ABSTRACTS

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ATHEROSCLEROSIS


The eysterma chyli of rats placed in restraining cages were cannulated in order to study the composition of chyle chylomicrons which were separated by ultra centrifugation. Analysis of lipid composition of chylomicrons showed that the feeding of cholesterol led to a 3-fold increase in the cholesterol content of the chylomicrons as compared with chyle from animals fed a similar diet without the cholesterol. Feeding of large amounts of lecithin did not raise the concentration of phospholipids, indicating that practically all of the phospholipids fed were hydrolyzed in the intestine and that their fatty acids appeared as triglycerides in the chylomicrons. Chylomicrons obtained from rats absorbing olive oil contained approximately 0.5 per cent protein, which could not be reduced by repeated washings with physiologic saline, indicating that protein was an integral part of the chylomycin. Following the feeding of radioactively labeled amino acids, the protein in the chylomicrons showed high specific activity in the first hour suggesting that at least some of the chylomicron protein was synthesized in the intestinal wall.

MAXWELL


Extending previous studies of fatty acid metabolism, the authors determined the rates of oxidation and plasma turnover at C14 palmitic acid administered intravenously to dogs as either chylomycin triglyceride fatty acids (TGFA) or as albumin-bound unesterified fatty acid (UFA). Analysis of specific activity in both plasma fatty acids and expired carbon dioxide showed that palmitate oxidation proceeded at similar rates following administration as either TGFA or albumin-bound UFA. Specific activity data and derived fluxes of radioactivity in both plasma as UFA and expired air as carbon dioxide showed that all chylomycin TGFA was not retransferred to blood as UFA prior to oxidation. It was inferred that approximately one half of the TGFA was directly oxidized without first appearing in the UFA fraction of plasma lipid. The authors believed that chylomycra represented a plasma vehicle for transport of fat which was directly available for oxidation. Comparison of data from animals given a high carbohydrate diet with that from dogs fasted prior to fatty acid infusion showed that carbohydrate feeding decreased both the oxidation of TGFA and the amount of UFA appearing in the blood after administration of TGFA, although the time of appearance of labeled UFA was unrelated to the previous diet.

FREEDBERG


A sustained reduction of the serum cholesterol levels in a group of 53 patients with hypercholesterolemia was obtained with a combination of niacin and pyridoxine. The dose of each vitamin administered during a 10-week period was 3 gm. daily in combination. The effect was obtained in those with familial or idiopathic hy-
percholesterolemia as well as those with diabetes and myxedema. Dietary fat restriction was not essential indicating that endogenous cholesterol metabolism was affected. A protein intake of 100 Gm. daily was provided to avoid liver damage and no alteration in liver function tests was observed. The side effect of flushing was combated with ascorbic acid, reserpine and Metrazole with some improvement, however, 15 patients refused continuation of the medication after 1 week. Nausea and vomiting were prevented by taking the tablet after meals. In 20 patients completing the 10 weeks of treatment the serum cholesterol fell from an average of 338 mg. per 100 ml. to 203 mg. per 100 ml. Upon discontinuing the drugs, the serum cholesterol values rose to pretreatment levels. The mechanism of action was not known although it was suggested that niacin has some effect upon the clearing factor of the blood and upon lipid transport.

**SHUMAN**


Currently, dietary fat is commonly implicated in the production of ischemic heart disease. The authors accepted the thesis that the level of serum cholesterol may be associated with a high intake of fat foods. However, the hypothesis that ischemic heart disease resulted from a disturbance in fat metabolism was founded upon assumption than fact. Other factors, such as genetics and environment, were probably equally important. Nevertheless, of all variables in our life which we can control, the dietary fat can best be related to the disease process. Much of the accumulated data related a fat diet to ischemic heart disease by pathology, metabolic studies, and epidemiology were reviewed. The author suggested caution in literal interpretation of these data.

**Krause**


The authors reviewed the possible role of the hormones on circulating lipids. They stress caution in transferring data obtained through animal experiments to those of the human. As a representative lipid, they discussed those factors that raised and lowered the level of blood cholesterol. For example, menopause, pregnancy, diabetes, myxedema, bilateral ovariectomy and androgens raised the blood cholesterol, whereas thyrotoxicosis, ACTH, cortisone, thyroxine, and estrogens lowered it. The concentration of circulating lipids was dependent upon changes in hepatic-cholesterol biosynthesis, degradation and excretion, interchanges between the plasma and the interstitial fluid, and changes in plasma volume. Hormones may affect the concentration of the circulating lipids by influencing any of these parameters. At present, it was concluded that there was insufficient evidence to reach any definite conclusions concerning the mechanism of the effect of any hormone on the circulating blood lipids.


Lipids are for the most part insoluble in water and in the blood they are linked with proteins as complex water-soluble molecules (lipoproteins) and as emulsion particles (chylomicrons). The 2 main classes of lipoproteins are alpha and beta lipoproteins. Chylomicrons consist chiefly of triglyceride, but they also contain a small proportion of cholesterol and phospholipid, and in the blood they are apparently stabilized by a surface layer of protein. In general, lipoproteins are removed from the blood through the capillary membranes. The permeability of the capillaries varied for the different lipid complexes. Since beta lipoprotein particles are larger than alpha, it is likely that the capillary membrane is less permeable to them. At certain sites, cells in contact with the blood, such as reticuloendothelial cells or possibly hepatic parenchymal cells may be able to take up lipids directly. When heparin was injected into the blood there was an increase in the concentration of unesterified fatty acid in the blood and this was associated with an increased rate at which chylomicrons were removed from the circulation. The latter apparently was accomplished by the production of an enzyme which hydrolyzed chylomicron lipid. This phenomenon was responsible for the "heparin-clearing" reaction. Unesterified fatty acids occurred in the blood as soluble complexes with the plasma albumin. These complexes were very readily removed from the blood through the capillary membranes.

**Krause**


During recent years attention has been drawn to the association of cholesterol and polythenoid fatty acids and to the possible connection of these esters to the pathogenesis of atherosclero-
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sis. With the advent of radio-isotope techniques, acetate has been shown to be a precursor of cholesterol. Furthermore, more recently data have demonstrated that at least 2 substances are concerned in the intermediate phase between acetate and cholesterol, namely: squalene and mevalonic acid. Exactly how mevalonate is synthesized from acetate and how squalene is synthesized from mevalonate remains to be discovered and is in the process of investigation.

KRAUSE


Nicotinic acid (nicacin) in relatively large doses can reduce the serum cholesterol in man and rabbits. In rabbits it can also inhibit the production of experimental cholesterol atherosclerosis. The reports on the toxicity of nicotinic acid were contradictory. However, it was pointed out that the high acidity of the compound rather than a specific action may be responsible for the occasional disturbances, such as the gastrointestinal reactions. Tests conducted on 12 healthy young individuals showed that a buffered solution of nicotinic acid was as efficacious as the pure nicotinic acid in decreasing the serum cholesterol. Hence, when nicotinic acid is poorly tolerated, a solution of nicotinic acid buffered with sodium bicarbonate (or sodium and potassium bicarbonate) deserves to be tried.

KRAUSE


Study of autopsy findings in 16,269 patients from Basel, Switzerland, and 5,836 patients from Marburg, Germany, showed that age was the greatest single factor in the incidence of general atherosclerosis and coronary sclerosis, which became practically 100 per cent after the age of 70. At the same age, this incidence was greater in men than in women; the difference was greatest under 50 years. Atherosclerosis involved the coronary arteries more often in men than in women. At the same age, the incidence of arteriosclerosis was greatest in patients with diabetes, hypertension and gallbladder disease; smallest in those with malignancies, tuberculosis, and leukemias. In Basel no differences were found in the incidence of atherosclerosis during the war (1939-1945) and after the war (1946-1953). A marked decrease during the war years, which were accompanied by deficiencies in alimentary fats, was previously found in Marburg in clinical observations but this must yet be confirmed on a larger autopsy material.

LEFESCHTIN


Various tissues of the rat were analyzed for their cholesterol content during phosphatide-induced hypercholesterolemia. Rats prefed a sterol-free diet showed an increase in cholesterol content of the liver and decreased cholesterol content of the adrenal gland at the peak of hypercholesterolemia. There was no change in the cholesterol content of other organs or tissues. In rats prefed excess cholesterol, a decline in liver as well as adrenal cholesterol occurred with no discernable change in other tissues. It was postulated that induced hyperphospholipidemia appears capable of mobilizing only stored or excess cholesterol from any tissue.

KAYDEN


Low-density lipoproteins and serum cholesterol concentrations were increased in dogs after bilateral nephrectomy maintained by peritoneal dialysis. The high-density fraction, which is the major lipoprotein fraction in the normal dogs, decreased moderately. When a high-protein diet was fed, the lipid changes were accentuated. Blood pressure rose in all nephrectomized dogs, but there was no correlation between elevation of blood pressure and changes in concentration of cholesterol and lipoproteins of the serum. Extensive arteriolar necrosis was present in many of the dogs at necropsy but this did not appear to be correlated with the changes in cholesterol and lipoproteins, except that the more marked changes occurred in high-protein-fed animals. No significant serum lipid changes were noted in starved dogs after 5 days. It was suggested that the postnephrectomy lipid pattern may be related to stimulation of adrenal activity.

