ABSTRACTS
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HYPERTENSION

The blood volume was measured before and during treatment with guanethidine in 12 patients with severe hypertensive disease. In all instances, the blood volume increased from 80 to 750 ml. in a 7 to 21 day period. In eight of the 12 patients there was a simultaneous increase in weight. The increase in weight and blood volume is attributed to the retention of sodium and water incident to guanethidine therapy. As a rule, the fluid retention could be satisfactorily controlled by simultaneous treatment with diuretics.

Rakita


Nortropine and norpseudotropine both had hypotensive activity in the renal hypertensive rat. The effect of the latter was significantly greater. The duration of action was considerably longer with norpseudotropine. Slight hypotensive action was observed with norpseudotropine in normotensive animals, whereas nortropine was inactive. In normotensive, unanesthetized dogs norpseudotropine produced a decrease in systolic and diastolic pressures and a reduction in the heart rate. Nortropine in these animals caused a slight increase in the blood pressure. The inhibitory activity of norpseudotropine on the carotid occlusion pressor reflex was much greater with norpseudotropine. Inhibition of epinephrine pressor response was twice as great with nortropine as with norpseudotropine. Both preparations had a sedative effect; it was greater with nortropine. In addition, a mild to moderate hypothermia occurred with both preparations. The utilization of these preparations in patients with hypertension is discussed, and it is noted that the undesirable degree of sedative effect with the higher doses preclude its full clinical acceptance.

Rakita


The pressor response induced by the renal venous effluent of a kidney grafted to a bilaterally nephrectomized rat has been ascribed by Omae to the secretion of renin. But the present experiments suggest that the apparent secretion of a pressor agent is a consequence of trauma, hemorrhage, and anesthesia. Ordinarily, preparation of the donor rat causes ischemia, indicated by extensive fluctuations in mesenteric artery pressure and by gross changes in the appearance of the kidneys. Under these conditions, the average blood pressure rise in the recipient animal was 15 ± 12 mm. Hg. When the donor's blood pressure was maintained above 80 mm. Hg during the manipulations, the recipient's pressure change was only 3 ± 1 mm. Hg and no pressor.
agent in the venous effluent could be implicated in the kidneys of normotensive and hypertensive donors. Nevertheless the technic is suitable for determining the secretion rate of pressor agents. When the renal artery of a normotensive donor kidney was perfused with saline at 100 mm Hg, and the renal blood supply was interrupted for 10 minutes, an average blood pressure rise of 31 ± 11 mm Hg was observed. The pressor response was similar in hypertensive donor kidneys. With infarction of the donor kidney, the pressor response diminished and there was virtual absence of response when bilateral infarction had occurred prior to the transplant. This is in agreement with Omae’s findings.

**MARCH**


Diabetic patients sustained a smaller increase in blood pressure during the cold pressor test and a greater increase following intravenous injection of angiotensin II than did nondiabetic patients. This was true whether both groups were hypertensive or whether they were normotensive. Hypertensive patients had greater increases than normotensive subjects in response to both cold and angiotensin.

**METABOLIC EFFECTS ON CIRCULATION**


Administration of 0.1 mg. of digitoxin per 100 Gm. of body weight daily for 28 days to rats resulted during the first 3 days in an increase, during the second week in normalization, and during the fourth week in renewed increase of free myocardial glycogen, whereas bound glycogen showed little change. The initial accumulation of glycogen is not considered to be a toxic reaction.

**PATHOLOGY**


There is inadequate information regarding the frequent failure of cardiac resuscitation of arrested hearts. To investigate this problem from a morphologic point of view a systematic study of fine structure of the myocardium by electron microscopy was performed on dog heart undergoing hypoxic arrest at normal and hypothermic temperatures. The dog hearts were perfused with heparinized blood oxygenated by means of a disc oxygenator. Temperature was controlled by a standard heat exchanger. Four groups of animals were studied. In the first, the hearts were perfused at 37 C., exposed to hypoxic arrest for 30 minutes, and then perfused at 37 C. for 30 minutes before sections were taken for study. A second group was exposed to perfusion and hypoxic arrest at 17 C. The third and fourth groups were perfused at 37 and 17 C., respectively, but without hypoxic arrest. Some alteration in fine structure was apparent in all groups. In hearts perfused but not arrested at 37 C, the only consistent change was intracellular edema. In hearts perfused at 37 C. and then exposed to hypoxic arrest for 30 minutes there were striking increases in intracellular edema, festooning of the sarcolemnnal sheaths, loss of large granules in the mitochondria as well as condensation of the matrix, and occasionally condensation of the inner mitochondrial membrane. Nuclei showed peripheral clumping of chromatin. Glycogen granules were relatively abundant. Little change was noted in the sarcomeres aside from distortion by edema. Similar but less pronounced changes were noted after hypoxic arrest at 17 C. and, interestingly, were about comparable to changes in fine structure noted after perfusion at 17 C. without hypoxic arrest.


In a series of 1,500 necropsies on patients aged 70 years or more, heart disease and malignant disease were the major causes of death, each accounting for 21 per cent of the total. Coronary disease was exceedingly prevalent and showed some distinguishing features compared to younger age groups. A striking leveling of the sex incidence was found. The clinical presentation was often atypical and sudden death occurred in 25 per cent. There seemed to be a greater tendency for coronary occlusion to follow shock, however induced. No significant pathologic differences were found in this older age group, and complications such as mural thrombosis, cardiac rupture, aneurysm, and rupture of the interventricular septum or a papillary muscle were similar in incidence to other age groups. Only 30 examples of hypertensive heart failure were found. A total of 12 fatal cases of calcific aortic steno-
sis were seen and in an additional 60 patients, it was an incidental finding. A degenerative etiology of this disorder was thought most likely, since evidence of previous rheumatic carditis was found in only 33 per cent. Only 10 patients died of rheumatic heart disease but the incidence of rheumatic stigmata in the entire series was 4 per cent, including 12 patients with asymptomatic mitral stenosis. Aschoff nodules were found in the myocardium of one patient. There were 10 fatal cases of bacterial endocarditis of which eight were acute. A localized form of amyloid was discovered in 12 cases (11 M, 1 F) and in none did it contribute to heart failure.

