PATHOGRAPHY


Findings at necropsy on a 16-year-old female baboon that died of infection in a North American zoo revealed many atheromata in the lower part of the abdominal aorta, similar to the lesions of atherosclerosis in the human. Because baboons may have a higher incidence of atherosclerosis than has been suspected for most primates and because these lesions may develop in the absence of excessive dietary cholesterol, a study was undertaken to determine the precise incidence of arterial lesions in baboons that had lived in their natural habitat. Study was made of 183 such animals immediately after they were trapped in Kenya, British East Africa. Some deposition of lipid was found in the intima of the aorta in approximately three fourths of the 67 adults, and this was extensive in a few animals. No sex difference was observed. Electron microscopy disclosed that most of the lipid droplets in the intima were intracellular. Fibrous plaques were infrequent. However, in one elderly male they were noted, and hemorrhage had occurred into the bases of the plaques. Sections of coronary arteries showed many small musculo-elastic intimal plaques in which lipids could be demonstrated only rarely. The aortic lesions occurred in the absence of excess intake of animal fat or hypercholesterolemia. It was suggested that the baboon is highly susceptible to lipid deposition in the arterial intima and, therefore, that it will lend itself well to the experimental study of atherosclerosis.


The peripheral arteries of 81 subjects, ranging in age from 1 month to 95 years, were examined at necropsy. No hypertension was evident clinically or at necropsy in the group. The radial artery at the wrist was examined in 65 cases, and segments obtained from the brachial artery, the upper third of the femoral artery, from the popliteal artery, and from the posterior tibial artery. Three changes were seen to occur in the structure of the peripheral vessels during the first two decades of life. During the first decade the only change observed was some increase in size of the muscular cushions previously observed in the popliteal and lower end of the brachial artery of the fetus. By the end of the second decade further cushions had formed at the mouths of branches in other peripheral vessels, particularly the femoral artery. These cushions were less prominent in the radial and posterior tibial arteries. Simultaneously, with the development of...
cushions, bands of longitudinal muscle developed in the brachial and popliteal arteries. At the end of the first and in the second decade the internal elastic lamina began to split to form the muscular elastic layer of the intima. Muscle cells could be observed passing from the media into the newly formed musculo-elastic layer through openings in the internal elastic lamina. The third and later decades were characterized by the development of the elastic hyperplastic layer of the intima and by regressive changes in the muscular cushions and media of the peripheral vessels. Simultaneously, progressive fibrosis of the media with atrophy of its longitudinal muscle occurred. It was suggested that the muscular cushions in the peripheral arteries showed good correlation with the severity of pulsatile stress. In vessels with marked pulsations cushions developed earlier than in the small arteries where the pulse wave was flattened and less steep. The development of the musculo-elastic layer of the intima was thought to occur in response to a gradual rise of the blood pressure throughout life. The authors stated their belief that the development of the musculo-elastic layer of the intima represented hypertrophy of the circular muscle of the vessel in the same way that the fetal cushions represented local hypertrophy of the longitudinal muscle. It was believed that the muscular cushions of the fetus and the later development of the peripheral arteries noted in the study confirmed the presence of pulsatile stress and indicated its importance in the localization of intimal plaques.


Histologic study of four hearts with predominant left ventricular hypertrophy showed that in three of these, the initial subendocardial portion of the right bundle-branch was shortened while in one heart it was completely missing, the branch showing an intramyocardial course from the beginning. These changes were in direct relation with the degree of ventricular septal hypertrophy.

LEFESCHSCHKIN


Gross and histologic observations were made on the rabbit kidney after various degrees of obstruction of venous outflow were produced. The degree and duration of partial obstruction were varied with production of different degrees of enlargement of the anastomotic channels and thus different grades of renal damage were produced. Necrosis occurred in the tubules in the outer part of the cortex, in the inner intermediate zone of the cortex, and in the outer medulla; no correlation could be made between the lesions in the various zones. Large mononuclear cells were found in the sinuses of the intermediate zone and in the lumen of the cortical veins; these were presumed to be endothelial or mononuclear cells that had been washed free into the lumen by the flow of interstitial fluid, which occurred immediately post mortem.