KAYDEN


The degree of saturation of the fatty acids of the various plasma lipid fractions of 8 normal
subjects was compared to that of 7 patients with myocardial infarction. If a deficiency of unsaturated fatty acids predisposed to atherosclerosis, a significant difference in the iodine number of at least 1 lipid fraction should be detected. The results failed to demonstrate any significant difference in the iodine numbers of the plasma cholesterol esters, phospholipids, triglycerides, or unsaturated fatty acids in the group with coronary artery disease as compared to normal controls. This would indicate that the plasma fatty acids in respect to unsaturation were similar in the 2 groups. The theory that a deficiency of unsaturated fatty acids was of etiologic importance in atherosclerosis was not supported by this study.

**SHUMAN**


Postmortem findings in 250 deaths from coronary sclerosis were compared to the findings in a group of 250 individuals of similar age and 6 who had died of natural or violent causes. The thyroid gland weighed more and the incidence of goiter was greater in the group with coronary sclerosis although no other endocrine organ was significantly different. Among these with coronary sclerosis those with goiter were heavier than those without goiter. The heart weighed more in the goitrous coronary sclerosis subjects than in the nongoitrous group. A pathogenetic relationship between goitre and arteriosclerosis through the possible role of hypothyroidism and increased thyrotropin production was postulated.

**KURLAND**


The epidemiology of cardiovascular disease in Finland was of special interest because the mortality rate of men from coronary disease was higher there than in any other European country. To determine whether the higher incidence in East Finland as compared to West Finland was due to diet, food consumption was determined by weighing, and the daily calories and nutrients were calculated. Thirty-five per cent of daily energy was derived from the 98.9 to 105 Gm. of daily fat which was similar in East and West, both in summer and winter. There was a higher consumption of bread, milk, butter, and fish in the East and of vegetables, margarine, and eggs in the West. More protein was consumed in the East, especially in summer. No significant statistical difference existed in the intake of saturated fatty acids or poly-ones. In both areas, the intake of saturated acids compared to poly-ones was rather large. The intake of iodine, ascorbic acid, and vitamin E was significantly larger in the West.

**KURLAND**


The surprising incidence of coronary disease in Finland, particularly East Finland, led to a field study of total cholesterol and alpha- and beta-lipoproteins in 869 healthy men in Helsinki and in 2 rural regions. The average total cholesterol in men in the populations studied in Finland was higher than that of men studied elsewhere. The difference was due to the beta-lipoprotein fraction. At all ages and work grades, the averages were higher in East than in West Finland particularly over age 30. Environmental rather than hereditary factors seemed to be important. The cholesterol level appeared to be somewhat related to the habitual level of physical activity among men aged 40 to 44. Smokers tended to have higher cholesterol levels and lower blood pressures than nonsmokers. Women had higher levels of alpha-lipoprotein though the level of total cholesterol was similar to that for men.

**KURLAND**


Extensive immigration to Israel has produced a population of diverse backgrounds permitting extensive epidemiologic investigation. For arteriosclerotic heart disease, there was a distinct preponderance of people of occidental over those of oriental origin, but this preponderance was absent or even reversed for vascular lesions of the nervous system. Similarly, men exceeded women in the incidence of coronary localization but not of cerebral. It is suggested, tentatively, that coronary and cerebral arteriosclerosis may be 2 basically different phenomena.

**KURLAND**

*BLOOD COAGULATION AND THROMBOEMBOLISM*


Warfarin was used to treat 175 patients with thromboembolic disease. It acted rapidly and 95 per cent of all patients reached therapeutic prothrombin levels in 28 hours. With daily doses of the drug adequate to maintain a therapeutic prothrombin time the duration of action was...
about 36 hours. In large doses warfarin had a sustained effect up to 5 days. The authors recommend 35 to 50 mg. for initial therapy. They found the average maintenance dose to be 9 mg., and 80 per cent of all patients were maintained on daily doses of 5 to 15 mg. Prothrombin time was rather easy to control with warfarin both for short- and long-term therapy. Care must be taken to allow for its cumulative action. Variations in daily dosage of as little as 0.5 mg. are suggested for optimum control of the anticoagulant effect.

**Krause**


After discussing the many difficulties involved in the evaluation of results and the choice of patients in the long-term ambulatory anticoagulant treatment of myocardial infarction, the authors urged that some standard method for the expression of data be adopted so that the results of various series would be mutually comparable. They presented a diagram and table used for this purpose which separated primary from recurrent infarction and concerned itself with recurrences, thromboembolic complications, and deaths during short- and long-term therapy in both groups. In order to make the plan applicable to varied periods of treatment, the results were recorded for each 6-month period following institution of treatment.

**Freedberg**


The author reviewed 169 cases of pulmonary embolism and infarction. In 47 instances pulmonary thromboembolism was the cause of death, in 26 it was a contributory cause, and in 96 it was an incidental cause of death. In this particular series, pulmonary embolism or infarction occurred in 11.2 per cent of 1507 autopsied cases in a 6-year period. Fifty-six per cent of the patients came from the medical service and 26 per cent from the general surgical service. Evidence was presented to support the contention that this was a disease of the aged, especially the cardiac patient or those with metastatic malignant disease. In the surgical patient it was a particularly prominent problem in those who had undergone laparotomy or lower extremity amputation. Pulmonary infarction complicated embolism in about one half of the cases, and about two thirds of the infarcts were found in the lower lobes of the lungs. As in other studies, the author agreed that the source of the majority of pulmonary emboli was asymptomatic leg-vein thrombosis. When adequate study was obtained and the diagnosis of pulmonary embolism or myocardial infarction was still in doubt, it was recommended that anticoagulant therapy be used (providing no contraindication to it existed). It was conceded that an occasional patient without the disease may be treated with this regimen.

**Krause**


The measurement of serum enzyme activity has been increasingly employed as an adjunct for the diagnostic confirmation of myocardial infarction. Several drugs may influence such activity and among them are certain anticoagulants (including bishydroxycoumarin and ethyl biscoumacetate). When such drugs are used in patients in whom diagnostic enzyme levels are obtained, cognizance must be taken of the potential hepatic effect of the anticoagulants and the reflection of this phenomenon in alteration of serum transaminase and lactic dehydrogenase activity.

**Kitchell**


The hypothesis that the incidence of coronary-artery disease is inversely related to the general level of physical activity was studied by measuring the effect of activity on the increase in the recalcified-plasma-clotting (R.P.C.) time which follows ingestion of a high-fat meal. The R.P.C. time at 3½ hours after a fat breakfast was significantly shorter than the fasting value while the subjects were sedentary. This significant shortening was abolished as the result of moderate exercise. The fasting R.P.C. time was shorter, and its reduction after 85 Gm. of fat was greater in convalescent-ward patients than in sedentary students.

**Kurland**


Myocarditis with necrosis and hemorrhage was produced in the hearts of mice by adding Di-
Cumarol to either purified or pellet diets at levels of from 40 to 200 mg. per Kg. diet. Vitamin E supplements to the diet did not modify this effect of Cumarol, but it was prevented by vitamin K, at 2 times or Menadione at 8 times the dietary level of Cumarol.

Rinzler


The records of 90 patients who were followed for at least 6 months off and 6 months on therapy were analyzed to assess the benefit of anticoagulant therapy and the clinical factors associated with its failure. Although a marked reduction in the recurrence rate of thromboembolism during anticoagulation was confirmed, a statistically significant effect was not demonstrable by the chi-square test in individual patients unless they had been treated for 2 years or exhibited a strong thrombotic tendency off therapy. Thromboembolism was more likely to occur during anticoagulant therapy in patients with marked impairment of cardiac function evidenced by congestive heart failure, atrial fibrillation, and double mitral lesions. Even in the group with heart failure, there was a marked reduction in the rate of thromboembolism during therapy. The danger of recurrent thromboembolism was highest shortly after a previous episode and diminished to a steady level after the first 6 weeks. It was therefore recommended that all patients with 1 embolic episode due to rheumatic heart disease be given at least a 6 weeks' course of anticoagulants. Since there was an increased tendency to thromboembolism within 6 weeks after stopping anticoagulants, the prothrombin level should be lowered gradually when therapy is to be discontinued.

Kurland

CONGENITAL ANOMALIES


The author defined the Eisenmenger complex in the light of present knowledge as pulmonary hypertension at systemic level, due to a high pulmonary vascular resistance (over 800 dynes sec./cm.²), with reversed or bidirectional shunt through a large ventricular septal defect (1.5 to 3 cm. across). As a syndrome he widens his concept to include a shunt at any level and then lists 12 causes of the syndrome. These are patent ductus arteriosus, aortopulmonary septal defect, persistent trunae arteriosus, transposition of the great vessels (with ventricular septal defect), single ventricle, ventricular septal defect, common atrioventricular canal or persistent ostium primum, single atrium, atrial septal defect, hemianomalous pulmonary venous drainage, total anomalous pulmonary venous drainage, and corrected transposition (with ventricular septal defect). As defined in his paper the incidence of the Eisenmenger syndrome was 8 per cent of the first 1,000 cases of congenital heart disease in his series. All patients with Eisenmenger syndrome had cyanosis, clubbing, polycythemia, and effort dyspnea, usually dating from infancy or early childhood. Recurrent hemoptysis began in adult life and can prove fatal. If patients survive other risks, such as cerebral abscess, bacterial endocarditis, and ill-advised surgical intervention, they succumb finally to heart failure, usually in the fourth or fifth decade. Physical signs common to all include a small or normal pulse, normal venous pressure, with or without slight predominance of the a waves, an impalpable left ventricle, and a slight or moderate lift over the right ventricle and pulmonary artery. On auscultation a loud pulmonary click followed by a short pulmonary systolic murmur, a palpable and sharply accentuated pulmonary component of the second heart sound, and often a loud pulmonary diastolic murmur can be heard. The characteristic venous pulse and auscultatory signs of tricuspid incompetence may complicate the picture. The electrocardiogram shows a normal or rather prominent P wave and usually moderate or considerable right ventricular preponderance. X-rays revealed conspicuous dilatation of the pulmonary artery, slight to moderate cardiac enlargement (chiefly of the right ventricle), and peripheral vascular markings that are usually oligemic, but which may be normal or even slightly plethoric.

