORPORATION OF H^3-CYTIDINE INTO RNA OF BONE CELLS OF RATS. Han Z. Park* and Roy V. Talmage. Rice University, Houston, Texas

For this study, endogenous parathyroid hormone (PTH) secretion was elicited by the technique of peritoneal lavage in 180-210 gm. rats, using a calcium-free isotonic rinse for periods of 20 mins. to 8 hrs. Following lavage the distal metaphyses and diaphyses of the femurs of intact and parathyroidectomized (PTX) rats were incubated in plasma for 1 hr. with tritiated cytidine and/or thymidine. The results were expressed as specific activity of the radioactive precursors. In the metaphysis of rats with intact parathyroids, the H^3-cytidine activity in the RNA fraction increased significantly by 20 mins. of lavage reaching a maximum increase of 50% by 8 hrs. of lavage. The H^3-thymidine activity in the DNA fraction increased at the 5th hr. with a maximum increase of 100% at 8 hrs. PTX without lavage increased the activity in the RNA fraction by 10%, but was not further influenced by lavage. All changes in activity in the DNA fraction were negated by PTX. In the diaphysis of the femur of the intact rat, the activity in the RNA fraction decreased 20% by 20 mins. It remained low until 5 hrs. of lavage at which time the increases in activity paralleled those in the metaphysis. Specific activities in the DNA extracted from the diaphysis paralleled those from the metaphysis at all time periods. Activities in both diaphyseal fractions taken from PTX rats were the same as in the metaphysis. These data demonstrate the rapidity of the effect of endogenous PTH on bone cells and provide further evidence that trabecular and compact bone respond differently to this hormone.

Supported by a grant from the AEC

ALTERATIONS IN SALT AND WATER METABOLISM IN SHEEP WITH RENAL HYPERTENSION. Harold R. Parker and Rajen S. Anand (intr. by Leo Bustad) University of California, Davis, California

Partial renal artery constriction in sheep produces a sustained hypertension in which the mean arterial blood pressure may exceed 200 mm Hg. In addition to elevated blood pressure there is profound disturbance of salt and water metabolism. A group of ewes in which total body water, body water turn-over, plasma volume, salt consumption, serum electrolytes, urine production, urine electrolytes and urinary aldosterone had been measured for several months was made hypertensive by a modified Goldblatt technique. In some unilateral and in others bilateral renal artery constriction was performed. By the tenth post surgical day the biological half life for body water decreased from 5.4 to 3.1 days. Total body water decreased slightly in some ewes and increased in others; changes in plasma volume were also variable. Salt consumption increased from an average of 16 g to 47 g/day. Average water intake increased from 3.8 to 6.1 l/day. Average urine production increased from 1.8 to 5.6 l/day and represented the main avenue of accelerated water turn-over. In most ewes, during the early hypertensive period, serum sodium decreased and serum potassium increased. Urinary aldosterone levels were usually less than normal. Several ewes exhibited a cyclical change of water consumption with a periodicity of 5-7 days between elevated and near normal water intake. Urine production paralleled imbibition. The altered patterns of salt and water metabolism continued during the chronic stage of hypertension (over 1.5 yr). (Supported by U.S.P.H. grant FR 05457).

EFFECT OF PROLONGED CONTINUOUS RECUMBENT BED REST ON RESPONSE TO HEAD-UP BODY TILT AND FORWARD ACCELERATION (+G_x). R. M. Patton,* G. J. Haupt* and N. C. Birkhead. Div. of Research, Lankenau Hosp., Philadelphia, Pa.

Although prolonged bed rest is known to produce circulatory deconditioning, little information is available on the effects of acceleration stress under such circumstances. To study this further, 4 healthy males 18-22 years were hospitalized in a metabolic ward and fed a weighed diet of 2500 Calories (74 gm protein, 99 gm fat, 341 gm CHO). For 18 days before and after an 18 day period of continuous recumbent bed rest (RBR) all subjects trained on a bicycle ergometer for 1 hour daily at 600 kpm/min. Before and after the RBR period, blood pressure (cuff) and heart rate (HR) response to 10 min 70° head-up body tilt, and HR and arterial blood saturation (ear oximeter) response to +3.6 G_x acceleration (Johnsville Human Centrifuge) were determined. Heart rate increase averaged 44% and 56% respectively over control values after 10 min of tilt before and after RBR. Despite this, no difference in HR response to acceleration occurred but acceleration arterial oxygen saturation decreased 1 1/2% before and 3% after RBR.

(Supported by U. S. Naval Air Development Center, Johnsville, Pa.)

METABOLISM OF PLASMA GLUCOSE AND FFA IN NORMAL AND PANCREATECTOMIZED DOGS DURING STEADY STATE EXERCISE. P. Paul,* H. Miller and B. Issekutz, Jr. Div. of Research, Lankenau Hosp., Philadelphia, Pa.

Dogs with indwelling arterial and venous catheters ran on a treadmill (slope: 15%, speed: 100 m/min) for 3-5 hours at a 5- to 6-fold elevated O_2 uptake. Glucose-C^{14}(U) or albumin-bound palmitate-1-C^{14} was infused i. v. at a constant rate. O_2 uptake, CO_2 output and the specific activities of CO_2, plasma glucose, or FFA were measured. In both normal and diabetic dogs, exercise increased the turnover rate of FFA and its percent participation (70-90%) in exhaled CO_2. The 5-16% contribution of plasma glucose to CO_2 output was not altered or decreased by exercise. In normal dogs glucose turnover was increased and immediately converted to CO_2; in diabetic animals exercise little altered the already high turnover rate, only a small fraction of which was oxidized. When in normal dogs glucose turnover was elevated by continuous glucose infusions (12-17 mg/kg min) to rates comparable to those of diabetic dogs, the plasma insulin level (immunoassay) rose 3- to 4-fold. At rest 50-80% of CO_2 derived from plasma glucose and 5-20% from FFA. Exercise decreased the insulin level, the RQ and the percent CO_2 from plasma glucose. It increased the turnover rate of FFA and its percent contribution to CO_2 output. Despite high glucose turnover and its complete oxidation, exercise shifted the metabolism toward fat oxidation.

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D_L, D_M and V_c in Normal, Asthmatic and Emphysematous Subjects. L. J. Pecora, I. L. Bernstein* and D. P. Feldman.* VA Hosp. & Depts. of Physiol., Med. and Ped., U. of Cincinnati Coll. of Med., Cincinnati, Ohio.

In a previous study of children with intractable asthma and chronic overinflation, we observed a stat. sig. increase in pul. diffusing cap. (D_L) and membrane diffusing cap. (D_M) while the cap. blood vol. (V_c) was slightly less than predicted. These observations suggested that this might be a method of distinguishing adult asthmatic and emphysematous patients. We studied 28 asthmatic patients, 21-62 years, 17 with obstructive lung disease (emphysema) age 37-71 years, and 16 normal subjects, 22-47 years. The overinflated asthmatic patients had approximately normal TLC, increased RV/TLC and FRC, while the emphysematous patients had increased RV, TLC and RV/TLC. The mean D_L values were over 100% of predicted for all groups studied. The asthmatic group had near normal D_M and V_c while the emphysema group had markedly decreased D_M and increased V_c. From our studies we also concluded that the use of the effective alveolar volume obtained by helium dilution gives the same single breath D_L as that obtained from the sum of the inspiratory vital capacity and residual volume measured separately.

Comparative alveolar volumes are:

	Norm.(32)	Asth.(56)	Emphys.(36)	Other Pul.Dis.(75)
Meas. AV $\bar{x}$	5733	4815	6318	4588
Eff. AV $\bar{x}$	5728	4802	6217	4656
Cor.coef.r	0.816	0.863	0.803	0.903
p	<0.01	<0.01	<0.01	<0.01

DEPRESSION OF RESIRATION OF A SCREENED CELL SUSPENSION FROM KIDNEY WITH L-THYROXINE. Hugh J. Phillips. Creighton Univ. School of Med., Omaha, Nebraska.

A cell suspension was prepared from male rat kidney by passing chopped, washed tissue through a 35 mesh stainless steel screen. The suspension had moderate endogenous respiration for an hour and could be stimulated with various substrates such as succinate and glutamate. Each reaction vessel contained 5.2 - 9.5 mg. cell protein in a volume of 2 ml. Respiration was depressed in the presence of 2.2×10^{-2} μ moles L-thyroxine per flask (10^{-5}M) and the depression could not be accounted for by the presence of free mitochondria. The depression of respiration followed a typical dose-response curve. D-thyroxine and 3,3',5-triiodo L-thyronine also depressed respiration. Diiodotyrosine, potassium iodide, L-thyronine and thyroglobulin had no effect on respiration. In the presence of .25% crystalline albumin L-thyroxine did not depress respiration. When respiration was measured at 4 hour intervals for 32 hours respiration of controls and thyroxine treated cells progressively became less. The addition of glucose did not restore respiration to the initial rate in either case. Initially respiration rate was less for the thyroxine treated cells. Eight to twelve hours later controls and the thyroxine group were about the same, from then on the thyroxine treated cells had a greater rate of respiration than controls. The total amount of oxygen used for 32 hours, as determined by planimetry, was the same for controls and thyroxine treated cells. In short it appeared that thyroxine first decreased and then increased the rate of oxygen utilization as compared to the controls.

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Fatty Acid Induced Glycogenolysis in Ruminants. R. W. Phillips (intr. by R. M. Johnson). Colorado State University, Fort Collins, Colorado.

Butyric acid has long been known to be unexpectedly glucogenic in ruminants. In certain cases this appears to be the result of specific organ of utilization of the butyric acid. Under more dramatic circumstances evidenced by a rapid increase in blood sugar, it is due to liver glycogenolysis. The mechanism of this glycogenolysis has been investigated and butyric acid has been found to act through the release of glucagon by the pancreas in sheep and goats. Butyric acid induced hyperglycemia is completely abolished by total pancreatectomy. Further the degree of glycogenolysis is directly related to the chain length of fatty acid administered in sheep but not in other animals, as dogs do not show a similar hyperglycemic response to either short or long chain fatty acids nor do cattle, another ruminant species.

THE EFFECTS OF ACUTE METABOLIC ACIDOSIS AND ALKALOSIS ON RENAL EXTRACTION OF GLUTAMINE AND AMMONIA PRODUCTION. Lou Ann Pilkington and T.K. Young*, Cornell Univ. Medical College, New York, N.Y.

Renal extraction of glutamine and total renal production of ammonia were measured for as long as 5 hours in two series of dogs: a) chronically acidotic animals rendered acutely alkalotic with bicarbonate infusion; b) chronically alkalotic animals rendered acutely acidotic with acid infusion. The results show that, in series (a) animals, extraction of glutamine and ammonia production decreased progressively and in parallel to low values as alkalosis was sustained. Conversely, in series (b) animals extraction of glutamine and ammonia production increased progressively and in parallel as the acidotic state was maintained. Excretion of glutamine was essentially zero in each series. The results indicate that a) the adaptation of renal ammonia production in chronically acidotic dogs is mimicked in alkalotic animals made acutely acidotic over a time course of 5 hours and b) adaptation occurs predominantly through changes in the extraction of glutamine.

PROTECTION OF THE ISCHEMIC HEART WITH DMSO ALONE OR DMSO WITH HYDROGEN PEROXIDE. H. P. Pingree and J. W. Finney (intr. by H. L. Dorman). Baylor Univ. Grad. Div. at the College of Dentistry, Dallas, Texas.

From studies already reported, one fact remains pertinent to this presentation: Oxygen can be supplied to the hypoxic myocardium by either pericardial perfusion or coronary artery infusion of dilute hydrogen peroxide. Some difficulties are encountered in attempting to supply sufficient oxygen to a large myocardium to maintain normal function. These difficulties are primarily due to diffusion rates and distance that oxygen diffuses into the anoxic myocardium during the perfusion period. The studies reported here will deal primarily with the effect of hydrogen peroxide or hydrogen peroxide with dimethyl sulfoxide on the myocardium following acute coronary ligation and subsequent myocardial infarctions. The lesion is created by ligating approximately 50 per cent of the anterior descending branch of the left coronary artery and the right coronary artery at its root. Preliminary evidence indicate that the addition of DMSO to this model system assists in the diffusion of oxygen into the ischemic myocardium restoring the electrostability and ability of the myocardium to do work.

THE INFLUENCE OF RIGHT VENTRICULAR EJECTION ON PULMONARY VENOUS PRESSURE AND FLOW IN DOGS. A. L. Pinkerson (intr. by E. D. Freis). V. A. Hospital and Department of Physiology and Biophysics, Georgetown University School of Medicine, Washington, D. C.

Pulsations of blood flow and pressure in pulmonary veins and the left atrium have been attributed by some primarily to right ventricular ejection and by others to left atrial and ventricular contraction and relaxation. To analyze the influence of right ventricular ejection alone, pressure and flow in a cannulated pulmonary vein and in the main pulmonary artery were recorded simultaneously with electromagnetic probes and pressure catheters in open-chested anesthetized mongrel dogs. Blood from the cannulated vein was drained into a constant level reservoir and returned to the femoral vein. Pulmonary arterial and venous pressures and flows were compared at different heart rates (15-187 beats/min.), after the administration of acetylcholine, and with changes in pulmonary vascular resistance. In every instance distinct pressure and flow pulses were transmitted from the pulmonary artery to the cannulated pulmonary vein. Foot to foot transmission time from the main pulmonary artery to the pulmonary vein was 80-160 msec. for both pressure and flow pulses. Peak to peak transmission time was 30-150% more prolonged. Similar venous pulsations were also recorded in animals after the thoracotomy incision was closed around the pulmonary vein cannula and spontaneous negative pressure respirations resumed. When the pulmonary vein cannula was removed from the reservoir and drained directly into the left atrium the flow and pressure contours appeared similar except for a phase of decreased flow associated with the atrial pressure "A" wave. These studies agree with the concept that right ventricular ejection is an important determinant of the pressure and flow pulses recorded in the pulmonary veins and left atrium.

CONTROL OF PURPOSIVE BEHAVIOR BY PROGRAMMED STIMULATION OF THE BRAIN. Lawrence R. Pinneo. Delta Reg. Prim. Res. Ctr. Tulane Univ. Covington, La.

We are studying the neural basis of purposive behavior in primates by programmed electrical stimulation of the brain through three approaches: (1) Observations and cinematographic analysis of the elementary movements involved in various goal-directed acts, such as eating, drinking, grooming, climbing, progression, fighting, sexual behavior, and the like. (2) Mapping in acute, anesthetized animals, the various loci in the brain (primarily the brain stem and cerebellar nuclei), that upon electrical stimulation produces the elementary movements involved in the goal-directed behavior. (3) Chronic implantation of many electrodes (6 to 200) for programmed stimulation of cites found in (2) that, when stimulated with the proper electrical parameters in the correct sequence, produces the purposive movements observed in (1) A ten-minute film demonstrates some of the many movements elicited during the mapping studies including: flexion and extension of limbs at the wrist, elbow, shoulder, ankle, knee, or hip; clenching or spreading of the fingers; opening and closing of the mouth; movement of the tongue in and out; curling and other movements of the tail; movement of the eyes and dilatation of the pupils. Optimum electrical parameters for all movements were 200 to 300 rectangular p.p.s., 0.1 to 1.0 msec. duration, 50 to 200μA base-to-peak, monophasic with active electrode negative. Each site was very specific, movements ceasing if the electrode was moved as little as 100 micro at threshold current. In all locations examined, the mechanical effect of movement was proportional to current strength. Programmed stimulation of six cites in the cerebellar nuclei and brain stem of a chronic squirrel monkey was sufficient to control the right arm and produce behaviors such as feeding, scratching, and climbing, even in a monoplegic limb.

EFFECT OF ADRENERGIC BLOCKADE ON THE CORONARY HEMODYNAMIC RESPONSE TO EXCITEMENT AT FIXED VENTRICULAR RATE IN THE UNANESTHETIZED DOG. B. Pitt*, E. C. Elliot*, E. M. Khouri* and D. E. Gregg. Dept of Cardiorespiratory Diseases, Walter Reed Army Inst. of Res., Wash., D. C.

Coronary hemodynamic studies during excitement have shown a rise in coronary blood flow (CBF), cardiac output (CO), ventricular rate (VR) and aortic pressure (AP). To eliminate the role of cardio-acceleration during excitement, surgical heart block was produced in 5 dogs and the heart paced. Phasic CBF and CO were recorded from implanted electromagnetic flow transducers along with AP in the unanesthetized dog. Mild excitement was produced by squirting ice water in the dog's face or by banging 2 pans together. During excitement at fixed VR, CBF increased 59%, CO 22% and AP 32%. After beta adrenergic blockade (BB) with I.V. Propranolol, similar excitement led to a 30% increase in CBF, CO 14%, and AP 10%. A diminished response to excitement after BB was found in all 5 dogs although there was considerable variation in the results. Data obtained from 2 unanesthetized dogs with intact conducting systems showed a similar reduction in CBF and CO after BB, due in part to diminished cardio-acceleration. To eliminate the effect of increased AP (in addition to cardio-acceleration) which normally occurs during excitement, alpha adrenergic blockade was produced with i.v. Dibenzyline in 2 heart-blocked animals. In one, CBF increased 76% along with CO 30%, while AP and VR remained constant during excitement. In the other, CBF increased 116% while AP fell 5%. In summary, studies at fixed and variable heart rate demonstrate that BB can diminish the coronary hemodynamic response to excitement. Also excitement can cause a rise in CBF independently of cardio-acceleration and a rise in AP.

GENERALIZED HYPOTHERMIA ENHANCES ANTI-CANCER DRUG ACTION ON NORMOTHERMIC TUMORS. Vojin Popovic and Roberto Masironi. Dept. Physiol., Emory Univ., Atlanta, Ga.

In experiments reported earlier it has been shown that subsequent to cooling of the whole body of golden hamsters their normothermically kept tumors disappear (Popovic, V. and Masironi, R.; Disappearance of euthermic tumors after 10-hour generalized hypothermia. Life Sci. 4: 533-43, 1965. Popovic, V. and Masironi, R.; Disappearance of normothermic tumors in shallow, 30°C, hypothermia. Cancer Res., May 1966. Popovic, V. and Masironi, R.; Effect of generalized hypothermia on normothermic tumors. Am. J. Physiol., Aug. 1966). However, in order to induce tumor disappearance the differential hypothermia (tumor-body) has to last at least 10 hours. Since extreme hypothermia lasting several hours is not well tolerated by non-hibernators, experiments were now undertaken in which the differential hypothermia was combined with 5-fluorouracil, an anti-cancer drug. It was reasoned that the anti-cancer drug might become preferentially effective in the tumor tissue because of higher volume blood flow as well as of higher metabolic rate of normothermic tumors when compared to the rest of the hypothermically kept body. For this purpose the bodies of 75 hamsters were cooled to a temperature of 4°C while their tumors (Toolan H.Ad. #1U) remained uncooled at 37°C. The FU (50 mg/kg) was administered i.v. in a single injection. One hour later the animals were rewarmed. Twenty days later all tumors regressed and disappeared completely without resuming their growth afterwards. When the same amount of FU was administered into normothermic tumor-bearing animals or into hypothermic animals with hypothermic tumors, neither tumor size nor body weight of the animals was affected. The same results as described above with Toolan tumors were obtained in 35 hamsters with chemically induced (isologous) tumors.

VASCULAR CONDUCTANCE AND CAPACITY IN SKELETAL MUSCLE. Camilo I. Porciuncula*, Reginald Carter*, Carlos E. Rapela and Harold D. Green. Bowman Gray School of Medicine, Winston-Salem, North Carolina.

These studies were initiated to determine whether vascular conductance may behave independently of vascular capacity in response to various stresses. The dog's hind leg skeletal muscle bed was isolated from collateral vasculature by tourniquets and ligation of communicating channels. Denervation of the bed was accomplished by section of the femoral and sciatic nerves. Vascular conductance was computed from flow, measured simultaneously by electromagnetic meter (venous outflow) and indicator concentration (IHSA-I^{131} Albumotope), divided by the perfusion pressure (femoral artery minus vein pressure). Vascular volume was computed as flow times mean transit time. Perfusion pressure was decreased stepwise by a screw clamp on the femoral artery. Measurements were made only after a steady state was established. During the stepwise reductions in perfusion pressure conductance tended initially to increase and thereafter to remain constant or fall. Conductance tended to be lower at most levels of pressure during occlusion of the common carotid artery and to be higher after denervation. As the perfusion pressure was lowered vascular volume tended to increase; and reciprocal time (1/mean transit time) to decrease more rapidly than pressure. It appears that conductance and vascular capacity may vary in opposite directions when the skeletal muscle bed is subjected to low perfusion pressure. (Supported by PHS grants 5 T1 HE 5392 and HE 00487, and a grant from NCHA).

EFFECT OF INTERSTITIAL FLUID PRESSURE, VENOUS PRESSURE, AND ARTERIAL PRESSURE ON FLUID MOVEMENT THROUGH THE CAPILLARY WALL. John W. Prather* Arthur C. Guyton, Konrad Scheel* and James McGehee*. Department of Physiology, Univ. Miss. Medical Center, Jackson, Mississippi.

The effects of changes in interstitial fluid pressure, arterial pressure, and venous pressure on fluid movement through the capillary wall have been studied in dogs having perforated capsules implanted four to eight weeks prior to the experiments. The capsules filled with fluid and were used as implanted plethysmographs. With arterial and venous pressure held constant, decreasing the interstitial fluid pressure from its normal value of -7 mm Hg resulted in increased flow across the capillary membrane such that the following linear equation was applicable: fluid flow = $\alpha\Delta P + \beta$. This linearity still held even at -40 mm Hg interstitial fluid pressure. The filtration coefficient calculated to be 0.058 µl/min/mm Hg/gram tissue. Increasing the interstitial fluid pressure above its control value resulted in only transient flow of fluid from the tissues into the capillaries. Holding the arterial pressure constant and increasing the venous pressure resulted in filtration into the tissues. However, the filtration rate was only 79% as great as that caused by decreasing the interstitial fluid pressure. The arterial pressure was reduced from its control value(105 to 135 mm Hg) to a value within the range of 40 to 75 mm Hg. During this procedure the venous pressure was held constant. The rate of absorption from the tissue was extremely slight or none at all, and that which did occur ceased in less than one minute. It is likely that autoregulation prevented absorption in these experiments.
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DIFFERENTIAL l-NOREPINEPHRINE SENSITIVITY IN THE FOUR CARDIAC CHAMBERS AFTER UNILATERAL DENERVATION. *Donald V. Priola.* Department of Physiology, Loyola University Stritch School of Medicine and the Graduate School, Chicago, Illinois.

Efforts to determine the specific chamber distribution of the cardiac sympathetic nerves from the right and left sides have been equivocal. It is conceivable that right or left cardiac sympathectomy should produce supersensitivity to norepinephrine in the denervated chambers, and distribution patterns should be more clearly delineated. Thirty-seven mongrel dogs, 15 control, unoperated animals, 12 with right sympathectomy two weeks earlier, and 10 with left sympathectomy were used. Cardiac sensitivity to norepinephrine was tested by recording pressures from the four cardiac chambers before and during constant infusions of six different doses of norepinephrine. The doses employed were: 0.03, 0.07, 0.17, 0.34, 0.68, and 1.69 µg/kg/min. Dose-response curves were constructed by relating the absolute change in pulse pressure, maximum dP/dt, or heart rate to the log dose of norepinephrine. The dose-response curves thus generated were compared and the changes in sensitivity measured as the horizontal displacement of the denervation curves from the control curves. Right sympathectomy produced a tenfold increase in atrial and heart rate sensitivity while causing little increase in ventricular sensitivity. Left sympathectomy, on the other hand, caused no change, or even a decrease, in atrial and heart rate sensitivity, while producing a threefold increase in ventricular sensitivity, left ventricle more than right. These data are interpreted to mean that the atria and the SA node are supplied almost entirely by the right sympathetics, while the ventricles receive fibers from both sides, left contributing the majority. The data argue for the functional unit hypothesis of cardiac innervation and for the heart's obedience to "Cannon's Law of Denervation."

CHANGES IN THE ADENINE NUCLEOTIDES AND ADENOSINE TRIPHOSPHATASE ACTIVITY DURING AESTIVATION OF THE INDIAN APPLE-SNAIL.
S. Raghupathiramireddy+ and Karumuri S. Swami. Dept. Zool., Sri Venkateswara Univ., Tirupati, A.P., India. (Intr. by James W. Campbell).

In view of the recent hypotheses implicating adenine nucleotides in the regulation of energy metabolism, these compounds were analyzed in the tissues from active and aestivating snails (Pila globosa). In the aestivating snail the level of ATP is significantly higher and the ADP level lower than in the active snail. No changes were found in the AMP levels. In accordance with these changes in adenine nucleotides the activity of the enzyme adenosine triphosphatase was markedly low in aestivation suggesting a decreased utilization of ATP in this torpid state. However the ATPase activity was found to be restored to the pre-aestivation level when the snail awakens from aestivation and this probably makes the stored ATP available for the energy requirements of the snail during recovery from torpor. These changes in the adenine nucleotides and adenosine triphosphatase activity may be important in regulating the rate of anaerobic glycolysis so that the glycogen reserves of the body are economically used over a prolonged period of aestivation. (Supported by a research grant from the CSIR of India).