KARPMAN


Fifteen extremities amputated for complications of arteriosclerosis obliterans and one from a case of thromboangiitis obliterans were studied for arteriolar disease. The Schlesinger radiopaque injection mass was used. Sections for histologic study were taken from major arteries, and additional sections included skin, subcutaneous tissue, and muscle. Sections were taken from four autopsies for controls. All patients were normotensive. Eight patients had diabetes mellitus. Major arteries were frequently occluded in several areas. This was generally more extensive among the patients with diabetes mellitus. The arterioles in the 40- to 150-micron range were given special attention. All the limbs showed alterations in these vessels. Those located in the dermis and generally in the more distal areas showed the greatest number of arteriolar changes. Proliferative changes were seen in thick walled vessels—the adventitia and the intima were thickened while the media was thinned. Some arterioles also showed hyaline changes. These usually showed a smaller lumen but occasionally the lumen appeared increased in relation to the wall thickness. The media sometimes showed no smooth muscle. The changes were classified as severe in two cases, moderate in eight, and minimal in five. The case of thromboangiitis obliterans did not show hyaline or proliferative changes. The patients with diabetes mellitus did not differ. The authors comment that these changes are similar to those described as being the basis for hypertensive ischemic ulceration although these subjects were normotensive. It is postulated that involvement of the arteriolar bed may so greatly increase the resistance to blood flow as to compromise the results of angioplastie procedures and lumbar sympathectomy.

SHEPPS

Circulation, Volume XXIV, September 1961
ABSTRACTS

PHARMACOLOGY


The authors injected rabbits with SU5864 (guanethidine), 12.5 mg. per Kg. intravenously, and cats, 15 mg. per Kg. subcutaneously. They found that in both animals the SU5864 lowered the norepinephrine level of the heart and spleen, but did not effect the norepinephrine level of the brain or adrenal medulla. The failure of guanethidine to lower the content of brain norepinephrine level was believed to be due to its extremely low lipid solubility and, hence, its difficulty in crossing the blood-brain barrier. These findings suggest that guanethidine acts as a hypotensive agent by producing a chemical sympathectomy through depletion of norepinephrine from peripheral nerve endings. However, the catecholamine depletion observed after guanethidine is slower than after reserpine.

LEPESCHKIN


Rats receiving daily doses of digitalis in ethanol showed a steep decline of free glycogen in the liver and in skeletal muscel, persisting during the entire experiment. This decline was present also in animals receiving only the solvent, but it was not as pronounced as in animals receiving digitalis. Bound glycogen in skeletal muscel did not show significant changes, while in the liver it persisted on a lower level throughout the experiment; these changes were less pronounced than those of free glycogen.

LEPESCHKIN


White male rats that received a daily dose of 0.4 mg. per 100 Gm. of digitoxin dissolved in ethanol intraperitoneally and were killed on the first to sixth day of the experiment showed a statistically significant increase of free myocardial glycogen during the first 2 days as compared with animals that received only the solvent.

LEPESCHKIN


The action of benzthiazide was compared with that of chlorothiazide. The drugs were first tried on two young men in good health who were hospitalized for investigation of minute tuberulous foci. Both men had relatively similar food and fluid intakes and a similar electrolyte pattern. Observations were made before and after the administration of the drugs, benzthiazide being given in a 100-mg. dose and chlorothiazide in a dose of 1 Gm. Urine volume with both drugs reached maximum excretion within 6 hours and returned to control levels within 10 hours. Electrolyte excretion ran parallel to water excretion with both drugs, but benzthiazide caused a greater loss of the chloride ion. Chlorothiazide led to excretion of alkaline urine in the first 6 hour period, while benzthiazide produced little alteration in either pH or titrable acidity. Benzthiazide minimally affected bicarbonate excretion, but chlorothiazide greatly increased bicarbonate excretion in the first 6 hours. The drugs were then tried on 15 hospitalized patients of whom nine were in cardiac failure and six had cirrhosis. In the cardiac patients both drugs were equally effective and produced similar results. Four patients responded well with weight loss of 12 pounds during 8 days of therapy. The other five did not do so well, losing an average of only 1.5 pounds during the same period. These five had been on diuretics and low-sodium diets for a long period of time. However, in all patients benzthiazide caused a greater chloride loss than sodium, whereas chlorothiazide tended to cause equal excretion of both sodium and chloride. Potassium loss was the same with both drugs. There was no disturbance of serum electrolytes with either drug and blood urea levels were reduced after treatment with both drugs. No gastrointestinal, hepatic, or hematologic disturbances were observed with use of either agent. Among the cirrhotic patients only 1 had a good response and this patient was the individual in whom sodium excretion during the control period exceeded the dietary intake. The authors believe that benzthiazide, 100 mg., is a good oral diuretic as compared with chlorothiazide, 1 Gm., the biggest difference being in bicarbonate excretion.