Krause

CONGESTIVE HEART FAILURE


Patients with congestive heart failure accompanied by gross peripheral edema, hepatic congestion, and venous hypertension with failure due to rheumatic, arteriosclerotic, or hypertensive heart disease were studied. All patients were on a metabolic balance ward where measurements of water, sodium, potassium, chloride, and nitrogen were performed. All patients received a low-sodium diet and digitalis, and certain of the patients received Thiomerin while the others received no additional diuretic ther-
apy. Sodium, potassium, chloride, and nitrogen were analyzed in diet, urine, and stools; changes in extracellular fluid were calculated from chloride space, and in those subjects studied body water was determined by deuterium dilution before and after diuresis. In all patients studied with or without additional diuretic therapy, chloride space contraction approximated total water loss, indicating an insignificant change in the cellular water compartment during diuresis. In those subjects showing spontaneous diuresis and in those who responded readily to mercurial diuretics with a loss of gross edema, the ratio of sodium to chloride exceeded unity. However, in those patients in whom a suboptimal response to diuretic therapy occurred and who never became entirely edema free, chloride loss exceeded sodium loss. This latter group was clinically felt to have more severe and advanced heart disease and had previously been partially or completely refractive to conventional forms of treatment. No consistent pattern of potassium metabolism could be established throughout the entire patient group. Nitrogen balances were also variable. No uniform cellular cation shifts could be demonstrated during diuresis. In those subjects in whom loss of cell potassium occurred, there was a reciprocal shift of sodium into the cells. In the majority of subjects the calculated decrease in total cation exceeded the observed negative balance, a finding interpreted by the authors as evidence of cation binding or osmotic inactivation.

MAXWELL

CORONARY ARTERY DISEASE


Seven instances are described in which cutaneous petechiae were found at necropsy in patients who had died of acute coronary insufficiency. These petechiae were found to have occurred in areas commonly associated with referred cardiac pain. Two of the 7 patients had been subjected to frequent clinical examinations before death and in neither cases had cutaneous petechiae been noticed. In 4 of the 7 patients there were hemorrhages directly related to the coronary arteries themselves; in 3 of these there were hemorrhages in the coronary adventitia, and direct involvement of the nerve elements may have played some part in the production of vasoconstrictive reflexes of the skin and coronary arteries. In the fourth patient there was subintimal hemorrhage in the wall of the coronary artery.

MAXWELL


One hundred fifty-five patients with a primary diagnosis of central nervous system disease were analyzed. In 66 (43 per cent) of these patients the acute symptoms were ascribed to cerebrovascular disease. Of the 66 patients, 8 (12 per cent) had simultaneous acute myocardial infarction associated with their illness; 3 had concomitant acute coronary insufficiency; 4 had other concurrent cardiac disease productive of emboli to cerebral arteries; and in 4 additional patients with cerebral symptoms there was a strong likelihood of associated acute coronary insufficiency. It was rather surprising to find that of the 66 patients who had presenting symptoms of strokes, 15 (23 per cent) had associated acute cardiac disease. Hence, in all patients with the clinical picture of cerebrovascular disease, it is important to be aware that not uncommonly cardiac disease may be the mechanism primarily at fault. Prompt recognition of this situation with an accurate diagnosis will enable specific therapy to be employed and this may result in a more favorable prognosis for the patient.

KRAUSE


The T wave is normally asymmetrical with a slow rising, ascending limb, and a more rapidly descending terminal portion. The vector TsE loop showed this uneven angular velocity. Tall symmetrical T waves were often seen in the precordial leads when myocardial infarction had occurred in the posterior, lateral, or inferior walls and could also occur in infarctions of the anterior wall that extended to the lateral or diaphragmatic surfaces of the heart. Although hyperpotassemia and certain gastrointestinal diseases may produce similar electrocardiographic changes, these conditions can usually be differentiated clinically. The most acceptable reason for the production of a symmetrical T wave was a change in the direction of the vector TsE loop to a more anterior position when the posterior portion of the myocardium was injured. When ischamic S-T depression first appeared, the T wave often became symmetrical. It increased in amplitude during the healing phase, and could remain, often permanently, as the only sign after scar formation was complete. It was suggested, but not proved, that when the myocardium was injured, potassium was released into the extracellular fluid, producing the same
electrocardiographic effect as hyperpotassemia. However, the base of the "hyperpotassemic T wave" was narrow as contrasted to the broad base of the "coronary T wave."

KRAUSE


In order to determine the feasibility of applying direct surgical methods in the treatment of coronary artery disease, the coronary circulation of 190 autopsied hearts was studied after injection with a barium-glycerine mixture. Occlusive coronary lesions were found in 114 hearts. Of this group 35 patients had had no clinical manifestations. Of the 79 patients with clinical arteriosclerotic disease, 23 had had angina pectoris as their sole or main clinical manifestation. The earliest and most sharply localized occlusive lesions were found in the subclinical group and the most advanced and widespread involvement occurred in those patients with angina pectoris. Taking into consideration the topographic accessibility of the lesions, as well as the luminal size and outflow characteristics of the main coronary branches, the rate of possibility of surgical palliation was judged to be 17 per cent in the subclinical group and 43 per cent in the clinical group, whereas the possibility of surgical curability was estimated to be 40 per cent in the subclinical group and only 13 per cent in the clinical group. This study pointed out the limited role of direct surgical procedures in the treatment of coronary atherosclerosis at the present time and indicated the need for a safe, reliable method of coronary angiography in selecting those few patients who may be helped by such surgery.

SAGALL


In a 78-year-old woman without cardiac symptoms, who died in hepatic coma, autopsy showed a fusiform aneurysm of the intermediate branch of the ramus descendens of the left coronary artery, about 20 mm. in cross section. The aneurysm was filled with a partly organized thrombus. The internal elastic lamina had practically disappeared in the wall of the aneurysm, while the media contained numerous thin-walled blood vessels resembling those found in aneurysmas. These findings were probably responsible for the formation of the aneurysm.

LEFESCHKIN


Based on a study of 867 patients seen during 1948-55, the Indian point of view on etiological aspects of coronary heart disease was presented. Observations relative to age, profession, family history, body build, and the association with diabetes and hypertension did not differ from those of the Western world. The sex ratio, too, was much the same as that described by Western authors. Feminine immunity was no greater in India in spite of the fact that women lived a more sheltered and indoor life, that they were mostly vegetarian, and that addiction to alcohol and smoking was almost unknown to them. The fat content of the Indian diet was poor as compared with European standards. Consequently the authors doubted that dietary fats played a significant role in causing coronary heart disease. Also, it was noted that vegetarians were no less prone to develop coronary disease, and the same was true of non-smokers. One-half of the patients belonged to the Sikh community, whose religion forbids smoking. Obesity, long considered in the etiology of coronary heart disease, was particularly evident in the female patients. The authors recognized that the standard of vital statistics in India was not equal to that of the Western world. Hence, the true incidence of coronary heart disease was probably not accurately known. However, coronary artery disease was present in 867 cases or 28.4 per cent of 3,054 cardiac patients. The writers concluded that coronary disease was not uncommon in materially less favored countries such as India.

KRAUSE


The problems in developing technics for measuring ischemic heart disease in unselected populations and ensuring comparability of the medical indices were demonstrated in 2 surveys of ischemic heart disease made on a random sample of miners and ex-miners and, for contrast, the inhabitants of an agricultural area. The population at risk was a random sample of inhabitants enumerated by a private census. The diagnosis of ischemic heart disease was based on clinical, radiologic, and electrocardiographic evidence. The last was most valuable but suffered from technical difficulties and considerable difference of interpretation by independent cardiologists. No significant difference between the 2 areas in prevalence of ischemic heart disease was proved. Those persons diagnosed as having ischemic
heart disease were taller and heavier than the others. The siblings of men with ischemic heart disease had a higher mortality than the siblings of the controls. There was no significant difference in the mean serum cholesterol levels.

Kurland


The effects of atropine cardioacceleration on the coronary circulation were studied in 6 patients. Coronary flow was measured by the nitrous oxide desaturation method following catheterization of the coronary sinus. One to 1.4 mg. of intravenous atropine sulfate increased the cardiac rate and, in parallel fashion, oxygen consumption. Coronary vascular diastolic resistance decreased, and coronary flow increased in proportion to the increase in myocardial oxygen consumption. Atropinization produced virtually no other changes in hemodynamics once a steady-state was reached.