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CAPILLARIES IN NORMAL, HYPERTROPHIC AND INFARCTED HEART. K. Rakušan*, W. du Mesnil*, C. Cowan* and R.J. Bing. Wayne State University, School of Medicine, Detroit, Michigan.

Blood content in the terminal vascular bed (BC) as an indicator of the capillary density was determined by means of I^{131}. Results are expressed in ml of blood per 100g of tissue. Postnatal development of the capillary density in the rabbit heart was investigated. An increase of the BC from 6.94 to 10.22 was observed in the first postnatal weeks. Values in adult animals were 8.03 and in old animals 6.54 (all differences are significant, $p < 0.01$). Cardiac hypertrophy (+35% of the left ventricle weight) was produced by means of aortic stenosis in adult rabbits. BC in hypertrophic hearts was 5.52 as compared to 8.03 in the controls. ($p < 0.01$). Regional differences were found in the dog heart (apex > left ventricle > septum, right ventricle). In ten dog hearts with experimental infarct BC was 3.10 in the center of infarcted tissue as compared to 5.20 in the borderline and 4.61 in the normal areas (sign. $p < 0.01$).

PUBERTY AFTER NEURAL ISOLATION OF THE MEDIAL BASAL HYPOTHALAMUS (MBH) IN THE FEMALE RAT. J. A. Ramaley* and R. A. Gorski, Dept. Anatomy and Brain Res. Inst., University of California, Los Angeles, Calif.

Neural connections of the MBH of 150 female 22-day-old Sprague-Dawley rats were completely or partially severed by means of the Halász knife, and the development of gonadal activity was studied. Compared to intact controls (34.8±1.8) the day of vaginal opening following complete deafferentation of the MBH was advanced (29.1±1.4; $P<0.02$). Sham surgery delayed both vaginal opening (41.0±1.2 days) and ovulation. Animals with a neurally isolated MBH failed to ovulate and developed persistent vaginal estrus; upon autopsy at 90 days the ovaries of these rats contained only large follicles and weighed less (17.7±3.5; $P<0.01$) than intact (38.5±2.3) or sham operated (36.8±2.9) controls. There were no significant differences in uterine, adrenal, thyroid, or anterior pituitary weights of deafferented and intact rats. The deafferented region extended from just behind the optic chiasm to the mammillary body and about 1.2mm laterally and dorsally. Partial deafferentations which were unilateral or incomplete anteriorally, leaving frontal connections to the MBH intact, had no effect. When only fibers passing through the retrochiasmatic area were severed (frontal cut), ovulation was prevented, and precocious vaginal introitus occurred (29.3±1.2 days). Prepubertal injection of 25 or 50 I.U. PMS accelerated vaginal opening in rats with frontal cuts, but ovulation did not occur. At autopsy, one day after vaginal introitus, polyfollicular ovaries of PMS-treated, deafferented rats equalled or exceeded in weight the heavily luteinized ovaries of similarly treated intact rats. It appears that the MBH-hypophyseal unit in the absence of neural input can sustain gonadal maturation and the shift to adult levels of GTH secretion at puberty as indicated by the time of vaginal opening and the response to exogenous PMS. As in the adult, however, ovulation does not occur. (NIH grant HD 01182.)

THE EFFECT OF O-ACETOXY BENZOIC ACID ON IONIC REABSORPTION IN THE RENAL TUBULE. A. G. Ramsay and H. C. Elliott, (intr. by E. B. Carmichael), University of Alabama Medical Center, Birmingham, Ala.

Previous work demonstrated that o-acetoxy benzoic acid (aspirin) profoundly decreased the urinary excretion of sodium in man. This was surprising as it is well known that salicylate increases ionic excretion. To investigate the mechanism involved, clearance experiments were performed in dogs. These showed a 25 to 75% decrement in excretory rates of Na^+, Ca^{++}, Mg^{++}, Cl^- and HCO_3^- following the administration of aspirin 8 mg./Kg. and subsequent infusion at 1 mg./min. There was no change produced in GFR or plasma concentration of univalent ions. Therefore it appeared that the compound profoundly increased tubular univalent ionic reabsorption. Although determinations of the ionic component of plasma Ca and Mg were not made, it seemed more than likely that the compound had the same effect on the tubular reabsorption of the divalent cations. Other congeners including salicylic acid, coumarilic acid, and o-acetyl and o-ethoxy benzoic acids all either increased the rate of ionic excretion or had no effect. Aspirin had no consistent effect on K excretion. Although the dog has a plasma aromatic esterase, analysis showed that at least half of the total plasma salicylate remained in the form of o-acetoxy benzoic acid during the period of the experiment. The absence of effect with salicylate would indicate that the action on tubular ionic reabsorption was primarily due to aspirin. The ortho acetoxy group of benzoic acid appeared to be specific for the effect. Aspirin may act by increasing permeability of the luminal membrane to ions, by increasing the capacity of the tubule cell carrier system, or by augmenting the production of energy required for active transport.

Supported by NIH

AUTOMATED MEASUREMENT OF CARDIAC OUTPUT BY USE OF A DIGITAL COMPUTER. William Medden Rand*, Max Harry Weil, and Herbert Shubin*. Department of Medicine, University of Southern California School of Medicine, Los Angeles, California.

A computer system has been developed for high speed monitoring and immediate reporting on the condition of patients in shock. Determination of cardiac output by indicator dilution technique using indocyanine green dye is accomplished by transmitting the electrical output of the dye densitometer to a digital computer. The dye curve is numerically integrated and the downslope of the curve corrected, using a standard extrapolation technique to exclude recirculating dye. The correlation between cardiac output reported by computer and the value based on manual calculations indicates no systematic differences and a high correlation ($r = 0.994$). The value for cardiac output is used, in combination with the values for other hemodynamic parameters measured by the computer system, such as arterial pressure and heart rate, to calculate values for peripheral resistance, stroke volume, central blood volume and cardiac work. The determination of these variables in "real time" and their immediate display greatly assist the physician in his bedside evaluation of the patient's circulatory status and the effects of treatment. Supported by Public Health Service Research Grants HE-07811 and HE-05570 from the National Heart Institute and The John A. Hartford Foundation, Inc., New York.

VENTRICULAR AUGMENTOR AND INHIBITORY RESPONSES TO VAGAL STIMULATION IN THE DOG. *Walter C. Randall, Donald V. Priola* and *Clarence N. Peiss*. Department of Physiology, Loyola University Stritch School of Medicine and the Graduate School, Chicago, Illinois.

The presence of cardioaccelerator fibers in the vagosympathetic trunk is well established, and DeGeest *et al* have demonstrated direct inhibitory innervation of the left ventricle. Employing a four-chamber pressure recording technique, differential inhibitory and excitatory responses were examined during vagal stimulation both before and after sympathetic and/or parasympathetic blockade. In the open-chest, anesthetized (Sernylan-chloralose) dog, stimulation of the distal end of the vagus resulted in suppression of contractility in all four chambers, as indicated by decreased systolic pressure and dP/dt in the presence of rising end-diastolic pressure. Differential pressure changes reflect variable distribution of vagal inhibitory fibers. Responses after atropine reveal the presence of direct ventricular augmentor fibers as signalled by prompt and sometimes profound rise in systolic pressure with decreasing end-diastolic pressure, increasing dP/dt and acceleration in heart rate. Differential responses in right and left ventricles after atropine were also common, and indicate variations in distribution of vagal augmentor fibers to the ventricles. Ventricular augmentation may occur in the absence of demonstrable direct changes in atrial dynamics. The augmentor response to vagal stimulation was blocked by Inderal, suggesting an adrenergic nature of the mechanism. Following conventional cardiac sympathectomy, results were inconsistent and emphasize considerable variability in derivation of vagal augmentor fibers to the heart. (Supported by NIH Grant HE 08682.)

EVOLUTION OF MOLLUSCAN HEMOGLOBINS

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The number of amino acid residues in the protein moieties associated with one heme group in the molluscan hemoglobins ranges from 137 for the hemoglobin Hb-1 of the bivalve Phacoides pectinatus to 284 for the myoglobin Mb-1 of Busycon canaliculatum. If other invertebrates are included we find that this range is extended at the lower end to 124-125 residues for the α-chain of the insect Chironomus thummi and to 332 residues at the upper end for the subunit of Ascaris lumbricoides (Nematoda) hemoglobin. Chain lengths of the vertebrate hemoglobins and myoglobins and other homologous proteins from different phyla and kingdoms vary up to 18 percent, at the outside, in the proteins so far studied.

The variation in amino acid composition among the molluscan or invertebrate hemoglobins is vastly greater than the variation in amino acid composition of putative homologous proteins including the vertebrate hemoglobins and myoglobins.

It is concluded, in the absence of sequence data, that the molluscan and other invertebrate hemoglobins and myoglobins, so far studied, are unlikely to be homologous either with each other or with the vertebrate pigments.

EFFECT OF TAURINE ON THE REFRACTORY PERIOD OF HEART MUSCLE. W.O. Read and Jeffrey E. Byrne*. Univ. So. Dak., Sch. of Med., Vermillion, S.D.

Taurine has been shown to be an effective non-toxic agent for suppressing ventricular premature contractions due to large doses of epinephrine or digoxin (Read and Welty, J.P.E.T., 139:283, 1963). In the present study, the effect of taurine on the refractory period of canine ventricular tissue was measured using intramyocardial electrodes. Paired square wave stimuli of equal duration and magnitude (1.25 X threshold) from a Grass model S4C stimulator was delivered to the intact beating dog ventricle. The delay between the paired stimuli was increased until the second stimulus elicited an action potential. This time was taken as the refractory period. The event was visualized on a Tektronic dual beam oscilloscope. The results show that taurine increases the refractory period of canine ventricular tissue about 15 percent (from control value of 170 m sec. to 198 m sec.). (Supported by USPHS grant No. HE-06044 and South Dakota Heart Association.)

PATTERNS OF POSTNATAL DEVELOPMENT OF PULMONARY AND BRONCHIAL ARTERIAL CIRCULATIONS IN THE CALF AND THE EFFECTS OF CHRONIC HYPOXIA. John T. Reeves and James E. Leathers.* Dept. of Med., Coll. of Med., Univ. of Ky., Lexington, Ky.

Calves living from birth at low altitude decrease their pulmonary arterial pressures to near adult levels in the first 7 to 14 days of life. Radiographs of the lung vessels showed rapid growth of both pulmonary and bronchial arteries within the first week of life. The increase in the pulmonary arterial circulation is sufficiently great to account for part of the early decrease in pulmonary vascular resistance within the first week of life. Calves living from birth at a simulated altitude of 11,000 feet rapidly developed pulmonary but not systemic arterial hypertension. The pulmonary arterial pressure was labile, responding in particular to small changes in oxygen tension. Radiographs of the lung vessels showed a restricted pulmonary arterial and an increased bronchial circulation. These calves probably maintained from birth increased tone in the pulmonary but not systemic arterioles. The normal growth pattern of the lung vessels was altered. There may be, therefore, a reciprocal blood supply to the lung by these two arterial systems even when there is vasoconstriction in the smallest radicles of the pulmonary arterial tree. The mechanisms which provide a different regulation of the two arterial supplies to the same organ remain an important area for investigation.
(Supported by NIH Grants HE 08932-03 and HE 06780-05.)

BLOOD pH AND BODY TEMPERATURE IN THE HETEROTHERMIC MAMMAL, MYOTIS LUCIFUGUS. R. B. Reeves and W. A. Wimsatt*. Div. of Biol. Sci., Cornell Univ., Ithaca, N. Y.

Blood pH in cold-blooded vertebrates has been shown to vary in vivo with temperature in a systematic way, namely, -0.0176 unit/deg. C. To examine whether this relation obtains for heterothermic mammals, measurements of blood pH were made on Little Brown Bats, Myotis lucifugus. These animals when quiescent have a body temperature near that of their environment. Animals were exposed to a controlled temperature environment for 72 hours, then duplicate 0.08 ml blood samples were taken and deep visceral temperature was measured. Blood pH and pCO_2 measurements were made with a Radiometer blood gas analyzer calibrated at each measured body temperature with appropriate standards. Blood pH was found to be constant, $7.53 \pm .037$, in 63 animals over the range of 6 - 37°C; the slope of the least-squares regression line was not significantly different from zero. Seven measurements, made after animals had been flying for periods up to 10 min, showed no significant alteration in blood pH. Deep visceral temperature was found to be 3 - 4° above ambient below 30°C; above this temperature deep visceral temperature was below ambient by 5 - 8°. Bats flown for periods longer than 3 min had body temperatures of 37 - 38°C. Carbon dioxide blood gas tension rose with body temperature from 10.7 mm Hg at 7.0°C to 22.6 mm Hg at 36°C. This alteration of pCO_2 was just sufficient to compensate for gas solubility changes with temperature and thus maintain constant blood pH. We conclude that extracellular fluid pH is closely regulated in this species at all physiological body temperatures by appropriate respiratory compensation in pCO_2.

EFFECTS OF ACETYLSALICYLIC ACID ON THE HEMODYNAMIC RESPONSE TO ENDOTOXIN. D.A. Reins*, L.B. Hinshaw, L.A. Solomon*, and E. Erdös*. V.A. Hospital and Depts. of Surgery, Physiology and Pharmacology, University of Oklahoma Medical Center, Oklahoma City, Oklahoma.

The acute response of the dog to an injection of endotoxin is characterized by portal pooling, decreased venous return, and irreversible systemic hypotension; accompanied by acidosis, hemoconcentration and abdominal visceral lesions. In the present study, adult dogs anesthetized with intravenous sodium pentobarbital, were infused with aspirin in alcoholic solution (40 mg/kg) or buffered aspirin (100-130 mg/kg) (Alka-Seltzer) 30 minutes prior to receiving an LD_{80} equivalent injection of E. coli endotoxin. Pretreatment with Alka-Seltzer blocked the acute response to endotoxin; portal hypertension did not occur, venous return and systemic arterial pressure remained near control levels; acidosis did not develop; hemoconcentration, diarrhea and intestinal hemorrhage decreased in severity. Pretreatment with aspirin diminished pooling, brought about a reversal of hemoconcentration during a two-hour observation period and blocked the portal hypertension effect. The prevention of acidosis and hemoconcentration after endotoxin is postulated to occur because of diminished venoconstriction and a stimulatory effect on the central nervous system. Alka-Seltzer alone brought about an increased body temperature, respiratory rate and cardiac output.
(supported by USPHS grant HE-09381)

THE EFFECT OF CALORIC VESTIBULAR STIMULATION ON SIMULTANEOUS BILATERALLY ELICITED H REFLEXES IN NORMAL MAN. Donald J. Reis and David Fraser,* Cornell University Medical College, New York.

The effect of unilateral caloric vestibular stimulation on the magnitude of simultaneously elicited bilateral H reflex responses was studied in 10 normal males. H reflex responses were elicited repetitively from posterior tibial nerves at 0.3/second in prone subjects. Individual H reflex responses were filmed and 40 consecutive responses averaged by computer before, during and following the nystagmus induced by ice water stimulation. Differences in H reflex latencies between legs was never greater than 1.5 msec and the average difference was 0.5 msec. The aperiodic fluctuations of H reflex magnitude which occurred with repetitive testing were never synchronized between legs. Startle, Jendrassik or Valsalva maneuvers resulted in brisk bilateral augmentation of H reflex responses. With vestibular stimulation 9 subjects developed nystagmus to the stimulated side with average latency of 42 seconds and average duration of 150 seconds. The magnitude of the H reflex increased in 8 subjects an average of 57% above control. Augmentation was ipsilateral in 4, contralateral in 2, bilateral in 2 and absent in 2 subjects. We conclude that the effect of calorically activated vestibular output onto extensor lumbar spinal motoneurons in man is inconstant, facilitatory, and of variable laterality in contrast to the invariant and potent effect on oculomotor function. (Supported by NIH grant NB-03346.)

RECRUITING AND BARBITURATE SPINDLE SEPARATION. John M. Rhodes and Allan Netick*. University of New Mexico, Albuquerque, New Mexico.

Recruiting responses were obtained from low frequency stimulation of the intralaminar and midline nuclei of the thalamus through implanted electrodes in acute preparations of 40 cats under moderate barbiturate anesthesia. The technique of reversible functional lesions with subcortically injected KCL was employed to explore possible generators and pathways for both the cortically recorded recruiting response and for barbiturate spindle bursts. Differential effects upon the recruiting response and the barbiturate spindles could be obtained depending upon the site of KCL injection (25 microliters of 10% solution). Injection into the prothalamic area abolished both recruiting and spindling; into the ventralis anterior abolished recruiting but spared spindling; into the medialis dorsalis spared recruiting while abolishing spindling. Injection into the head of the caudate did not consistently influence spindling or recruiting amplitudes. The results support the separation of generators and/or pathways for recruiting and barbiturate spindles despite gross resemblances between these cortically recorded responses. In addition, the possibility of obtaining specific effects with intrathalamic injection of KCL in the cat is demonstrated.

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EFFECTS OF GASTRIN AND HISTAMINE ON THE ACID AND PEPSIN RESPONSES TO VAGAL ACTIVATION IN ANTRECTOMIZED DOGS. P. T. Ridley, L. Olbe*, and B. Uvnäs. Department of Pharmacology, Karolinska Institute, Stockholm, Sweden.

These studies were designed to investigate the role of gastrin in gastric acid and pepsin secretion following vagal activation mediated by sham feeding. Antrectomized, innervated gastric pouch dogs were used to determine the effect of sham feeding (SF) alone, and SF in combination with various doses of exogenous hog gastrin (SF+G) on gastric acid and pepsin secretion. In the latter experiments a ten minute SF response was superimposed on a gastric acid secretory response induced by i.v. infusion of gastrin. The acid secretory responses with gastrin alone ranged from threshold to 2/3 maximal. SF alone was characterized by high pepsin and low acid secretion. SF+G resulted in a potentiated acid secretion with a dose-response relationship. However, the degree of potentiation [total acid output - (SF acid output + G acid output)] remained the same with increasing doses. Pepsin secretion was the highest with SF alone and with SF+G in threshold amounts, and was significantly suppressed with higher doses. Similar studies with histamine replacing gastrin yielded comparable results. The cooperation between neural and gastrin mechanisms does not seem important for the pepsin secretory response mediated by vagal activation. (Supported by USPHS. Grant 1-F2-AM-24,030-01.)

CORONARY DIASTOLIC FLOW TIME AND VASCULAR CONDUCTANCE. Simon Rodbard. City of Hope Medical Center, Duarte, California.

Coronary vascular conductance (C) (flow rate/arterial pressure) was calculated in terms of diastolic (d) flow time/beat. Bazett's formula: $d = 60/F - 0.4\ (60/F)^{0.5}$ in which F is cardiac frequency/minute was used; d/minute diminished as F increased. F was regulated by an electrode on the right atrium. Diastolic conductance/minute C_d was evaluated in 452 tests on 9 anesthetized dogs. C_d varied with F ($r = 0.87$). Thus, each contraction appeared to generate a unit of conductance. C_d correlated poorly with arterial pressure ($r = 0.18$), stroke volume or cardiac work ($r = 0.10$). The correlation of C_d and F can be accounted for on mechanical bases without invoking metabolic, hormonal, or neurogenic factors. Thus, during each contraction, myocardial parenchymal compression expresses intercellular fluids. The reduced tissue pressure during the succeeding diastole permits the capillaries to open more fully, increasing conductance. Experiments on isolated dog hearts and on models support this thesis. Conclusions concerning coronary vascular conductance drawn from interventions which modify frequency or duration of systole therefore appear to deserve re-evaluation. The present study offers further support for the thesis (Angiology, August, 1966) that vascular conductance is normally regulated at the capillary. Aided by HE 08721, NHI, USPHS.

MECHANICAL RESPONSES OF THENAR MUSCLE IN NORMAL INFANTS. Robert D. Roe. (Intr. By Stefan Shanzer) Depts. of Pediatrics and Neurology, Mount Sinai Hospital, New York City.

Mechanical responses of adductor pollicis were examined in infants to establish criteria of normal neuromuscular function and development. The simultaneously evoked action potential and contraction were recorded following supramaximal stimulation of the ulnar nerve. Infants, 10 days to 10 months of age and young adults were examined. Stimulus frequencies of 1/10sec through 50/sec were given. "Staircase" potentiation, post train potentiation, contractile summation and tetanus were observed. These phenomena and the stimulus frequencies at which they occur are the same in infants and adults. Both groups showed a reproducible single twitch at 1/10sec and "staircase" potentiation at low frequencies (1/2sec through 4/sec). The staircase effect was always present at the same frequency; it was not associated with a change in the supramaximal evoked action potential. In infants and adults, potentiation of the single twitch was particularly prominent following conditioning trains of pre-tetanic frequency (1-8/sec). The onset of summation occurred at 5-8/sec with rapid increase in tension to almost complete fusion at 20/sec. Tetanus occurred at 40/sec. The results indicate that these characteristics of contraction are fully developed functions in the normal infant.

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INTERNAL HYDRAULIC CONTROL OF AN IMPLANTABLE HEART. Adair Rogers, Kirkley R. Williams and Livingston B. Morris (intr. by J. E. Rhoads). University of Pennsylvania, H.D.S.R., C.V.R.C., Phila., Pa.

A surgically implanted prosthesis to provide a useful extension of human life when heart failure or damage are beyond surgical repair. Procedure: An artificial replacement for the heart has been designed and engineering prototype tested. Implantable size units are being built for use in animals in 1966.
Results: After more than two years of continuous unattended operation, the engineering prototype has (1) simulated blood circulation in physiological circuits comparable to the human circulation in all essential particulars; (2) automatic internal control of arterial and pulmonary pressures and pulse rate within the limits existing in normal human beings; (3) automatic adjustment of all cardiac pressures to correspond to the barometric changes; (4) cardiac outputs automatically controlled over a range of 30 to 100% of capacity as a function of the venous return pressure variation from -2 to +10 mm Hg: (5) response times of under 200 ms for full range of cardiac output; (6) pulse by pulse control of ventricular discharge volumes as a function of venous return; (7) dissipated internal heat to the blood with a temperature differential under 1°C; (8) over 16,000 hours of automatic operation to substantiate the ultimate 10-year design life expectancy made possible by internal hydraulic control and actuation; (9) the following space requirements. With the unit divided the ventricles occupy the normal pericardial space and the control and power section require about 1500 cc in the abdomen. Foreign bodies simulating the power unit have been implanted in calves for periods up to one year.
Conclusion: Artificial hearts meeting the requirements of implantability, internal automatic control and adequate life expectancy can be used this year in animals to ascertain long term acceptance.

EFFECT OF ATROPINE ON HISTAMINE STIMULATED GASTRIC SECRETION IN MACACA MULATTA. E. F. Rosato*, G. P. Smith* and F. P. Brooks. Dept. of Physiol., School of Med., Univ. of Pennsylvania, Philadelphia, Pa.

To extend our recent observation that atropine inhibits the maximal histamine response in rhesus macaques (Fed. Proc. 25:513, 1966), 5 male macaques (4.5-5.5 kg) were prepared with chronic gastric fistulas and venous catheters, and adapted to chronic restraint in primate chairs. Acid-pepsin responses to constant iv infusions of histamine (0.2-1.6 μg/kg/min) were determined in each monkey. When atropine (0.2-0.6 mg/kg, iv) was given prior to a maximal histamine infusion, acid and pepsin outputs were inhibited (mean acid inhibition=48%, n=5; mean pepsin inhibition=62%, n=3). When atropine was given prior to a supramaximal histamine infusion there was less inhibition of acid and pepsin (mean acid inhibition= 19%, n=5; mean pepsin inhibition=40%, n=5). When atropine was given during a maximal histamine infusion, significant acid inhibition (>10%) occurred in 1/4 tests, pepsin inhibition occurred in 2/3 tests. When atropine was given during a supramaximal histamine infusion, inhibition of acid occurred in only 1/7 tests, but pepsin outputs always decreased. That atropine produced less inhibition when given during a histamine infusion than when given prior to histamine suggests that histamine produced spatial interference at muscarinic receptor sites. The marked inhibition of the MHR by prior treatment with atropine is the first evidence in monkeys that acetylcholine is involved in the normal parietal and peptic cell responses to histamine.

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SINGLE BREATH CARBON MONOXIDE DIFFUSING CAPACITY (D_L) AND LUNG PERMEABILITY (K) IN NORMAL MAN BREATHING 99% O_2 AT ONE AND 3 ATMOSPHERES. Edith Rosenberg and Lloyd D. MacLean, Department of Surgery, McGill University, Montreal, Canada.

It has been reported that D_L decreases in normal man after breathing 99% O_2 at one atmosphere (at.) for 3 hours (Proc. Roy. Soc. Med. B. 53:96, 1960). D_L is the product of the lung permeability, K, and alveolar volume, V_A. We repeatedly measured K and V_A in 8 healthy men between the ages of 21 and 36 after 0.5 hours of rest in the sitting position and compared these values to measurements of K and V_A 5 minutes after they breathed 99% O_2 at one or 3 at. for periods up to 3 hours. Breathing 99% O_2 at one at. for 3 hours had no effect on V_A or K. Exposure to 99% O_2 for 2 hours at 3 at. had no effect on 4 of the 6 subjects studied but significantly increased K in the 2 others. One of the latter had normal V_A but the other had a reduction of one liter in his vital capacity. Two of the subjects who showed no change in K or V_A after 2 hours had an increase in K after 0.75 to 1 hour of breathing O_2 at 3 at. Thus, inhalation of O_2 at 3 at. causes an initial increase in CO uptake, (K), followed by a return to resting values. This suggests that the primary response of the human pulmonary system to O_2 at 3 at. is an increase in the pulmonary capillary volume. After prolonged exposure this increase may be obscured by a thickening of the alveolar capillary membrane.