GUREWICH


Sections of vessels were obtained from necropsies of 36 cases ranging in age from newborn to 94 years. In addition, a series was obtained from 23 necropsies of children and young adults. Peripheral arteries from the head, neck, viscera, and extremities were examined. An accumulation of ground substance in the arterial media and small foci of calcification of the internal elastic lamina was found in young adults in the large leg arteries and progressively in a wider series of arteries throughout life. No relationship was found to hypertension, Mönckeberg’s sclerosis, or atheromatous formation. A notable quantity of ground substance may be a feature of early intimal development, and of a thickened intima in adult life, and probably the major constituent of an organizing thrombus. Organizing thrombi seemed to be incidental findings at several sites even in young adults, and showed no association with the state of the arterial wall beneath the lesion, the wall being in fact normal, though accumulated mucopolysaccharide was always present. The incidence of atheroma increased with age. Occlusive peripheral artery atheromata were found only in cases where the cause of death was severe atheroma, such as coronary artery disease or myxedema, in which the incidence of occlusive lesions may differ from that in severe generalized atheroma. Elastic tissue is described in all coats of the artery. Longitudinal muscle bundles are almost confined to the popliteal artery, where they may form an essential buttress for a large branching artery subject to unusual external stresses.

GUREWICH

PHARMACOLOGY


Magnesium dependent ATPase activity was found to reside primarily in the nuclear-cell debris fraction. However, some activity was demonstrated in other subcellular components. The magnesium (Mg) + sodium (Na) + potassium (K) dependent G-strophanthin sensitive ATPase was primarily located in the microsomal fraction although activity could be demonstrated in every subcellular fraction. The Na + K activated component was inhibited by G-strophanthin. The Mg activated component of the microsomal enzyme was not affected by G-strophanthin. Strophanthin did, however, slightly inhibit the Mg activated ATPase present in other cellular fractions. The data suggest the possible presence of an inhibitory substance. The problems of cross contamination in the various fractions is indicated and further purification of the enzyme is being carried out.

RAKITA


Patients were satisfactorily anesthetised with thiopentone and suxamethonium for electrical atrial defibrillation. When quinidine was given intravenously (300 mg.) to a refractory patient in the process of recovering from an earlier dose of suxamethonium, he again became paralyzed. Subsequently, observations in six patients receiving intravenous quinidine after recovery from suxamethonium have revealed return of paralysis in two patients, muscular weakness in three, and no effect in one. It is cautioned that the use of quinidine in this manner may cause unexpected respiratory arrest.

NESSON


Thioridazine hydrochloride was found to reduce the heart rate and arterial blood pressure in anesthetized, vagotomized dogs. With smaller doses, administered intravenously, the effects lasted from 5 to 25 minutes. With doses of 10 mg./Kg., however, only partial recovery was observed in some instances up to 140 minutes. After a dose of 10 mg./Kg. there was only partial restoration of the blood pressure to pre-treatment levels; in some instances even as long

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as 140 minutes after administration. In addition, the larger doses resulted in prolongation of the PQ and QT intervals in the electrocardiogram. The drug also prevented the blood pressure alterations due to vagal stimulation and epinephrine when administered prior to either of these procedures. Cardiac arrhythmias secondary to ephedrine administration did not occur when the animal was pretreated with thoridazine. Small doses of the preparation resulted in an increase in femoral blood flow. In frog heart perfusion experiments thoridazine produced a slowing of heart rate and a decrease in the amplitude of contractions. Similarly, in isolated rabbit atria amplitude of contractions was also diminished by the drug. Prior utilization of thoridazine did not modify the positive inotropic and chronotropic effects of epinephrine in these preparations. However, the inhibitory effects of acetylcholine were prevented by the prior treatment of the preparation with thoridazine. The possible mechanisms of action of the antiarrhythmic drugs are discussed.

**Rakita**


Chlorothiazide was administered to male rats that had been fed a potassium-deficient diet, and also to their pair-fed controls. Daily urine collections were carried out on the experimental and control rats before and during administration of chlorothiazide. The drug caused a persistent increase in the daily urinary volume of the potassium-deficient rats, but only a transitory increase in the control rats. The striking increase in the daily urinary volume of the potassium-deficient rats was unaccompanied by an increase in solute output. Chlorothiazide did not affect the urinary potassium loss in the potassium-deficient rats. No significant difference was found between the creatinine clearances of the potassium-deficient rats and their controls, nor did the creatinine clearances differ from those found in separate groups of potassium-deficient rats and controls to which chlorothiazide had not been administered.

It is concluded that potassium deficiency does not interfere with the diuretic effect of chlorothiazide in the rat, but rather enhances it. The findings are consistent with the view that chlorothiazide interferes with sodium reabsorption at a site proximal to that at which free water may be formed and at which complementary reabsorption of sodium takes place during the administration of chlorothiazide. An alternative explanation is that chlorothiazide may enhance the thirst of potassium-deficient rats.

**Kayden**


Quinidine therapy for all patients with atrial fibrillation, except those with complete atrioventricular block, was carried out during a 4½ year period. The results of quinidine therapy in 200 unselected patients who had atrial fibrillation for more than 7 days were presented. All patients were digitalized and given anticoagulants before and during quinidine treatment. Sinus rhythm was restored in 107 patients; it was maintained during hospitalization in 84 and for at least 6 months in 65. The conversion rate was greatest in patients with thyrotoxic heart disease and in those with uncomplicated mitral stenosis, but poor in those with mitral insufficiency. Significant cardiomegaly, marked congestive heart failure and fibrillation of several years' duration, especially when combined, adversely influenced success and increased the risk of complications. Sudden loss of consciousness occurred in 11 patients, all of whom recovered. There were no deaths and only one possible incident of embolism. Bundle-branch block was present in 13 patients prior to quinidine therapy, but no serious toxicity was observed in those patients. The dosage schedule was 0.2 Gm. three times a day on the first day, four times a day on the second day, six times a day on the third day, eight times a day on the fourth day, 10 times a day on the fifth day and then continued at 0.2 Gm. 12 times a day until toxicity or a therapeutic response occurred. Maintenance dosage was 0.9 Gm. to 1.2 Gm. per day. In 17 patients more than 1 week's treatment was necessary for conversion, and sinus rhythm was maintained for at least 6 months in 11 of these patients. Successful restoration and maintenance of sinus rhythm was possible in some patients with a combination of severe congestive heart failure, cardiomegaly, and fibrillation of several years with pronounced clinical improvement.