KRAUSE


Bendrofluazide is a benzothiadiazine derivative with greater potency than either hydrochlorothiazide or hydroflumethiazide. Volumetric and
biochemical studies of its action were performed in 19 edematous patients and two healthy subjects. Optimal dosage in most patients was 7.5 mg. Maximum dosage was in the first 12 hours and still appreciable in the second 12 hours. Urinary sodium and chloride were both greatly increased; maximum water diuresis was closely related to them in time. Potassium excretion was increased but to a lesser extent than that of sodium or chloride. Plasma levels of sodium, chloride, and urea showed no change after a single dose, but there was a slight fall in plasma potassium. No toxic effects were noted.

KURLAND


In a previous paper by the authors digitalis antagonism by potassium salts was discussed. In the dog at rather low levels of K-strophanthin intoxication, potassium in the form of any of its soluble salts appeared capable of reversing electrocardiographic evidence of toxicity. At higher levels of toxicity, however, only the L-glutamic and A-keto glutamic acid salts retained this antitodal property. Actual quantitation of digitalis intoxication was impossible, but an empirical approach by the authors permitted differentiation into "acute" and "subacute" high-level digitalis intoxication in animals. On the basis of these experiments clinical trial of monopotassium glutamate as an antagonist against digitalis intoxication seemed warranted. The drug appeared to be safe even in the presence of altered renal function. Furthermore, correction of electrocardiographic abnormalities due to excess digitalis occurred at the low dose levels of 10 mEq. of potassium. This study confirmed the fact that monopotassium glutamate appears to be just as effective in human as it is in animal digitalis intoxication.

KRAUSE


The physiologic disposition of hexamethonium and certain similar compounds was studied in animals. Absorption was poor from the small intestine. There was no biotransformation in the intact mouse. Hexamethonium was found in the blood for an hour following an intravenous dose of 30 mg. per Kg. and was distributed rather uniformly to all tissues including muscle and some adipose tissue depots, but not brain tissue, following an oral dose, about 40 per cent of hexamethonium was excreted in the urine within 5 hours. Biliary excretion does not represent the major pathway of elimination.


The contractile force of the heart was measured directly with the strain-gage arch in open-chest dogs with intact circulatory systems. Phosphorylase activity was analyzed from small samples of myocardium cut from the contracting heart "in situ." The positive inotropic effect of epinephrine, norepinephrine, Isoproterenol, Ephedrine, and stimulation of the cardiac sympathetic nerves was accompanied by augmentation of enzyme activity. Methoxamine affected neither contractile force nor phosphorylase activity, while naphazoline produced small increases in force with no change in enzyme activity. Other agents with positive inotropic action (ouabain, theophylline, serotonin, and phenoxycbenzamine), had no effect on the enzyme. Calcium in large doses augmented phosphorylase. Dichloroisoproterenol prevented both the positive inotropic and phosphorylase-activating effects of epinephrine and sympathetic nerve stimulation. Phenoxycbenzamine blocked the vasopressor effect of epinephrine, but failed to prevent either physiological or biochemical stimulation of the heart. Pretreatment with reserpine prevented the positive inotropic and the phosphorylase-activating effects of cardiac sympathetic nerve stimulation but did not alter the effects of epinephrine. This was presumably through the mechanism of depleting cardiac catecholamines. It was not possible to decide which was the primary event in the action of catecholamines on the heart—the effect on phosphorylase or on the contractile mechanism—or whether both were concomitant phenomena with no immediate causal relationships.


Alpha-phenoxy-alpha-dimethylaminomethyl propiophenone hydrochloride (U-0882) when administered intravenously in an anesthetized animal, produces a transient depressor effect and concomitant stimulation of respiration. The electrocardiogram and direct measurements show that
the refractory period of the ventricular myocardium is greatly prolonged without depressing intracardiac conduction. This compound is also a weak atropine-like blocking agent. Ventricular fibrillation is easily induced by a subsequent intravenous injection of epinephrine, levaterenol, isoproterenol, or electrical stimulation of the right atrium, the right ventricle, or the stellate ganglion. In the unanesthetized dog, the administration of this compound intravenously produces spontaneous ventricular fibrillation. U-0882-epinephrine fibrillation is not prevented by dibenzylene, quinidine, procaine amide or functional hepatectomy—measures which protect against hydro-carbon-epinephrine fibrillation. Previous administration of toxic doses of Ouabain or dichloroisoproterenol will prevent fibrillation from U-0882. The authors suggest that ventricular fibrillation is a state of continuous conduction and not a state of increased ventricular automaticity. The maintenance of fibrillation depends upon continuous conduction of one or more impulses in relatively refractory tissue. The authors present evidence against the existence of an "excitable gap."