Kurland


The experience with myocardial infarction at the Harlem Hospital, New York City, from 1950 through 1954 was reviewed. This diagnosis was suspected in 312 of 111,323 patient admissions and confirmatory and confirmatory methods were available in 152 of these. One hundred thirty-one were Negro; 20 were Caucasians, the incidence ratio being 1:2.5 respectively. Of the Negro patients, the average age was 58 years and 52 per cent were men. Eighty-seven per cent described precordial pain accompanying the infarction, which contrasts with a number of reports claiming that the Negro was less subject to cardiac pain than the Caucasian. The case fatality rate was 47 per cent, which was probably heightened by the presence of other heart disease or diabetes mellitus in 71 per cent of the whole Negro group. The authors concluded that myocardial infarction in the Negro was similar in incidence and in clinical characteristics to that occurring in the general population.

Rogers


The rarity of cardiac infarction in the Bantu and to a lesser degree in other native Africans was confirmed. Coronary atherosclerosis in the Bantu was even rarer, and adequate explanation of this was lacking. Cardiac infarction was found in 3 of 188 adult Bantu autopsied in the 1952-1956 period in 2 Capetown hospitals. The same number of cases was detected electrocardiographically during those 5 years in which there were 760 such instances in Europeans. Of the autopsied patients, 1 was a 40-year-old obese man who had angina pectoris for 3 months, then died suddenly from thrombosis of diffusely atherosclerotic coronary arteries. The other 2 patients were men aged 39 and 45 years. Both had cardiac infarcts apparently resulting from insufficiency of nonatherosclerotic coronary arteries; 1 had severe hypertensive heart disease and the other had syphilitic aortic regurgitation and heart failure but no significant coronary ostial narrowing.

Rogers


In 77 patients with acute myocardial infarction, observed within the first 24 hours, the active blood volume has been measured. The blood volume was calculated from venous hematocrit and Evans-blue dye dilution in samples obtained 4 to 9 minutes after injection. No systematic error has been found in previous independent studies comparing isotope tagging and dye-dilution methods to measure the red cell mass. Other hemodynamic data included arterial pressure, direct venous pressure, and fluorescein or decholin circulation time; estimates of the cardiac output were obtained from the amplitude/rate product (Liljestrand-Zander) and also from simultaneous blood volume and circulation-time determinations. In 70 of these patients a decrease in active circulating blood volume was found; 58 of these had no evidence of cardiac failure; 35 had also initial hemococoncentration, indicative of shock as defined by Wollheim; 23 were in simple hypovolemia. Actual circulatory collapse, with arterial pressure below 80 mm. Hg, was uncommon in myocardial infarction. In 19 patients the venous pressure was increased, and the circulation time prolonged, indicating mechanical cardiac incompetence: the blood volume was then increased in 7 patients (with decompensation); it remained low in 12 others (without decompensation). Evidence of cardiac failure had very serious prognostic implications: mortality was 80 per cent in this series. In the treatment of circulatory failure those sympathomimetic amines were advocated that increased the circulating blood volume and had little hypertensive effect; digitalis should be used only when there is evidence of cardiac incompetence. Transfusions were less beneficial in these patients than in other patients with shock, and were potentially dangerous. In view of its effect on
active blood volume the armchair treatment was contraindicated.


In a total of 760 consecutive autopsies of cardiac subjects, coronary atherosclerosis was found in 27.9 per cent: 70 of these 212 patients had had typical angina pectoris without prolonged attacks, except the terminal event in 35 of them. Detailed macroscopic study of the heart failed to show coronary artery occlusion in only 10 cases; 1 of the 3 main branches was occluded in 22 hearts, 2 in 20, all 3 in 18. Myocardial changes, absent in 15 specimens, were relatively small in 29, and large in 26: as some hearts had more than 1 large lesion, 30 infarcts were counted in this series. The average weight in 23 cases of pure coronary atherosclerosis of this series was 533 Gm.; therefore, pure atherosclerosis may induce cardiac hypertrophy. Angina of effort, pure or associated with other types of cardiac pain, was present in 148 of the total 760 autopsies: only 19 of them (12.8 per cent) did not have significant coronary atherosclerosis. It was concluded that angina pectoris was usually due to coronary atherosclerosis; coronary occlusion was common, although not always present; myocardial infarction was frequently found at autopsy. Pathologic myocardial changes were more severe in patients with spontaneous angina than in those with pure effort angina, but no great difference was noted. More than the type and circumstances of the painful episodes, the evolution of the disease suggested the degree of the arterial changes: more severe coronary and myocardial lesions were seen in cases with rapid evolution, in those of very long duration, and especially in patients with status anginosus (defined as frequent attacks of short duration). As all of these 70 subjects died of causes independent of coronary disease, and showed similar distribution of anatomic changes as the total group, it was tentatively inferred that the present series was representative of "ambulatory" patients with common angina.

ELECTROCARDIOGRAPHY, VECTORCARDIOGRAPHY, BALLISTOCARDIOGRAPHY, AND OTHER GRAPHIC TECHNICS


Considerable elevation of the RS-T segment occurs in pathologic states, such as acute myocardial infarction, acute pericarditis, and ventricular aneurysm. Persistent elevation is also seen in the right precordial leads in association with intraventricular block, especially of the left bundle-branch type, and left ventricular hypertrophy. Various investigators have placed emphasis on the specific amount of elevation for it to be significant as well as on the contour of the are that is formed when the RS-T segment rises above the junction. The electrocardiographic sign of injury is a characteristic type of displacement of the RS-T segment. This was thought to be due to failure of the injured zone to become depolarized when the muscle was stimulated. The excitatory wave was completely blocked at the boundary which separated the uninjured from the injured region. The latter, therefore, remained polarized and was positive with respect to the uninjured segment. The authors presented 5 patients with the following electrocardiographic findings: prolongation of the QRS complex, considerable elevation of the RS-T segments on the right side of the chest, inverted or diphasic T waves over the right precordium, and no change in the pattern over a long period of observation. In none of these patients was there definite evidence of organic heart disease. One of the 5 died from a neurologic disorder and at autopsy had a normal heart. It has been suggested that this pattern may result from overlapping of ventricular activation and recovery with simultaneous recordings of potentials due to depolarization and repolarization. This was manifested by the fusion of the terminal portion of the QRS complex with the initial portion of the ST-T complex. This was apparently due to prolongation of the depolarization proved by the right bundle-branch block, although an unusually early onset of repolarization may also play a role.

Krause


In 18 autopsied patients with decompensated chronic cor pulmonale secondary to pulmonary emphysema, the electrocardiograms showed evidence of P-pulmonale in 20 per cent and right ventricular hypertrophy in 38 to 72 per cent, depending on the criteria employed for that electrocardiographic diagnosis. Study of these patients also showed that in chronic cor pulmonale a pattern of evolution of the electrocardiogram developed. The first and earliest stage showed no deviation from the normal electrocardiogram with the major electromotive force being di-
rected leftward and posteriorly. The second stage consisted in the development of a rightward direction of the major electromotive force but with posterior orientation remaining. This change resulted in a rightward direction of the axis in the frontal plane and a prominence of S waves in the left precordial leads, but no prominent R waves in the right precordial leads. In the third and final stage the major electromotive force was directed anteriorly as well as rightward, producing tall R deflections over the right chest leads and rightward orientation of the axis in the frontal plane. In 4 patients with serial electrocardiograms this evolution was demonstrated. The authors pointed out that the success of various criteria proposed for the detection electrocardiographically of right ventricular hypertrophy depended directly on which stages of the evolution of cor pulmonale the criteria encompassed. No criteria could detect the right ventricular hypertrophy found at autopsy of those patients with cor pulmonale and normal electrocardiograms (30 per cent in this series of 18 patients) and criteria depending on the anterior orientation of the major electromotive force of stage 3 will detect fewer cases than those dealing with the changes of stage 2.

SAGALL


Thirty-one patients with either right or left ventricular hypertrophy, submitted to pulmonary or cardiac surgery, were studied with direct epicardial electrocardiographic leads to determine the spread of ventricular activation and the morphology of the QRS complex at different points on the anterior and lateral ventricular surfaces. With slight right ventricular hypertrophy only a delay in the onset of activation in all points of the right ventricular surface was found. With severe right ventricular hypertrophy the pattern of activation spread was altered in the heart as a whole. The principal change consisted of a delay of the activation in the outflow tract of the right ventricle with resulting patterns in this region of rsR'S', RsR'S', RsR'S, and qRs. With left ventricular hypertrophy a delay in the activation was found over all points of the left ventricular surface, particularly in the most basal and lateral points of the lateral surface, but the sequence of activation and the morphology of the QRS complex were not significantly altered. In left ventricular hypertrophy the electrocardiographic transition zone occupied the same points as in normal hearts, but in right ventricular hypertrophy it extended to the right ventricle's intermediate zone and occasionally to the pulmonary conus. In 1 patient with pure pulmonary stenosis an inversion in the spread of septal activation was found.

SAGALL


The effect of mephentermine upon cardiac arrhythmias found in 12 patients with various forms of heart disease was analyzed using a 12-lead electrocardiogram following intravenous administration of the drug. In 4 patients with atrial fibrillation and 1 with atrial tachycardia, no salutary effect on cardiac action was noted. Effective reduction in a functional atrioventricular block was produced and it was believed that supraventricular tachycardia with second-degree block represented a contraindication to the use of the drug. The frequency of premature ectopic impulse formation was decreased in 5 of 6 patients studied. Of these 5 patients, 2 sustained an increase in heart rate while 3 did not. The mechanism of action was described as a decrease in the refractory period, an increase in velocity of conduction and a positive inotropic effect. The antibrillatorary effect of mephentermine suggested that it may be of value during induction of anesthesia and during open heart surgery with therapeutic cardiac arrest and in hypothermia. The direct action of the drug upon the heart muscle in increasing the force of contraction and facilitating conduction may prove useful as adjunctive treatment in patients with chronic congestive heart failure.