**Kayden**


The effects on myocardial contractility of vasodilator agents that are produced by direct depression of vascular smooth muscle were studied in anesthetized dogs in which cardiac denervation and ligation of the adrenal vein had been performed. The agents tested included isopropyl arzenol, theophylline, papaverine, khel-
line, and caffeine. There were positive inotropic and chronotropic actions with all these agents. The largest increase in myocardial contraction was obtained with isopropyl arEinol and the minimum with caffeine. The duration of action for all these agents varied from 10 to 17 minutes after a single intravenous dose. The increase in cardiac rate followed the same order of magnitude as was observed with the effect on myocardial contractility. Arterial blood pressure was decreased, the maximum occurring with isopropyl arEinol and the minimum with papaverine. Other vasodilators without specific effect on myocardial contractility included the nitrates, procaine, and nicotine acid. It was pointed out that the increase in coronary blood flow occasioned by the use of vasodilators may do no more than cover the increased needs resulting from the positive inotropic and chronotropic actions of the vasodilators. It was felt that drugs like the nitrates, which produce vasodilatation without the associated positive actions, were in principle, more suited to achieve an amelioration of impaired coronary circulation.

**Rakita**

**ABSTRACTS**


The effects of digitoxin intoxication on the free glyco-gen, esterified fatty acids, phospholipids, and cholesterol of the myocardium were determined. The free glyco-gen increased for the first 2 days and subsequently decreased over the succeeding 3 days so that at the time of sacrifice, 5 days after the initiation of the experiment, there was a significant decrease of the free glyco-gen content of the myocardium. Bound glyco-gen behaved in a similar fashion. Esterified fatty acids were unchanged for the first 3 days and subsequently decreased significantly. Phospholipid levels were unchanged except just before death at which time there was a significant decrease. The cholesterol values were above normal levels except that at death on the fifth day there was a significant decrease. The increase in the myocardial glyco-gen was thought to be due to the therapeutic action of digitalis, whereas the subsequent decrease was related to its toxic action.

**Rakita**

**PHYSIOLOGY**

Alexander, N., and De Cuir, M.: Role of Aortic and Vagus Nerves in Arterial Bar-


The mechanism that eventually restores heart rate to normal during continuous arterial baroreceptor stimulation is not known. One step toward an understanding of this mechanism was to assess the relative contribution of afferent and efferent nerve pathways to the initial reflex bradycardia elicited by a rise of arterial pressure. The amount of reflex slowing at the end of a 10-minute infusion of angiotensin into conscious rabbits was studied before and after sectioning vagus or aortic nerves. A 20 to 30 mm. Hg rise in arterial pressure caused an average decrease in heart rate of 23 per cent in control rabbits, 10 per cent in aortic denervated, 3 per cent in vagus denervated, and 9 per cent after atropine block. These results indicate that the major contribution from afferent pathways to cardiac reflex slowing is through aortic nerves rather than carotid sinus or other afferent nerves. On the efferent side, vagus nerves have more effect on cardiac slowing than does sympathetic nerve inhibition.

**Kayden**


Effects of various drugs on coronary blood flow in dogs were evaluated. Coronary flow was measured by thermostromuhr with femoral vein administration of drugs and by rotameter when given via the anterior descending branch of the left coronary artery. A strain-gage arch sutured to the ventricular myocardium recorded changes in contractility. Eledoisin, a polypeptide first isolated from salivary glands of Eledone and later synthesized, exhibited potent vasodilator properties. It was compared to nitroglycerin, bradykinin, and I-epinephrine in the present study. Eledoisin increased coronary blood flow without change in heart rate or muscular contractility. Bradykinin had a similar effect, but was 100 times less potent. Nitroglycerin acted like Eledoisin and increased blood flow, independent of change in blood pressure. When the dosage of nitroglycerin was raised 100 times, the minimal active dose, heart rate, and myocardial contractility fell slightly. The initial coronary flow increase was followed by a transient fall. The experiments suggest that Eledoisin acted directly on the coronary vascular bed as does nitroglycerin. Further investigation is needed to confirm this point. Epinephrine caused an increase in coronary blood flow and simultaneously en-
hanced myocardial contractility. This occurred even in the absence of change in blood pressure and heart rate.

KALTMAN


In measurements of the permeability of capillaries in situ, diffusion is possible. By injecting a nondiffusible substance (Evan's blue dye) into the arterial supply of an organ and measuring its concentration in the venous outflow, a measure of the degree of dilution is possible. Injection of a diffusible test substance (inulin, sucrose) with the Evan's blue dye, and measurement of the difference in concentration between the diffusable and nondiffusible agents give a measure of loss of the test substance through the capillaries. Loss of the test substance so calculated is not a direct indicator of permeability. An expression between loss of the test substance and permeability is made in the formula P = Q/A × Loge 1/1 - E (P = permeability, Q = blood flow, A = capillary surface area, E = initial extraction of the substance in question). Permeability coefficients for inulin and sucrose varied considerably from organ to organ. Permeability coefficients for inulin were 0 in brain and lungs, 0.26 in the hind limb, 2.9 in the liver, and 14.4 in the kidney. Sucrose permeability coefficients were 0 for brain and lung, 0.74 for hind limb, and 6.6 for liver. The pore model of capillary permeability should result in pronounced deviation of the ratio between the permeability coefficients of sucrose and inulin from the ratio of their free diffusion coefficients. This was found not to be the case.