Influence of renal artery infusion of NaCl on Renin Release. H.H. Rostorfer, R.L. Wathen*, E.G. Schneider* and R. Manalis*. Anatomy and Physiology Department, Indiana University, Bloomington, Indiana.

The effect of renal artery infusion of NaCl (RA-NaCl) at 1.3m Eq/min on renin release, known to occur within 1-2 minutes in anesthetized dogs upon (a) renal artery infusion of catecholamine, (b) a fall in arterial blood pressure when i.v. catecholamine is stopped, or (c) a decrease in kidney perfusion pressure, has been studied in the left kidney of male dogs anesthetized with pentobarbital. Plasma renin was estimated by plasma incubation and rat bioassay of incubation-formed angiotensin. When 1.3m Eq NaCl/min was infused into the renal artery during renal artery infusion of catecholamine or during i.v. infusion of noradrenaline, renin release responses were greatly diminished. The depression of release (V-A plasma renin) occurred within two minutes of the onset of NaCl infusion. This was accompanied by a rise in renal vein plasma sodium and urinary excretion of sodium. In three experiments in which RA-NaCl (1.3m Eq/min) was given during the period of rapid fall in blood pressure following i.v. catecholamine infusion, renin production [GU/min/g kidney=V-A plasma renin (GU/ml) differences between simultaneous samples drawn continuously over 15 minute periods times RPF (ml/min/g kidney)] was only 1/20 that found for three similar experiments in which NaCl was not infused into the renal artery. Renal artery infusion of NaCl after the onset of large renin releases induced by decreasing the perfusion pressure (without added catecholamine) did not noticeably depress renin release even when Na excretion was elevated to 3 times the control. These results indicate sodium may play a role in the control of catecholamine-induced renin release but give no real indication of the mechanism involved. Supported by USPHS HE05625

EXPERIMENTAL SPINAL CORD INJURY IN THE MONKEY. F. Hermann Rudenberg, John E. Coe, and Travis H. Calvin, Jr. (intr. by E. A. Blair). Department of Physiology and Division of Neurosurgery, The University of Texas Medical Branch, Galveston, Texas.

In order to investigate the physiological changes produced by spinal cord injuries an apparatus was designed which will rapidly flex the cervical spine of the monkey. Controlled flexion-compression deformity may be applied with the head fixed in order to reduce any associated head acceleration-deceleration injury. In addition to testing the neurological status before and after the injury, continuous recordings were made of blood pressure, heart rate, respiration, EKG, and EEG. High speed movies were made during the flexion in addition to x-rays and movies both before and after the injury. Various grades of disability were produced but all animals showed marked autonomic changes similar to those associated with experimental head injury (Rudenberg, Fed. Proc. 20:329, 1961). These included transient bradycardia and apnea; longer lasting EEG slowing also was seen. X-rays showed many monkeys to have cervical column fractures but these were not always associated with motor or sensory deficits. Alterations in conscious state appear to be related to significant spinal cord injury as indicated by motor and sensory deficits. In several animals unconsciousness appeared within the first two minutes following the flexion, definitely not at the time of flexion, but no gross pathology was observed at autopsy.

Supported by the Mary Katherine Peterson Foundation and by grant NB-05675-01 of the USPHS.

COMPARATIVE METABOLIC ACTIVITY OF HEPATIC PARENCHYMAL AND KUPFFER CELLS. Thomas M. Saba* and N. R. Di Luzio, Dept. of Physiology & Biophysics, Univ. of Tenn. Med. Units, Memphis, Tennessee.

In an attempt to define the relative role of Kupffer and parenchymal cells in the metabolism of lipids, a new technique has been developed for the isolation of specific cell homogenates. Phagocytizable iron particles were administered intravenously to rats; Kupffer cells were isolated from parenchymal cells by magnetic means and homogenates prepared. Magnetic techniques were also employed to prepare iron free Kupffer cell homogenates. Acetate-1-C^{14} or albumin-bound palmitate-1-C^{14} was added to the homogenate and $C^{14}O_2$ production determined. All incubations were carried out in Krebs-Ringer phosphate, using a specially designed metabolic flask which permitted the direct trapping of $C^{14}O_2$ into liquid scintillation counting vials. Kupffer cell homogenates manifested a 5 fold enhancement in $C^{14}O_2$ production in the presence of palmitic acid as compared to the parenchymal cell preparation. These findings suggest Kupffer cell involvement in lipid metabolism. In marked contrast, the oxidation of acetate to $C^{14}O_2$ was approximately 3 times as great by the parenchymal cell preparations. These studies not only indicate a differential metabolic behavior by the phagocytic and non-phagocytic hepatic cells, but also that metabolic data obtained from experiments utilizing whole liver homogenates can not be ascribed to a specific cell population. (Supported by USPHS Grant HE-05367.)

PHOSPHATASE REACTIONS OF TRANSPORT ATPASES. G. Sachs*, J. D. Rose*, R. L. Shoemaker*, and B. I. Hirschowitz. Department of Medicine, University of Alabama Medical Center, Birmingham, Alabama.

Frog and rat brain microsomal ATPase consists of at least 2 partial reactions [A] an Na^+ dependent protein phosphokinase and [B] a K^+ dependent phosphoprotein phosphatase. Reaction B may be reflected in a K^+ stimulated p-nitrophenyl phosphatase (PNPase) or a K^+ stimulated acetyl phosphatase (AcPase) reaction with pH optimum 7.8, Mg^{++} dependence and Km 5mM. Ouabain 10^{-3}M, nucleotides such as ADP, ATP, AMP and mercurials inhibited the AcPase or PNPase. Pyrimidine nucleotides, iodoacetate (IAA), N-ethyl maleimide (NEM) were without effect. Concentrations of K^+ for 1/2 maximal activation was 1.2mM compared to 1.4 for ATPase. Concentration of Ca^{++} for 1/2 maximal inhibition of ATPase, AcPase and PNPase was approximately 2 mM. AcP^{32} showed Mg^{++} stimulated protein P^{32} labelling. A K^+ dependent AcPase or PNPase were also detected in frog gastric microsomes, which show an SCN^- inhibited Na^+, K^+ and ouabain insensitive ATPase. Mercurials and purine nucleotides inhibited and pyrimidines, IAA, NEM, ouabain were also without effect. However, SCN^- did not inhibit PNPase. Concentration of K^+ for 1/2 maximal activation was 3mM and Ca^{++} inhibited PNPase in presence of Mg^{++} (1/2 maximal inhibition at 0.7 mM), but was without effect on ATPase or AcPase. There was Mg^{++} stimulated transfer of P^{32} from AcP^{32} to protein. It is concluded that AcPase is a partial reaction of ATPase, but Ca^{++} effects on PNPase raise the possibility that PNPase is not part of ATPase system in gastric mucosa. (NIH, NSF support).

A NEW REACTIVE PHOSPHORUS COMPOUND FROM CAT MUSCLE. Jacob Sacks and William D. Duckett*, Dept. of Chemistry, Univ. of Arkansas, Fayetteville. A hitherto unknown P compound has been found in cat striated muscle in the course of experiments with tracer phosphate. It is eluted together with glucose-6-phosphate from Dowex-1 ion exchange resin, and is hydrolyzed by heating for 30 minutes at 100° in 1 N sulfuric acid. The concentration in resting muscle is of the order of 1 micromole per gram, and more is formed in tetanic contraction. In muscles frozen *in situ* 2 hours after the injection of the tracer, the specific activity of this compound is significantly higher than that of phosphocreatine or the terminal P of ATP. This suggests a possible role of the compound in P transport across the cell membrane. Evidence has also been obtained for a functional compartmentalization of the compound in the muscle. The finding of this compound with its high specific activity in the same eluate as glucose-6-phosphate brings the tracer data on the phosphorylating glycolysis in contracting muscle into complete harmony with the known enzymatic mechanism. Experiments are under way to look for this compound in other vertebrate species. Supported in part by grant No. AM 07273 from the National Institute of Arthritis and Metabolic Diseases.

IMPACT OF EXERCISE OR PHYSICAL STRESS ON THE CARDIO-VASCULAR SYSTEM OF ANIMALS. Stellos C. Samaras, Kwan S. Chang* and David R. Meranze* Department of Pathology, Albert Einstein Med. Center, Southern Division, Philadelphia, Pennsylvania.

More research is needed to improve performance, prevent damage, and speed rehabilitation, from the effects of stress. Forty-eight Wistar rats and 25 Swiss mice, young males, were properly subdivided. Blood cholesterol and glucose were low in the exhausted animals compared to controls. Animals swimming 30 min. repeatedly, at room temperature, initially gained and later lost weight, and one heart showed advanced degenerative and necrotizing changes. Animals subjected repeatedly to 2 hours swimming, showed early necrotizing changes and focal myocarditis. Animals stressed 4 hours repeatedly, showed cardiac fiber disorganization and necrobiosis. After 6 hours stress, microhemorrhages and myocardial foci of degeneration were seen. Animals stressed once 20 hours, showed almost complete exhaustion, extensive G.I. hemorrhages and tarry feces, myocardial and epicardial hemorrhages and focal necrotizing myocarditis. Glycogen staining showed no discernible trend. Swiss mice swimming in ice-cold water survived only 6-10 min. and showed acute myocarditis. Animals subjected to complete exhaustion disclosed varying degrees of interstitial pneumonia. Further studies are underway.

In conclusion, the pathology of one form of excessive exercise is demonstrated in this study. The physiologic and metabolic alterations induced require elucidation and correlation with the anatomic changes shown.

Work supported by the Albert Einstein Medical Center Research Fund

EFFECTS OF READMISSION OF O_2 AFTER ANOXIA IN FROG GASTRIC MUCOSA BATHED IN CL^--FREE MEDIA. S. S. Sanders,* G. Sachs* and W. S. Rehm, Dept. of Physiology and Biophysics, Alabama Medical Center, Birmingham.

Mucosae were bathed in sulfate media and gassed with either O_2 (95% O_2-5% CO_2) or N_2 (95% N_2-5% CO_2). Changing O_2 to N_2 reduces H^+ rate to zero and changes PD from about -15 mv (nutrient negative) to about +5 mv. Changing N_2 to O_2 on secretory side (N_2 still on nutrient side) or simultaneously on both sides results in a positive spike of the PD (3 to 15 mv) followed by a return of the PD to a negative orientation and the reestablishment of H^+ secretion. Changing N_2 to O_2 on the nutrient side (N_2 still on secretory side) results in reestablishment of H^+ secretion and a return of the PD to a negative orientation without a positive spike. The hypothesis that the positive spike is associated with a Na^+ and/or K^+ transport system in the surface epithelial cells was tested by studying the effects of changing N_2 to O_2 in K^+-free sulfate media and in Na^+-free (choline for Na^+) sulfate media. It was found that the positive spike was still present in K^+-free and in Na^+-free sulfate media. In K^+-free sulfate media (in the presence of O_2) the H^+ rate goes to zero and the PD to a positive value, and with K^+-free sulfate nutrient solution on both sides (H^+ gradient abolished), N_2 to O_2 still gives a positive spike. Concurrent measurement of the redox state of a given member of the electron transport system (ETS) with the Aminco-Chance technique revealed that following N_2 to O_2 the PD started to change in about 4 sec and was at 30% of its peak value by the time (10 sec) a change was seen in the redox state of the cytochromes a_3 or c. Thus the positive spike seen in sulfate media is not dependent on external K^+ or Na^+ or upon a H^+ gradient across the mucosa and precedes any observable changes in the ETS. (NIH and NSF support.)

EFFECTS OF X-RAYS AND LIGHT ON MOLLUSCAN NERVE CELLS IN VITRO. M. Sato* G. Austin, H. Yai* Univ. of Oregon Med. Sch., Portland, Oregon.

Abdominal ganglion cells of Aplysia were isolated from surrounding connective tissue and perfused with artificial blood. Two microelectrodes were inserted in a single cell to record changes in membrane conductance and potential. D-type response of postsynaptic membrane to acetylcholine (ACh) was not affected by X-irradiation of 9300r. Excitatory postsynaptic potentials (EPSP's) activated orthodromically were slightly increased following exposure to 4500r. Threshold firing level of the soma was not altered by exposure to 13,000r. However, a slight hyperpolarization of 1-3 mV was often observed during exposure to 1700-5000r. Light increased the frequency of spontaneous spike discharge of some cells and decreased that of others. Light did not significantly alter ACh-response of D- or H- membrane. Light markedly raised threshold firing level. Spontaneous EPSP's and IPSP's were immediately depressed on illumination, suggesting a depression of presynaptic activities. White or blue light, but not red, produced these changes. It is suggested that the site of action of X-irradiation is the Na-pump whereas that of blue light is the molecular arrangement within the membrane. (Supported by a grant from U.S. A.E.C.)

GASTRIC EMPTYING OF SOLID AND COMPLIANT SPHERES IN DOGS. Jerry F. Schlegel, William M. Coburn, Jr.,* and Charles F. Code. Mayo Clinic and Mayo Foundation, Rochester, Minn.

Will the stomach while emptying discriminate between particles of different size and compliance? To answer this, six intact healthy dogs were fed 1-cm or 1.5-cm radiopaque spheres which were either hard or compliant. All types were of the same specific gravity. The number fed was adjusted so that the volume given was constant. Each of the four types of spheres was swallowed by each dog on at least six occasions. The number of spheres in the stomach was counted during roentgenographic observations at intervals of 2 hours or less until the stomach was empty. As anticipated from the work of others, the emptying of the stomach was exponential; therefore, when the percentage of each type of sphere remaining in the stomach was plotted logarithmically against time, straight lines emerged, enabling calculation of the rate of emptying as per cent per hour. The smaller objects left the stomach quicker. The solid and compliant 1-cm spheres emptied at the same rate, 12% per hour. The stomach moved 6% of the solid 1.5-cm spheres into the duodenum per hour and 9% of the compliant; and this difference was significant. The difference between the rates for the compliant 1.5-cm and 1-cm spheres was not significant. When the square root of the number of spheres remaining in the stomach was plotted against time, the closest fitting of the data to a straight-line function was obtained. The stomach therefore did discriminate between hard objects 1 and 1.5 cm in diameter and between solid and compliant spheres when their diameters were 1.5 cm. (Supported in part by NIH Grant AM-2015.)

COMPARISON OF 131I-LABELLED DIATRIZOATE, METHYLGLUCAMINE AS AN INULIN SUBSTITUTE FOR CLEARANCE AND EXTRACTION DETERMINATIONS IN THE DOG. H. E. Schmid, C. A. Muehlbaecher,* F. C. Watts,* and I. Meschan.* Bowman Gray Sch. of Medicine, Winston-Salem, N. C.

Clearances of 131I-diatrizoate, methylglucamine (Renografin, Squibb) using the single injection technic have been found to compare closely with those for inulin with a 131I-Renografin/inulin clearance ratio of 1.00 in dogs and 0.90 in humans. Clearances of 131I-Renografin and inulin were determined simultaneously in 22 experiments in 12 trained dogs with a constant sustaining infusion during which urine flow rates were varied by giving water per os. 131I-Renografin/inulin clearance ratios averaged 0.85 and varied from 1.00 at urine flow rates less than 1.00 cc/min. to 0.73 at rates greater than 8 cc/min. The decreased clearance ratio at higher urine flows was due primarily to an increase in the clearance of inulin. Clearance ratios of 131I-Renografin and inulin determined during meralluride sodium-induced diuresis demonstrated no significant changes at urine flow rates ranging from 1 to 6 cc/min. (av. 0.86). The extractions of 131I-Renografin and inulin averaged 23.0±1.0 and 26.8±1.0 per cent respectively in 9 acute dog experiments with exposure of the left kidney and renal vessels via a flank incision. Centrifugation ultrafiltration studies of dog blood containing 131I-Renografin and inulin revealed that 13.6% of the total 131I-Renografin was associated with plasma protein and RBC's. Adjustment of the clearance and extraction values of 131I-Renografin by this amount resulted in 131I-Renografin-inulin ratios of essentially 1.00. Stop flow studies in 3 dogs revealed no significant differences in the 131I-Renografin/inulin ratios along the nephron. Supported by grants from NIH HE- 5418 and HE-5948.

EFFECTS OF BARIUM ON FROG GASTRIC MUCOSA. M. Schwartz,* T. N. MacKrell,* A. Jacobson,* and W. S. Rehm, Depts. of Engineering Physics, Anesthesiology, and Radiology, Univ. of Louisville and Dept. of Physiology and Biophysics, University of Alabama Medical Center, Birmingham.

Frog gastric mucosae were mounted between chambers and bathed by regular secretory and Cl^--Ringer solutions. The PD, resistance (ΔPD/applied current) and H^+ secretory rate (pH stat method) were measured. Barium from 0.1 to 1.1 mM in the nutrient solution resulted in an increase in resistance of 108% (SD±41%, $P<0.01$), a decrease in PD and H^+ rate of only 10% (SD±14%, $P>0.05$) and 18% (SD±9%, $P<0.01$) respectively. The new steady state levels were maintained for the duration of the experiments (1 hr.). Addition of Ba^{++} to the secretory solution (2.0 mM) produced no significant changes. Other agents (anoxia and DNP) that produce a marked increase of the resistance result in a drastic reduction in H^+ rate (AJP 208:922, 1965). During the increased resistance with anoxia, DNP produces no further increase and vice versa. The possibility was considered that Ba^{++} acts on the nutrient membrane and anoxia and DNP on the secretory membrane where the active H^+ and Cl^- mechanisms are assumed to be located. If this be so then the effects of anoxia and Ba^{++} on the resistance should be additive. This prediction was verified in experiments in which Ba^{++} was added during anoxia and also in experiments in which anoxia followed the addition of Ba^{++}. If the resistance increase following Ba^{++} is localized in the nutrient membrane then the total conductance of this membrane is insufficient to account for the steady state movement of Cl^- and HCO_3^- across this membrane (assuming reasonable concentration gradients for these ions). The above together with unpublished studies on the PD as a function of $[HCO_3^-]$ and $[Cl^-]$ suggest a carrier exchange mechanism for HCO_3^- and Cl^- transport across the nutrient membrane. (NIH and NSF support.)

PROPERTIES OF NECTURUS GASTRIC MUCOSA. R. L. Shoemaker*, G. Sachs*, and B. I. Hirschowitz. Department of Medicine, University of Alabama Medical Center, Birmingham, Alabama.

Necturus gastric mucosa, stripped of external muscle layers mounted in a flux chamber, with standard frog Ringer bathing solutions had no spontaneous H^+ rate in 16 of 19 experiments with P.D. 10.7 ± 0.87mv (±SEM, lumen negative) resistance 531 ± 21Ω cm^2, I_{sc} 25.1 ± 1.8 μa cm^{-2}. Minimal concentration of gastrin for stimulation was 10^{-8}M, and for histamine 10^{-4}M, with onset of secretion from 2-8 minutes following stimulus. This stimulation in the 16 resting mucosae resulted in an H^+ rate of 0.97 ± 0.17 μEq hr^{-1} cm^{-2}, P.D. 15.3 ± 0.8 mv, resistance 509 ± 21Ω cm^2 and I_{sc} of 33.8 ± 3.5μa cm^{-2}. The stimulation of H^+ secretion, accompanied by increased P.D. and I_{sc} is interpreted as concomitant stimulation of ancillary ion transport, presumably Cl^-. Mecholyl at 10^{-7}M resulted in a 2 min. spike of P.D. (5-15 mv in height) in resting or secreting state. SO_4'' substitution for Cl^- on both sides resulted in 70% inhibition of P.D. and H^+ rate of 0, while with SO_4'' on one side only, the P.D. was determined by the Cl^- gradient. Choline substitution for Na^+ on both sides resulted in initial inversion of the P.D. with declining H^+ rate, and when H^+ rate was 0, P.D. returned to normal orientation. Na^+ re-admission on nutrient side reversed P.D. effects.

Thus this tissue shows significant differences compared to other in vitro preparations, particularly with respect to sensitivity of resting state to gastrin, histamine, mecholyl and to ion substitution. (NIH, NSF support).

POSTNATAL ALTERATIONS IN EVOKED UNIT ACTIVITIES OF CEREBELLAR CORTEX. R.J.Shofer* and D.P.Purpura, Columbia University, New York.

Unit responses recorded with tungsten microelectrodes in cerebellar vermis of kittens have been studied following stimulation of inferior olive (IO), juxta-fastigial sites (JF) and auditory cortex. IO-evoked responses in the first postnatal week consist of 20 msec-latency "all-or-none" brief spike bursts associated with prominent focal negative-positive responses. Initial excitatory events occur in relation to the rising phase of focal negativity whereas unit discharges are blocked at peak of negativity or during early positive phase. JF-stimulation is less effective than IO-stimulation in eliciting unit discharges until after the second week. Prolonged (150-200 msec) inhibition of spontaneous discharges is occasionally observed with single or repetitive JF stimuli. IO-stimulation initiates typical 'inactivation responses' in the youngest preparations studied. Such responses exhibit rhythmically recurring behavior and occur as spontaneous bursts prior to the appearance of high-frequency spontaneous discharges typical of adult animals. Somewhat later unit discharges without prominent slow waves regularly follow low-frequency JF stimulation but fail to follow stimulation rates in excess of 20/sec. Cerebellar evoked responses to auditory cortex stimulation are detectable during the first week. Responses are surface-positive and accompanied by brief duration repetitive discharges in recordings from cortical depths. Marked decrease in threshold for eliciting these responses occurs during the 2 - 3 weeks. Click-evoked responses in vermis are not evident in the first month in contrast to findings in auditory cortex. PST-histograms at various stages after the appearance of well developed cerebellar click responses are compared with findings in adult animals. The data are discussed in relation to developmental features of afferent pathways activating different cerebellar neuronal organizations.

SOME SIMILARITIES IN COMPOSITION OF HIGH AND LOW POTASSIUM SHEEP RED CELL MEMBRANES. B. Shore and V. Shore. Bio-Medical Research Division, Lawrence Radiation Lab., University of California, Livermore, California.

Membranes prepared from high and low K red cells by stepwise lysis against hypotonic salt solutions were identical in percent N (9.1), P (1.3), lipid (43.2), protein (52.6), Cu, Zn, Ca, Mn, in carboxyl- and amino-terminal amino acids and in amino acid composition. Moles amino acid/10^5 g protein were: 43.0 lysine, 18.9 histidine, 39.7 arginine, 68.8 aspartic acid, 43.7 threonine, 53.0 serine, 107.2 glutamic acid, 45.6 proline, 62.7 alanine, 53.3 valine, 17.8 methionine, 37.5 isoleucine, 99.3 leucine, 20.7 tyrosine, 34.0 phenylalanine, 50.3 glycine, 13.2 cysteine. The membranes could be solubilized by sodium dodecyl sulfate. Ultracentrifugation of the resulting complexes showed a not greatly polydisperse schlieren peak that accounted for at least 90% of the material and some very high molecular weight material. Optical rotatory dispersion spectra of the complexes were identical over the 200-600 mμ range. Since neutral lipids, phospholipids and fatty acids of these membranes are identical (G. J. Nelson, unpublished), it appears unlikely that differences in cation content, membrane permeability and active transport in sheep red cells are the result of differences in composition of the membrane lipoprotein complex. Differences in amino acid sequence, tertiary structure or utilization of energy are possible. (Supported by Div. of Biol. and Med., U.S. Atomic Energy Commission.)

SUBCELLULAR LOCALIZATION OF BOVINE ENDOTHELIAL CELL ACTIVATOR OF THE FIBRINOLYTIC SYSTEM. Chakwan Siew* and D. R. Celander, Col. Osteo. Med. & Surg., Des Moines, Iowa.

Examination of the jugular veins of cows reveals that the endothelial cell layer contains an activator capable of bringing about the conversion of profibrinolysin to fibrinolysin. When such cells were removed by spatula or cold microscope slide, suspended in 0.25 M sucrose and homogenized with a Potter-Elvehjem homogenizer, a suspension was obtained which retained activity. Particles which were obtained at 3300 x g in 10 min were virtually without activity. Lysosomes sedimented at 25,000 x g in 10 min contained moderate activity. However, the greatest amount of activity was found associated with a fraction of particles which sedimented at 25,000 x g for one hour. This fraction, which predominated in microsomes, exhibited enhanced activity following a single washing and resedimentation from 0.25 M sucrose solution. Incubation of all systems with profibrinolysin-containing and profibrinolysin-free fibrin gave lysis only in the profibrinolysin-containing system. The fractions were not stable and rapidly lost activity in the refrigerator. Activator could not be adequately demonstrated after three days. It is concluded that an activator similar to that reported previously in the dog (Celander, D. R. & E. Celander, Am. J. Physiol., in press, 1966) is present in the microsomes of the endothelial cells of the jugular vein of the cow. (Supported by NIH Grants AM-6285 and HE-7260.)