**Sheps**


The action of Amarine and 10 congeners of U-0882 were studied. Like U-0882, Amarine prolongs atrial and ventricular refractory periods and sensitizes the heart to ventricular fibrillation; but Amarine differs in that it has more depressant action upon intracardiac conduction and does not block vagal slowing of the heart or the depressor response to metha-choline. Sensitization to ventricular fibrillation was shared by the three congeners of U-0882 that, like the parent compound, have a keto oxygen and an alpha methyl group. The remaining congeners do not sensitise but produce death by circulatory collapse without ventricular fibrillation.

**Sheps**


Dimecamine (3-dimethylaminoisocamphane), a derivative of mecamylamine, in a single dose of 2.5 to 10 mg. causes a maximum fall of blood pressure in 1 to 2 hours, this low level being maintained for some 12 hours. With subcutaneous administration, 85 to 90 per cent of this dose was excreted with the urine in 4 days, while with oral administration this percentage was 62 to 76 per cent. Simultaneous administration of ammonium chloride accelerated the rate of excretion slightly, streptomycin slowed it slightly, while diamox and especially chlorothiazide slowed it considerably. Therapeutic doses were given to 47 patients with hypertension over a period of 12 to 18 months, after a single test dose. This resulted, in most patients, in a marked fall in blood pressure, systolic pressure being affected more than diastolic pressure. A single dose of dimecamine did not cause a decrease in renal blood flow or in glomerular filtration rate, and no renal damage resulted from long-range treatment with the drug. The most serious side effect was constipation, which appeared in 31 patients and resulted in ileus in one. Constipation was most marked in persons who already had such a tendency before treatment, and could be counteracted by synthostigmine but not by conventional laxatives.

**Lepeschkin**


Acetylstrophanthidin was administered to dogs previously placed on an extracorporeal pump-oxygenator and the extracardiac vascular effects of the drug were measured. When the portal circulation was kept intact, a decrease in the venous return and intravascular pooling of blood occurred. If pooling in the splanchnic bed was prevented, a decrease in intravascular volume and an increase in venous return occurred. Elevations were noted in the pressures of both the superior and inferior venae cavae. The authors concluded that the hemodynamic alterations produced by digitalis are secondary to peripheral as well as inotropic actions.

**Karpman**


Hexamethonium has previously been demonstrated to exhibit positive inotropic responses without muscarinic activity. In order to correlate structure and activities, other bis-trimethylammonium compounds were studied on the isolated aatria of the cat, rat, and on the heart-lung preparation of the dog. A series of alkane, alkene,
and alkyne bis-trimethylammonium compounds was examined. All lacked ganglion-stimulating properties. In contrast, the saturated compounds exhibited little or no inotropic or chronotropic activities. Unsaturation, as well as an increase in internitrogen chain length from C4 to C5 or C6, enhanced cardioinhibitory activity. This was maximum when the internitrogen hydrogen chain contained five or six carbon atoms and a triple bond in the 2,3-position. When the triple bond in the C6 alkyne compounds was moved from the 2,3- to the 3,4-position, there was decreased cardio-inhibitory activity. A difference in receptor sites for the inotropic and chronotropic responses was suggested by the observed differences in dose-response relationships, and because negative inotropic activity was greater than negative chronotropic activity in the entire series of unsaturated compounds. Since there was no correlation between internitrogen distance and the observed differences in activities of the compounds, it was postulated that the differences might be related to the effect of the position of the unsaturated group on the reactivity of the nitrogen atom of the quaternary groups.

SHEPS


Medical literature is virtually devoid of data relating to toxic effects of vitamin K. Free use of this vitamin, and its analogues, in greater than adequate doses and continued over long periods, may harm the patient, especially the one with hypoprothrombinemia due to a seriously diseased liver; a condition that cannot be corrected by vitamin K. An 80-year-old woman, admitted for surgery, was found to have a prothrombin time of 18 seconds (40 per cent). She was given 150 mg. of menadion sodium diphasphate intramuscularly and 50 mg. of phytomandione intravenously. An abdomino-perineal resection performed the next day was uneventful and the liver was grossly normal to inspection. Vitamin K was continued for 11 days (menadion sodium diphasphate, 30 mg. intramuscularly daily supplemented by 50 mg. of phytomandione by vein on the eighth day through the eleventh) although her prothrombin time had reached the normal of 13 seconds (100 per cent) on the fourth postoperative day. Subsequently there was a fall in prothrombin activity to 29 per cent of normal on the twelfth postoperative day and an increasing hemorrhagic ooze from the wound. Transfusions of fresh blood and discontinuance of vitamin K resulted in improvement. The prothrombin time returned to normal in 3 weeks, but liver-function studies were abnormal for more than a month.