LUCCHI


Metabolism of fatty acid was studied in the isolated rat heart perfused with albumin-bound palmitate-C14. Uptake of fatty acid by the heart was related to the concentration of fatty acid present and the molar ratio of fatty acid to albumin in the perfusion fluid. Disappearance of lipid-bound radioactivity from the perfusion fluid (palmitate-C14 uptake) was consistently greater than disappearance of titratable fatty acid. This was attributed to failure of equilibration of unlabeled "endogenous" fatty acid on albumin with added palmitate-C14 and possibly to release of unlabeled fatty acid from the heart to the perfusion fluid. The principal fate of palmitate-C14 were C14O2 and saponifiable tissue lipid. The maximal rate of recovery of palmitate-C14 as C14O2 was equivalent to 83 per cent of total CO2 production of the isolated perfused heart in 30 minutes.

KAYDEN


At the time of cardiac surgery silver tantalum clips were sutured to three points on the external surface of the ventricles. Cineradiography was used to determine distances between the clips. This procedure was carried out in 68 patients between 3 months and 1 year after operation. In this manner, dimensions of the cardiac chambers were studied in intact unanesthetized subjects. The measurements were of changes in distances between fixed points on the ventricular surface, but were felt to be indicative of variations in heart size. The technic permitted evaluation without the necessity of contrast media reducing the physiologic effect and the potential hazards of such injections. The studies were limited to patients undergoing cardiac surgery. With this method, the effects of respiration upon left and right ventricular dimensions were observed. The end-diastolic dimensions increased during inspiration and decreased with expiration. The magnitude of the changes was related to the depth of respiration. Both end-diastolic and end-systolic distances were reduced sharply by the Valsalva maneuver. This was reversed rapidly upon release. During this maneuver, the systolic excursions of pulse pressure of the right ventricle varied with the end-diastolic dimensions supporting the concept of the Starling mechanism in intact man. Changes in left ventricular dimensions were of smaller magnitude and followed those of the right ventricle by two or three cardiac cycles. This lag may explain the apparent reciprocal variations in the two ventricles with respiration. In the present study, left ventricular proportions remained constant even when changes in the right ventricle were marked. Reciprocal changes in the two ventricles were not seen even
during deep respiration or the Valsalva maneuver. The effects of exercise were studied in nine patients. Simultaneous right ventricular pressures were measured in four patients and left ventricular pressures in three. Cardiac output was determined by an indicator-dilution method. There were significant decreases of end-diastolic and end-systolic dimension in both left and right ventricles. These ranged from 5 to 6.5 per cent of the measurements, approximately half of the resting stroke volume. The rate of change of right ventricular pressure was increased as the end-diastolic dimensions decreased. This was interpreted as an indication of increase in myocardial contractility during exercise.

KALTMAN


With use of electrophysiologic technics, the transmission of excitation from atria to ventricles were studied in dogs. Histologic examination of the hearts was not performed. Electrodes were attached to the endocardial surfaces of the bundle of His, right and left bundle branches, and the Purkinje systems. Epicardial electrodes were placed over the right atrium and both ventricles. These were left in place for repeated experiments in the lightly anesthetized animal. Transmembrane potentials were recorded from isolated ventricular muscle, papillary muscle, and Purkinje fibers. The AV transmission of premature atrial stimulation was recorded. Transmembrane potentials of single fibers of the AV node and Purkinje system demonstrated a reduced rate of rise and diminished amplitude. Premature impulses were slowly conducted or in some cases not transmitted at all. Local delay or block could be demonstrated in certain instances. In the living dog, recordings from selected sites in the conducting system allowed the measurement of the transmission of premature atrial stimulation. The intact heart followed the same delay, and block was noted in the transmembrane potential of the conducting system. The delay in spread of activity from atria to ventricles following forced atrial stimulation varied in the AV node. This change was a reflection of the length of the effective refractory period between atria and ventricles. Delay distal to the AB node, in the His-Purkinje system could also be demonstrated. This was achieved by stimulation of the atria as well as direct stimulation of the bundle of His. The variations in transmission at the several sites in the conducting system as well as differences in transmembrane resting and action potentials of individual fibers seem adequate to explain changes in AV responses to premature stimuli. The authors believe that it is not necessary to invoke a distinct dual AV conducting system to explain their electrophysiologic results.

KALTMAN


Balance studies reflect a net gain or loss of a substance which would be cancelled by equal flows in both directions. Therefore, an attempt to determine the actual exchange of potassium in the dog heart was made after perfusion of a coronary artery with radioactive potassium chloride. The effects of coronary flow, perfusion pressure, and heart rate on the magnitude of potassium flux were measured. Distribution of activity in perfused and non-perfused areas of the heart and the specific activity of the plasma were measured. The buildup of radioactivity is a function of the influx of K into the heart less an increasing amount leaving the tissues at the same time. Changes in the flux of potassium varied with alterations in collateral blood supply to the perfused area. Two rates of exchange, similar in buildup and washout, were found in all experiments. A rapid compartment resembled the extracellular space. The slow phase is assumed to be the transmembrane transport of potassium between the intracellular and extracellular spaces. Changes in coronary flow and perfusion pressure had little effect in this potassium exchange. Increase in heart rate enhanced the flux in both directions. Efflux of potassium was influenced more than the influx of this ion. The efflux of potassium varied as much as 150 per cent from subject to subject. It averaged 0.68 mEq. K+/Kg. at a heart rate of 130; 1.85mEq. K+/Kg. were exchanged per beat above the resting flux of the non-beating heart.

KALTMAN


Actin preparations were isolated from cardiac and skeletal muscle of dogs and rabbits. These were subjected to starch gel electrophoresis, sedimentation coefficient determinations, amino acid analyses, and comparison of peptide patterns after trypsin digestion. By these methods, no difference between skeletal and cardiac muscle actin could be demonstrated. There is a marked similarity between the amino acid content of dog

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and rabbit skeletal muscle actin. However, the amounts of cysteine in the dog preparations was less than that of the rabbit. Because of the difficulty in accurate determination of this amino acid, further study of this point is being undertaken. The data are in contrast to lactic dehydrogenase differences in the two types of muscle. In addition, the myosins of skeletal and cardiac muscle differ enzymatically and structurally, and could be responsible for the physiologic variations noted in these tissues.