SINGLE UNIT ANALYSIS OF THE PRETECTAL REGION IN THE RAT. R. Siminoff*, H. O. Schwassmann* and L. Kruger. Department of Anatomy, University of California, Center for the Health Sciences, Los Angeles, California.

The pretectal region in the rat was explored for unit responses to visual stimuli. The responsive region appears to be principally within the nucleus prectalis anterior (PTA; prebigeminalis lateralis). In general the units could be classified into two broad categories depending on their response characteristics; phasic (i.e. brief on and off) and tonic (i.e. sustained discharge during visual stimulus). More than half of the units encountered in the pretectal region displayed phasic discharge properties. In general, receptive fields were less than 10 degrees in diameter. Some units showed simple receptive field organization while others displayed "on-off" centers with "off" peripheries. Directional sensitivity was observed in a small number of units. About one third of the pretectal units were tonic; a majority of these were "on" type. Receptive fields of these units were usually larger than those of phasic units. A small number of the tonic units were of the "off" type (i.e. sustained cessation of discharge during light stimulus). A few units showed both phasic and tonic properties depending on stimulus parameters such as size and position in receptive field. Electrode track reconstruction and correlation with unit properties suggests that the nucleus PTA might be subdivided into an upper portion containing phasic units and a lower portion containing tonic units. A distinct organized projection of the contra-lateral visual field was mapped onto each of the above portions of the PTA. Tonic units may subserve luminous flux detection for operation of the pupillary reflex. (Supported by NB-4578 USPHS).

EFFECT OF RESPIRATORY ACIDOSIS ON HEMODYNAMICS OF THE DOG HIND LIMB. D.H. Simmons and R.C. Powell* UCLA Medical Center, Los Angeles, Calif.

Under barbiturate anesthesia, multiple measurements were made in 30 dogs of femoral artery flow (electromagnetic flowmeter) and perfusing pressure, and arterial pH and pCO_2 during control periods and during respiratory acidosis induced by addition of 2.5, 5, 10, 20, and 30% CO_2 to inspired gas while holding ventilation constant. Under the same conditions, the partitioning of femoral flow between muscle, skin and paw was estimated by measuring gamma emission of HNO_3 digests of each of the tissues dissected free following injection of 50 microcuries of K^{42} into the femoral artery. The absolute flow and conductance of each tissue was then calculated at the various levels of respiratory acidosis. Total femoral flow increased minimally (3.4%) when pH decreased 0.9 and then fell progressively to 44% of control values at a pH of 6.76. Flow to muscle decreased progressively from 3.01 to 0.69 ml/min/kgm body weight and flow to skin and paw increased from 0.81 to 0.99. At normal pH and pCO_2, 79% of femoral flow was to muscle; this percentage decreased progressively with increasing acidosis to 41%. Femoral artery conductance increased 11% when pH dropped 0.9 units, then decreased progressively to 67% of controls at pH 6.76. The initial increase was accounted for by moderate increases in conductance of both muscle (2.1 to 2.2 cm^5/dyne-sec. $x10^{-7}$) and skin (0.4 to 0.6). During more severe acidosis, muscle conductance fell progressively approximately two-thirds to 0.7, while conductance of skin and paw increased from 0.6 to 1.1. It was concluded that the effects of respiratory acidosis on the hind limb of the anesthetized dog is primarily constrictor to muscle and dilator to skin and paw.

Plasma Free Fatty Acid and Glucose Concentrations in Houssay Dogs Following a Single Injection of Growth Hormone.

Otakar V. Sirek and Anna Sirek*. Dept. of Physiology. University of Toronto, Toronto, Ontario, Canada.

A marked reduction in the concentration of plasma free fatty acids (FFA) was observed within 30 minutes after an intravenous injection of bovine growth hormone (GH) into Houssay dogs. The animals were maintained without substitution therapy for at least five weeks prior to experimentation and by then had lost some 30 per cent of their initial body weight. The average plasma FFA concentration was 546 μEq/l. and remained at that even after adrenalin or glucose injections. GH did not change the blood sugar level but did reduce the plasma FFA concentration by some 40 per cent. The same reduction was observed after GH in depancreatized dogs, but in normal animals it was only 20 per cent. A direct stimulation of oxidation of plasma FFA by GH was likely the major cause of the lowering of FFA observed 30 minutes after a single injection of GH.

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THE EFFECT OF DENERVATION ON MERKEL CELLS IN HAARSCHEIBEN OF RATS. Kenneth R. Smith, Jr. (Intr. by Theodore Cooper) St. Louis University School of Medicine, St. Louis, Mo.

The Haarscheibe is a specialized disc of epidermis located near tylotrich hair follicles in mammals. It is a sensitive, slowly adapting mechanoreceptor containing numerous large neural endings closely applied to granulated epidermal cells, which lie in a row along the basement membrane of the epidermis. These distinctive cells, described by Merkel in 1875, also occur in other epidermal regions. With electron microscopy, Merkel cells are seen to contain secretory granules which consist of osmiophilic cores surrounded by limiting membranes. The chemical content of these granules is unknown. It has been stated that Merkel cells become degranulated and that the entire cells disappear within a few days after denervation of Haarscheiben in cats (Brown & Iggo, J. Phys. 165:28, 1963) and after denervation of the nasal skin of opossums (Palmer Anat. Rec. 151:396, 1965). Dorsal lumbar cutaneous nerves (which transmit action potentials when Haarscheiben are mechanically stimulated) were transected and Haarscheiben were observed electron microscopically after intervals of 3 to 20 days. Typical Merkel cells were readily identified in Haarscheiben 20 days after denervation. The secretory granules of some cells appeared to undergo degenerative changes, but many granules remained morphologically intact. This would indicate that Merkel cells are not completely dependent upon neurites in order to maintain their structure in the rat. The reasons for this apparent difference are unknown.
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CENTRAL NERVOUS SYSTEM STRUCTURES INHIBITORY TO THE CAROTID SINUS REFLEX. Orville A. Smith, Jr. and Marc A. Nathan.* Regional Primate Research Center and Department of Physiology and Biophysics, Univ. of Wash., Seattle, Washington.

The central control of baroceptors has recently been studied by Reis and Cúenod. They demonstrated augmentation of the depressor component of the sinus reflex following decerebration and cerebellectomy but did not reveal direct inhibitory control of the depressor component. Previous work by Moruzzi and by Hilton have implicated the cerebellum and hypothalamus respectively in this inhibitory function. Recent anatomical studies of central autonomic pathways have shown an input to the inferior olive from cardiovascular reactive areas of the rostral brain stem. The depressor sinus reflex was elicited by stretch of the carotid arteries in chloralose anesthetized cats. Stimulation of the medial portion of the inferior olive exerted a strong inhibitory effect on this reflex while stimulation of the olive alone produced no cardiovascular effects. This finding provides a link for the elucidation of potential hypothalamic, cerebellar and basal ganglia effects on autonomic regulation. (Supported by a grant from the Life Insurance Medical Research Fund and USPHS FR00166.)

SKIN BLOOD FLOW RESPONSE TO CEREBRAL TEMPERATURE CHANGES. Robert E. Smith (intr. by L. D. Carlson). University of Kentucky, Lexington, Kentucky.

The characteristics of skin blood flow and peripheral resistance have been examined in the ear of the lop-eared rabbit subjected to alterations in cerebral blood temperature. Chloralose/urethane anesthetized rabbits' carotid arteries were cannulated and connected to an extracorporeal circulatory system designed to permit the imposition of rapid temperature changes on the circulating blood. The rabbits' ear volume was measured, together with arterial and venous pressures at the base of the ear and the temperatures of the carotid blood, hypothalamus, ear and core. With the temperature of the ear itself held constant, ear blood flow has been found to vary as a direct function of cerebral temperature, and the time course of peripheral resistance changes so generated have been examined. (This research supported by U.S. Air Force under contract AF 41 (609)-2684 with the Arctic Aeromedical Laboratory.)

EFFECT OF HEMICHOLINIUM NO. 3 (Hc-3) ON POTENTIAL AND SHORT-CIRCUIT CURRENT ACROSS FROG SKIN. H. Sonnenberg* and D.T. Frazier. Dept. of Physiol., Univ. of New Mexico Sch. of Med., Albuquerque, N.M.

Current concepts of the inhibition of cholinergic mechanisms by Hc-3 postulate interference with choline transport. To test the hypothesis that cations other than choline may be similarly affected, sodium transport across frog skin was studied in the presence of varying concentrations of Hc-3. Excised frog skins were mounted in a chamber and bathed on both sides with aerated amphibian Ringer's solution. After potential and short-circuit current had stabilized Hc-3 in concentrations ranging from 10^{-5} to 10^{-3}M was added to either the inside or outside compartment. A concentration-dependent increase of both skin potential and short-circuit current was seen when Hc-3 was added to the inside. Conversely, addition to the outside compartment resulted in a decrease of current and potential. Choline, atropine or curare added to both compartments had no effect on the Hc-3 response. Substitution of sulfate for chloride in the bathing fluid did not alter the response. These results cannot be explained on the basis of interference of Hc-3 with cholinergic mechanisms. The finding that Hc-3 affects the two sides of the frog skin differently also excludes from consideration a simple permeability change to sodium. It is concluded, therefore, that in addition to its effect on choline transport in other systems, Hc-3 interacts with the active sodium transport mechanism in frog skin.

(Supported by grant from NIH, HE-08477.)

ROLE OF OXYGEN IN THE ELABORATION OF RENAL PRESSOR SUBSTANCE; RENAL LYMPH AND RENAL VENOUS PLASMA AS ROUTES OF RELEASE OF THE PRESSOR SUBSTANCE. J. Spath*, R. M. Daugherty*, J. B. Scott, S. Swindall*, B. Swindall*, and F. J. Haddy. Dept. of Physiol. University of Oklahoma Medical Center, Oklahoma City, Oklahoma

Samples of renal venous plasma were obtained for pressor assay from 10 dogs in which the left kidney was pump-perfused through an extracorporeal lung circuit. The lung was ventilated with various gas mixtures. In this way it was possible to locally alter blood flow and/or oxygen tension of the blood entering the experimental kidney while maintaining pH constant. Plasma samples were assayed for pressor activity using vagotomized, pentolinium-treated rats after the method of Skinner, McCubbin, and Page (Circ.Res.15:64, 1964). Assay of plasma samples obtained during periods of altered renal blood flow and/or altered renal oxygen tension indicates: 1) with flow held constant at control levels, the near absence of oxygen in the blood perfusing the kidney does not increase pressor output, 2) reduction in renal blood flow(and,therefore, also renal blood pressure) is followed by increased pressor activity appearing in renal venous blood even during an extreme reduction in the oxygen tension of the perfusing blood. We conclude that, under the conditions of our experiments, oxygen, per se, is not an important determinant of renal venous pressor activity. Additional experiments in 13 naturally-perfused kidneys were performed to determine whether the pressor material also appears in renal lymph. A renal hilar lymphatic vessel was cannulated and renal lymph and renal venous plasma were collected before, during, and following a period of partial renal artery constriction. Assay of lymph and plasma, in the presence of either EDTA or calcium-complexed EDTA, revealed that, per unit volume, the pressor activity was always greater in lymph than in the corresponding plasma.

STUDIES ON URIC ACID BIOSYNTHESIS AND NITROGEN EXCRETION IN THE LAND SNAIL, OTALA LACTEA. K. V. Speeg, Jr.* and J. W. Campbell, Rice University, Houston, Texas.

Uric acid biosynthesis in Otala involves intermediates common to the avian pathway, the pathway that is present in all species capable of de novo synthesis of the purine ring (T. W. Lee & J. W. Campbell, Comp. Biochem. Physiol. 15, 457 [1965]). In the present work, we have attempted to assess the contribution of purine synthesis to the overall excretion of nitrogen by estimating the in vivo rate of formation and accumulation of these compounds. The levels of kidney purines (uric acid, xanthine, and guanine) were determined in active snails and in snails which had been in aestivation for prolonged periods of time. The in vivo rate of uric acid synthesis in active snails was estimated by the rate of incorporation of 1-C^{14}-glycine. The effect of two inhibitors of uric acid synthesis on this incorporation was also determined: azaserine, an inhibitor of glutamine-requiring reactions, and azathioprine, an apparent inhibitor of the shunt pathway and a suppressor of plasma and urinary uric acid levels in primary gout were the inhibitors used.

An alternate method of nitrogen excretion may be present in Otala which involves the extrarenal excretion of gaseous NH_3. During aestivation, NH_3 gas is given off by the snails but whether this is due to an active physiological process remains to be established.

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RESPIRATORY AND CARDIAC ACTIVITY OF THE KILLER WHALE (ORCINUS ORCA). M. P. Spencer, D. L. Johnson* and T. A. Gornall, III*. Virginia Mason Research Center, Seattle, Wash., and T. C. Poulter*, Stanford Research Institute, Menlo Park, California.

Observations of free ranging orca in Puget Sound and the American San Juan Islands indicate these animals maintain respiratory balance in 5-7 minute submersions spaced with 2-4 breaths between soundings. The longest observed sounding was 12 minutes. Respiratory flow curves on a 2500 lb., 14 ft. female orca (Shamu) were recorded by a large special design calibrated "basket" pneumotachygraph. Tidal volume averaged 46.2 liters over 4 breaths; duration of expiration averaged 0.59 sec. and inspiration 0.75 sec. Peak expiratory flow averaged 129 liters/sec. while inspiratory flow averaged 90.2 liters/sec. The time course of the respiratory flow curve indicates expiration is active and inspiration is initiated by a passive recoil phase with a superimposed active phase. The ECG obtained on Shamu and on a 25 ft. male orca (Namu) by means of a large suction cup electrode and insulated wires to a clinical ECG machine disclosed a simple R and inverted T wave complex with no visible P wave. Heart rate was normally 60 beats/min. just before and extending 15 sec. after the blow to 30/min. when submerged. (Supported by NIH research grant HE 10258.)

POTENTIATION OF RECURRENT INHIBITORY ACTION ON CAT SPINAL MOTONEURONS. W. A. Spencer. New York Univ. Med. School, New York, N. Y.

The inhibitory pathway from motoneuron axon collaterals to adjacent motoneurons, mediated by Renshaw cells, was studied with respect to two questions: (1) Do inhibitory interneurons show post-tetanic potentiation (PTP)? (2) Does PTP occur at natural motoneuron discharge frequencies? Ventral roots (V.R.) were stimulated at various frequencies in pentobarbital anesthestized, acute spinal cats. The responses of Renshaw cells and motoneurons were studied with extra and intracellular microelectrode and ventral root electrotonic recordings (Werman, 1964). In confirmation of Eccles et. al. (1961) and Haase (1963), Renshaw cell discharges exhibited depression when V.R. volleys were delivered at frequencies above 7/sec. At lower frequencies, Renshaw cell discharges were essentially constant, but the motoneuron IPSP's generated by Renshaw cells showed potentiation of their earliest phase at stimulus frequencies of 10/sec to 0.2/sec. This potentiation could not be accounted for by steady changes in motoneuron membrane potential. These results suggest that the inhibitory action of Renshaw cells can be potentiated.

With respect to the second question, PTP of both Renshaw cell discharges (Eccles et. al., 1954) and motoneuron recurrent IPSP's (the later phase) was noted following tetani at 30-50/sec for short (10 sec) periods. Since cat motoneurons are known to discharge at these frequencies during strong muscular contractions, it may be concluded that potentiation of recurrent excitation of Renshaw cells by motoneurons probably occurs physiologically. Since the recurrent inhibitory pathway could assist in localizing the operation of the gamma loop (Brooks and Wilson, 1958), potentiation of its action may be important in the phenomenon of "warm-up" in skilled motor performance. (Supported by USPHS Grant NB 05980.)

THE EFFECT OF NOREPINEPHRINE ON HEPATIC FATTY ACID METABOLISM. John J. Spitzer, H. Nakamura* and M. Gold*. Hahnemann Medical College, Philadelphia, Pa.

Hepatic metabolism of fatty acids was studied under in vivo conditions in anesthetized dogs. A constant infusion of C-14-labeled palmitic and H-3-labeled oleic acid was administered as free fatty acids bound to albumin. Hepatic arterio-venous differences of the labeled substrates, triglycerides, CO_2, glucose, glycerol and β-OH-butyrate were calculated from simultaneously drawn blood samples from the femoral artery and portal and hepatic veins. During the control period, both of the labeled fatty acids were removed by the liver, some of the label was incorporated into triglycerides and released in the hepatic vein. Glycerol was removed, and glucose and β-OH-butyrate were released by the liver. Although a net hepatic uptake of free fatty acids was a consistent finding, it could be calculated that the liver also released some free fatty acids in the hepatic vein. A constant infusion of norepinephrine (0.4μg/kg/min) increased the blood level of free fatty acids and glycerol. The flux of free fatty acids was elevated, as was the flux across the liver. The net hepatic uptake of free fatty acids and glycerol, and the production of β-OH-butyrate were increased. (Supported by a grant from NIH.)

DETERMINATION OF BOVINE PLASMA PROGESTERONE USING GAS-LIQUID CHROMATOGRAPHY WITH ELECTRON CAPTURE DETECTION. G. H. Stabenfeldt*, L. L. Ewing* and L. E. McDonald. Dept. of Physiology and Pharmacology, College of Veterinary Medicine, Stillwater, Okla.

The detection of progesterone in the peripheral blood of cows has been difficult due to the low levels present requiring large quantities of blood for assay. The technic of van der Molen and Groen (J. Clin. Endocr. 25:1625, 1965) has been modified so that 20 ml samples of plasma can be analyzed. The problem of bovine plasma pigments has been avoided by the use of cold dichloromethane for extraction; initial purification was by thin-layer chromatography (TLC). Progesterone was converted to 20β-hydroxypregn-4-en-3-one (20β-ol) by incubating with 20β-hydroxysteroid dehydrogenase. 20β-ol was acetylated with chloroacetic anhydride followed by further purification on TLC. Detection and quantitation was accomplished by a gas-liquid chromatograph (GLC) equipped with an electron capture detector. 4-20 ml aliquots averaged 730$\pm$33 nanograms/progesterone/100 ml plasma in a cow 167 days pregnant; this is in agreement with reported values. Recovery rates averaged 37.9%. A set of 5-20 ml aliquots from the same pool of plasma averaged 623$\pm$38 nanograms/progesterone/100 ml plasma following 5 days refrigeration at 5° C. This suggests progesterone breakdown following collection may occur quite rapidly. Recovery rates for these samples averaged 40.4%. Extraction losses were followed by the use of tritium-labeled progesterone. Blank samples which contained only tritium-labeled progesterone were carried through the entire procedure. At recovery rates comparable to the plasma samples no labeled progesterone was detected by GLC. This technic will allow detailed progesterone studies in individual animals.

EFFECTS OF ANDROGEN ADMINISTRATION AND CASTRATION ON GLAND AND ORGAN WEIGHTS OF MALE PSEUDOHERMAPHRODITE RATS. Allan J. Stanley*, Laurence G. Gumbreck* and Ronald B. Easley* (Introduced by M. Jack Keyl), University of Okla. Medical Center, Oklahoma City, Oklahoma.

Androgen administration to 120 day-old male pseudohermaphrodite rats in 6 mg. doses of testosterone propionate on alternate days for 30 days gave the following results: pituitary weights were reduced by 29%; thyroid weights by 36%; adrenal weights by 20% and testis weights were 17% less than those of control male pseudohermaphrodite animals. The kidneys, however, failed to exhibit any growth response. No stimulus to penile development occurred and thymus weights were unaffected. Body weights were not changed from those of controls. Castration was without effect on any of the above mentioned glands or organs except the thymus which was found to be from 50% to 100% larger than that of non-castrate controls of the same age. Assay of the pituitary glands of male pseudohermaphrodite animals for F.S.H. content against the NIH-S-3 ovine standard gave a value of 12.8 $\pm$ .8% of the standard while pituitaries of normal sibling male controls gave a value of 65.0 $\pm$ .8% of standard by use of the assay method of Payne and Hellbaum and the five point statistical analysis of Finney.

SULFHYDRYL GROUP OF THE RELAXING PROTEIN OF SKELETAL MUSCLE. I. Staprans*and S. Watanabe. Cardiovascular Res. Inst., Univ. of Calif. Med. Center, San Francisco, Calif.

A minor component of Szent-Györgi and Kaminer's "metin" was found to be the relaxing protein of Ebashi and Ebashi and its relaxing activity was reported to be unaffected by NEM, thus suggesting that SH groups are not responsible for the relaxing activity: The Physiologist 7, No. 3 (1964). On the other hand, Mueller found that Bailey's "tropomyosin", if prepared in the presence of dithiothreitol (DTT), gained the relaxing activity, thus suggesting an important role of SH groups in the relaxing activity: Nature 209, 1128 (1965). We have observed that although the relaxing activity of the Ebashis' relaxing protein is not improved by having DTT during its preparation, DTT prevents a decrease in the relaxing activity which occasionally occurred during a chromatographic purification of the relaxing protein. Moreover, blocking SH groups of the relaxing protein by CMB results in a decrease in the relaxing activity of the relaxing protein preparation. However, we have found evidence that the observations made in using DTT, including Mueller's, are not due to the SH group protective action of DTT. (Supported by research grants from NSF (G-19442 and GB-4754) and USPHS (HE-06285).

THE "LIQUID VEINS" OF THE LUNG. N.C. Staub. Cardiovasc. Res. Inst. and Dept. of Physiol., Univ. Cal. San Fran. Med. Ctr., San Francisco, Calif.

In the anesthetized, open-thorax cats or in freshly isolated air-inflated lobes of cat lung I have used glass micropippettes (tip diam. 10 μ or under) to directly inject 1 μL or more of fluids into the subpleural alveolar airspaces under continuous microscopic observation. In every experiment there has been a rapid (few seconds) clearance of either 0.9% NaCl, blood serum, 6% dextran in saline or 0.3M urea (tagged with 0.5% trypan blue) from the alveoli principally into and away from the injection site along the 3-dimensional network of alveolar wall junctions. The fluid clearance is independent of blood flow and the dye particles, at least, do not enter blood vessels. Kerosene and 1.5% NaCl (460 mOsm) are also cleared. There does not appear to be any selective particle or osmotic barrier. The phenomenon is consistent with Plateau's (1869) analysis of foam drainage. At the junctions of foam bubble walls there is sharp curvature such that any existing interfacial tension generates a force directed centripetally (Laplace's formula). At equilibrium the hydrostatic pressure in the junctional space must be less than that in the bubbles. Any excess or added fluid flows immediately into these junctions. The 3-dimensional network of foam bubbles are called "liquid veins" or Plateau's border. In the lung the mechanical pull of the alveolar walls may be an important factor as well as interfacial tension. These results support the hypothesis that pulmonary alveoli do not normally contain free fluid and that the drainage of fluid in early edema is within the alveolar walls, not in the airspaces. (Supported in part by USPHS grant HE-06285.)

ON-LINE COMPUTER ANALYSIS OF CARDIOVASCULAR DATA. M.M.Stauffer*, T.A. Pryor*, R.M.Gardner*, W.C.Day* and H.R.Warner. Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S.Hosp., Salt Lake City, Utah. Supported by a grant from NIH #FR 00012.

A computer program has been developed to provide on-line analysis, reporting and storage of cardiovascular data. The program consists of a main control program which uses data acquisition and analysis subprograms. These are called by a code which also indicates the position of the catheter tip and state of the patient. Results of the analysis are reported back on an oscilloscope (CRT) and saved on magnetic disc. The program may be used simultaneously by up to six physiologists. The first subprogram reads directly the output of the red and infrared cells of a Wood oximeter, performs the logarithmic calculations and reports the O_2 saturation of the blood; the second reads pressure and EKG for six seconds, obtains an "averaged" waveform and displays it along with the mean, systolic, diastolic or, in some locations, the end-diastolic or A and V wave peaks. The waveforms may be saved on a disc and compared with others for selective pressure gradients. The third subprogram samples an indicator-dilution curve directly from the output of an IR photocell, does the logarithmic conversion, calibrates and plots each point on a CRT. The exponential extrapolation is superimposed on the original plot and cardiac output, central blood volume and other parameters are displayed. A fourth subprogram calculates and plots beat-by-beat stroke volume, cardiac output, mean pressure, heart rate and peripheral resistance from central aortic pressure and displays the average values upon completion of sampling. All past data may be viewed and edited from the CRT. A printed report may be obtained including dye curves, pressure waves and abnormal findings and the whole record saved on magnetic tape. This program is currently used for patient monitoring, animal experiments and diagnostic catheterization.

REGIONAL VASOCONSTRICTION DURING ACCELERATION. H.F. Stegall and W.K. Brown (Intr. by H.L. Stone), Biodynamics Branch, USAF School of Aerospace Medicine, Brooks AFB, Texas.