KITCHELL


Gamma-amino-N-Butyric Acid (GABA) has been obtained from extracts of mammalian central nervous system. This has been reported to possess significant cardiovascular activity. This amino acid and similar compounds were studied. GABA, beta-alanine, 5-amino-N-valeric acid, taurine, sodium butyrate, and butylamine induced a transient, dose-related, blood pressure fall when administered intravenously to anesthetized dogs. Respiratory stimulation was observed following GABA, beta-alanine, and 5-amino-N-valeric acid. GABA also produced a transient pressor response and bradyardia preceding the depressor response. A more prolonged depressor response was occasionally observed following large doses of 6-amino-N-caproic acid, 8-amino-N-caprylic acid, and butyalmine. The latter agent also elicited a more transient dose-related depression of blood pressure. Tachyphylaxis to this prolonged blood pressure fall was observed. There was a 25 to 30 second latent period before the response was manifest. The depressor responses induced by GABA were antagonized by beta-alanine, 5-amino-N-valeric acid, and 6-amino-N-caproic acid. It is suggested that in dogs the depressor response induced by GABA may be due in part to peripheral autonomic ganglionic blockade. The pressor and respiratory stimulation induced by this compound may be due to carotid and aortic chemoreceptor stimulation.
ABSTRACTS

disease of the right heart and transmitted to the femoral vein, and that the second sound was produced by left ventricular systole and transmitted to the femoral artery.

Rogers


The authors reviewed 30 patients with loud opening snaps associated with a pansystolic murmur attributed to mitral regurgitation. In 12 patients the valve was examined at operation; in all instances the aortic cusp was found to be pliant and mobile whereas regurgitation was caused by shrinkage of the mural cusp. A mitral diastolic murmur of variable duration and intensity was heard in all patients. In this series the opening snap did not appear to depend upon the degree of mitral stenosis or the mobility of the mural cusp but rather upon a pliant aortic cusp moving rapidly under the influence of a high left atrial pressure. The patients with dominant regurgitation usually had a third heart sound, left ventricular thrust, and the explosive onset of the diastolic murmur. The authors believed that they could distinguish the latter group, those patients with pliable aortic cusps who would, therefore, be amenable to present-day surgical procedures.

Kalmansohn

PHYSIOLOGY


Serum free fatty acid levels were followed before, during, and after the infusion of saline in one group of patients, and after infusions of Arfonad in a second group of patients. There was a gradual and sustained rise in free fatty acid levels during the saline infusion; in addition, the blood pressure increased although the heart rate and blood sugar values did not change. Ganglionic blockade (with Arfonad) resulted in a fall of free fatty acid levels during the infusion with a sharp rise after infusion; during ganglionic blockade, the blood pressure decreased, with a secondary increase in the pulse rate, and the serum glucose remained unchanged. Ganglionic blockade inhibited the rise of free fatty acid levels following presentation of a threatening stimulus. The authors concluded that the autonomic nervous system provides a stimulatory component to lipid mobilization and that the mechanism is operative in the resting and in the stimulated individual.

Karpman


The history of previous investigations on the mechanism of cardiac fibrillation is reviewed. The circus theory of Lewis, which remained unchallenged for 30 years, is cited. Also described is the production of fibrillation in the dog heart during vagal stimulation and applying a single shock early in the relative refractory period (the vulnerable period). The works of Scherf and Prinzmetal, individually with different techniques, are described in support of atrial fibrillation originating from, and perpetuated by, a single rapidly discharging ectopic focus. The combination of an infusion of acetycholine and rapid stimulation produced fibrillation in the atria but not in the ventricles. Since acetycholine shortens the action potential of the atria, but not the ventricles, this is probably an important mechanism for the production of atrial fibrillation. When the atria are fibrillating due to this procedure and the infusion of acetycholine is stopped, the atrial fibrillation stops. In fibrillation the muscle fibers are not contracting simultaneously and are out of phase. When a muscle fiber contracts, excitation spreads to adjacent fibers, which will also contract if they are excitable. In the presence of acetycholine, muscle fibers are rapidly repolarized and after contracting are promptly re-excited so long as the acetycholine keeps the action potential and the refractory period short. In addition to a short refractory period, the muscle fibers must be out of phase, in order to produce fibrillation. This occurs with rapid stimulation electrically, or can be produced by a rapid stream of impulses by applying aconite. The long refractory period (or the long action potential) of cardiac muscul as compared with that of skeletal muscle protects the cardiac muscul from fibrillation. Energy is required to maintain its length, since, when there is lack of oxygen or glucose, or in the presence of metabolic inhibitors, the action potential is shortened and fibrillation is facilitated.