SHERMAN


This article summarized the practical aspects of ballistocardiography and was based on a broad experience of over 20 years. Of the recording techniques in use, the author favored a high frequency table from which displacement was registered simultaneously with an electrocardiogram for timing. Each instrument should be individually standardized. Artifacts arising from respiration, movement of the patient or the building, or from resonance occurred frequently but could usually be overcome. The normal ballistocardiogram was described, emphasizing the systolic components which were the more in-
formative. The diastolic components usually were not clearly produced by shin-bar instruments, and they tended to superimpose on the systolic area in marked tachycardia. In healthy young adults, the tracing was extremely consistent in form; but in older healthy persons it was less so, probably because the older heart was weaker or occult cardiovascular disease was present in some instances. Interpretation of the abnormal tracing was to a considerable extent subjective and depended first of all on a thorough knowledge of the normal record. The structure of the I wave was regarded as an important indication of the force of cardiac contraction. In general, the more abnormal the ballistoeadiogram was, the more abnormal was the heart action. Four stages of abnormality were described. The utility of the ballistoeadiogram was considered to be mainly one of evaluating cardiac strength and coordination, and it was of less value in detecting cardiovascular structural defects. The overall value of the method when properly used was said to be comparable to that of a knowledge of blood pressure.

Rogers

ENDOCARDITIS, MYOCARDITIS, AND PERICARDITIS


Brief accounts are given of 3 elderly men who received sulfamethoxypyridazine for infections of the urinary tract and who died in 1 to 3 weeks with heart failure. Autopsy in each case disclosed extensive infiltration of eosinophilic leukocytes and histiocytes in the myocardium, particularly perivascularly, but without necrosis. Coronary atherosclerosis with myocardial fibrosis also was uniformly present. No other clinical or pathologic evidence of allergy was mentioned nor was it said whether any patient had received a sulfonamide in the past. The previous reports of similar myocarditis attributed to other sulfonamides and the absence of other likely etiologic factors led the authors to believe that the sulfamethoxypyridazine therapy produced the myocarditis.

Rogers


In various species of laboratory animals, predominantly subendocardial necroses can be produced after suitable conditioning with corticoids by sodium salts and stress, and these can be prevented by oral administration of potassium or magnesium chloride. Studies were undertaken to relate this experimental situation to the endomyocardial fibrosis found widely in man. Accordingly, lesions were induced by this technic in 1 group of rats and were prevented by magnesium chloride in another. In a third group, the rats were killed 20 days after cessation of treatment. In the first group, in eight of 10 animals, thick layers of subendocardial fibrosis had developed in those areas where the necroses were most plentiful. The histological appearance of these changes bore striking resemblance to the changes found in patients who died of endomyocardial fibrosis. In rats in which cardiac necroses were prevented by the prophylactic administration of magnesium chloride the secondary fibrosis did not develop.

Kuhlman


Pericardiectomy is useful in the management of tuberculous and chronic pericardial effusion of nonspecific etiology. The authors were concerned with the applicability of this procedure to all types of pericardial effusion. A case report of a successful operation in suppurative pericardial effusion is described. The procedure in conjunction with appropriate antibiotic therapy provided wide drainage of the infection into the pleural space where infection was more readily controlled by a dependently placed, indwelling tube. Although pericardiectomy was performed in a case of pericardial effusion due to malignant origin, the authors recognized that first, local instillation of radioactive colloidal gold or nitrogen mustard should be employed to alleviate tamponade before resorting to surgery.

Krause


Aortic or mitral valvular injury was produced in dogs with laryngeal biopsy forceps inserted in the right carotid artery, advanced to the level of the aortic valve and used to remove tissue. Animals that had evidence of valvular disease manifest by heart murmurs but with no evidence of complicating infection were given 1 to 4 intravenous injections of a suspension of Streptococcus mitis on succeeding days. Development of a persistent fever of 39.5 C. or more was con-
siderd indicative of active bacterial endocarditis. Positive blood culture was obtained in all febrile animals. Streptokinase and Streptodornase were administered intravenously at 12-hour intervals for 6 injections. The dogs that received intravenous enzymes survived only 3 days longer than the infected dogs that received no intravenous enzymes. This difference was found to be statistically insignificant. Only 4 of 11 enzyme-treated animals had vegetations measuring more than 6 mm., whereas 10 of 14 untreated dogs had lesions greater than this dimension. Application of the Chi-square test failed to establish a statistically significant difference. While inflammatory responses of the valves were not significantly altered in the dogs receiving enzymes as compared to the controls, it was the authors' conclusion that reduction of the vegetation suggested that fibrin deposition was impeded in the presence of active infection.

MAXWELL


The clinical findings and hemodynamic and angiocardiographic studies are reported in a 14-year-old boy with Marfan's syndrome; the diagnosis of endocardial fibroelastosis was advanced by exclusion of other disease processes. The pertinent literature was reviewed. Only typical cases, without evidence of degenerative and inflammatory changes, should be included; the etiology of this disorder remains obscure, although its origin during embryonal life appeared likely; the causal relationship of myocardial hypertrophy and failure was discussed.

CALABRESI

HYPERTENSION


The management of a patient with phaeochromocytoma who had an unusually wild and unpredictable fluctuation of the systemic blood pressure with periods of alarming hypertension alternating with profound shock was discussed. The use of intramuscular phentolamine ("regitine") was ineffective. However, the use of intravenous phentolamine produced dramatic improvement. This procedure of intravenous titration permitted leisurely control of the operative and postoperative periods of surgical excision of the tumor.

KRAUSE


While measuring systemic arterial blood pressure uterine ischaemia was induced in gravid dogs, cats, and human beings by raising intra-ovular pressure with balloons in the ovarian cavity. In dogs, increasing intra-ovular pressure for 7 to 20 minutes was accompanied by a slow increase in blood pressure which the authors found difficult to distinguish from physiologic variations in blood pressure. In cats, a biphasic blood pressure response to uterine ischaemia was found with an early rapid rise of 15 to 65 mm. Hg followed by a second prolonged rise after the intrauterine pressure had been released. Taehyphlaxis to repetition of filling and evacuation of the uterus was demonstrated. In 4 human subjects, intra-ovular filling of the uterus increased the blood pressure by 20 to 30 mm. Hg. Injection of concentrated perfusate of the uterus of the gravid dog elicited in the cat an initial fall in blood pressure followed by a slow and then a rapid rise. A similar effect was seen following injection of perfusate of the uterus of a gravid cat to the male cat. In both groups when an antihistamine was administered with the uterine perfusate, only the pressor effect was seen. The authors concluded that at least part of the pressor effect depended on a humoral mechanism and thought that this was most likely the second gradual rise seen in the cat. They concluded from the perfusate experiments that vasoactive substances can enter the circulation from the placenta and that these must at least in part include histamine or some histamine-like substance, and possibly also an acetyl choline-like substance that may be involved in the depressor effect because of associated changes observed in intestinal peristalsis after administration of the perfusate.

MAXWELL


The properties of Pempline, a tertiary amine and simple derivative of piperidine were investigated. Like mecamylamine, it was completely absorbed from the gut, but its elimination was delayed if there was renal failure. Its excretion was greater in acid than in alkaline urine. It was concentrated in tissues rich in nuclear material, readily crossed the blood-brain barrier and was found in high concentration in the nervous system. Following intravenous injection, a fall
in blood pressure occurred in 2 minutes and lasted from 2 to 6 hours. After an oral dose, a hypertensive effect was usually observed within an hour and lasted for 6 to 7 hours. A steady hypertensive effect was maintained on an oral 5-hour schedule. Rapid elimination permitted early attainment of a stable therapeutic dose with reasonable safety. In this respect, it was superior to mecamylamine. This characteristic also resulted in early subsidence of toxic effects which were similar to those of all ganglionic-blocking agents.


The arterial flow and pressure in the digital circulation were measured in hypertensive and normotensive pregnant women in the third trimester. Flow was measured calorimetrically, pressure with the cuff method and with a Gartner capsule: indirect heating and ganglionic blockade were used to inhibit vasoconstriction. Calculations for the work, work index, and force of vasoconstrictions were made from the data obtained. The effect of pregnancy upon digital circulation was the same as that for any factor increasing heat production. The vasoconstrictive force was decreased as was the brachial-digital systolic pressure gradient. The latter effect may be attributed to a reduced level of brachial arterial pressure in pregnancy. In the hypertensive group an increase in neurogenic vasoconstriction was observed. This finding represented the only significant difference between the 2 groups.


After sympathetic nerve inhibition by indirect heat (cradle baker) and ganglionic blockade (Pendimidine or SC 1950), the sensitivity of the digital blood vessels to infused norepinephrine was measured in 15 patients with primary hypertension and 15 normotensive patients from the work of digital vasoconstriction per milligram of norepinephrine infused per minute. Sensitivity to norepinephrine was uniformly increased in the hypertension group. This was attributed to the following: the increased response in hypertension due to hypertrophy of the smooth muscle of blood vessels; the enzyme defect in the smooth muscle of hypertensive patients which rendered the effect of infused norepinephrine more intense because it was more slowly destroyed; rates of excretion of norepinephrine; and a phenomenon of nerve-ending sensitization by the ganglion-blocking drug.