Despite the reduction in man's cardiac output induced by the stress of prolonged $+G_z$ (headward) acceleration, mean aortic pressure rises and elevations of 40% in total peripheral resistance may be detected well below blackout levels (Lindberg et al, Aerospace Med 31:817). This study was directed at identifying the organ vascular beds responsible for such compensation. In one group of healthy volunteers exposed for 15 min. each to +2 and $+3G_z$ on the USAF SAM centrifuge, disappearance of intravenously injected indocyanine green was used to estimate changes in splanchnic flow. Hepatic extraction ratio was presumed unchanged by the exposure. Average estimated splanchnic flow was 1200 ml/min at $+1G_z$ (control). At $+2G_z$ flow fell to 70%, and at $+3G_z$ to 60%, of control; splanchnic resistance rose by 40% and 90%, respectively. In a second group, strain gage plethysmography was used to estimate blood flow in a forearm supported at heart level. Average control value was 4.2 ml/min/100 ml forearm. Flow after several minutes at $+2G_z$ was 60%, and at $+3G_z$ 40% of control, and vascular resistance rose by 110% and 180%. From these figures it would appear that most of the rise in total peripheral resistance may be attributed to vasoconstriction in these two major beds. More surprising was the observation that, despite the assumed severity of the $+3G_z$ stress, vasoconstriction was not maximal. The hydrostatic gradient between carotid sinus and brain may explain why vasoconstrictor response is not complete despite the fact that cerebral blood pressure and flow are falling to marginal levels.

ALVEOLAR MECHANICS IN LIQUID FILLED LUNGS AT LOW LUNG VOLUME. Edward J. Stemmler* and Arthur B. DuBois. Dept. Physiol., Div. Grad. Med., Univ. of Penna., Philadelphia, Pa.

Cavagna, Stemmler & DuBois (Fed. Proc. 25:No. 2, Mar-Apr 1966) have shown that transpulmonary pressure becomes negative before the airways or alveoli close when lung volume is decreased toward 'zero', whether oxygen is absorbed from the alveoli or air is withdrawn mechanically from the trachea. Surface forces acting on the lung through the range of negative pressure have not been determined previously. In order to study the effect of surface forces on the lungs in the range between 'zero' and 'minimal air' volume the pressure-volume (PV) diagram was determined in isolated saline filled rabbit lungs and compared with the PV diagram of the gas filled lungs of the same rabbits measured in vivo with the chest open. Transpulmonary pressure was measured as tracheal pressure minus plethysmographic pressure. In gas filled lungs, volume was measured from the pressure change in an air filled plethysmograph. In saline filled lungs, volume was measured by volume displacement from a saline filled plethysmograph. The present results show that transpulmonary pressure in saline filled lungs becomes negative as 'zero volume' is approached and before the airways close. The range of negative transpulmonary pressure developed by slowly withdrawing saline from the trachea is -1 to -2.5 cm H_2O and is similar to that recorded by slowly withdrawing gas from the trachea when the lungs are gas filled. The general conclusions are: (1)during deflation of the lung from 'minimal air' volume, surface forces in the gas containing lung act as if they were zero, (2)the alveoli support a negative pressure in saline filled lungs, (3)the increased viscosity of saline as compared to air does not appreciably affect the pressure at which the airways close, and (4)airway closure appears to be relatively independent of surface forces.

RELATIONSHIP BETWEEN STIMULUS STRENGTH AND ISOMETRIC ACTIVE TENSION (AP) DEVELOPMENT OF ISOLATED CANINE PULMONARY ARTERY (PA). by N. L. Stephens and A. Naimark, University of Manitoba, Winnipeg Canada.

This study of the stimulus-response characteristics of vascular smooth muscle consisted of 7 experiments on the isolated canine PA. Stimulation was effected from a 60 cycle constant voltage, AC source. In developing maximum AP, (P_O), the relation between voltage and response was initially curvilinear and then appeared to reach an asymptote at 11 volts, as read from the stimulator. This facilitated identification of the supramaximal voltage. The maximum rate at which AP developed (dP/dt) showed qualitatively the same relationship to stimulus strength as P_O. The time to reach P_O, however, was independent of stimulus strength, averaging 25 seconds. This was longer than for skeletal and cardiac muscle. We conclude that (1) PA smooth muscle develops maximum active tension very slowly and its supramaximal stimulus must encompass both voltage and time and (2) both its maximum active tension and its maximal rate of active tension development are stimulus strength dependent, while the time it takes to achieve maximum active tension is stimulus strength independent.

EVIDENCE FOR ACTIVE TRANSPORT OF ACETATE ACROSS BOVINE RUMEN EPITHELIUM. C. E. Stevens and B. K. Stettler, N.Y. State Veterinary College, Cornell University, Ithaca, N.Y.

The isolated, short circuited rumen epithelium was used to study acetate transport between initially identical acetate-Ringer's solutions. The bathing solutions were buffered with bicarbonate, imidazole or tricine. When 10 mM acetate-Ringer's was added as bathing solution there was a net transepithelial transport of acetate in the direction of blood to lumen. This was against its concentration gradient, in the absence of a transepithelial electrical gradient, and in an opposite direction to the net movement of water. This transport was of small magnitude but quite consistently seen with the bicarbonate buffered system. It was of much larger magnitude and statistically significant when imidazole or tricine was used. Time-course studies showed that during the first 30 minutes the tissue showed a rapid uptake of acetate from the solution bathing its blood-facing surface. Acetate was also absorbed from the lumen bath during this period unless the tissue was previously incubated in acetate-Ringer's solution. After the first 30 minutes the rates of acetate uptake and transport remained quite constant. These and previous results suggest that limiting membranes between lumen and epithelial tissue contents are relatively permeable to the passive movement of acetate while those between tissue contents and blood are relatively impermeable to passive transport of acetate anion and actively transport acetate from blood to tissue contents. (Supported by NIH grant AM 09280-02).

AN EFFECT OF INSULIN ON PROTEIN SYNTHESIS BY RIBOSOMES FROM HEART MUSCLE INDEPENDENT OF SUBSTRATE TRANSPORT. William S. Stirewalt* and Ira G. Wool. Univ. of Chicago, Chicago, Ill.

The administration of insulin to diabetic rats one hour before they are killed and the ribosomes from heart muscle are isolated leads to an increase in the catalysis of protein synthesis by the particles. To determine if the increase in activity of the ribosomes was the secondary result of an increase in substrate transport, hearts isolated from alloxan-diabetic rats were perfused for 15 min. with bicarbonate buffer and with or without insulin. Ribosomes from the perfused hearts were isolated and assayed for their ability to effect the transfer of radioactivity from C^{14}-phenylalanyl-sRNA to protein in an in vitro system where the extent of protein synthesis was directly proportional to the concentration of ribosomes. In two experiments ribosomes from hearts perfused with insulin, but without added substrate, were more active in carrying out protein synthesis than were ribosomes from diabetic hearts perfused without insulin. (Expt.1-no insulin, 387 cpm; insulin, 479. Expt.2-281 and 366.) We conclude that the effect of insulin to increase the efficiency of the ribosome for protein synthesis is not the result of the transport into the muscle cell of some critical substrate, nor is the effect on the ribosome mediated by a product of some tissue other than muscle.

VENTRICULAR FUNCTION FOLLOWING BETA-ADRENERGIC BLOCKADE. H.L. Stone and V.S. Bishop, Biodynamics Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.

The effect of beta-adrenergic blockade on ventricular function was studied in 6 mongrel dogs ranging in weight from 13 to 20 kg. The animals were instrumented under sterile surgical conditions with an electromagnetic flowmeter probe around the pulmonary artery and catheters in the left atrium, right atrium and left jugular vein. After a two week recovery period, ventricular function curves were determined by rapid infusion of Tyrode's solution into the left jugular vein catheter while recording right and left atrial pressure, mean arterial pressure, heart rate, mean cardiac output and pulsatile pulmonary artery flow. Eighteen control curves were determined in the animals. The beta-adrenergic blocking drug propranolol in a dose of 1 mg/kg given intravenously was used following the determination of control ventricular function curves in all animals. A total of 21 ventricular function curves were determined in the six animals after beta-adrenergic blockade. During the control period, the average plateau value of cardiac output was 316 cc/min/kg; the average heart rate at this plateau value was 156 bpm, and the average stroke volume at the plateau of cardiac output was 2.0 cc/beat/kg. Following beta-adrenergic blockade, the average plateau value of cardiac output was 241 cc/min/kg, the average heart rate at this plateau was 130 bpm, and the average stroke volume at the plateau of cardiac output was 1.9 cc/beat/kg. The reduction in the plateau value of cardiac output and heart rate following beta-adrenergic blockade was statistically significant. Thus, the reduction in ventricular function in these animals appears to be primarily a result of the decrease in heart rate at the plateau of cardiac output. The decreased heart rate response is apparently a consequence of blockade of the sympathetic nervous system to the heart.

PROSTAGLANDINS AND VASCULAR SMOOTH MUSCLE. Cameron G. Strong* and David F. Bohr. Dept. of Physiol., Univ. of Mich., Ann Arbor, Mich.

Intravenous infusions of prostaglandin E (PGE) decrease blood pressure in man (Bergstrom, S., et al, Acta Physiol. Scand. 45, 145, 1959). In the intact dog intravenous infusion of PGE_1 lowers blood pressure and total peripheral resistance, but high concentrations of prostaglandin-containing tissue extracts cause contraction of isolated rabbit aortic strips (Lee, J.B., et al, Circ. Res. 17, 57, 1965). We are examining this paradox, making more detailed observations of the action of prostaglandins on isolated smooth muscle from various levels of the vascular tree. Indeed, the angiotensin-induced tension of isolated helical strips of rabbit aorta is slightly augmented by PGE_1 in concentrations of 10^{-9} and 10^{-8} gm/ml, and greatly augmented with PGE_1 concentrations of 10^{-7} gm/ml and more. However, vascular smooth muscle from smaller arteries shows a biphasic dose-response relationship with the prostaglandin E compounds. Helical strips of dog mesenteric artery (500μ o.d.) partially contracted with epinephrine or vasopressin are relaxed by PGE_1 and PGE_1-217 in concentrations of 10^{-9} to 10^{-5} gm/ml, but at concentrations greater than 10^{-5} gm/ml their contraction is augmented. The finding that low concentrations of the prostaglandin E compounds relax isolated smooth muscle from resistance vessels affords an in vitro model for their depressor action.

REFLEX RESPONSES TO SINUSOIDAL STRETCH OF THE GASTROCNEMIUS, SOLEUS AND TIBIALIS ANTICUS MUSCLES. *Douglas Stuart*, *Eugene Engel** and *Koichi Ishikawa**. University of California, Davis, California.

A servo-regulated electromagnetic ergometer was used to impart single and repetitive sinusoidal waves of 2.5 and 5 mm stretch to the gastrocnemius, soleus and tibialis anticus muscles of decerebrate cats at rates from 0.1 to 20 cps beginning from resting muscle lengths that yielded 25 and 50 gms initial tension. Reflex electromyographic response, length, tension and zero tension were monitored simultaneously throughout the stretching procedures. Length-tension relations were similar for the three muscles. Peak tension preceded peak length (90°) by 5-10° at 0.1 cps stretch and shifted in phase 20-25° toward the peak velocity of lengthening (45°) at faster stretch frequencies. During single stretches, a consistent retardation in tension release appeared during muscle shortening between 0.2 and 1 cps. The change in extent of stretching from 2.5 to 5 mm and initial tension from 25 to 50 gm yielded greater tension development but little change in the phase relations between peak length and peak tension. At 2.5 mm stretch and 25 gm initial tension, a reflex electromyographic response was evident in the gastrocnemius and soleus muscles at 0.1 cps stretch. In contrast, it did not appear in tibialis anticus until 1 cps stretch. In gastrocnemius and soleus, the ratio of the duration of electromyographic response to the duration of lengthening and the ratio of latency of onset of electromyographic response to the duration of lengthening remained relatively constant at all frequencies of stretch. *(Supported in part by USPHS Grants NB 05199 and FR 05457.)*

FUNCTIONAL RECOVERY OF POST-THYMECTOMY WASTED MICE BY THYMUS GRAFTS. O. Stutman*, E. J. Yunis* and C. Martinez, Depts. of Physiol. and Lab. Med., Univ. of Minnesota, Mpls, Minn.

Neonatally thymectomized mice of some inbred strains develop lymphopenia, have impaired homograft reactivity and show a wasting syndrome characterized by failure of body growth and early mortality. In the present experiments attempts were made to reverse wasting in thymectomized mice of the C3H/Bi, A and DBA/2 strains by the subcutaneous or intraperitoneal grafting of one or five syngeneic, hemiallogeneic or allogeneic thymii. It was found that wasting could be reversed in 13/62 (20.9%), 14/61 (22.9%) and 4/40 (10%) of the animals grafted with five subcutaneous thymii from syngeneic, hemiallogeneic or allogeneic donors, respectively. When similar hemiallogeneic or allogeneic thymii were grafted intraperitoneally, recovery from wasting was obtained in 9/19 (47.3%) and in 4/21 (19%), respectively. Although one subcutaneous hemiallogeneic thymus graft was ineffective in reversing wasting, one similar intraperitoneal thymus saved 2/28 (7.5%) of the treated animals. Animals salvaged from wasting showed a return to normal weight gain, 170 day survival, normal lymphocyte counts and a normal rejection of allogeneic skin grafts. Furthermore, spleen cells from mice rescued from wasting were immunologically active in the Simonsen's graft-versus-host spleen assay. It is concluded that reversal of the post-thymectomy wasting syndrome can be accomplished by multiple subcutaneous or by single or multiple intraperitoneal thymus grafts. (Aided by U.S.P.H. Grants #CRT-5023, CA-3511 and by the American Cancer Society, N.Y.).

RELATION OF RENAL ARTERIAL PRESSURE TO THE OBLITERATIVE REACTION OF THE TUBULES. H. G. Swann, Dept. of Physiology, Univ. of Texas Medical Branch, Galveston, Texas.

When the renal artery is occluded, the hitherto open tubules of the kidney rapidly become obliterated with an eosinophilic colloid, the reaction starting 10 sec after occlusion. The relation of blood pressure to this reaction was ascertained in rats. The blood pressure was lowered to a certain level and maintained therefor 5 min, using an adjustable tourniquet set on the proximal abdominal aorta. The exposed kidney was then snap-frozen in situ with isopentane at -150C. Sections were prepared for microscopic examinations with a microtome-cryostat. When mean blood pressure was lowered to 80 mm Hg, obliteration did not occur, but when lowered to 50 mm, all tubules except thin loops of Henle and distal collecting ducts became obliterated. Between these two levels, fractions of the tubular sections were found obliterated. In interpretation, the reaction is thought to be an inward swelling of tubular cells when hypoxic. In this experiment hypoxia was caused by lowering the blood pressure, thus producing a relative ischemia. In addition, cellular swelling is thought related to the tonicity of the urine adjacent to the hypoxic cell: if relatively hypertonic, hypoxic swelling does not take place.
(Supported in part by USPHS Grant HE 08814.)

EFFECTS OF EXOGENOUS IRON ON THE ERYTHROCYTE SEDIMENTATION RATE OF YOUNG PIGS. Melvin J. Swenson and Rachel B. Shireman.* Department of Physiology and Pharmacology, College of Veterinary Medicine, Iowa State University, Ames, Iowa.

A rapid ESR (erythrocyte sedimentation rate) develops in pigs during the first few days of life. These pigs are usually kept on a concrete floor and deprived of iron. They develop an iron-deficiency anemia. Exogenous iron corrects the rapid ESR quickly but a portion of the anemia persists. The ESR is also increased greatly in bacterial, viral, and certain metabolic diseases but the PCV (packed cell volume) is usually not decreased as in the anemias. The plasma iron is frequently decreased in these diseases and in adrenocortical insufficiency. Therefore the hypothesis was advanced that low plasma iron may be responsible for an increased ESR. Four litters of 42 pigs were assigned at random to two treatments. One half of the pigs served as controls and the other half received 150 mg elemental iron as iron dextran. Serum iron was determined by the bathophenathroline method (Beale et al. 1961). Wintrobe tubes were used in measuring ESR. Pigs were bled at 12 to 36 hours of age and at 1, 2, 3, 4, 5, and 6 weeks. The ESR was significantly faster in iron-deficient pigs and the serum iron significantly lower. Based on regression coefficients the increased ESR in iron-deficient pigs was due to low PCV values rather than serum iron. The latter paralleled the PCV values. In some instances the PCV was low and a normal ESR was present. Apparently plasma iron affects the ESR indirectly by supplying iron for erythrogenesis which increases the PCV and decreases the ESR in postnatal anemia of pigs. It does not explain, however, the rapid ESR in animals with a normal PCV.
(Supported by a research grant from the Iowa Heart Association).

ACTIVATION OF CORTICOSPINAL TRACT FIBERS BY GROUP I AFFERENT VOLLEYS. JOHN E. SWETT AND CHARLES M. BOURASSA* UPSTATE MEDICAL CENTER, SYRACUSE N.Y AND GOOD SAMARITAN HOSPITAL, PORTLAND, OREGON.

Weak cutaneous and high threshold muscle nerve volleys evoke discriminative behavior in the cat, whereas Gp I afferent volleys, causing a large evoked response in the postcruciate gyrus, do not provide adequate sensory cues for discrimination. Recordings were made from pyramidal and corticospinal tracts to help identify the cortical cell types influenced by Gp I volleys. In cats anesthetized with chloralose, a weak Gp I shock (1.5 X threshold) produced a response (best seen with averaging methods-Enhancetron 1024) in the bulbar pyramid as early as 7.2 msec (mean 9.5 msec), about the same as the pyramidal response to a cutaneous volley (9.6 msec). Amplitude of the response was maximal for both inputs at 15.5 msec. The pyramidal response to Gp I was distinguished from the ascending Gp I discharge in the medial lemniscus by its longer latency and disappearance at rates above 4/sec. Of the 57 cells observed in the Gp I cortical projection zone, 37 responded to Gp I and 38 responded to cutaneous volleys. Of these 23 cells responded well to both, often at very low thresholds. Mean latency for Gp I cortical unit activation was 8.6 msec; mean latency after cutaneous shock was 11.1 msec. Several units were identified as Pt cells because they were antidromically activated from the bulbar pyramids at constant, short latencies (2 msec or less) and responded to rates of 400-625/sec. Some units were classified as non-Pt cells but others remained unidentified. Units responding to Gp I volleys were observed at depths of 0.5 to 2.5 mm below the cortical surface. Pt cells activated by Gp I, that could also be antidromically activated (1.2-1.5 msec) from cervical cord levels, were identified as corticospinal tract neurons. (Supported by USPHS NB 05048 and NB 02289.)

THE PATTERNS OF CONTRACTION OF THE CIRCULAR AND LONGITUDINAL MUSCLE LAYERS OF CANINE SMALL INTESTINE FOLLOWING DESTRUCTION OF THE MYENTERIC PLEXUS. Joseph H. Szurszewski* and F. R. Steggerda. Department of Physiology and Biophysics, University of Illinois, Urbana, Illinois.

To study these changes, a jejunal segment of the dog was isolated and perfused with Ringer-Tyrode solution according to the Hukahara method. During this operation, the anoxic segment is without circulating blood for 4 hours, a sufficient time to produce destruction of 80% of the ganglion cells of Auerbach's plexus. After restoration of circulation, extraluminal force transducers are implanted on the intestinal area just perfused as well as on the non-perfused area above. The leads were connected to a sensor unit inserted in the back of the neck. The results showed a significant drop in the frequency of contraction in both layers of the perfused segment. In addition, there was a significant increase in the "bursting" pattern and a significant decrease in the "intermediate" pattern of contraction in the transverse axis. The longitudinal axis showed no significant changes in either pattern of contraction. Cinefluoroscopic observations demonstrated a marked increase in tone of the perfused segment. At times, complete obstruction of the lumen was observed. It is proposed that the myenteric plexus regulates the tone of the intestinal musculature and coordinates the type of motility demonstrated by the two muscular layers. (Supported by NIH 1-FL-GM-29, 523).

TISSUE REGENERATION (MITOSIS) UNDER CONDITIONS OF ALTERED GRAVITY. K. S. Talarico*, E. D. Neville* and D. D. Feller, Physiology Branch, Ames Research Center, NASA, Moffett Field, California.

This study was undertaken to determine the effects on liver regeneration of rats exposed to artificial changes in weight by centrifugation. Partial hepatectomies were performed on 7 week old male Sprague-Dawley rats that were then centrifuged at 2.5 *g* or 4.7 *g* and sacrificed during the periods of initiation and peak activity of mitosis. No regeneration was noted in rats centrifuged at 2.5 *g* 24 hours after operation; at this time period the control rats at 1 *g* showed initiation of mitosis. At the 28 hour period, regeneration at 2.5 *g* was noted but the value was significantly lower than controls. The delay in initiation of mitosis was prolonged beyond the 28th hour in the group of animals that was centrifuged at 4.7 *g* and a significantly lower mitotic index still prevailed at the 36th hour. To study the effects of removing rats from high to normal gravity, 3 week old weanling rats were centrifuged for 4 weeks at 4.7 *g*, removed from the centrifuge, hepatectomized, and sacrificed during the period of onset of mitosis. These animals showed an earlier onset of time of mitosis. Greater mitotic activity was observed in the high gravity conditioned rats 24 and 28 hours after hepatectomy than in rats not exposed to centrifugation. Thus, the onset of liver regeneration is delayed in rats exposed to high gravity and is accelerated in rats conditioned to high gravity when they are subsequently returned to normal gravity.

EFFECT OF BULBOCAPNINE ON MONOSYNAPTIC REFLEXES. G. W. Tate*, W. D. Willis, J. C. Willis*, and R. D. Ashworth*. Department of Anatomy, University of Texas Southwestern Medical School, Dallas, Texas.

The action of bulbocapnine upon monosynaptic reflexes was studied in spinal cats. The alkaloid produced a long lasting reduction in the amplitude of monosynaptic reflexes evoked by stimulation of dorsal roots, extensor or flexor muscle nerves. This reflex depression occurred independently of concomitant alterations in the blood pressure of the animal. However, the depression was contingent upon there being an intact pathway between peripheral receptor organs and the spinal cord. The depression could be reversed by severance of the dorsal roots. It is concluded that the reduction of the monosynaptic reflex by bulbocapnine is due either to an action of the drug upon peripheral receptor organs or to an increased central responsiveness to a constant input from the peripheral nervous system.
(Supported by U.S.P.H.S. grant NB 04779.)

HUMORALLY MEDIATED BLOOD PRESSURE RESPONSE TO RETICULAR FORMATION STIMULATION IN "ENCEPHALE ISOLE" CATS. A.Newman Taylor. Depts. of Anatomy & Psychiatry, Baylor Univ. Coll. Med. & Houston State Psychiatric Inst., Houston, Texas.

Activation of the mesencephalic reticular formation is known to be accompanied by sustained cortical arousal and motor and vegetative responses. The present studies indicate that a prolonged elevation of blood pressure may also occur. In "encephale isolé" bilaterally vagotomized cats, maintained with Flaxedil and artificial respiration, ECoG and blood pressure were monitored and the mesencephalic reticular formation stimulated with a bipolar concentric electrode (0.2 ms pulse, 300/sec, 2.5-30secs). Brief stimulation of points throughout the pontine and midbrain tegmentum consistently results in a sustained rise in blood pressure (10-60 mm Hg) commencing 9-41 secs after the onset of stimulation and lasting for 2.5-8.5 mins. Since the spinal cord was sectioned at C-1, the blood pressure elevation must be hormonally mediated. The response can be mimicked by small doses of pitressin (our results and those of S.K.Sharpless and A.B.Rothballer, Am.J.Physiol.200:909, 1961). However, preliminary results indicate that the response persists following complete transection of the brain stem at the level of the mammillary bodies, i.e. in the absence of pathways to the hypothalamic-hypophyseal system, suggesting that other pressor substances may be released by the brainstem during activation of the reticular formation. (Supported by grants from the Heart Assoc. Northeastern Ohio and the American Heart Assoc., Inc.)

SODIUM TRANSPORT PROPERTIES OF ISOLATED TADPOLE SKIN. R. E. Taylor, Jr.* and S. B. Barker, Depart. of Physiology and Biophysics, Univ. of Alabama Medical Center, Birmingham.

Failure of isolated Rana catesbeiana tadpole skin to show a spontaneous transepithelial potential difference (PD) until late in metamorphosis (Taylor, R.E., Jr. and S.B. Barker, Science 148:1612, 1965) suggests absence from this tissue of the mechanism for active Na transport. Alternatively, active transport may occur but fail to engender a PD. To rule out the latter possibility, bidirectional Na fluxes through skin from tadpoles at various stages of thyroxine-induced metamorphosis were measured simultaneously. Net movement of Na was noted only after 12 days exposure to thyroxine (T_4, 100 ng/ml) in aquarium water, coinciding exactly with first appearance of a spontaneous PD and measurable short-circuit current (SCC). Net Na flux was in the inward direction and accounted for 99.0±2.1% of the SCC. Prior to development of a PD, the mean ratio of Na influx to efflux was 0.98±0.02. Thereafter, the ratio rose to 2.70±0.31, a value still somewhat less than that reported for adult frog skin. Ohmic resistance of isolated skin, usually less than 100 ohm cm^2 for premetamorphic tadpoles, increased with continued exposure of tadpoles to T_4 and exceeded 600 ohm cm^2 in skin showing net Na transport. Partial conductance of Na (calculated from unidirectional Na flux) equalled about 50% of the total electrically-measured conductance of young tadpole skin. This value increased during T_4 administration and usually exceeded 100% in actively transporting skin. Although there are unproven assumptions in this analysis, it suggests development of a mechanism which allows movement of Na without transport of charge. Thus a carrier-mediated, forced exchange of Na for some other cation may develop simultaneously with the mechanism for active Na transport. (Supported by NIH research grant AM 10436).