KALTMAN


It has been established previously that the 2-day embryonic chick heart contains a high sodium concentration that declines rapidly from 600 to 700/mM to about 80/mM/Kg. of wet ventricle in 7 days. Subsequently there is a slower decline to about 30/mM shortly after hatching. In the present communication, the physico-chemical state of the myocardial electrolytes is clarified. Data from Na24- and K42-labeled myocardia indicate that 35 to 94 per cent of tissue sodium (Na) is bound (Na+ linked to molecules too large to traverse dialysis tubing during ultrafiltration) in the cells of 2 to 3 day hearts. After 5 days, Na binding remained constant at 25 to 30 per cent potassium. Bound potassium remained constant at 25 to 30 per cent during this period. It is suggested that the Na+ binding relates to the cardiac jelly of the tubular embryonic chick heart. This jelly is a macromolecular system, and Na+ may be required to stabilize the protein-polysaccharidecation complexes. The cardiac jelly is situated between layers of cells at the inner and outer surfaces of the tube, and even relatively free Na+ might have difficulty in traversing this viscous substance.

MARCH


In 51 rats the distribution of the aortic depressor fibers that travel in the cervical region with the vagus, sympathetic, laryngeal, or as a separate aortic nerve, was investigated by recording the action potential or by stimulating these nerves. A separate aortic depressor nerve was found in only 20 per cent of the rats on the left side and in 5 per cent on the right side. In these animals no depressor fibers were identified in the sympathetic trunk but the laryngeal nerves usually still exhibited depressor fiber activity. In those rats with no separate aortic depressor nerve the aortic fibers were present almost equally in the sympathetic trunk and laryngeal nerves, and on both sides of the neck. Only exceptionally was depressor activity found in the vagus trunk, and stimulation elicited depressor instead of pressor effects in 2 of 12 rats. Optimal stimuli for obtaining hypotensive effects from the aortic depressor fibers were 80 to 150 per frequency and of 1 to 2 msec. in duration.

KAYDEN


The measurement of coronary blood flow with Rb 86 previously described, involved an application of the Fick principle in which the total myocardial uptake of Rb 86 as well as the coronary AV difference for the isotope had to be measured. Coronary sinus sampling could be eliminated, and the technic could be applied under more physiologic conditions, if it could be shown that coronary blood flow was closely correlated with the myocardial clearance of the Rb 86, in which case coronary flow during infusion of Rb 86 could be estimated from the mean arterial concentration of the tracer and the total amount of radioactivity accumulated in the heart. The present data indicate a close relationship between myocardial blood flow and myocardial Rb 86 clearance for both the right and left ventricles. The percentage error in predicting flow from clearance is greater as flow increases. At flow rates below 6 ml./Gm. ventricle/10 minutes the mean error is 4.7 per cent. From 6-12 ml./Gm. the mean error is 14 to 10 per cent in animals with and without induced pulmonary artery obstruction respectively.

MARCH


Heart rate could be slowed and sinus arrest induced by perfusion of the canine sinus node with digitalis glycosides. This effect was unaltered by vagotomy or atropine. Epinephrine administered via the sinus node artery could restore sinus rhythm. Dogs were prepared with a catheter in the sinus node branch of the right coronary artery. The right stellate ganglion was exposed for direct electrical stimulation. Resting basal heart rate and acceleration produced by epi-

Calcium uptake and release were both increased during activity in the beating frog heart, as was the cellular calcium exchange with extracellular calcium. The calcium release from the ventricle followed an approximately exponential time course. The extra influx of calcium associated with activity in 1 mM-Ca-Ringer was approximately 10 to 20 times larger than the resting influx of calcium. The rise in efflux during activity was of similar magnitude to that of the influx. Activation of contraction during a myocardial muscle twitch was explained by the author by assuming that the action potential caused a sudden increase in calcium influx and consequently raised the concentration of activator calcium in the cell; this sequence of events initiated contraction, and the fairly rapid inactivation of this "activator" was responsible for relaxation after cessation of the action potential.

Karpman


Acute cardiac tamponade was produced in anesthetized thoracotomized dogs by rapid infusion of 0.9 per cent sodium chloride solution at 37 C. into the pericardial sac in amounts of 125 to 200 ml. The sac was rapidly drained after 5 to 7% minutes. Catecholamine levels in arterial plasma were measured by a modification of the fluorimetric method of Weil-Malherbe and Bone before, during, and after tamponade. Before tamponade the values were 0.2 to 1.2 (mean 0.8) μg./liter. During tamponade the arterial blood pressure decreased by 14 to 70 mm. Hg, the venous pressure increased by 4 to 13 mm. Hg, and the heart rate increased by 24 to 108 beats per minute. The catecholamine levels were 1.0 to 7.1 (mean 3.0) μg./liter. On recovery, the levels declined to 0.8 to 1.6 (mean 1.2) μg./liter. In individual cases, the alteration in catecholamine levels was related to the severity of the tamponade. Endogenous release of catecholamines in man may help to explain the improvement in the circulation noted 2 to 3 minutes after the onset of acute tamponade. It is doubtful, however, whether prolonged infusion of catecholamines would be of therapeutic benefit, since they increase the oxygen demand of the myocardium to which the coronary blood flow is severely restricted by the raised intrapericardial pressure.