Krause


The threshold strength of electrical stimuli on the lumbar sympathetic chain in the intact dog.
and in perfused preparations were measured by studying vasoconstrictive phenomena plethysmographically in the intact animal while changes in arterial resistance and venous outflow were measured in the perfused preparations. An infusion of norepinephrine reduced the threshold of sympathetic stimulation (after the direct effect had abated), whereas epinephrine had little or no effect. The authors suggest that at the post-ganglionic sympathetic nerve ending there is a mechanism for taking up circulating norepinephrine as well as for releasing it. They hypothesize that the norepinephrine sequestered into the blood by the adrenal gland replenishes the stores at the sympathetic nerve ending and that if the secretory activity of the adrenal medulla is excessive, the tone maintained by the sympathetic impulses may also be excessive. Furthermore, the disappearance of norepinephrine from the blood may be partly due to its uptake and storage and not due to its destruction.

**Karpman**


The existence of a physiologic communication through the foramen ovale and through the ductus arteriosus was demonstrated in the newborn infant by means of dye-dilution curves. Communication through the foramen ovale occurs from right to left and the blood passing in that direction comes from the inferior vena cava. Closure of the foramen may take place early (within the first 6 hours of life) or late (more than 8 days after birth). Communication via the duct is left to right. Functional closure of the duct may be early (in the first 6 hours) or late (more than 14 days after birth). Crying, which produces rapid variations in pressure in the right atrium, can activate a right-to-left shunt through the foramen ovale that is not present in the resting state.

**Brachfeld**


Eighty healthy subjects were studied to determine the effect of cigarette smoking on blood flow, surface temperature, blood pressure, pulse rate, ballistocardiogram, and electrocardiogram; the same subjects were skin tested with each of the various tobacco extracts. Forty-seven and a half per cent revealed changes in at least one of the circulatory measurements; 40 per cent showed a positive skin test to the tobacco extracts; of the 48 subjects with negative skin tests, 43 revealed no change in peripheral flow after smoking. The authors concluded that simple skin testing might be a fairly reliable way of screening those people in whom smoking will in all probability not cause any decrease in peripheral blood flow.

**Kalmansohn**


The cardiovascular response to transfusions was studied in seven normal human subjects before and after ganglionic blockade induced by a constant, continuous intravenous infusion of Arfonad. The cardiac output was not significantly affected by transfusions or by venesection prior to ganglionic blockade, but it did increase after a transfusion during an Arfonad infusion; this latter effect was presumed to be due to a substantial increase in blood volume, associated with a striking increase in the output and work of the left ventricle. The authors conclude that acutely induced hypervolemia stimulates the autonomic nervous system with subsequent reflex venodilation and depression of myocardial contractility, thereby preventing marked alterations in the circulatory dynamics. When hypervolemia was induced after the activity of the autonomic nervous system had been reduced, more profound hemodynamic changes occurred resembling those changes noted in the Starling heart-lung preparation.

**Karpman**


Oxygen utilization, lactic acid metabolism, myocardial oxygen availability, and left ventricular work capacity were studied in a series of 47 dogs in whom 1-hour cardiac arrest was produced utilizing potassium citrate, acetylecholine, or cold. The oxygen consumption of the normothermic, non-working, beating canine heart was 3.7 cc. per 100 Gm. of heart per minute. This decreased sharply from 37 to 30 C. and more gradually from 30 to 5 C. The oxygen consumption of the perfused arrested heart was 1 cc. per 100 Gm. per minute or less during all methods of cardioplegia. Following arrest, however, the
ABSTRACTS


Eighteen mongrel dogs were premedicated, anesthetized, and had blood samples drawn as well as cardiac catheterization during the control period. Subsequently, sustained hypotension was induced by bleeding the dogs from the femoral artery. After shock was induced, one group of 12 dogs was treated with L-norepinephrine and the other six were treated with infusion of whole blood. During the period of shock a negative pyruvate balance was found as well as a decrease in the per cent extraction of lactate. Infusion of L-norepinephrine did not change this picture, but reinfusion of whole blood caused immediate reversal of both pyruvate and lactate levels toward normal. An important finding was the variation in glucose during shock and after treatment with blood or norepinephrine so that the main change of significance is the increased arterial level of glucose during shock. The abnormal metabolic pattern of the myocardium responded to the administration of blood by increased blood pressure and, thus, increased cardiac output, as well as decreased vascular resistance of the extremities. L-norepinephrine did not correct the oligemia or the cardiac output and, hence, further increased vascular resistance in the extremities. The use of L-norepinephrine alone in the treatment of shock in dogs does not increase per cent of survival because it does not correct the abnormal metabolism of the myocardium and, in fact, actually causes an increase in incidence and severity of myocardial damage according to the authors.