Comparison of direct effect of purified gastrin and histamine on the total resistance of the gastric circulation of dogs. E. C. Texter, Jr. and H. C. Laureta.* V. A. Research Hosp., Hektoen Inst. of Cook County Hosp., Northwestern Univ. and Univ. of Phillipines.

Partially pure gastrin (Grossman) has been shown to be vasodilator in the gastric as well as the mesenteric circulation; when compared to histamine gastrin is a weak vasodilator. Pure gastrin (Gregory) on weight basis has been shown to be 30 times and on molar basis 500 times more powerful as a gastric secretory stimulant than histamine. Because of the evidence for a direct relationship between gastric secretory function and blood flow it is reasonable to expect purified gastrin (PG-Leo Pharm.) also to be more potent than histamine (H) as a vasodilator. The direct effects of PG and H on the total resistance of the gastric circulation of dogs were compared using the constant flow perfusion technique. With this technique the response of the blood vessels is reflected by the change in total resistance (RT) (arterial minus venous pressure divided by blood flow). At sequentially increasing flow rates (0.123-4.94 ml/min) isotonic solutions of PG (0.5 mg/ml) and H (1 mg/ml) were infused i.a. into the constantly perfused stomach of 16 dogs. Mean blood flow was 0.3 ml/min/gm of wet stomach tissue. Mean control RT was 2.73 $\pm$ 0.63 and 2.35 $\pm$ 0.79 PRU for PG and H respectively. At maximum infusion rates, PG (2.47 mg/min) caused 30% (0.78 $\pm$ 0.34 S.D., difference from control, $p<0.001$) and H (4.94 mg/ml a 50% (1.32 $\pm$ 0.76 S.D., difference from control, $p<0.001$) decreased in the respective RT. On weight basis 2.9 mg/ml/Gm stomach/min PG produced 30% and H 50% fall in RT; on molar basis a 30% fall in RT was produced by 1.3×10^{-13} moles/ml/Gm stomach/min PG and 9×10^{-13} moles/ml/Gm stomach/min H. On weight basis H is more potent than PG but on molar basis PG is 7 times more potent vasodilator than H in the gastric circulation. (Supported by Grant R01-AM 02651).

POTENTIATION OF THE PRESSOR EFFECT OF ANGIOTENSIN BY ADRENERGIC DRUGS. P.H.Thomas*, E.A.Ohler, R.W.Sevy and C. Harakal*. Temple University School of Medicine, Philadelphia, Pa.

The pressor effect of angiotensin was potentiated by norepinephrine (NE) and by adrenergic agents (tyramine, mephentermine, ephedrine) which cause release of endogenous catecholamines, including NE. On the other hand, potentiation of the pressor effects of NE or tyramine by angiotensin could not be demonstrated. Prior depletion of catecholamine stores by reserpine abolished the potentiating effect of the NE releasing agent, tyramine. Neither non-catecholamine adrenergic drugs (phenylephrine, methoxamine) which act directly on alpha adrenergic receptors and produce vasoconstriction, nor vasopressin, a non-adrenergic vasoconstrictor, potentiated the pressor effect of angiotensin. Either alpha adrenergic receptor blockade (phenoxybenzamine) or beta adrenergic receptor blockade (dichloroisoproterenol, propranolol), but not ganglionic blockade (hexamethonium), significantly reduced or abolished potentiation of the pressor effect of angiotensin by NE or tyramine. It may be concluded that: 1) pressor effects of angiotensin may be potentiated by NE and by adrenergic drugs which release catecholamines, including NE; but the reverse could not be demonstrated, 2) this potentiation is dependent upon the presence of catecholamines (probably NE) and it is intimately related to functional integrity of both alpha and beta adrenergic receptor sites.

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EFFECT OF PROLONGED INTRAVENOUS HISTAMINE AND GASTRIN PENTAPEPTIDE ON GASTRIC PEPSIN SECRETION. J.C. Thompson, W.D. Davidson*, J.H. Miller*, and C.A.E. Lemmi*. Depts. Surg. & Med., Harbor Gen. Hosp., Torrance, Cal., and UCLA Sch. of Med.

Babkin concluded that histamine acted only to wash out pre-formed pepsin and was not a true stimulant. The present study was designed to test the effect of prolonged (6-8 hrs.) intravenous administration of histamine and a gastrin pentapeptide (t-butyloxycarbonyl-β-Ala. Tryp. Met. Asp. Phe. NH_2, "ICI-50,123") on pepsin secretion. Ten adult female mongrel 20-30 kg. dogs with Heidenhain pouches were used. Continuous iv infusions of histamine (H) (24 mcg./kg./hr.) and pentapeptide (5P) (5 mcg./kg./hr.) were performed; these doses yield c. ½ maximum acid stimulation. Secretory collections were made every half-hour, the acid titrated with N/10 NaOH (phenol red), and pepsin determined by the method of Grossman and Marks.

Results: ACID: both stimulants provoked vigorous secretion. Average hourly output (mEq.) 3rd through 5th hour = 2.67 (H); = 1.62 (5P). PEPSIN: good stimulation was obtained with both agents. Average hourly output (mcg.) = 1st hour: 402 (H), 150 (5P); 4th hour: 1212 (H), 1540 (5P); 5th hour: 1404 (H), 2480 (5P); 6th hour: 2412 (H), 2228 (5P).

Conclusions: Intravenous histamine and the gastrin pentapeptide provide continuous stimulation of acid and pepsin output in 6 hour infusions. The ratio of pepsin output during the 6th hour as compared with the 1st hour was 6 for histamine and 14 for the pentapeptide. There was no evidence for a wash-out phenomenon.

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EXERCISE AND LIGAMENTOUS STRENGTH. C. M. Tipton, R. J. Schild and S. L. James (intr. by C. C. Wunder). University of Iowa, Iowa City, Iowa.

Exercise has long been advocated to improve ligamentous strength although there is meager scientific evidence to justify this practice. Medial collateral ligament preparations from the knees of male Sprague-Dawley rats and mongrel dogs were used to investigate this matter. Results were expressed in separation force (SF) units and evaluated with regard for body weight. There is a low ($r=0.55\pm05$) but statistical relationship between BW and SF (N=203). A single exercise period (0.5 hr. by 34 rats) had little influence on rat SF values; however, a 6-12 week training program (1-3 hr./day with 50 rats) significantly increased ($30\pm2\%$) this measure. Ten rats detrained for 4 weeks also had SF results ($31\pm10\%$) that were higher than controls. SF data from 32 trained hypophysectomized rats followed this same trend ($5\pm1\%$). Immobilization of dog limbs (N=12) by plaster casts caused a SF reduction of $32\pm9\%$. When ligaments were surgically sectioned, repaired and permitted to recover (6-12 weeks) the SF of the repaired ligament increased as the amount of exercise increased; however, the strength of the repaired ligament never equaled the strength of the nonsectioned ligament. Analysis of the hydroxyproline, hexosamine and water content data from various experimental groups revealed no measureable differences. It was postulated that the differences associated with exercise levels were due to changes that have occurred at the ligamentous insertion site.

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ACTIVE SUBSTANCES IN THE BLOOD DURING STIMULATION OF THE VAGUS NERVES. Y. Tomiyama*, T. Geisel*, N.C. Jefferson, A. Doi*, P. Lott, Jr.* and H. Necheles. Michael Reese Hospital and Medical Center, Chicago, Ill.

We have reported earlier on gastric contractions in dogs by stimulation of the central ends of the cut vagus nerves. This effect appeared to be caused by a humoral factor from the head of the animal, as found in experiments with isolated heads and perfused isolated stomachs. Presently, we report a search for substances in the blood during stimulation of the vagus nerves. In a dog under nembutal anesthesia a control venous blood sample was taken and then samples were collected during and after stimulation of the intact vagi and of the central ends of the vagi cut in the neck. These samples were transferred immediately into 4 volumes of cold ethanol and filtered. The filtrate was evaporated and shaken with ethyl ether. The aqueous phase was lyophilized, the powder dissolved in distilled water and applied on a Sephadex G-25 column, using saline as eluent and collecting 5 ml-fractions which were tested on isolated guinea pig's ileum. Spectrophotometric determinations were carried out at 280μm and 570μm after the ninhydrin reaction. Distinct differences in activity were found between fractions of control blood and fractions from the period of vagus stimulation. The active substance appears to be a kinin, related to but apparently not identical with bradykinin.

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COMPARISON OF METHODS FOR CALCULATION OF LEFT VENTRICULAR STROKE WORK. W.S.Topham (intr. by H.R.Warner), Dept. of Biophysics & Bioeng., Univ. of Utah, Salt Lake City, Utah. Supported by a grant from NIH #HE 03607 and a grant from the Utah Ht. Assoc.

Physiologists have used a variety of equations to calculate the effective stroke work of the left ventricle. Stroke work (SW) is defined by the following equation:

$$SW=\int_{t=0}^{t=\tau} p(t)f(t)dt$$

where $p(t)$ is the time-varying pressure generated by the left ventricle, $f(t)$ is the time-varying flow from the left ventricle and τ is the duration of systole. In these experiments $p(t)$ was measured with a catheter tip manometer in the ascending aorta and $f(t)$ was obtained from an electromagnetic flowmeter probe implanted around the ascending aorta. Using the above equation the total output work of the heart, with exception of that producing coronary flow, was determined because the measured flow becomes zero during diastole. Results of calculations made with this method were compared with SW calculated from $SW=\overline{P}\cdot SV$, where

$$\overline{P}=\frac{1}{\tau}\int_{t=0}^{t=\tau} p\,dt$$

and

$$SV=\int_{t=0}^{t=\tau} f\,dt$$

in dogs under conditions of rest and exercise. The values obtained from the two methods were equal within three percent when calculations were made at both rest and exercise. SW increased 30 percent with moderate exercise.

A CORRELATION BETWEEN THIRST SATIETY AND ELECTROPHYSIOLOGICAL STUDIES OF TASTE. E. J. Towbin and C. B. Ferrell*. VA Hosp. and Univ. of Arkansas School of Med., Little Rock, Ark.

Three experimental protocols were designed to determine the correlation between thirst behavior and gustatory electrophysiology in the cat. In the first two the cats had access to a dry food for 16 hours before the drinking solution was made available. In one protocol this liquid was alternately water, or one of three concentrations of NaCl, or Na acetate. The animals drank more NaCl than sodium acetate at the 0.2 M level, while at 0.1 M and 0.05 M consumption of the two salts was equal. At 0.1 M and above more salt solution was drunk than was water on alternate days. In the second experiment the lapping of the animals was recorded. In the four animals tested, none showed a significant increase in the time necessary to reach satiety when drinking saline vs. drinking water. In the third protocol animals had access to dry food and two drinking solutions. Water, physiological saline, Ringer's solution, sodium acetate, choline chloride, potassium benzoate, ethyl alcohol, pH 3 saline, and pH 11 saline were presented in various combinations. In this situation half the cats prefer saline to water. The animals that show a preference for water maintain this preference throughout. Those animals preferring the saline also prefer Ringer's solution, select water rather than the ethyl alcohol solution and show no preference for potassium benzoate solution. Four of the five cats showed a preference for 0.1 M potassium chloride. In choosing between water and sodium acetate or choline chloride solution there was no consistency in this group; half showed no preference while half preferred the electrolyte solution.

EFFECT OF DIFFERENT VENTRICULAR STIMULATION SITES ON CARDIAC DYNAMICS. Theofilos J. Tsagaris* and Hiroshi Kuida. Univ. of Utah College of Medicine, Salt Lake City, Utah.

The hemodynamic effect of altering the site of ventricular pacing was studied in ten anesthetized open-chest dogs. To facilitate ventricular pacing complete heart block was induced by injecting formalin into the AV node. A pair of teflon-coated stainless steel wire electrodes was placed in each of four ventricular sites: apex and lateral basal wall of the left ventricle (LV) and inflow and outflow tract of the right ventricle (RV). Pacing at a rate of 100/minute for 10 minutes was performed in a pattern which permitted comparison of each site sequentially with every other at least once and usually twice. The following variables were measured: cardiac output (CO), femoral artery pressure, LV diastolic pressure, LV isometric dp/dt, and LV stroke work (LVSW). Comparison of variables was made only between successively stimulated ventricular sites. In comparison with LV apex pacing, RV inflow pacing produced slight but statistically significant increases in LVSW, LV diastolic pressure and CO. However, no significant differences were found comparing RV inflow pacing with the other two sites. There were five other instances of small but significant differences in the variables between the different pacing sites. It is concluded that among the pacing sites used only minor and inconsistent differences in left ventricular function could be demonstrated. (Supported by USPHS grants HE-4530, HE-07618 and the Utah Heart Association)

COMPARISON OF RESPONSIVENESS OF PERFUSED RESISTANCE VESSELS FROM RABBIT MESENTERY AND BRAIN. Eiichi Uchida*, David Bohr and Sibley W. Hoobler. Depts. Physiol. and Medicine, Univ. of Mich., Ann Arbor, Mich.

A technique has been developed for studying the reactivity of single, minute blood vessels. Segments (0.6 to 5.0mm long) of small resistance vessels (60 - 250μ o.d.) from mesojejunum and from a branch of the a. cerebri media were perfused with physiological salt solution at constant rate (0.17 to 1.9 ml/min). Vasoactive agents (in 0.002 to 0.02ml vols) were injected into the inflow system and the resultant pressure changes were recorded. Doses required for threshold response were:

Vasoactive agent	Mesenteric vessel	Cerebral vessel
Potassium Chloride	9-60μM	15-60μM
Epinephrine	0.01-0.1μg	>5μg
Norepinephrine	0.02-0.5μg	>10μg
5-hydroxytryptamine	0.2-5.0μg	>10μg
Angiotensin II	0.1-0.5μg	0.25-0.5μg
Vasopressin	>50mU	2-6mU

Tachyphylaxis was observed in responses to angiotensin II, vasopressin and 5-hydroxytryptamine, in preparations from both organs; tachyphylaxis to angiotensin II was so pronounced that it was difficult to evaluate the threshold concentration correctly. Since the differences in responsiveness of vessels from the two sources are not the same for all stimulating agents it seems probable that smooth muscle of the cerebral vessels is not generally less sensitive than that of mesenteric vessels to all stimuli, but that vessels from the two sources differ in the number and distribution of receptors for the several vasoactive agents. The results obtained with these small, functionally important vessels corroborate those with larger vessels, that differences in receptor population exist among vessels from different organs. Supported by a grant from the National Institutes of Health, HE-02578.

PREVENTION OF PEPTONE SHOCK BY INHIBITORS OF PROTEASE ACTIVATION AND ANTIHISTAMINE. G. Ungar, A. L. Ungar* and B. Chan Yip† Baylor Univ. College of Medicine, Houston, Texas.

Injection of peptone is known to produce in dogs a shock of the anaphylactoid type but the mechanism of this effect is unknown. We observed that addition of peptone to dog serum in vitro induces activation of a protease. This observation has been repeatedly confirmed but its significance in the production of shock is still uncertain. More recently, we found that protease activation is prevented by hexadimethrine Br (Polybrene), ε-amino caproic acid (EACA) and Trasylol, a naturally occurring inhibitor. These agents were administered intraperitoneally to dogs 30 min before intravenous injection of peptone but the shock produced was not significantly different from that observed in untreated controls. However, when an antihistamine drug, pyribenzamine, was given together with the enzyme inhibitors, the shock was considerably reduced:

Drug + Pyribenzamine	Fall in B.P. ± S.D.		N
Control	74.0	11.2	7
Polybrene (20 mg/kg)	24.3	18.5	7
EACA (1 g/kg)	21.7	12.4	4
Trasylol (4000 U/kg)	45.5	--	2

Pyribenzamine alone (1 mg/kg) had no effect. The results suggest that peptone produces shock by two main mechanisms: histamine release and protease activation; the latter acting probably through plasma kinin formation. The bearing of these observations on other types of shock is being investigated. (Supported by PHS grant GM 12650.)

A METHOD FOR DETECTION OF BLOOD FLOW IN THE DENTAL PULP. D. D. Upthegrove*, J. G. Bishop, and H. L. Dorman. Baylor University College of Dentistry, Dallas, Texas.

Enamel and dentin form an enclosure which is sufficient to protect the pulp from various forms of trauma, e.g., mastication. As a result of this barrier highly sensitive instrumentation is required in order to study the blood flow in intact teeth. This investigation has developed instrumentation sufficiently sensitive and stable to record changes in the phototransmittance of the pulp which occur with each heart beat. The apparatus was arranged so that a prefocused tungsten bulb illuminated the anterior surface of the tooth. Transmitted light was received by a photoconductive resistor placed on the opposite side of the tooth. A wheatstone bridge detected the resulting resistance changes and the pulsitile signal was amplified and read out on one beam of a Tektronix 502 oscilloscope. In this manner the optical density charges of the pulp could be monitored. The second beam of this oscilloscope was used to display the subject's electrocardiogram or in some cases the carotid artery pulse wave. Comparisons of the two traces indicated that the optical density rise was correlated with each QRS complex and with each pulsitile pressure increase. This correlation is explained by assuming that the optical density increase is caused by surges of oxygenated arterial blood driven through the pulp by each heart beat. This view is supported by the finding that occlusion of the carotid arteries abolished the optical density changes while injection of 1/2 cc. of normal saline into the carotid artery resulted in a prompt but transitory fall in the optical density of the tooth. Injection of cardio-green dye into the carotid artery increased the optical density.

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STUDIES OF VISCOMETRIC BEHAVIOR OF BLOOD AT LOW SHEAR RATES. Shunichi Usami*, Shu Chien*, Robert J. Dellenback* and M.I. Gregersen. Columbia University, New York City.

In studies of the viscometric behavior of human blood at low shear rates (0.1 to 0.01 sec^{-1}) using the GDM couette viscometer equipped with modified rotor drive mechanism (Chien et al., J. Appl. Physiol. 21:81, 1966) it has been found that at the same red cell concentration (H = 45%) the recorded torque curves at 0.01 sec^{-1} show marked and characteristic differences depending on the suspending medium. Comparisons include red cells suspended in plasma (heparinized blood), serum (defibrinated blood) and red cells washed and suspended in Ringers or in modified Eagle solution containing 0.25% human albumin. The torque curves differ in a) the maximal torque value, b) the time required to reach maximal torque (rise-time) and c) the rate of decay in torque after the peak value is attained; in heparinized blood the rise-time is about 40 seconds followed by decay; in defibrinated blood the rise-time is 2-4 minutes and decay is absent or gradual; with red cells suspended in Ringers or modified Eagle solution the rise-time is 15-20 seconds with no decay in torque. The torque-curve changes induced by defibrination are reversed by addition of fibrinogen or HMD (D x 375).

(Supported by U.S. Army Contract DA-49-193-MD-2272.)

RHINENCEPHALIC CELLS AND CONDITIONED DISCRIMINATION. A. A. Uyeda and J. M. Fuster (intr. by N. A. Buchwald). School of Medicine, University of California, Los Angeles, Calif.

Monkeys trained to lever-press to visual cues associated with food or electric shock were prepared for chronic micro- and macroelectrode recording. Extracellular spike discharges and EEG were recorded from the rhinencephalon during the discrimination tests.

From a population of over 500 units, cells of the amygdala and the hippocampus were selected for a study of relations between unit discharge and the sequence of experimental events. Though generally showing a high level of spontaneous discharge, over half of the amygdaloid units were found to be indifferent in their firing frequency to the experimental procedures. Hippocampal units maintain a lower rate of spontaneous activity and are even less reactive.

Considering the responsive units, firing frequency is most often affected by the appearance of the conditioned visual stimuli, a common mode of reaction being a depression of the ongoing discharge rate. Approximately 40% of reactive amygdaloid and hippocampal units fall within this category. Some units, especially in the amygdala, show reaction to one cue (food or shock) and not to the other. Increased rate of firing of cells in the two sites is the most notable change occurring at removal of a conditioned stimulus and reinforcement of level-pressing.

Spectral analysis indicates EEG changes in the amygdala in response to discriminanda. At presentation of the two discrimination stimuli the power of lower frequencies becomes noticeably prominent at the expense of that of higher frequencies.

BLOOD FLOW DISTRIBUTION IN ALASKA SLED DOGS DURING EXTENDED EXERCISE. R.L. Van Citters, E. Evonuk and D. Franklin U. of Washington, Seattle, Artic Aeromed Lab, Alaska and Scripps Clinic Research Foundation, La Jolla, California

The Alaska sled dog is a remarkable athlete; trained teams can pull a sled and driver 20 miles cross-country at subzero temperatures in under 75 minutes. We studied the effects of such exercise on distribution blood flow. In each of six trained dogs, Doppler telemetry flow meter transducers were implanted chronically on ascending aorta, terminal abdominal aorta, and renal and mesenteric arteries. Training was resumed and within six weeks the dog's performance matched that of control animals. Two days before the study a miniature pressure gage was implanted in the external carotid artery under local anesthesia. Aortic blood pressure and flow through three arteries were telemetered simultaneously from individual dogs as the team pulled sled and driver around the track. At a receiving station one-half mile away, pressure and flow responses were continuously recorded during extended exercise runs. Heart rate, 60/min at rest, was 300/min during vigorous runs; aortic pressure rose from 120/80 to 230/90. Stroke volume fell slightly at these high rates. During severe exertion, when cardiac output increased nearly six-fold and terminal aortic flow seven to ten-fold, renal and mesenteric flows remained at basal levels or increased slightly. These findings do not support the view that, during exercise, muscle flow is augmented at the expense of visceral flow. (Supported by grants from USPHS, AHA, Arctic Aeromed Lab, and Wash. State Heart Association.

Changes in cerebral cortical extracellular space during asphyxiation and spreading depression. A. Van Harreveld, S.K. Malhotra* and F.I. Khattab.* Calif. Institute of Technology, Pasadena, California.

Electron micrographs of the molecular layer of the cerebral cortex prepared by freeze substitution show an appreciable extracellular space mainly in bundles of nonmyelinated axons. This space is only present when the tissue is frozen shortly (within 30 sec.) after circulatory arrest; when the tissue is asphyxiated for 6 min. before freezing the tissue elements are closely packed and tight junctions are often observed. These observations parallel those made previously on the molecular layer of the cerebellar cortex. The loss of extracellular material during asphyxiation is in accordance with the impedance increase and the transport of water and chloride into cellular elements observed under these circumstances. Spreading depression also causes an impedance increase and transport of water and chloride. Cortical tissue frozen while spreading depression was in progress showed a similar loss of extracellular space as that caused by asphyxiation. The depression was in some experiments elicited by applying an isotonic KCl solution to the cortex. In the micrographs of these cortices an enormous swelling of certain tissue elements was observed. Some of these were identified as dendritic structures (spines). When spreading depression was elicited by electrical stimulation the swelling of the elements was much less. This suggests that part of the material in the swollen structures was derived from the solution bathing the cortex. When the cortex was bathed with Ringer's solution during asphyxiation a similar enormous swelling of certain tissue elements was observed. (Supported by a grant from the National Science Foundation G. B. - 4028).

A THEORETICAL APPROACH TO TREATMENT OF DECOMPRESSION SICKNESS. Hugh D. Van Liew. Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N. Y.

Rates of diffusion of gas out of bubbles in blood vessels or tissues can be predicted from assumptions as to permeation of gases through living tissues and geometry of the bubbles. One can predict the relative efficacy of treatments with compression, oxygen, or combinations of the two, even though the exact locations or characteristics of the bubbles are not known. Experience with absorption of gases from subcutaneous gas pockets in rats (Am. J. Physiol. 202: 53-58, 1962, and J. Appl. Physiol. 20: 927-933, 1965) lends support to this approach. Some predictions from the theory are: (a) At any environmental pressure a spherical bubble will cease to exist five to ten times sooner when the patient breathes pure oxygen than when he breathes air. (b) In an O_2-breathing patient, the time for a spherical bubble to disappear is inversely proportional to the cube root of the environmental pressure. (c) In air-breathing patients, disappearance time is no simple function of pressure. Effectiveness of pressurization decreases markedly as environmental pressure increases; with air-breathing at two atmospheres a bubble may disappear in one-half the time required at one atmosphere, but five atmospheres would be needed to reduce the time to one-third.
(Supported in part by a grant from the NIAMD, NIH.)

TRITIATED ALPHA-AMINOOCTANOIC ACID: PREPARATION AND INTESTINAL TRANSPORT. Francia Vishno,* Kenneth R. Brody,* Richard P. Spencer. Dept. of Radiology, Yale University School of Medicine, New Haven, Connecticut.

It has been recognized that the affinity ($1/K_m$) of amino acids for the active transport system in the mammalian small intestine increases with the length of the lipophilic side chain. For example, in the rat intestine, $1/K_m = S/(3.9x10^{-6})$ where S is the ethanol-to-water solubility for glycine, alanine, valine and leucine. Therefore, amino acids with very long side chains should have great transport affinity (and low net transport). To test this further, amino acids of composition C_8 to C_{16} are under investigation. D,L-α-aminooctanoic acid was tritiated by exposure to tritium gas (Wilzbach technique) at 26°C for 2 weeks. Purification was by dissolving in glacial acetic acid & water (50:50, v/v), filtering, flash evaporating, and extracting the residue with butanol to remove impurities. The final product was white in color and had the correct melting point (230°C). Thin-layer chromatography on 250 micron cellulose showed R_f values of 0.87 in isopropanol:NH_4OH:H_2O (40:5:55), and 0.83 in butanol:acetic acid:water (4:1:1). Radioactivity corresponded to the peak revealed by ninhydrin spraying. The final specific activity was about 440 millicuries/millimole. Transport did occur against a concentration gradient ($1x10^{-4}$M) using everted intestinal sacs (hamster and mouse). The K_m value is low (high affinity). Studies on possible inhibition of the transport of other amino acids by α-aminooctanoic acid are complicated by the limited solubility of the compound. The affinity of the long chain amino acids for the transport system may be of use in attempts to physically separate the transport site.