Marshall


Radioactive calcium was utilized to study the uptake and release of calcium in frog ventricles at rest and during contractures that were induced by the application of sodium-depleted or potassium-rich fluids; the calcium uptake was found to be larger in the presence of these fluids and the extent of the increase appeared to be dependent upon the degree of sodium depletion. With constant sodium concentrations, however, an increase in calcium uptake occurred on raising the external potassium concentration. Calcium efflux also increased upon application of the contracture fluids and a large net efflux of the ion was observed on return to normal Ringer's fluid after a large calcium uptake had been induced by periods of exposure to sodium-free fluids. The author devised a tentative model to link movements of calcium with the activation of contraction and he interpreted the results by assuming that entry of the calcium occurred after a combination of this ion at the cell surface with the carrier molecules and, that the intracellular exchange of calcium was present in two interacting forms; that is, the activator-calcium, which induced contraction, and a larger store of inactive calcium.

Karpman

The role of extracellular K⁺ in the transmission of excitation along atrial and AV pathways was studied in the isolated, perfused rabbit heart. The hearts were driven at a selected frequency by electrodes attached to the right atrial appendage, and the electrocardiogram was recorded from the bath with a pair of salt (1M KCl) electrodes. In several experiments an electrogram was also recorded from the upper His bundle. Atrial propagation velocity reached a maximum when K⁺ was 7 mM. Higher levels depressed both atrial and His-ventricle propagation. AV nodal transmission was markedly impaired at K⁺ below 2.7 mM. Propagation velocity increases above this level and the higher K⁺ concentrations that depressed the atrium and His bundle had no obvious depressive effect on the AV node. Appropriate K⁺ levels abolished AV block induced by acetylcholine. The authors speculate that an increased K⁺ would decrease the K⁺ equilibrium potential. This would reduce the driving force promoting an outward K⁺ current, facilitating depolarization. Clinical counterparts are cited in which AV block has been associated with hypokalemia and AV conduction could be corrected by raising the extracellular K⁺ levels.

March


In six dogs, the main pulmonary artery was banded to reduce the cross-section area by about 84 per cent. This was less than the 90 per cent considered necessary to cause chronic heart failure. The resulting right ventricular end-diastolic pressure was less than 5 mm. Hg in three, between 5 and 10 in two, and 10 to 15 in the other. Catheters were placed in the carotid artery, right ventricle, and right atrium. Hemodynamic data were obtained in the resting state and after response to treadmill exercise in 2½ to 3 months. Three dogs were studied after 6 to 9 months of this induced pulmonary stenosis. At rest, the right ventricular systolic pressure averaged 89 mm. Hg after 3 months. On exercise, the cardiac output doubled without change in stroke volume. This was accomplished by increase in heart rate and decrease in duration of systole. The right ventricular systolic rose to a height of 158 mm. Hg. In four dogs, whose heart rate exceeded 180 beats/minute, pulsus alternans was noted. Under these circumstances, the maximal pressure reached 228 mm. Hg. Normal right atrial pressures were present at rest in five of the six animals. On exercise, these increased by at least 15 mm. Hg. There was a 100 per cent rise in right ventricular stroke work. Left ventricular stroke work was not altered by exercise. After 6 to 9 months of pulmonary artery banding, there was a mean rise of only 9 mm. Hg in the right ventricular systolic pressure in the three dogs subjected to a second study. On exercise, there was no significant change in the hemodynamic effects previously demonstrated. Late cardiac failure was not seen in any of the animals.

Kaltman


Human ventricular tissue obtained within 28 hours after death was homogenized in ammonium hydroxide and tested for its ability to catalyze the hydrolysis of the following substrates: 2 per cent cottonseed oil emulsion activated by incubation with plasma at 37 C., tributyrin, tricaprylin, trilaurin, triolein, and plasma lipid particles from a patient with carbohydrate-induced hyperlipemia. Lipolysis, as indicated by a rise in fatty acids, was observed in fresh homogenate. The lipolytic activity of these homogenates shows the following characteristics in common with other lipoprotein lipases: greater hydrolysis of "activated" triglyceride emulsions, hydrolysis of chylomicrons, and inhibition by 1M sodium chloride, but not by sodium fluoride. The study suggests that human heart contains a lipoprotein lipase, and that this lipase may function in the myocardial extraction of plasma triglyceride fatty acids.

March


Chorda tendinea tension (CTT) was measured in dogs on total cardiopulmonary bypass. The sensing device was a small displacement transducer introduced through a 3.0-cm. incision in the left atrium. Both ends of the transducer were sutured to a selected chorda tendinea connecting a papillary muscle with the aortic leaflet of the mitral valve, and this chorda was cut between the attachments. Since each papillary muscle ends in several chordae, total papillary muscle tension was not recorded, nor, of course, that of the ventricle as a whole; but the instru-
ment is capable of measuring the true tension in the structure to which it is attached. The CTT curves rose rapidly during isovolumetric contraction. A peak or shoulder was inscribed at the onset of ejection, and during early ejection CTT fell at a time when left ventricular pressure was still rising. A more rapid decline in CTT was noted from 15 to 40 seconds before aortic valve closure. Increases in stroke volume or arterial pressure increased CTT, but at larger stroke volumes the tension slope fell more steeply during ejection, whereas with increasing outflow resistance the initial tension peak was maintained during ejection. When left ventricular diastolic pressure was elevated as a consequence of lowered coronary perfusion pressure, CTT decreased; whereas if left ventricular diastolic pressure had become increased due to systolic pressure or volume overloading, CTT increased in the first instance and was unchanged in the second. With the pericardium open in “failing” hearts, the left ventricular diastolic pressure fell and the CTT increased.

**March**

**Surawicz, B.: Effect of Ca on Duration of Q-T Interval and Ventricular Systole in Dog.**


The relation between the duration of the Q-T interval and of the left ventricular systole was studied in dogs with induced hypocalcemia and hypercalcemia. At all studied Ca++ concentrations the change in the duration of both intervals was of similar magnitude and the relation between the duration of Q-T and ventricular systole was nearly constant as long as the heart rate was regular and the ventricular end-diastolic pressure did not change abruptly. Changes in the Q-T duration were due to changes in the duration of the interval from the end of QRS to the apex of T. In the postextrasystolic beats and during alternans the duration of left ventricular systole changed independently of the duration of the Q-T interval. It was concluded that the ventricular systole adjusts its duration to the duration of repolarization, more specifically to the duration of the plateau of the ventricular action potential, within a wide range of Ca++ concentrations. An escape from this adjustment occurs when the ventricular filling pressure or volume changes abruptly.