Rinzler

METABOLIC EFFECTS ON CIRCULATION


Slices of heart muscle obtained from adult rats were placed in oxygenated modified Ringer-glucose solution and studied by the Warburg method, using 100 per cent oxygen. The digitalis preparations were strophanthid G and desacetyl-digitoxin. Because of the fluctuations in the basal respiration of heart muscle in vitro that had been observed from heart to heart but much less from slice to slice of the same heart, all studies of the digitalis effect were done with simultaneous controls on slices from the same heart. An ouabain concentration of 2.5 \( \gamma \)/ml. was without any effect on the heart; a concentration of 5 \( \gamma \)/ml. caused a slight stimulation and in the range from 10 to 50 \( \gamma \)/ml. a significant stimulation of the oxygen consumption was found, increasing with dosage. A dose of 100 \( \gamma \)/ml. did not stimulate; it had a depressing effect in half the cases. The dose maximally increasing the \( Q_{O_2} \) of heart muscle had a slightly depressing effect on kidney and liver respiration and a depressing effect on the oxygen consumption of the diaphragm, increasing with the dosage of ouabain. The effects on the same organs using desacetyl-digitoxin C were similar qualitatively with variations dependent on dosage.

Maxwell


Hearts from adult rats were obtained immediately after death, were placed in oxygenated, modified Ringer-glucose solution, and were sliced and transferred into Warburg vessels. Kidney, liver, and spleen slices were handled in the same manner and diaphragm was also used. Oxygen consumption was calculated on the basis of the dry weight of the tissue, and wet weight was assumed as 4 times the dry weight for the heart, 5 times the dry weight for other tissues. Under optimal conditions using 100 per cent oxygen, the basal respiratory rate of heart slices not exceeding 0.5 mm. in thickness was 17.4 ± 3.0. In air instead of pure oxygen, the respiratory rate of heart muscle slices was 9.9 ± 1.9. Average
QO₂ values for heart slices at various oxygen concentrations showed that the respiratory rate was constant between 100 and 60 per cent oxygen and decreased progressively from 50 per cent downward. When oxygen concentrations less than that found in air were used, requirements of adequate diffusion required slices of such thickness that the condition of the slices was found to be inadequate. The effects of corresponding reductions in oxygen concentrations on slices of various tissues showed that the effect of the same reduction was greater in heart muscle, kidney, and diaphragm than in liver and spleen. It was found that with decreasing oxygen concentration and decreasing QO₂ the lactate concentration increased, indicating anaerobic glycolysis.

In experiments using slices of variable thickness, it was shown that there was a correlation between the limiting thickness for each oxygen concentration and the point where the QO₂ started to decrease. These latter 2 groups of experiments were taken to indicate that insufficient oxygen diffusion was responsible for the reduced oxygen consumption found in heart slices under the influence of reduced oxygen concentrations.

MAXWELL


This is a radioisotopic tracer study on the protein binding of digitoxin. Both biosynthetically labeled C¹⁴-digitoxin and self-radiation labeled H³-digitoxin were used in this study. Starch block electrophoresis was used as the method for studying drug-protein binding. Drug binding by equilibrium dialysis of salt-fractionated proteins was also used. By zone electrophoresis, digitoxin binding by serum albumin could not be shown. By salt precipitation and dialysis methods, results in the radiotracer portion agreed qualitatively but not quantitatively with other investigators. The authors found that within the therapeutic range 1 mg. of rat serum protein will bind 0.01 mg. of digitoxin.

RINZLER


The myocardial carbohydrate metabolism of the isolated dog heart was studied in the beating and in the arrested stage. Under the circumstances of these experiments the carbohydrate metabolism of the isolated perfused beating heart proceeded at a relatively stable rate with glucose serving as the primary substrate. The uptake of glucose or lactic acid was not correlated with the arterial oxygen concentrations. In the arrested heart the energy was found to be approximately 1/1000 to 1/2000 of that of the isolated beating heart for the same time period. This energy came primarily from residual aerobic carbohydrate metabolism that was finished within the first 10 minutes of arrest. During arrest a marked fall in the pH of the blood contained in the coronary circulation was found; but unlike the abrupt drop in aerobic metabolism, this occurred gradually being 0.14 in 10 minutes and 0.38 in 30 minutes.

SAGALL


No significant changes in cardiac output, heart rate, or electrical potential were produced by 0.2 to 0.8 mg. of thyronine. Low concentrations of thyroxine (0.2 mg.) usually produced a slight increase in heart rate with no change in cardiac output. Triiodothyronine at this dose increased both heart rate and cardiac output. At higher concentrations, (0.6 mg. and above) both the latter agents decreased the heart rate and cardiac output, and produced variable degrees of heart block, arrhythmias, and electrical alternans. Electrocardiograms showed minimal effects on the P wave; the R wave was usually decreased, the S-T segment was depressed, and the T wave became increasingly inverted. The changes caused by triiodothyronine occurred earlier and were also more pronounced than those caused by thyroxine. There were no electrocardiographic effects of thyronine. The introduction of iodine atoms into the thyronine nucleus produced compounds that had marked activity on myocardial function.

KAYDEN

PATHOLOGY


In 67 consecutive autopsies coronary atherosclerosis was evaluated on the basis of the following: crude morphologic grading, a measurement of the thickness of the largest plaque, determinations of the total amount of concentration of lipid and of calcium present in the inner coats of the arteries. Mast-cell counts of the myocardium were also done. The authors could find no correlation between mast-cell counts and any of the 6 parameters measured. No correlation
could be made between the mast-cell concentration and the severity of the disease in any particular age group. A correlation could be made, however, between the mast-cell concentration and the incidence of myocardial infarction or other complications of coronary atherosclerosis.

**MAXWELL**

**ABSTRACTS**

**PHARMACOLOGY**


The vascular actions of 1,1-dimethyl-4-phenylperazinum (DMPP) and tetramethylammonium (TMA) were compared in anesthetized dogs. The rate of blood flow in the femoral artery was determined with a recording rotameter. The blood pressure was recorded with a pressure transducer at the inflow tubing to the rotameter close to the arterial cannula. The blood pressure and the blood flow were recorded simultaneously on a direct-writing electronic recordor. Intravenous injection of both agents produced an initial transient fall in blood pressure followed by a more prolonged rise in pressure. Hexamethonium blocked both phases of the DMPP action but the hypotensive phase of TMA persisted; this was subsequently blocked by atropine. The hypotensive phase of both compounds was selectively blocked by atropine, whereas the hypertensive phase of both compounds was selectively blocked by Regitine. Intrarterial injection of TMA into the hind limb produced local vasodilation which was blocked by atropine but not by hexamethonium. DMPP most frequently produced local vasodilation on intrarterial injection but vasoconstriction was observed in a few animals at the start of the experiment. This later changed to vasodilatation. The dilator response to DMPP was blocked or converted to a constrictor response by hexamethonium, Regitine, and Iliard, but not by atropine. Acute denervation of the limb did not alter the response to DMPP or TMA. The results indicated that TMA can stimulate both at the autonomic ganglia and at the peripheral cholinergic effector sites (cholinomimetic action). The mechanism of the local vasodilator action of DMPP was not clear except that it was located in the periphery. It was suggested that it may involve peripheral ganglion cells, an axon reflex, or direct stimulation of the smooth muscle in the vessel walls.

**RINZLER**


The antiarrhythmic action of the tranquilizing agents, reserpine, alseroxylon, benzylzine, and meprobamate was studied and compared with that of quinidine sulfate. Alseroxylon, reserpine,
and beta-tyzine possessed significant quindine-like activity in prolonging the refractory period of isolated rabbit atria as well as in abolishing experimentally induced atrial fibrillation and flutter in anesthetized dogs. Meprobamate was not efficacious in the atrial arrhythmias although it shared the effect of quinidine to increase atrial refractoriness. It, however, equaled quinidine in the suppression of ectopic activity produced by 2-stage coronary ligation in unanesthetized dogs. In this test procedure, beta-tyzine and alseroxylon were stronger than quinidine, while reserpine was considerably weaker.

**Rinzler**


In dogs, norethandrolone was investigated for effects on atrial flutter, blood pressure, heart rate, ventricular arrhythmia, and the electrocardiogram. Progesterone and testosterone propionate were evaluated for effects on atrial flutter and blood pressure. Further, all 3 compounds were studied in the isolated rabbit heart for their effects on rate, rhythm, and strength of contraction. Norethandrolone (17-ethyl-19-nor-testosterone), testosterone propionate, and progesterone all depressed the amplitude of contraction of the isolated perfused rabbit heart. Norethandrolone had appreciable potency in abolishing atrial flutter in dogs. Progesterone was approximately as effective as norethandrolone in this regard. Testosterone propionate did not show such activity to the same extent as the other 2 steroids. Norethandrolone did not affect ventricular arrhythmia caused by coronary occlusion. It had negligible effects on blood pressure, heart rate, and electrocardiogram, even at very large doses.

**Rinzler**


The relationship between the actions of acetylcholine and nicotine in isolated perfused frogs’ hearts was studied in normally beating hearts and in hypodynamic and spontaneously stopped hearts. Both the excitatory and inhibitory effects of acetylcholine were antagonized by nicotine. It was suggested that acetylcholine and nicotine act through the same neuronal receptors and that the antagonistic effects observed in these experiments were due to competition for these receptors.