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CENTRAL BLOOD VOLUME IN HEMORRHAGIC SHOCK IN THE DOG
John A. Waldhausen*, Francis L. Abel, and William L. Pearce*
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Five dogs with chronically implanted electromagnetic flow probes on the pulmonary artery (PA) to measure cardiac output (CO) and with silastic catheters inserted into the PA and left atrium (LA) were subjected to a standard hemorrhagic shock procedure. In order to measure mean transit time (MTT) in the lesser circulation ascorbic acid was injected into the PA and monitored in the ascending aorta by a platinum electrode. Central blood volume (CBV) was calculated as CBV=(CO x MTT)/60. Pressure was measured in the aorta, PA and LA. Pulmonary vascular resistance (PVR) was calculated as PVR=(PA-LA)/CO. Total blood volume (TBV) was measured with I^{131} serum albumin. All parameters were studied at 30 minute intervals throughout the bleeding and postinfusion period until death. During the control period the mean CBV was 9.9 ml/kg of body weight or 11.2% of the TBV (101.1 ml/kg); with bleeding the CBV fell to 7.5 ml/kg at 20% time and 6.7 ml/kg at 80%. After reinfusion the CBV rose to 8.5 ml/kg or 9.6% of TBV (mean 88.6 ml/kg) but fell to 6.4 ml/kg at 80% of postinfusion time. PVR rose to 286% of control at 80% of the oligemic phase and remained elevated (170% of control) in the postinfusion period. These studies suggest that the pulmonary vascular bed in hemorrhagic shock in the dog is selectively constricted and its blood volume decreased when compared to the body as a whole. (Supported by USPHS Grants HE-09211, H-6308, and HE-08042).

Rapid Interaction with a Digital Computer--Plusses and Minusses by D.O. Walter , Dept. of Physiol. and Brain-Research Inst., U.C.L.A. Three remote console systems (typewriter-like keyboard and memory oscilloscope) have been connected to the computer (Scientific Data Systems 930; 2 μsec, 16K 24-bit words) in the Brain Research Institute. The three operate concurrently with each other and with other, "background" jobs; the system was originally conceived for use with a disk, but production delays have forced us to use tapes. Response time of the system varies from imperceptible (300 μsec) to unbearable (if two users try to access the same scratch tape, the second waits for the first). Operations programmed under single buttons one mathematical manipulation on real or complex scalars and vectors), set-up and control of analog-digital conversion packages for spike and/or wave data, and real or complex plotting. Applications have included simple data plotting, spike interval histograms, amplitude distribution functions of EEG data, simulation of lateral inhibition, some teaching programs illustrating digital filtering or illustrating diffusion of particles with entropy calculation.

THE PHYSIOLOGY OF CENTRAL PAIN. Thomas A. Waltz and George Ehni (intr. by Robert Vick). Baylor University College of Med. Houston, Texas.

Relief of central pain has been attempted in human subjects by placing thalamic lesions. The lesions were made stereotaxically with a leukotome aiming at centrum medianum and parafascicularis. The patients are 5 in number, 3 of whom suffered strokes and had pain beginning in the recovery period. Another had central pain as a result of an arterio-venous malformation in the lateral thalamus and the fifth had a cervical-thoracic hydromyelia as a basis for the painful state. In patients recovering from stroke, the painful state worsened as improvement in sensation occurred. Spinal anesthesia resulted in relief of pain in the distribution of the anesthesia as well as diminution of pain in the body area cephalad to the anesthesia. In one patient, there was resolution of the pain presumably by drug induced block in the C fibers before the agent affected the sensations of light touch and pin prick. Another patient reported a phantom sensation during induction and resolution of the block, the foot feeling as if it were attached to the hip. Thalamotomy has resulted in a 50-100% reduction in central pain with resolution of the hypersensitivity to stimulus. Examination demonstrated no change in sensation and 2 of the patients spontaneously volunteered that sensation seemed to be improved. It is concluded that with both fast and slow pain systems intact the fast system exercises a degree of inhibition on the slow pain system, and that differential interruption of fast pain input to the nucleus VPL results in thalamic syndrome. Loss of input to the nucleus VPL from the secondary sensory area of the parietal cortex is responsible for production of thalamic pain with purely suprathalamic lesions.

CHARACTERIZATION OF CIRCULATORY STATUS USING A MATHEMATICAL MODEL. H.R. Warner, Dept. of Biophysics & Bioeng., Univ. of Utah and L.D.S.Hosp., Salt Lake City, Utah. Supported by a grant from NIH #FR 00012.

A mathematical model of the circulation which describes the relationship between pressure, flow, volume and time in the closed-loop system has been developed and programmed to run on a Control Data 3200 computer under the MEDLAB time-sharing monitor system. The physiologist may enter parameters from a keyboard and observe the results of solution of the set of 26 differential equations in the form of plots of variables and lists presented on a memory oscilloscope at his remote station. Physiological data previously recorded from a patient such as heart rate, stroke volume, mean pressure, time-course of pressure in the ascending aorta and total blood volume are called from disc or tape into the program and provide sufficient constraints on the model solution to permit unique definition of the model parameters for that particular patient. Since many of these parameters are being determined for the first time, much experience will be needed to define their usefulness as indicators of the subsequent course of a patient and as aids for the physician in determining therapy.

ACTION SPECTRA OF OMMATIDIAL CELLS IN THE LATERAL EYE OF LIMULUS. Gerald S. Wasserman (intr. by M.G.F. Fuortes). Natl. Insts. of Health, Bethesda, Md.

An early report[1] of the existence of two classes of ommatidial cells in the lateral eye of Limulus with different action spectra has been confirmed and observations have been extended into the near ultraviolet region of the spectrum. Using micropipettes, responses of single receptor cells have been measured as a function of wavelength and energy; equal response action spectra have been constructed from these data. Two types of cells have been found. Alpha cells: These cells have action spectra which agree well with the density spectrum of rhodopsin which is the only photopigment thus far extracted from the rhabdome of this eye[2]. The most sensitive wavelength is around 525 nm. Beta cells: The action spectra of these cells do not resemble any photopigment spectra; beta cells are almost (±1 dB) equally sensitive to all wavelengths from 350 to 550 nm, whereupon sensitivity drops rapidly. The data on hand suggest that beta cells are less sensitive than alpha cells in the visible spectrum (which agrees with the earlier report) and more sensitive in the near ultraviolet.

1. Graham, C. H. and Hartline, H. K., J. gen Physiol., 1935, 18, 917-931.
2. Hubbard, R. and Wald, G., Nature, 1960, 186, 212-215.
(Supported by NIH postdoctoral fellowship, F2-NB-22, 408)

ULTRASTRUCTURE, HISTOCHEMISTRY, AND AMINO ACID COMPOSITION OF THE SHELL OF NEOPILINA SP. N. Watabe,* V. R. Meenakshi,* P. E. Hare,* R. J. Menzies* and K. M. Wilbur. Dept. of Zoology, Duke University, Durham, N. C., and Geophysical Lab., Carnegie Institution of Washington, Washington, D. C.

The shell consists of an outer uncalcified periostracum of two layers, a predominant prismatic region, and a thin lamellar nacreous region on the inner surface. Chemical and histochemical tests show that the periostracum is a weakly tanned protein with neutral mucopolysaccharides and traces of lipids. The prismatic region contains weakly tanned proteins, lipids, and traces of acidic and neutral polysaccharides. The nacreous layer shows the presence of proteins soluble in dilute acids, acidic mucopolysaccharides and traces of neutral polysaccharides and lipids. Chitin is absent from all layers. Neopilina shell differs markedly from non-nacreous calcified shell in its amino acid residues and resembles uncalcified periostracum except for valine, leucine and tyrosine.

THE SITE OF IMPULSE FORMATION WITHIN THE ATRIOVENTRICULAR JUNCTION. Yoshio Watanabe* and Leonard S. Dreifus, Hahnemann Med. Col., Phila, Pa.

Precise localization of the site of impulse formation was attempted in 15 isolated, perfused rabbit hearts showing spontaneous atrioventricular (A-V) nodal rhythm. Transmembrane potentials of various A-V junctional fibers were recorded utilizing ultramicroelectrodes and their time of activation was determined with reference to the electrograms recorded from the sinoatrial (SA) nodal region as well as the ventricles. Mapping of the A-V nodal fibers was accomplished by topography, characteristic action potential configuration and microscopic sectioning of the recording sites. The earliest sites of activation during A-V nodal rhythm consistently occurred in an area near the atrio-nodal junction adjacent to the fibrous A-V ring and below the ostium of coronary sinus These fibers were activated 60 to 138 msec before the sequential retrograde excitation of the SA nodal region. Diastolic (phase 4) depolarization was observed in some fibers in and around the points of earliest activation. A distinct difference in both timing and action potential configuration of these A-V junctional fibers was seen upon spontaneous return to SA nodal rhythm. It is concluded that impulse formation within the A-V node occurs in a specific area near the atrionodal junction and below the coronary sinus under these experimental conditions. Diastolic depolarization observed in these fibers suggests the potential of automaticity within this region.

E. COLI ENDOTOXIN, MYOCARDIAL CONTRACTILITY AND CORONARY FLOW. W.R. Webb, D.N. Gupta,* S. Nakae,* and W.A. Cook.* The University of Texas Southwestern Medical School, Dallas.

The characteristic hemodynamic alterations in dogs after injection of E. coli endotoxin are well known. The following study evaluated the effects of endotoxin on myocardial contractility under precisely controlled circumstances to differentiate the primary myocardial effects of endotoxin per se. In open chest dogs, with controlled cardiac output, aortic pressure, heart rate, body temperature, pO_2, pCO_2 and pH, left ventricular pressure and its dp/dt were studied after injection of a 5 mg/kg dose of E. coli endotoxin. Coronary flow was measured by coronary sinus catheterization. The potency of endotoxin was demonstrated separately in intact chest dogs who received a 3 mg/kg dose of E. coli endotoxin from the same stock. Following injection of the endotoxin, hypotension was produced in about two minutes and reached shock levels in 4 to 6 minutes. After staying at that level for about 5 minutes the arterial pressure slowly rose to near control levels in 12 to 15 minutes. This was followed by the classic slowly progressive deterioration leading to severe shock. In the controlled preparation, which did not allow a fall in blood pressure, measurements of dp/dt of the left ventricular pressure pulse at 2 minute intervals for a period of 15 to 20 minutes following the injection of 5 mg/kg E. coli endotoxin did not show any change. Continuing measurements at one-half hour intervals over the subsequent two hours likewise showed no significant changes. Coronary flow remained at the control levels throughout. These studies demonstrate that E. coli endotoxin has no direct pharmacologic effect on myocardial contractility or coronary flow.

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ISOPROTERENOL FOR THE TREATMENT OF EXPERIMENTAL SHOCK PRODUCED BY HEMORRHAGE. Max Harry Weil, Howard Whigham*, and Edward P. Marbach*. Dept. of Medicine, University of Southern California School of Medicine, Los Angeles, California.

The effectiveness of isoproterenol, a sympathomimetic drug with vasodilator activity, was tested in 29 Wistar rats to determine its potential benefit for treatment of "irreversible" hemorrhagic shock. Femoral arteries were cannulated for bleeding into a reservoir which was maintained at 35 mm Hg pressure for 240 min. Following reinfusion of blood, isoproterenol (Isuprel) was infused in amounts of 1.16 µg/min for 60 min. Untreated animals survived for an average of 21 hrs (range 8-36 hrs). All treated animals survived for more than 72 hrs, a highly significant difference, $p < 0.001$. After blood had been reinfused and isoproterenol administered, arterial pressure was reduced to 35mm Hg; simultaneously, it was elevated to 87 mm Hg in control animals. In isoproterenol treated animals the pH was elevated from 7.22 to 7.34 in the hour after reinfusion, $p < 0.005$. Thirteen identically treated, unbled control animals, five of whom received isoproterenol, survived permanently without significant change in pH. Pressure fell from 96 to 39 mm Hg after isoproterenol in the control animals. A significant increase in O_2 uptake occurred in the 60 min following reinfusion of blood in those animals treated with isoproterenol when compared to the untreated controls, $p < 0.001$. These observations provide additional evidence that blood pressure may be a totally invalid index of the effectiveness of circulation during shock. In confirming previous studies in dogs, and more recently in patients, these experiments invite further study of isoproterenol as a potentially useful drug for reversal of advanced circulatory shock. Supported by USPHS grants HE-07811 and HE-05570 and The John A. Hartford Foundation.

A COMPARISON OF OVERALL AND TISSUE OXYGEN CONSUMPTION RATES WITH AGING. A. Kurt Weiss and Robert J. Cossey*. Univ. of Okla. Med. Ctr., Oklahoma City, Oklahoma.

There is general agreement that the basal metabolic rate of man declines with age. This is not invariably true of the laboratory rat whose minimal resting oxygen consumption rate, whether based on surface area or on an exponential function of body weight, increases after the first year of life. In contrast, the surviving oxygen consumption rates of 4 tissues, expressed on a weight basis, taken from rats between the ages of 1 month and more than 2 years, decline. The slopes of the regression lines of the linear least square fit for the oxygen consumption rates are -.009 for liver, -.016 for kidney, -.014 for brain, and -.017 for diaphragm. The reasons for the diverse trends in the intact animal and in some tissue slices are not immediately apparent. Perhaps slices from tissues other than those studied may make a significant contribution to the overall metabolic increase which is observed in the intact animal. Conceivably the units in which the data are expressed may not properly convey the existing metabolic pattern. It is also possible that some functional aspects may progressively gain importance in the intact rat with aging, but that these aspects are not reflected in the tissue preparations.
(Supported by grants from NIH).

RESISTANCE OF THE QUAIL, COTURNIX JAPONICA, TO OXYGEN TOXICITY: ROLE OF FOOD INTAKE. H. S. Weiss, R. A. Wright,* E. S. Kreglow,* and J. F. Pitt,* Department of Physiology, The Ohio State University, Columbus, Ohio 43210.

The extended survival time of chickens in 100% O_2 at one atm (OAP) (Nature, 208:1003, 1965) could be an isolated phenomenon or a more general function of the structural difference between avian and mammalian lungs. To test the species concept, quail were exposed to OAP in sealed, recycling, polyvinyl chambers in which CO_2, temperature and relative humidity were controlled. In four 14-day trials involving 32 sexually mature Coturnix, only 13 birds died (41%), all between the 5th and 10th day. Survivors were generally in good health; several were maintained for an additional 10 days in OAP without signs of deterioration. All of a group of mice exposed simultaneously died within 13 days, half by the 5th day, as is typical of rodents in our system. The quail as the chicken thus appears considerably more resistant to OAP than small mammals, tending to support a protective role for the birds' semi-rigid continuous-air-capillary pulmonary system. Quail which succumbed virtually ceased eating 3-4 days before death, resulting in a 40-50% loss of body weight by the time death ensued. Force feeding reduced this weight loss by half but did not improve the mortality pattern. Inanition thus does not seem to be important as a cause of mortality of birds in OAP. Apparently OAP inhibits appetite factors more than the digestive processes which follow ingestion of food. Supported by grants from NASA and NIH.

VIBRATION EFFECTS ON THE ENDOCRINE SYSTEM OF RATS. Weltman, A. Stanley, Arthur M. Sackler*, Joseph Gennis* and Paul Steinglass*. Lab. for Therapeutic Research, Brooklyn College of Pharmacy, Brooklyn, New York.

Previously, we reported that in a 3 week study of male Wistar rats, vibration stress administered daily for 15 and 30 minutes stimulated adrenal activity and inhibited body growth, food consumption and gonadal function. The frequency of nose-bleeds during the vibration sessions and abdominal adhesions and pleural lesions at autopsy suggested the need of increasing the thickness of the protective foam-rubber sidings from 1 cm to 2.5 cm. Two test groups with appropriate controls were now subjected to similar peak acceleration forces of 2.1 g for 1 hr periods administered daily for 7 and 21 days. The reciprocating shaker produced a horizontal amplitude of 4.6 cm and a frequency of 283 cpm. Parameters studied involved alterations in body weights, urinary steroids, adrenal ascorbic acid, total leukocyte counts, food consumption, O_2 consumption, fecal elimination and the endocrine and associated organs (adrenal, thyroid, pituitary, testes, seminal vesicles, thymus, spleen and liver). Despite the absence of visible physical and pathological trauma, the findings indicated that vibration induced significant and/or pronounced decreases in body weights, body weight gains, food utilization and fecal elimination patterns. The adrenal weights and adrenal ascorbic acid levels were significantly or markedly increased, accompanied by comparable weight reductions of the thymus, spleen and thyroids in both test groups while gonadal changes were not pronounced. The heart weights were significantly lowered in the one week stressed rats. The present vibration study again demonstrated stimulated adrenal function and inhibition of body growth, food consumption and food utilization. Indications of some acclimatizations to vibration stress were noted.

GLYCINE AND POSTSYNAPTIC INHIBITION IN CAT SPINAL CORD. R. Werman, R. A. Davidoff*, and M. H. Aprison, The Institute of Psychiatric Research and V.A. Hospital, Indiana Univ. Med. Center, Indianapolis, Indiana.

Extracellular iontophoresis of glycine during intracellular recording from neurons in cat lumbar cord enabled us to demonstrate reversible and rapid inhibitory effects in all motoneurons impaled. Minimal amounts of iontophoretic current (<50nA) were frequently able to block invasion of the SD region leaving an IS spike. The size of the presynaptic volley did not change. Concomitantly, a hyperpolarization of 0.5 to 8mV was noted when K citrate electrodes were used for recording. Following intracellular iontophoresis of Cl^- ions, glycine produced depolarization. A marked decrease in membrane resistance (up to 80%) accompanied these changes. EPSP's and IPSP's recorded in the same neurons showed a marked decrease in amplitude and time constant. The threshold to direct stimulation of the cell by depolarizing current was also increased. All of the above effects were reversible and related to the dose of glycine applied to the cell. Interneurons were also inhibited by glycine. A close similarity between the actions of glycine and the naturally occurring postsynaptic inhibitory transmitter was demonstrated. This conclusion is strengthened by the pattern of distribution and the high concentration of glycine in cat spinal cord (Life Sci. 4: 1075, 1965) and the decrease of glycine associated with loss of spinal interneurons (Physiologist, this issue).

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CIRCULATORY CHARACTERISTICS OF THE TRANSPLANTED BRAIN
R.J.White, M.D.,Ph.D., M.S.Albin*, M.D., M.Sc.(Anes.)
G.E.Locke, M.D., E.Davidson*, M.D. Section of Neurosurgery, Cleveland Metropolitan General Hospital and Western Reserve University School of Medicine, Cleveland, Ohio.

To date ten isolated canine brains have been successfully transplanted to the vascular environment of a surgically created neck pouch in large recipient animals. Serial x-rays were made of the isolated brain following the injection of 50% Hypaque into the recipient carotid artery supplying the isolated brain vasculature. Opacification of the Circle of Willis and its major branches was repeatedly demonstrated for as long as three days after transplantation. Estimations of cerebral blood flow (electromagnetic flow meter and direct measurement of cerebral venous return) demonstrated average values of cerebral blood flow in the range of 30 cc's per 100 gram of brain per minute at an average intracerebral temperature of 32° C. Viability of the transplanted brain was attested to by the presence of electrocortical activity and significant oxygen and glucose uptake. The eventual removal of the isolated brain transplant was necessitated because of blood loss due to the use of an anticoagulated state in the recipient.

Supported by NIH Grant NB 03859

EFFECTS OF GRADED VAGAL AND SYMPATHETIC STIMULATION ON THE LEFT VENTRICLE IN DOGS STUDIED WITHOUT THORACOTOMY. John C. P. Williams,* Russell A. Vandenberg,* A. Clark Nolan,* and Earl H. Wood. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The inotropic effects on the left ventricle of stimulation of the cardiac autonomic nerves were studied, under conditions such that changes secondary to chronotropic effects or alteration of left atrial dynamics were controlled or eliminated, in anesthetized dogs (morphine-pentobarbital) with acute heart block (Fed. Proc. 23:413, 1964), cardiac denervation, electronically induced atrial fibrillation, and controlled ventricular rates. Bipolar electrode catheters in the right atrium and right ventricular outflow tract were used to regulate the sequence of atrial and ventricular systoles or to produce atrial fibrillation by rapid, paired-pulse stimulation of the atrium. The spontaneous atrial rate on cessation of cardiac pacing and the height of atrial cannon A waves during synchronous atrioventricular driving provided a measure of the degree of vagal (bilateral cervical) and sympathetic (left anterior cardiac nerve) stimulation. When atrial fibrillation was established, mild degrees of cardiac sympathetic stimulation (6 v, 2-3 cps) produced marked changes in cardiac output, determined from indicator-dilution curves, and in systemic and left ventricular pressures. Conversely, graded vagal stimulation (6 v, 5-20 cps) had little effect on these parameters. Minimal increases in aortic pressure and cardiac output were sometimes recorded on cessation of the highest level of vagal stimulation in some dogs. It is concluded that, by comparison with the marked positive inotropic effect of sympathetic nerve stimulation, a negative inotropic effect of the vagus nerves on the left ventricle if it exists is small. (Supported in part by NIH grants H-3532 and FR-0007 and AHA CI 10.)

CHLORIDE AND POTASSIUM DEPLETION AND INTRACELLULAR pH.
Archie F. Wilson* and Daniel H. Simmons. Cedars-Sinai Medical Research Institute and Departments of Physiology and Medicine, University of California Medical Center, Los Angeles, California.

Hypochloremic, hypokalemic alkalosis was produced in eleven dogs on a low electrolyte diet by five daily infusions of 11 mm/Kg of .335 M Na NO_3. Whole body intracellular pH (pH_i) was measured by the distribution of C^{14} DMO while using ^{36}Cl for measurement of extracellular volume and ^{3}HOH for measurement of total body water. Mean control pH_i was 6.96; pH_i in the same animals after induction of alkalosis was 6.75. Extracellular volume fell about 25%. Infusion of 11 mm/Kg of .335 M NaCl for two days without provision of K corrected the hypochloremia, the extracellular alkalosis, and the extracellular volume depletion. There was an additional excretion of K and a small rise in plasma K but no further change in pH_i or extracellular volume. Two additional days of NaCl infusion resulted only in further reduction of extracellular pH with little or no change in pH_i. Restoration of K to the diet resulted in return to control intra- and extracellular pH. The data fit the hypothesis that pH_i is inversely related to plasma K and that extracellular pH is related to plasma chloride concentration.

EFFECT OF ERYTHROPOIETIN ON THE PRIMING OF RNA POLYMERASE BY DNA-PROTEIN EXTRACTED FROM MOUSE SPLEENS.
J. Winkert, F. Wilkinson, E. Winkert* and M.A. Castellucci. State Univ. of N.Y. School of Med., Buffalo, N.Y.

The stimulatory effect of erythropoietin (ESF) on red cell development was blocked in vivo by actinomycin D, an inhibitor of RNA synthesis (Keighley and Lewy, 1966). The direct action of ESF on isolated marrow cells was studied by Krantz and Goldwasser (1965) who observed the early production of messenger type RNA 15 minutes after addition of ESF to the culture. To determine whether ESF can exert a direct effect on RNA synthesis in a cell free system a study was made of the action of ESF on the priming of RNA polymerase by mouse spleen deoxyribonucleoprotein (DNAP).

DNAP was isolated from mouse spleen by a modification of the method of Messineo (1964). RNA polymerase was isolated from M. lysodeikticus by the method of Nakamoto et al (1964). ESF was isolated from human urine by precipitation with ethanol followed by filtration of the dissolved precipitate through sephadex G-200. After separation of the proteins by acrylamide disc electrophoresis ESF was eluted from the disc by grinding the gel in saline with mortar and pestal. Assays of RNA polymerase and priming activity of DNAP were made by following the procedure of Fox et al (1964).

Spleen DNAP had only 3% of the priming activity of pure DNA. One unit of ESF (60 units/mg protein) per ml lowered the priming activity of DNAP to 89.4±3.0 % of what it was without ESF. An equal amount of human chorionic gonadotrophin had no effect. ESF may act by blocking regulator genes.

MODIFICATION OF HYPERBARIC OXYGEN TOXICITY BY EXPERIMENTAL VENOUS ADMIXTURE. P. M. Winter*, R. K. Gupta*, A. Michalski*, and E. H. Lanphier. Depts. Physiol. & Pathol., State Univ. of New York at Buffalo and Anesthesia Labs. of Harvard Univ. at Mass. Gen. Hosp., Boston.