**Kayden**


The use of heart block dog preparations allowed an investigation at constant ventricular rates of the hemodynamic effects that resulted when the timing of atrial systole was altered relative to ventricular systole. Ganglionic blockade and vagotomy precluded sympathetic reflex compensation in these animals. Lengthening or shortening the interval between left atrial and left ventricular systole (As-Vs interval) produced a decrease in left ventricular end-diastolic pressure (LVEDP), mean aortic pressure, and aortic flow. Mean left atrial pressure increased as did the relation of MLAP to LVEDP. The absence of atrial systole produced similar changes. Lengthening or shortening the As-Vs interval while holding aortic pressure and stroke volume constant resulted in an increase in MLAP and the relation of MLAP to LVEDP. The changes observed in the left atrial pressure tracings suggested, and a platinum electrode technic demonstrated, that mitral regurgitation can occur with improper timing of atrial systole. The data indicate that properly timed effective atrial activity can enhance ventricular filling and can precoalesce the atrioventricular valve.

**Kayden**


The distribution of renal blood flow in the unanesthetized dog was studied by disappearance of radioactive krypton after injection into the renal artery. Polyvinyl catheters were placed in the renal ureters and left in situ. Repeated experiments could be carried out for periods up to 1 year. Considerable variation was noted in 65 experiments on four trained unanesthetized dogs. Since 95 per cent of krypton is removed in one circulation through the lungs, the return to the kidney is negligible. External monitoring over the kidney with a scintillation counter revealed a multiexponential disappearance curve of this isotope. Acute experiments with use of autoradiographs of excised kidneys identified these exponential components. The first curve was cortical blood flow; the second, outer medullary; and the third, inner medullary blood flow. The fourth component consisted of hilar and perirenal blood flow. Initially 80 per cent of radioactivity went to the cortex, 16 per cent to the outer medulla, and 2 per cent each to the inner medulla and hilum. This low effective inner medullary flow is well suited for maintaining the high solute concentration of the antidiuretic state. When urine flow is markedly decreased, highly diffusible substances.
such as krypton, are trapped from tubular urine as well as from blood. Their deposition in the inner medulla and in the renal pelvis is thus retarded.

**KALTMAN**

**PULMONARY DISEASES**


Pulmonary hypertension was produced in 25 dogs by infusion of serotonin, lycopodium spores, or polystyrene spheres. Flow through one lung was doubled by balloon occlusion of the opposite pulmonary artery, and the changes in calculated pulmonary vascular resistance of the unoccluded lung were observed. In the presence of pulmonary hypertension produced by serotonin, balloon occlusion produced a 51-per cent fall of pulmonary vascular resistance in the unoccluded lung. A similar result was obtained with hypertension produced by small precapillary emboli 28 μ in diameter. Resistance fell 47 per cent with occlusion of one artery. These results suggested that vasodilatation had occurred in the unoccluded lung. When pulmonary hypertension was produced by larger spheres, the fall of resistance seen in the unoccluded lung was only 18 per cent. Significant vasodilatation had not occurred. The findings suggest active control of pulmonary vascular resistance by the precapillary arteriole.

**KAYDEN**


Right heart failure is a common complication and a major cause of death in obstructive pulmonary disease. An evaluation of the prognosis of this complication was undertaken through a review of all patients admitted to the Massachusetts General Hospital between 1950 and 1956 with a diagnosis of chronic cor pulmonale. Patients with clinical or postmortem evidence of hypertensive heart disease, marked coronary disease and left ventricular failure were excluded. A total of 61 patients were included, of which 47 were thought to have an obstructive ventilatory defect associated with chronic bronchitis and emphysema. Therapy, which included digitalization, salt restriction, and intermittent use of diuretics and bronchodilators was uniform. Antibiotics were employed when sputum cultures dictated their use. The average length of survival after onset of peripheral edema was 3.8 years, being somewhat longer below age 50 years and somewhat shorter in those above 50. The type of underlying pulmonary disease did not appear to influence prognosis. The incidence of carbon dioxide narcosis was higher in the patients with the shortest survival. Autopsy confirmation was available in 35 per cent of the total. These figures indicate a better prognosis than previously reported.

**GUREWICH**

**RENAL AND ELECTROLYTE EFFECTS ON THE CIRCULATION**


The effect of reduction of renal arterial perfusion on the release of pressor substance into renal vein blood and into lymph was compared in dogs. Although pressor material was found in thoracic duct lymph, this was in much smaller amount than that which appeared in the renal vein blood. In fact it did not add materially to the systemic pressor activity. The renal vein appeared to be the principal route of release of pressor substance into the circulation. This material in the renal vein blood probably was angiotensin formed from renin released by the kidney. Its concentration in the renal vein far exceeded that of the systemic arterial circulation confirming its kidney origin. When renin is secreted into blood, angiotensin I is produced. Angiotensin II is formed and inactivated by an enzyme, angiotensinase. These experiments did not isolate the various components of this system, but merely identified its existence and degree of activity. The primary route of its release from the kidney was established. This appeared to be the renal vein although its appearance in lesser amounts in lymph was confirmed.

**KALTMAN**

**ROENTGENOLOGY**


The incidence and clinical findings in acute rheumatism at the Western Infirmary, Glasgow, during the years 1954 to 1961 were reviewed. Diagnosis was based on a modification of the original criteria of Jones. A total of 159 patients fulfilled the diagnostic criteria during this 7-year period. An additional 140 were rejected, many because arthralgia was confined to one joint or was evanescent, suggesting that many attacks of acute rheumatism caused so little
arthralgia that a few aspirin tablets settled the discomfort and the patient never saw a physician. The incidence of carditis in the 139 patients with acute rheumatism over age 12 was 18 per cent, further documenting the recently reported decline in carditis. The high incidence (60 per cent) of Aschoff bodies in surgically removed atrial appendages is noted and observations casting doubt on the specificity of this lesion are reviewed. Polyarthritis was the presenting symptom in 92 per cent of the cases. The erythrocyte sedimentation rate is the most sensitive measure of rheumatic activity, and it fell to less than 10 mm. per hour in 88 per cent of the patients within 8 weeks of treatment. A positive throat culture for Group A, beta-hemolytic streptococci was found in 33 per cent and the antistreptolysin-O titer was over 200 in 70 per cent of the patients. The patients were treated with salicylates and penicillin. All patients were maintained on oral penicillin-V for 3 to 5 years and no recurrence was seen in any patient maintaining this regime.