**Kayden**


The subcellular localization of digitoxin was studied with biosynthetically labeled C14-digitoxin and self-radiation labeled H3-digitoxin to gain insight into the intracellular site of action of cardiac glycosides and the manner in which intracellular particulates interact to affect myocardial contraction. Twenty minutes after a single intravenous injection, the rat cleared its vascular system of digitoxin. Upon cell fractionation of in vivo preparations, over 90 per cent of the unchanged digitoxin present in the cell was found in the soluble supernate of rat heart, kidney, and liver cells. No marked quantitative binding was demonstrated with any of the particulate fractions. Animals for in vivo study were exsanguinated and perfused before their tissues were fractionated. No functional significance concerning the intracellular localization of digitoxin could be made.

**Rinzler**


The nature and degree of diuresis obtained with chlorothiazide were studied in 26 acute experiments on 22 patients with various clinical states associated with fluid retention. Following a single oral dose of 2 Gm. of chlorothiazide, there was a considerable increase in the flow of urine, particularly in the 6 hours immediately after its administration. This was associated with increased output of sodium, chloride, bicarbonate, and potassium, in that order, with little alteration of serum electrolytes. The diuresis was chiefly of the former electrolytes but if their serum level was low, the excretion of the latter was promoted. A satisfactory diuresis may occur in the absence of corresponding electrolyte loss. In general, the best diuretic response occurred in the patient who responded well to mercurials. In patients with pulmonary heart disease the response was disappointing.

**Kurland**


This report dealt with the mechanisms underlying the peripheral action of hexahydro-1-azipinepropionamidoxime (SU-4029). Three milli-
grams per Kg. of phentolamine hydrochloride given by vein markedly reduced the pressor response to epinephrine in 7 dogs. Subsequent intravenous administration of 180 mg. per Kg. of SU-4029 in a series of 30 to 60 mg. per Kg. doses produced a stepwise return of the pressor response to norepinephrine to control dimensions in 4 dogs and partially returned the pressor response in 3 dogs. The reversal of the epinephrine pressor response evoked by phentolamine was not affected in the 7 animals by these doses of SU-4029. The blockade of norepinephrine produced by the irreversible blocking agent Dibenamine was not negated by SU-4029. Since phentolamine and Dibenamine are generally considered to function at the same site in the adrenergic receptor substance, the indication was that SU-4029 may have an action in the substance of the alpha receptors and that it may be at the same locus as that affected by Dibenamine and phentolamine. It was further suggested by the response of a series of pressor phenylethylamines following SU-4029 pretreatment that part of the action of SU-4029 was to deform that portion of the alpha receptor system affected by adrenergic blocking agents.

RINZLER


Acetylcholine, 1 mg. per liter, restored the rate of isolated rabbit atria (but not of ventricular fibers), depressed by quinidine 2.5 to 5 mg./L. Norepinephrine 1 to 100 mg./L. had no such effect. Quinidine-arrested atria could be restarted by acetylcholine, possibly by an action on the sodium “carrying system” (excitatory mechanism) without increasing the membrane resting potential. The usual inhibitory action of acetylcholine on the rate of beat of pacemaker cells was thought due to an increase in potassium permeability which diminished the rate of diastolic depolarization.

Rogers


Measurements of contractions, conduction velocity, and intracellular potentials were made by photographing simultaneous oscilloscopic tracings from electrically driven isolated rabbit atria bathed in varying concentrations of quinidine sulfate. Quinidine in concentrations up to 10 mg. per liter did not affect the resting potential and either shortened or did not change the half-time for repolarization, the latter corresponding with the failure of quinidine to prolong the absolute refractory period. However, the effective refractory period was prolonged by slowing the rate of rise of the action potential. Also, the conduction velocity and height of the overshoot were reduced. Quinidine thus lowers the frequency at which atria can respond to a stimulus and therefore has an antiarrhythmic action.

Rogers


Pempidine is a tertiary amine and therefore is chemically similar to mecamylamine but not to bis-quaternary ammonium compounds such as hexamethonium and pentolinium. Its effects on cats and mice were those of a long-acting ganglionic-blocking agent without undue toxicity. While oral doses were ordinarily effective, hypotension in the anesthetized cat was difficult to produce unless the drug was injected into the duodenum. Other actions included neuromuscular paralysis of a curare-like type when large doses of Pempidine were injected intravenously, and central effects such as tremors occurred with near toxic doses. Its weak muscarinic properties, as seen on the isolated guinea-pig ileum, might be clinically advantageous by reducing the incidence of parasympathetic side effects.

Rogers

PHYSIOLOGY


Cardiac performance requiring oxygen determines coronary blood flow. The level of arteriovenous oxygen difference across the bed is altered by local conditions of oxygen and carbon dioxide concentrations and the presence of catecholamines. The initiating factor in the equilibrium between coronary flow and oxygen extraction by the heart cannot be decided. It is more than likely that hypercapnia and catecholamines have an effect on the basic vascular tone, probably at the level of the precapillary sphincter, that results in enhanced flow and reduced oxygen extraction.

Aviado

External constriction of the descending aorta elicited immediate inhibition of breathing in dogs under pentothal-chloralose anesthesia both before and after sino-aortic denervation. Impulses initiated by traction of a ligature on the aorta were conducted into the thoracic part of the cord. There was no indication that this mechanism was activated in experiments involving internal occlusion in the innervated animals. Internal occlusion of the descending aorta elicited inhibition of breathing in dogs under morphine sulfate-chloralose anesthesia having all neural pathways intact. The inhibition was related in large part to reflexes from the sino-aortic zones. In the majority of dogs studied, the delayed inhibition of breathing following internal occlusion of the descending aorta was greatly reduced but usually not entirely eliminated by sino-aortic denervation. Therefore, some other respiration-inhibiting mechanism was involved. That the respiratory center may be relatively insensitive to changes in blood flow under the conditions of these experiments was indicated by the fact that in individual cases sudden severe changes in blood pressure in sino-aortic denervated animals were not accompanied by changes in respiration.


Simultaneous records of the transmembrane potential from 2 points in a single cardiac fiber indicate that during the refractory period when repolarization is about half complete graded responses appear close to the site of stimulation. These responses to cathodal pulses vary in amplitude with stimulus intensity and may show spatial decrement even when an overshoot is present close to the stimulating electrode. The results obtained indicate that the transition from graded to all-or-none response does not depend solely on the restoration of membrane potential. In some experiments, stimulation was accomplished by employing 1 lumen of a double microelectrode; in others single Purkinje fibers were stimulated by action potential propagated from attached papillary muscle. Similar graded responses were elicited in both instances. The experiments employing propagating action potentials as stimuli suggest the possible occurrence of graded activity as a response mechanism in the intact heart.


A study of fibrillation induced in isolated rabbit atria by stimulating at high frequencies (600-1,200 cycles per minute) in the presence of acetylcholine revealed it to be dependent on the ionic composition of the medium. The effects of varying the sodium potassium and calcium ion content of the bath fluid on the incidence of fibrillation were interpreted on the basis that fibrillation only began at a time when the transmembrane flux of sodium and potassium ions exceeded a critical rate. Evidence was presented that the initiation and maintenance of fibrillation are governed by separate physiochemical processes. The onset of fibrillation resulted from a sudden transient increase in permeability of the cell membrane. This latter reaction set off other biochemical processes that maintained the phenomenon.


Effects of hemorrhage on blood pressure responses to epinephrine and to histamine were studied in dogs anesthetized with sodium pentobarbital. A series of graded doses of either l-epinephrine bitartrate or l-histamine diphosphate was given before and after hemorrhage, and the blood pressure effects of each dose of the administered drug were recorded. The amount of hemorrhage was determined as 10 per cent of the experimental animal's Evans-blue blood volume. Blood pressure records were analyzed in terms of minimum or maximum blood pressure attained, actual rise or fall in blood pressure and duration of primary blood pressure response before and after hemorrhage. The results showed that there was a significant change in the minimum and maximum blood pressures attained, but no significant change in the actual rise, actual fall or duration of primary response of blood pressure. The amount of change in minimum or maximum attainable blood pressure was directly related to the amount of change in blood pressure that resulted from the decrease in blood volume.


The sequence of hemorrhagic shock was studied in dogs with functional absence of the liver produced by ligation of vascular inflow circuits.
Establishment of a portal to jugular shunt permitted continued measurement of intestinal blood flow. It was found that this vascular bed exhibited the characteristic hyperemic response previously observed in dogs with intact livers, studied under similar condition. Other hemodynamic changes symptomatic of irreversibility were observed. It is concluded that the liver made anoxic during shock does not contribute to irreversibility, and that it is more likely that it exerts a protective role. A hypothesis is advocated that hypotension creates conditions in the intestinal bed that favor production or release of vasodepressor agents or material toxic to the cardiovascular system. In the absence or impairment of the normal protective role of the liver, these gain access into the general circulation with deleterious consequences to circulatory homeostasis.

**Wendkos**


The refractory period was measured at several points on the right atrial surface in anesthetized dogs. Under control conditions with the vagi cut, the values recorded at various points varied by no more than 40 milliseconds. During stimulation of the vagus nerves, singly or together, the refractory period varied widely. At some points marked effects were observed, while at others little or no effect was apparent. Reflex excitation of the vagi, induced by increased arterial pressure, yielded similar results. It was concluded that the effects of vagal stimulation were not uniformly distributed. It follows that an early ectopic impulse generated during a period of vagal stimulation was bound to be propagated along an irregular wave front as the impulse encountered areas in varying states of excitability. The likelihood of fibrillation must be enhanced by such irregularity.