KRAUSE


Rat heart cells were separated by trypsin treatment and grown attached to glass in a liquid medium. These cells exhibited periodic contractions similar to a whole beating heart. The beating ranged from intermittent, irregular twitches to steady, deep, rhythmic contractions at rates up to 150 per minute. Most of the cells ranged within 30 to 80 beats per minute. When two or more cells were observed in the same microscopic field, they appeared to beat independently. The effect of several drugs and metabolic substrates on these cells was noted. Acetylcholine produced either a marked slowing or complete stoppage of the beating. Recovery ensued in either instance. Eserine had no effect on the beating. When acetylcholine was added the beating slowed to 8 per minute which persisted until ouabain was added, which raised the rate to about 30 per minute. The effects of adenosine triphosphate and other metabolic inhibitors were studied. Observations were sufficiently interesting to suggest that this preparation may provide a unique system for the study of the requirements of the periodic contractility typical of mammalian hearts.

LEVINSON


Reversible transamination has been demonstrated in the isolated perfused rat heart between aspartic and glutamic acids, but not between other pairs of amino and keto acids. The glutamic/aspartic transaminase activity was only 3.4 per cent of that previously demonstrated in rat heart homogenates and no other transaminase activity was detected. At least a part of the glutamic/aspartic transaminase activity observed during perfusion was due to an enzyme released into the perfusate. Glutamic acid added alone to the perfusate was not utilized, nor was oxaloacetic acid produced during the perfusion. The glutamic acid content of the heart did not increase when it was added to the perfusate but alanine, leucine, and aspartic acid penetrated the heart cells when present in the perfusate. The authors conclude that, at least in the perfused heart, glutamic/aspartic transaminase is not concerned with energy metabolism.

KARPMAN

Circulation, Volume XXIV, September 1961

The normal individual responds to hypoxia at altitudes of 6,000 to 10,000 feet by increasing ventilation. At somewhat higher levels, tachycardia with or without increased stroke volume and then vasodilatation occur in order to maintain tissue oxygen supply. Circulatory collapse develops at 18,000 to 23,000 feet where the critical alveolar pO₂ of 30 mm. Hg is reached. Breathing pure oxygen preserves full blood oxygenation to 33,700 feet. At higher levels pressurized oxygen may be required, but its force cannot be permitted to exceed approximately 20 mm. Hg lest venous blood flow to the heart be inhibited and arterial hypotension result. This state may become obvious by wearing a pressurized g-suit. Sudden exposure to an altitude of 50,000 feet or higher allows the rapid loss of blood and alveolar oxygen into the surrounding air. If these circumstances continue for 5 seconds or longer, brain oxygen will be depleted and syncope will ensue, although there will be a lag period of 10 to 15 seconds. The decrease in ambient pressure above altitudes of 27,000 to 30,000 feet allows gaseous nitrogen to escape from the tissues, and the intravascular gas may produce circulatory impairment in any area causing pain or reflex bradycardia. Gravitational (g) force 3.5 times that at sea level is withstood for several minutes, but forces of 5 to 6 g decrease brain and ocular circulation to an intolerable degree in less than 1 minute. G forces are greatest during air maneuvers and depend upon the velocity squared divided by the vehicle's turn radius. Other effects of high g force are sinus tachycardia followed by bradycardia, dependent pooling of blood, edema formation, nausea, hypoglycemia, pain due to visceral dislocation, and collapse. The consequences of prolonged relative immobility on cardiovascular reflexes is an important area for investigation.

Rogers


Hypovolemic shock was induced in nine mongrel dogs by temporary occlusion of the portal vein. Five other animals that had undergone only a midline incision under pentobarbital anesthesia served as controls. All nine dogs in whom hypovolemic shock was induced recovered initially. In all nine, electrocardiographic signs of subendocardial ischemia appeared within 30 minutes of the beginning of the hypotensive phase. In four dogs these changes reverted to normal once the occlusion of the portal vein was released; in the other five dogs electrocardiographic patterns manifested high lateral myocardial infarction. Levels of glutamic oxaloacetic transaminase in serum increased to abnormal values in the five dogs with myocardial necrosis and in one other dog with a liver abscess. Sections of the myocardium showed multifocal necrosis extending from the endocardium to the epicardium.