Gurewich


The electrokymogram, or cinedensigram, is the record of pulsations of the heart and great vessels obtained by means of a photoelectric cell, which converts the variations of light intensity emitted by a fluoroscopic screen over the chest into electric current. It is recorded by an electrocardiogram. Its value is enhanced by recording simultaneously the electrocardiogram, phonocardiogram, and carotid pulse. The authors discuss how the construction of isophases, at different times in the cardiac cycle (isometric contraction, isotonic contraction, and diastole), facilitates the recognition of areas of paradoxical pulsation.

Marshall

SURGERY AND CARDIOVASCULAR DISEASE


One hundred fifty-one of 331 patients undergoing mitral valvulotomy had normal sinus rhythm. Forty-six of these developed postoperative atrial fibrillation, 19 within the first week. There was spontaneous reversion to normal sinus rhythm in 12 (60 per cent) of these 19. None of those developing atrial fibrillation after the first week spontaneously reverted to normal rhythm. Quinidine was not used prophylactically in any patient. Nineteen patients under the age of 50, with minimal cardiomegaly, little valvular calcification, and an adequate valvulotomy were selected for attempt at conversion with quinidine. While anticoagulant therapy was administered 2 weeks after the onset of the arrhythmia, quinidine was introduced. Thirteen patients returned to normal sinus rhythm with an average total dose of 1.4 Gm. Those remaining in atrial fibrillation were closer to 50 years in age and had more severe mitral regurgitation or other valvular involvement than the group with successful quinidine conversion. However, 11 of the 13 patients restored to normal rhythm relapsed into atrial fibrillation within 2 years. Maintenance therapy had been discontinued at widely varying periods before reappearance of the arrhythmia. Of 179 patients with atrial fibrillation at the time of valvulotomy, only one spontaneous reversion to normal rhythm was noted and this occurred 5 years postoperatively. Quinidine conversion attempted in 27 selected patients was successful in only six instances; five of these relapsed within 6 months despite continuous maintenance therapy in two. The remaining patient reverted to atrial fibrillation after 1 year. Embolism was not seen in the patients with either spontaneous or quinidine-induced conversion. Two of 46 patients treated with quinidine died unexpectedly.

Kaltman


Postoperative cardiac arrhythmias are more likely to occur in patients having preexisting heart disease—including premature beats, in those having operations involving the cardiopulmonary area, and in those who have disorders with systemic effects such as infection or hyperthyroidism. Arrhythmia prevention therefore involves control of metabolic derangements, infection, hypoxia, hypotension, and the use of digitalis. Prophylactic digitalization was advocated in the presence of premature atrial beats or cardiomegaly, and the drug was used routinely in cardiac surgical cases. Management of the arrhythmia requires accurate diagnosis, ideally made by comparing an electrocardiographic record of it with a tracing made shortly preoperatively. Digitalis was given to patients with supraventricular tachycardias; quinidine or pronestyl to refractory problems or to those with ventricular tachycardias. Vasopressors, potassium salts, oxygen, and electric shock were further measures of note.

Rogers

A retrograde phlebography was performed via a femoral vein puncture in over 2,500 legs with venous pathology and in greater than 100 normal legs. Instead of tilting the patient to the erect position after the injection of radiopaque dye, a Valsalva maneuver was utilized to obstruct venous return from the leg and, therefore, the entire examination was performed with the patient in a comfortable supine position. After the initial film was taken, the patient performed a second Valsalva maneuver and further radiographs were taken of the lower thigh and leg. In the author's experience, the phlebographic Trendelenburg test was capable of localizing the pathologic lower leg communicating veins and also indicated pathology in the short saphenous vein or in the veins of the calf muscles.

KARPMAN

UNCOMMON FORMS OF HEART DISEASE


A new aortic valve prosthesis with a fixed and mobile portion is described. The fixed portion is made of stainless steel in the shape of a ring with two projecting arms extending up and down. These arms have loops at the ends that guide a mobile portion. The mobile portion is a plastic plunger, hemispherical on its ventricular aspect with flexible guide rods placed in the loops of the steel arms. Thus far, replacement has been successful in four of five patients with a follow-up of 4 to 7 months. The fifth patient who died postoperatively also had severe mitral disease.

NESSON


The authors have developed an electronic device which, according to them, can accurately identify the cardiac conduction system. The probe or locator utilizes the comparative differences in impedance between myocardium and conduction system. The accuracy of the original probe in locating the atrioventricular node and bundle of His was only 50 per cent, and the circuit was redesigned, now employing a three-pole probe or "guard ring." The new design employs the principle that lines of current cannot cross and, therefore, a portion of the driving current would be forced deeper into the tissues. The deeper current detects sources of lower or relatively lower impedance in the atrioventricular node which lies up to a depth of 3 mm. below the endocardium. Since April 1961 the device has been used by several cardiac surgeons throughout the United States, the experience now totaling 54 patients with ostium primum defects, atrioventricular canal, ventricular septal defects, or tetralogy of Fallot. The conduction system was accurately located in 89 per cent of the patients. Complete heart block developed in two of the six patients in whom the conduction system had not been successfully located. The authors estimate that their device has reduced the incidence of complete heart block from 10 to 15 per cent down to 3.7 per cent. In view of the postoperative morbidity resulting from heart block, this probe would appear to have made a significant contribution to the safety of open-heart surgery.

MARCH