**Wendkos**


Changes in transmembrane flux of Na⁺ and K⁺ during acetylcholine (ACh) induced fibrillation were investigated. At a mean atrial rate of 160 per minute, the efflux of potassium was estimated to be 3-45 pmole/cm.²/sec. With the onset of fibrillation the efflux reached a mean value of 9.37 pmole/cm.²/sec. This rate was 50 per cent greater than the combined effects of ACh (8.0 × 10⁴ Gm./ml.) and stimulation (1,200 per minute) alone. With the onset of fibrillation a momentary increase of influx followed by a decrease to 1/20-1/40 the control was observed. ACh alone produced comparable effects. The rate of sodium influx was increased 10 to 15 times by both ACh and fibrillation. Similar changes in sodium eflux were noted but of a smaller magnitude. The change in fluxes noted was transient in nature with the rate returning rapidly to that of the control even though fibrillation continued. Upon cessation of the arrhythmia a momentary increase of potassium eflux was again observed. It is concluded that ACh and fibrillation increase the transmembrane flux of sodium and potassium. With the present method the onset of fibrillation is best correlated with an increase of potassium eflux above a critical rate. Since these changes are transient, it appears that the initiation and maintenance of the arrhythmia are governed by separate physiochemical processes.

**Wendkos**


Studies were made of the effects of histamine and 5 hydroxytryptamine (HT) on arterial and venous segmental resistance in the isolated perfused dog lung. The lung was perfused at constant flow while pressures were measured in the pulmonary artery, left atrium and in either the pulmonary artery wedge position or a small pulmonary vein. Arterial resistance changes were inferred from changes in the pulmonary artery-pulmonary artery wedge position, pressure drop, and venous resistance from the pulmonary artery wedge position-pulmonary vein pressure gradient. Changes in lung weight were recorded continuously. It was found that histamine usually caused a greater increase of the venous resistance than of the arterial resistance, while HT usually increased the arterial resistance more than the venous resistance. When the predominant resistance increase was arterial, the lung weight fell, but when there was a sizable increase of the venous resistance, the lung weight rose, presumably as a result of increased capillary blood content. The correlation coefficient between the change in lung weight and the change in venous resistance was +.791. Small pulmonary vein pressure rose after administration of epinephrine, norepinephrine, histamine, and HT. This result gives further proof of the constriction of pulmonary veins by these agents.

**Wendkos**
ABSTRACTS

RENNAL AND ELECTROLYTE EFFECTS ON THE CIRCULATION


The effects of constant intravenous infusions of serotonin with doses of 5 to 10 μg. per Kg. per minute on glomerular filtration rate, effective renal plasma flow, urinary flow, and sodium excretion were studied in trained, unanesthetized female dogs. A small but significant decrease in glomerular filtration rate associated with increased renal plasma flow occurred at the 5 μg./Kg./min. dose, indicating a specific effect of serotonin on the kidney. Similar changes were noted with 10 μg./Kg./min. dose plus a marked antidiuretic effect that occurred in the absence of any significant change in mean arterial blood pressure and an intact neurohypothesis, indicating a direct action on water reabsorption in the kidney. Urinary sodium excretion decreased with both doses as a result of a decline in glomerular filtration rate associated with increased tubular reabsorption. These results indicate that serotonin has a specific effect on the kidney and suggest that this substance may alter the caliber of the glomerular vessels to decrease renal vascular resistance.

WENDKOS

RHEUMATIC FEVER


Two comparable groups of patients with rheumatic fever were followed for 5 years. One group of 96, admitted in 1949 to 1950, were given no prophylaxis. The other group of 88 patients, admitted in 1951 to 1952, were given 1 Gm. of sulfonamide daily. The period of follow-up study in the 2 groups overlapped by 2 to 4 years. The mean incidence of recurrences per patient-year was 5.6 per cent in the unprotected and 1.2 per cent in the protected group. There was only small variation from year to year in each group and no tendency for the recurrence rate to decrease with time. Toxic reactions to the sulfonamide were minimal and none was serious. It was pointed out that the recurrence rate in America for the unprotected group was far higher (18 to 25 per cent) than that in Britain. This may, in part, explain the fact that prophylaxis of rheumatic fever was taken up less enthusiastically in Britain than in the United States.

KRAUSE

VALVULAR HEART DISEASE


An analysis of the rate of fall of the diastolic portion of the left atrial tracing obtained before and after mitral valvotomy as suggested by Owen and Wood for pulmonary wedge tracings failed to determine the degree of obstruction at the mitral valve or to differentiate the presence or absence of mitral regurgitation.

SOLOFF


The authors contend that when dissection occurs in the ascending artery just distal to a stenotic aortic valve, it is due to the hemodynamic effects of the stenosis. Repeated impacts on the vessels over a long period of time produce structural fatigue in an elastic artery with distention of its wall. These hemodynamic effects are due to changes in the velocity of blood flow, the development of lateral pressure, and eddies of alternating high and low pressures. In the case studied, the whole length of the aorta and pulmonary artery was examined for medial necrosis and this pathology was confined to the ascending aorta, where poststenotic dilatation was present. The authors state that medial necrosis can also occur in arteries remote from a stenotic valve in which event other factors besides hemodynamics must be considered abnormal. This, for example, can be found in the congenital form of aortic medial necrosis such as occurs in Marfan's syndrome.

KRAUSE


In 44 patients with mitral stenosis the transpulmonary pressure was recorded using a differential manometer, 1 side of which was connected with an intraesophageal balloon, while the other side was connected with the oral cavity; a spirometer recorded the pulmonary volume in the same tracing; a stopcock was used to interrupt the respiration at every displacement of 500 ml. of air. Data on pulmonary circulation, obtained by right heart catheterization, and on the ventilatory function were presented, with the calculated elastance and with clinical information for
each patient. It was found that the elastance increased in proportion to the severity of the mitral disease. Some relation was found between the elastance and the pulmonary arteriolar resistance. Changes in vital capacity, in the index of Tiffeneau, and in residual air were not important factors of changes in elastance. When the pulmonary capillary pressure was increased and fluid accumulated in the septa and in the alveoli, the elastance was also greatly increased. In patients undergoing mitral commissurotomy, it was found that the elastance was greatly increased in those patients in whom the biopsy of the lung showed interstitial fibrosis.


The diagnostic features of tricuspid stenosis are reviewed. A recording of the venous pulse in the neck was regarded as an important diagnostic aid. In the phlebogram of a patient with tricuspid stenosis and sinus rhythm there was a characteristically high a wave but if there were atrial fibrillation the a wave vanished. As the fall of pressure in the right atrium in tricuspid stenosis occurred gradually, there was no marked Y wave in atrial fibrillation in contrast to the findings in constrictive and exudative pericarditis. When there was coexistent mitral stenosis, the auscultatory findings in tricuspid stenosis could be difficult to assess. It was of value in the differential diagnosis between these 2 lesions to observe whether the diastolic murmur increased in intensity when the breath was held after a deep inspiration. When the negative intrathoracic pressure increased with inspiration the rate of flow of blood increased in the venae cavae and the murmur became higher pitched in tricuspid stenosis, whereas the opposite was true in mitral stenosis. It was characteristic of the murmur of tricuspid stenosis that it was accentuated with the patient on his right side. In a 10-year period, 54 patients with rheumatic heart disease were examined at autopsy and showed an incidence of tricuspid stenosis of 26.4 per cent. About one fourth of these had high grade stenosis, yet the correct diagnosis was made ante mortem in only 1 patient. This points up the fact that tricuspid stenosis is frequently not diagnosed ante mortem. An accurate clinical diagnosis of tricuspid stenosis assumes increasing importance in view of the operative treatment of rheumatic heart disease. The indications for mitral valvulotomy depend partly on whether there is co-existent tricuspid stenosis. Moreover, tricuspid stenosis itself is amenable to surgical treatment.

**Brothers**

**VASCULAR DISEASE**


The significance of the superior vena caval syndrome was reviewed on the basis of a series of 23 patients observed between 1947 and 1957. The symptoms and signs of the syndrome fell into 2 main categories: those of the primary disease and those due to venous obstruction itself. When compared with similar data collected before 1945, it was found that the incidence of primary thoracic tumor rose from 33 per cent to 38 per cent. Obstruction of the superior vena cava when caused by a benign lesion was compatible with long life; when caused by malignant disease, the outlook was extremely poor. When the diagnosis was suspected the adjuvant diagnostic measures of venous pressures, infrared photography, and contrast medium venography were recommended. The presence of the superior vena caval syndrome for longer than 6 months usually indicated that the lesion was benign and often could be relieved by surgery.

**Krause**


In 5 of 10 dogs with surgical anastomosis between the femoral artery and vein, repeated small injections of methylene blue caused less intense coloration of the arterial intima above the anastomosis than of the corresponding artery on the other side. This was attributed to a shorter time of contact between the dye and the intima due to increased blood velocity near the fistula. The ectasias in the artery leading to an arteriovenous fistula which are often found in human patients with such fistulas are attributed to deficient nutrition of the intima which is said to result from a decreased time of contact between blood and intima.
ABSTRACTS

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