Findings of Bean and others suggest that CNS effects contribute to lung damage in high pressure O_2 exposure. If so, the extent of damage should be modified by measures which limit elevation of arterial PO_2. In 10 dogs under pentobarbital anesthesia, venous admixture was produced by anastomosis of the inferior vena cava to the right inferior pulmonary vein, with subsequent ligation of the cava above the anastomosis. Two or more weeks after surgery, mean arterial values breathing air at 1 atm abs were: PaO_2 40.7 ± 4.79; $PaCO_2$ 26.2 ± 2.8; pH 7.47 ± 0.24. The shunted dogs and 10 controls were placed individually, awake and unrestrained, in a sealed, glass-walled cage ventilated with 99 - 100% O_2 at 10 l/min at 2.5 atm in a hyperbaric chamber. Convulsions occurred in control animals at 5.1 ± 2.7 hr. Upon convulsion, pressure was reduced to 2 atm. Shunted dogs had no convulsions and were exposed to 2.5 atm for 5 hr and then to 2 atm until death. Mean survival times: shunted 21.09 ± 2.21 hr; control 12.52 ± 4.91 hr; $P = < 0.001$. Lung surfaces in both groups showed patchy purplish discoloration. Microscopic examination showed patchy atelectasis, congestion, edema, and emphysema with destruction of respiratory bronchioles. All changes were more marked in the experimental group. Relative hypoxemia greatly prolongs survival in hyperbaric oxygen exposure. It does not prevent lethal lung damage but may delay its development. (Supported in part by ONR Contract Nonr-969(03) and Training in Anesthesia NIH 1T1GM 1273.)

Uptake of Fe^{59} by Rabbit Reticulocytes and Erythrocytes Related to Na-K ATPase Activities. W. C. Wise* and J. W. Archdeacon. Dept. of Physiology and Biophysics, University of Kentucky, College of Medicine, Lexington, Kentucky.

Fe^{59} uptake by rabbit reticulocytes was reported recently to be energy and sodium dependent, ouabain sensitive and depressed by potassium (Fed. Proc. 25 (2): 567, 1966). In present experiments rabbit reticulocytes were pulse labeled with Fe^{59} and sodium ion was found essential for movement of iron from the stroma to the cell interior (hemolysate). Reception of Fe^{59} by the stroma apparently was unrelated to sodium. Potassium inhibited movement of Fe^{59} from the stroma to the cell interior without affecting attachment. The K_m and V_{max} for Fe^{59} uptake by the rabbit reticulocyte in the presence and absence of sodium ion were determined. V_{max} values were found to be identical, but K_m values without sodium were higher than with sodium. Uptakes of Fe^{59} by rabbit and cat reticulocytes and erythrocytes were compared to stromal Na-K ATPase activities. The order of uptake of Fe^{59} was: rabbit reticulocytes > cat reticulocytes > rabbit erythrocytes > cat erythrocytes. Quantification of Na-K ATPase followed a similar sequence indicating a possible relationship between this enzyme system and iron uptake by the cell.

EFFECTS OF GLUCOSE, PHLORIZIN, AND PARATHYROID EXTRACT (PTE) ON RENAL TUBULAR TRANSPORT OF PHOSPHATE IN THE CHICKEN. Robert A. Wolbach and Roger K. Ferguson*, Department of Physiology, University of Utah College of Medicine, Salt Lake City, Utah.

Glucose, phlorizin and PTE (Lilly) were infused into chickens to determine their effects on phosphate excretion and renal tubular transport of phosphate. Exogenous glucose had no effect, phlorizin decreased phosphate excretion and PTE increased phosphate excretion. Plasma glucose concentrations always exceeded 200 mg%, even in the fasting state. For this reason, any influence which glucose may have on phosphate transport may be saturated by endogenous glucose. If glucose and phosphate are reabsorbed competitively, phlorizin may increase phosphate reabsorption as an indirect consequence of its inhibition of glucose reabsorption. Frequently PTE increased phosphate excretion by more than one filtered load. This implies that PTE enhances phosphate secretion, rather than simply blocking reabsorption of filtered phosphate. Since phlorizin did not block this action of PTE, the suggestion that phlorizin influences phosphate reabsorption and not phosphate secretion is further substantiated.

Aided by Grant AM 06973 and Training Grant GM 8407, National Institutes of Health.

ELECTRICAL RESPONSES FROM THE EYE OF O. LACTEA, A PULMONATE SNAIL. M. L. Wolbarsht and H. L. Gillary*, U. S. Naval Medical Research Institute, Bethesda, Md.

The eye of the land snail, Otala lactea Müller, appears to be similar in structure to that of Limax maximus, as described by Smith (Bull. Mus. Comp. Zool. 48, 233, 1906). The eye is at the tip of the long tentacle. Light microscopy has revealed only one neural cell type in the retina, with no interconnections between the separate photoreceptors. The axons of the photoreceptors form a discrete, unbranched optic nerve, approximately a centimeter long, which connects to the optic lobe of the brain. Recordings from the eye with wick electrodes showed a slow cornea-negative ERG in response to light. The ERG was similar in shape to that recorded from the squid eye (Hagins, CSHSQB 30, 403, 1965). However, in the snail eye, the latency of the ERG (0.5 sec to 1.5 sec at 10°C) was considerably longer than that of the squid eye (0.2 sec at 10°C). This suggests a relatively slow, chemical mechanism in the snail eye preceding the generation of electrical activity. The latency varied inversely with temperature. A burst of spike activity in the optic nerve started concurrently with the rise of the ERG, after which the nerve activity continued at a steady lower level until illumination ceased. No spontaneous spike activity was seen in the dark. Neither the ERG nor the nerve activity showed an "off" effect. This would be expected from such an anatomically simple eye. Preliminary spectral measurements indicate a single-moded action spectrum with its peak near 480 nm. (From the Bureau of Medicine and Surgery, Navy Department, Research Task MR 005.13-1500.05.)

CONTINUOUS INTRAVASCULAR MEASUREMENT OF BLOOD GAS PRESSURES BY MASS SPECTROGRAPHY. Sabbo Woldring* and Guy Owens. Roswell Park Memorial Institute, Buffalo, New York.

The mass spectrometer analyzes extremely minute amounts of gas. Such quantities are easily collected from gaseous mixtures or dissolved gases by drawing the gas molecules into the evacuated space of the spectrometer analyzer through a permeable membrane. The amount of gas that thus enters the mass spectrometer per unit of time, depends upon the partial pressure of the gas and upon the diffusion characteristics of the membrane. In the present study a rubber membrane was stretched over the tip of a 20 gauge polyethylene tubing (O. D. 1.1 mm, I. D. 0.4 mm, length 1 m) and tied with a silk ligature. The cannula was directly connected to the analyzing section of the mass spectrometer. Calibrations showed excellent stability and linearity; response time was determined by membrane permeability, with average time constant 3 sec. Membrane characteristics were different in wet and dry environment and were susceptible to changes in temperature. Continuous recordings of arterial carbon dioxide and oxygen pressures will be shown, measured simultaneously in the aorta of an anesthetized cat subjected to various respiratory maneuvers.
Supported by NIH Grant no. GM 09034.

EFFECTS OF RATE OF CHANGE OF SKIN TEMPERATURE ON SWEATING. *Robert D. Wurster**, *Robert D. McCook* and *Walter C. Randall*. Department of Physiology, Loyola University Stritch School of Medicine and the Graduate School, Chicago, Illinois.

In previous experiments, abrupt cessation of sweating was observed when subjects were shifted from high (63°C) to low (18-21°C) ambient temperatures. Tympanic membrane temperatures (Ttm) remained elevated, while skin temperatures (Ts) rapidly declined. The rate of decline in Ts from approximately 38 to 36°C is believed to be an important thermoregulatory drive. Experiments were designed in which a nude male subject was maintained at a Ta of 60°C for 20 minutes, and then shifted rapidly (approximately 1 sec) into Ta of 36°C. The latter ambient temperature was selected because the subject maintains a moderate sweat rate and distribution under static exposure to this environment. Skin, rectal, oral, and tympanic membrane temperatures were measured; mean skin temperature (Tms) was continuously electronically computed. Sweating was measured by the starch iodine technique, as well as by continuous multichannel resistance hygrometry. At the moment of transition (hot to "cool" chamber), sweating quickly decreased during the rapid change in Ts, but when the rate of change in Ts approached zero, the sweat rate increased despite altered Tms and Ttm. It is concluded that rate of decline in Ts is an important component in peripheral drive to control mechanisms mediating sweating. It is suggested that equations describing sweat gland regulation include dTs/dt. *(Supported by NIH Grant HE 08882.)*

ONTOGENESIS OF SODIUM PUMP IN THE VENTRICULAR MYOCARDIUM. Billy K. Yeh*, Brian F. Hoffman and David Spiro*. Departments of Pharmacology and Pathology, Col. of Physicians & Surgeons, Columbia U., New York, N. Y.

A histochemical method for the localization of sodium ions at the electron microscopic level was utilized in a study of chick heart embryogenesis. This technique has permitted both localization and comparison of the relative amounts of sodium ion present in cardiac tissue during embryonic development. Ventricular myocardium from chick embryos from 4 to 19 days of age was fixed in 1.5% osmium tetroxide in an acetate buffer containing 1.7% potassium antimonate and dehydrated in ethanol. Thin epon embedded sections of these specimens of ventricular myocardium were studied. It was found that the density of sodium antimonate precipitate was a function of the age of the embryo; more precipitate was observed in younger embryos. A considerable decrease in sodium content in the nuclei and cytoplasm of myocardial cells was apparent between 6 and 11-day old embryos. Little sodium was found after 11 days of age. In all different aged embryos nuclei had a higher sodium antimonate precipitate density than cytoplasm. These results suggest that the genesis and maturation of the function of sodium pump takes place during embryonic development of the organism and that an important phase of the initiation of this process in heart occurs between 6 to 11 days of embryonic chick development, i.e., during and immediately after the period when the aortic and pulmonic valves are formed and complete separation of right and left ventricle takes place. (Supported by a grant from the New York Heart Association, a USPHS general research support grant and USPHS research grant HE-5906.)

THE ROLE OF LIPOPROTEINS AND PHOSPHOLIPIDS IN HUMORAL TRANSMISSION. Wei Young, Dell Goldsmith*, Robert Hotovec*, and John Gofman*. Bio-Medical Division, Lawrence Radiation Laboratory, University of California, Livermore, California.

A series of blood lipoproteins, occurring in man and other animals, has been extensively characterized in this laboratory. Pathologic derangements in the control of blood levels of certain classes of these lipoproteins have been studied in connection with radiation lethality, several hereditary metabolic disorders, in diabetic acidosis, and in atherosclerosis. Yet, the physiologic role of essentially all the lipoprotein classes remains poorly understood. This study is directed toward understanding one possible physiologic activity of lipoproteins, namely, an effect upon humoral transmission. Our early work (Biochem. Biophys. Acta 64; 60-64, 1962) established a method for quantitative assay of acetylcholinesterase (AChE) activity in the frog vagal heart preparation. This system has now been utilized in a study of effects of lipoproteins upon humoral transmission. The addition of either low-density lipoproteins or high-density lipoproteins of human or rabbit origin to the perfused vagal heart preparations results in a decrease in AChE activity. The serum proteins, freed of lipoproteins ultracentrifugally, increase the AChE activity. In either case, for proteins or lipoproteins, the quantitative studies indicate non-competitive effects. Ultrasonically dispersed phospholipids (beef brain origin) decrease AChE activity non-competitively in the vagal heart preparation. Sphingomyelin is of especial interest in that competitive inhibition of AChE activity is observed.

THE EFFECT OF ESTRADIOL, GROWTH HORMONE, AND INSULIN ON NUCLEIC ACID LEVELS IN THE UTERUS OF THE HYPOPHYSECTOMIZED-OVARIECTOMIZED RAT. E. B. Yudkowsky* and Ardis J. Lostroh, Hormone Research Lab., Univ. of Calif., Berkeley.

Female rats were ovariectomized at 60 days, hypophysectomized at 67 days, and sacrificed at 77 days of age. In appropriate groups, single daily subcutaneous injections of bovine growth hormone (100 μg) and/or estradiol (5 μg) were initiated on days 68 and 73, respectively. In addition, alloxan monohydrate (13 mg/ 100 g body wt.) was administered to 8 of the 12 groups on day 71 and blood sugar determinations were made 48 hours later; animals with glucose levels of 300 mg% and above were adjudged diabetic; insulin (0.5 U/day) was administered to 4 of the 8 groups of diabetic rats from day 72 to sacrifice. Uteri were removed and nucleic acids extracted; RNA was determined using the orcinol reaction, DNA using the diphenylamine reaction. Estradiol effected increases of approximately 150% in both RNA and DNA in doubly-operated, and in doubly-operated diabetic rats. Growth hormone enhanced the effect of the estradiol (30% increase in RNA, none in DNA), but alone had no effect on nucleic acid content. In animals made diabetic with alloxan, no effect of growth hormone could be demonstrated unless insulin was administered. There is no indication from the data that insulin is required in order for estradiol to stimulate the synthesis of nucleic acids in the uterus of the ovariectomized rat. (Supported in part by grants from the U. S. Public Health Service, AM-6097 and DE-2008).

STUDIES OF THE ANTERIOR HYPOTHALAMUS OF THE OPOSSUM. G.A. Zeballos*, M.B. Wang*, and K. Koizumi, Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, New York.

Histological and electrophysiological techniques were used in studying the hypothalamus of the Virginia opossum (Didelphis virginiana). Staining of neurosecretory materials by the Gabé method (fuchsin paraldehyde) revealed that cells containing Gabé-positive granules were situated not only in supraoptic and paraventricular nuclei but also in columns extending between these two nuclei. Another group of "neurosecretory cells" was found in the median eminence. Many of these "neurosecretory cells" were located close to blood vessels, and in these aggregates some bipolar cells with many Gabé-positive granules were also found. The response of the hypothalamo-hypophyseal system of the opossum to hydration and dehydration was studied histologically. The increase and decrease of Gabé-positive materials observed in these conditions were similar to that seen in the rat and cat. A stereotaxic map of the opossum hypothalamic nuclei was constructed for use in recording from the cells of this area. Electrical activity of single neurons in supraoptic and paraventricular nuclei as well as in the preoptic area of the hypothalamus was recorded by means of a steel microelectrode as previously used in cats (J. Neurophysiol., 1964, 27:878). The rate of discharges of these cells in opossums anesthetized with chloralose-urethane or chloralose alone was similar to that found in cats (5 to 10 per second). Osmotic stimuli and other chemical agents affected the rate of discharge of these cells. The solutions were injected into a lingual artery to avoid any embarrassment of circulation to the hypothalamic area. (Supported by Public Health Service Grant (NB-00847-11) and (5 T1 GM 968-03)

SUPPRESSION OF CIRCADIAN BUT NOT STRESS-INDUCED PITUITARY-ADRENAL ACTIVITY WITH INTRACEREBRAL DEXAMETHASONE. E. Zimmermann and V. Critchlow. Dept. of Anatomy, Baylor Univ. Coll. Med., Houston, Texas.

In previous studies, sc injection of 100 μg/kg dexamethasone 21-PO_4 (Dex) at noon into adult female rats caused total suppression of the diurnal peak in plasma corticosterone (Cpd B) levels while leaving intact the 15-min steroid response to 3-min ether or immobilization stresses. To examine further this dissociation of pituitary-adrenal functions, agar pellets, each containing 2.5 μg Dex, were bilaterally placed into the anterior (AH) or posterior (PH) hypothalamus, midbrain (MB) or deposited sc (6-7 rats per location) between 7-9 a.m. At 4:30 that afternoon all but 2 animals receiving Dex implants in the brain showed marked suppression of peak non-stress plasma Cpd B levels (0-10 μg%) while rats with sc Dex or control AH and PH agar implants had Cpd B levels not differing from those of untreated controls (66± 12). However, all animals showed an unimpaired 15-min steroid response to the 3-min ether and initial bleeding procedure. In a similar study using 1 μg Dex pellets, 8/10 rats with AH, 7/10 with PH, 6/9 with ventral thalamus, 4/10 with MB, and 1/10 with amygdala implants showed suppression ($P < 0.05$) of peak circadian Cpd B levels, while 10/10 with Dex pellets in pituitary and 10/10 with AH agar implants had normal (64± 8) high levels that afternoon. Again, in no location did Dex suppress the response to ether stress. These observations following intracerebral dexamethasone support the previous suggestion that corticoid feedback preferentially suppresses circadian rather than stress-induced ACTH release and further implicate the brain, especially the hypothalamus, as the site of this feedback action.

LABELED MACROAGGREGATED ALBUMIN (^{131}I-MAA) FOR STUDYING PULMONARY BLOOD FLOW DURING THE ONSET OF RESPIRATION. Helen Z. Zweizig*, David E. Kuhl* and George Polgar. University of Pennsylvania, Phila., Pa.

To investigate the distribution of blood flow between newly aerated and non-aerated parts of the lung, ^{131}I-MAA was injected into the right heart of newborn lambs before the onset of breathing or after one to five breaths. The animals were sacrificed immediately after injection. Relative pulmonary blood flow was estimated from the distribution of ^{131}I-MAA in the lung, determined by scanning and sample counting. Relative aeration was estimated by inspection and radiography using both conventional and soft tissue techniques. Results: (a) before onset of breathing, the distribution of pulmonary blood flow was uniform (one lamb); (b) after the onset of respiration, the distribution of pulmonary blood flow depended on the extent of aeration: with no aeration, blood flow distribution remained uniform (one to five breaths in three lambs), with minimal aeration the distribution of blood flow was slightly uneven, in markedly aerated parts of the lung significantly higher blood flow was observed (three to five breaths in four lambs). These results suggest: (1) changes of regional pulmonary blood flow during initial lung expansion in the newborn are topographically related to aeration. (2) ^{131}I-MAA scanning is a useful study method for investigation of these relationships.

SYMPOSIUM

MAN'S PHYSIOLOGICAL RESPONSE TO THE SPACE FLIGHT ENVIRONMENT

Chairman: Charles A. Berry

SOME RESPONSES OF THE CARDIOVASCULAR SYSTEM OF MAN TO THE SPACE FLIGHT ENVIRONMENT by Lawrence F. Dietlein, M.D., NASA Manned Spacecraft Center
Houston, Texas

Orthostatic intolerance to passive tilt has been observed following Mercury and Gemini space flights. This intolerance is characterized by an increased pulse rate and a narrowing of pulse pressure on assuming the erect position. The degree of cardiovascular "deconditioning" as evidenced by cardio-acceleration during postflight passive tilt procedures was generally proportional to the duration of the flight with the notable exception of the 14-day Gemini VII mission. Passive tilt tolerance following this flight was markedly improved over that observed following the preceding Gemini missions lasting more than 2 days. Gemini VII differed significantly from all previous flights in that the crew were unsuited for the greater part of the mission, and their fluid and food intake were more nearly optimal, as was their programmed exercise regimen. Although prolonged weightlessness itself is doubtless a factor in the etiology of the postflight orthostatic intolerance syndrome, multiple factors most certainly are contributory, including thermal loading, dehydration, hypovolemia, relative immobility, and fatigue. Fluid volume studies performed after the 4-, 8-, and 14-day Gemini missions generally revealed a decreased total body hematocrit, diminished red cell mass, and increased pooling of blood in the lower extremities as compared with preflight values. Total blood volumes were diminished following the 4- and 8-day flight, but remained unchanged following the 14-day mission. Plasma volume values were diminished after the 4- and 8-day Gemini flight, but were increased following the 14-day mission, thus compensating for the decreases in red cell mass and resulting in unchanged total blood volumes for the Gemini VII astronauts. Crewmembers exhibited a loss of nude body weight following each mission.

VESTIBULAR EXPERIMENTS IN ORBITAL FLIGHT. Ashton Graybiel. U. S. Naval Aerospace Medical Institute, Pensacola, Florida.

Weightlessness offers a unique opportunity to investigate perception of the upright in the absence of gravitational cues. Our first step in this direction dealt with the role of non-visual factors in the perception of a luminous oriented line stimulus in darkness. A monocular goggle device permitted subject or experimenter to rotate a luminous line about its center, and a digital readout indicated its angle relative to the goggle. The astronaut's task was to set the line parallel to the horizontal axis of the spacecraft and thus involved a judgment correlating body and spacecraft orientation. Measurements were obtained on four astronauts at different times throughout orbital flight for comparison with pre- and post-flight measurements. These findings are discussed both on the basis of agravic contact cues which presumably influenced the setting of the line and on the basis of previous investigations of perception of the upright, including observations on normal persons and on subjects with bilateral labyrinthine defects exposed to systematic variations in the visual and force environments. Measurements were also obtained, pre- and post-flight, on the magnitude of the compensatory counterroll of the eye when the astronauts were tilted in the frontal plane, a test of otolith function. Significant differences were not observed.

HEMATOLOGICAL CHANGES IN SPACE FLIGHT. Scott N. Swisher and Craig Fisher. Univ. of Rochester School of Med. and Dentistry and Manned Space Craft Center, Rochester, N.Y. and Houston, Texas.

More detailed studies of hematological changes exhibited by astronauts were undertaken after it was appreciated that a slight decrease in hematocrit was observed in a number of early flight crews. Studies have been limited to pre- and post-flight observations under severe operational constraints that limit control of the observational situation. Standard methods of red cell mass measurement utilizing Cr^{51} were employed, and estimates of red cell life span were also derived in some instances. (in collaboration with Dr. Philip Johnson). Post-flight neutrophilic leukocytosis or a mild leukemoid reaction with little increase in immaturity has been seen commonly. These data suggest that leukocytic mobilization may occur in response to these stresses. Decreases of red cell mass of 7% and 19% were encountered in G.T. VII studies which have been the most satisfactory and comprehensive to date. This was accompanied by a slight rise in osmotic fragility and mean corpuscular red cell volume. There was concordant evidence of decreased red cell life span and splenic uptake of Cr^{51}. Interpretation of these data as indications of a hemolytic process of unknown mechanism is difficult in view of the complex environmental changes to which the pilots were exposed. The role of the oxygen atmosphere, severe immobilization and weightlessness deserve consideration and further study, as do other possible interpretations of these observations.

MINERAL AND NITROGEN BALANCE OBSERVATIONS ON THE GEMINI-VII FOURTEEN DAY ORBITAL SPACE FLIGHT. G. Donald Whedon and Leo Lutwak, National Institute of Arthritis and Metabolic Diseases (NIH), Bethesda, Maryland, and Graduate School of Nutrition, Cornell University, Ithaca, New York.

In an intensive collaborative effort with staff of Manned Spacecraft Center, metabolic observations were made of the effects on two astronauts of the several complex influences of Gemini space flight, including weightlessness, confinement, moderate to vigorous physical activity, slight hyperoxia, and low atmospheric pressure. Constant dietary intake of many elements and continuous collection of all excreta (plus periodic sweat collections) were carried out at Cape Kennedy for ten days before and four days after the December, 1965, fourteen day flight. Dietary intake and urine collections during flight were more difficult to control. One astronaut showed an increase in urinary calcium similar in pattern to that seen in bed rest-immobilization studies but to a lesser degree; negative shift in calcium balance in both astronauts was of borderline significance. Markedly negative phosphorous and nitrogen balances occurred. These first metabolic observations in space demonstrate the feasibility of such studies, predict the possibility of more definite derangements in longer flights, and indicate the need for such assessment by additional ground-based and in-flight metabolic studies under well controlled conditions.

SYMPOSIUM

PHYSIOLOGY AND BIOCHEMISTRY OF MOLLUSCS

Chairmen: J. W. Campbell and A. W. Martin

(Cosponsored by Division of Comparative Physiology, American Society of Zoologists)

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Molluscan Respiratory Pigments - K. R. H. Read

Excretion in Molluscs - A. W. Martin

Intermediary Nitrogen Metabolism in Molluscs - J. W. Campbell

Lipid Metabolism in Molluscs - G. A. Thompson, Jr.

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THE PERFECT MIXERS IN SERIES MODEL FOR FITTING INDICATOR DILUTION CURVES. E. J. Schlossmacher, H. Weinstein, S. Lochaya and A. B. Shaffer (intr. by L. N. Katz). Illinois Institute of Technology and Michael Reese Hospital and Medical Center, Chicago, Illinois.

The perfect mixers in series model represents the dispersion of a sudden impulse of tracer as it passes through a series of equal-sized perfect mixers. This approach is often used in modeling the mixing in chemical reactors. Resemblance of the resulting response curve to an indicator dilution curve was noted by Sheppard in 1954. Weinstein et al. in 1964 used this model to fit normal veno-arterial indicator dilution curves. It is shown that other mathematical treatments of indicator dilution curves, such as the gamma variate, the theoretical curves of Evans, and the forward triangle method can be expressed in terms of the perfect mixers in series model equations. The lagged normal density distribution is also shown to be related. Simple curve measurements derived from the mixers in series model equations yield primary curve area and first moment, as well as an "objective" appearance time. Using, for example, a five mixer model to fit the curve,

$$\tau = 1.43W,$$

where τ is the first moment and W is the width of the curve at 68.5% of its peak height. Then,

$$\text{area} = 1.025 \times \text{peak height} \times \tau,$$

$$\text{model appearance time} = \text{peak time} - 4/5\,\tau.$$

Such measurements applied to curves obtained in man, using a four or five tank model, showed good agreement with results found when using the Stewart-Hamilton method and the observed appearance time.

NOTES