Schirger


As a result of research upon Korotkoff's sounds, the author attempted to explain the action of the human heart. The right and left sides of the heart were each regarded as the mechanical analogue of a reflex klystron. The right and left atria on the one hand and the pulmonary and aortic sinuses on the other constitute cavity resonators wherein contraction and dilation of the walls and apertures generate fields through which the blood flows. The action of the two sides of the heart are similar. The function of the left atrium is to set the blood into motion while that of the orifice of the mitral valve is to produce velocity modulation of the blood entering the left ventricle during diastole. The blood impinges upon the ventricular wall, is reflected upon the aortic valve, with the correct angle of incidence being maintained by the papillary muscles and chordae tendineae. The mitral valve acts as a buncher, the aortic valve and sinuses as a catcher, corresponding to the resonance of the klystron. The function of the autonomic nervous system is that of tuning the resonators, assisted by the apposition of the aortic and mitral valves.

Kalmansohn


Quantitative studies of the changes in arterial pressure, venous pressure, and left ventricular output were made in dogs as pericardial pressure alterations were recorded following instillation of colored saline into the pericardial sac. This was done under pentothal anesthesia. Increments in pericardial volume were continued until it was thought that circulatory arrest was imminent. The fluid was then removed rapidly, and arterial pressure, cardiac output, and venous pressure were again measured. Peripheral resistance was calculated by dividing mean arterial pressure by cardiac output. It was noted that as cardiac output fell, venous pressure rose. Arterial blood pressure
was still maintained after there had been considerable drop in cardiac output and increase in venous pressure. At first peripheral resistance remained stationary and then later, during the tamponade, increased. Blood pressure fell when it appeared that the animal was at the point of circulatory cessation. It is concluded from this experiment that simple measurement of venous pressure is the best indicator as to the status of the circulation in cardiac tamponade. If blood pressure is depressed it is indicative of imminent circulatory collapse and here rapid pericardial aspiration may be lifesaving.

LEVINSON


Heating the carotid blood in anesthetized cats and in decerebrate cats where the hypothalamus had been removed resulted in a fall of blood pressure and increased respirations. The blood pressure fall was in the range of 40 to 70 mm. Hg and was not associated either with a significant change in heart rate or with detectable perspiration. The effect was not due to a reflex from the carotid sinus or carotid body, since it was present after bilateral section of the lower four cranial nerves. The authors note that recent studies have revealed a similar fall in blood pressure produced by local heating of the medulla and therefore conclude that the heated blood produces its effects by acting on the medulla.

KARPMAN


Experiments were conducted on dogs under intravenous pentobarbital anesthesia. Cardiac output was calculated from dye-dilution curves and the effects of respiration, asphyxia, and muscle relaxants were determined. Cardiac output was less at the beginning of lung inflation. During maintained lung inflation the cardiac output increased to the preinflation level. Cardiac output increased about 75 per cent on the average during short periods of asphyxia; muscle relaxants differed in their ability to reduce cardiac output, only d-tubocururaine significantly reducing cardiac output. The authors believe that, if it is desired to maintain output at the highest level, the fraction of the respiratory cycle time devoted to lung inflation must be kept to a minimum. The cardiac output increased to approximately the same level during asphyxia whether or not the dogs were pretreated with muscle relaxants, suggesting that muscle relaxants do not significantly interfere with the mechanisms responsible for the compensatory increase in cardiac output.

KALMANSON

PULMONARY DISEASE


The effect of intermittent positive-pressure breathing on cardiac output was studied, utilizing a group of 31 men, whose ages ranged from 24 to 70 years. All subjects exhibited chronic pulmonary disease, such as pulmonary fibrosis or pulmonary emphysema. All subjects were well acquainted with the use of the intermittent positive-pressure-breathing apparatus. Cardiac output was determined by an indicator-dilution technic using T-1824. Results revealed a small but consistent drop in stroke volume utilizing a peak pressure setting of 20 cm. of water at 20 minutes. Blood pressure and heart rate did not seem to be altered appreciably. Although changes in peripheral resistance were not remarkable, it was noted that a rise in peripheral resistance took place whenever cardiac output fell. Of particular interest was the fact that cardiac output returned to normal, and occasionally to above normal, following the cessation of intermittent positive pressure.

MAXWELL


Four cases of patients with pulmonary infarcts complicated by staphyloccocal infections are presented. One case terminated fatally. In all four patients, the sputum was positive for staphylococcus pyogenes and the patients were treated with a course of chloramphenicol and erythromycin. One patient was also given tetracycline. These drugs were given following sensitivity tests. The authors feel that patients with pulmonary infarcts are very susceptible to staphyloccocal invasion and that when sputum in such patients changes from blood streaked to hemorrhagic pus, staphylococci are almost always present. In addition, the hemorrhagic infarct provides an ideal site for bacterial growth. They stress the importance of septic technic, isolation of infected patients, careful epidemiologic study, and energetic and appropriate antibiotic therapy when staphyloccocal invasion does occur.

KRAUSE
ABSTRACTS

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