ABSTRACTS

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ATHEROSCLEROSIS


Cholesterol levels in random samples of populations in different areas were measured in the age group of 55 to 64. There is a general upward trend over the years 55 to 59 and then a fall to the age of 64. Levels were higher in women than in men. Results were consistent with findings in studies by other researchers. Six methods of estimating blood cholesterol levels were compared with a standard test solution and with each other by carrying out determinations in triplicate by each method on 10 sera. Trinder's method was the most reproducible, and those of Anderson and Keys (K5) and Sperry and Webb were the next. Sackett's method was the least reproducible. Mean levels obtained with the methods of Sperry and Webb and Anderson and Keys did not differ; the mean by Trinder's method was 4.2 per cent higher; by Sackett's method, 7.3 per cent higher; by Pearson's method, 8.8 per cent higher; and by Zlatkis' method, 51.8 per cent higher. For routine use Trinder's method is most suitable and involves less manipulation and time. Anderson's and Keys' method is also quite suitable. There are 2 major types of technic. Pearson's and Zlatkis' methods involve adding reagents directly to the serum. In the others, the cholesterol is first extracted, either by solvents or by digitonin precipitation. In all the methods, colorimetric technics are used.

Maxwell


Twenty-eight guinea pigs given a dietary supplement of goose liver and cholesterol and subjected to daily exercise for 102 days showed significantly lower serum lipids and cholesterol levels and incidence of aortic atheromatosis than 28 guinea pigs given the same supplement but not exercised. The blood pressure amplitude was also lower. It is concluded that athletic activity in man has a similar preventive effect on atherosclerosis.

Lepeschkin


One current hypothesis relates atherosclerosis to a deficiency in essential fatty acids and presumes that fatty acids esterified with cholesterol in atheromatous tissue will be more saturated than those esterified with cholesterol in normal plasma. Studies were performed to ascertain how much difference in saturation there might be between cholesterol esters in normal blood and in atheromatous tissues. Tissues obtained at post-mortem examination were extracted and the extracts subjected to chromatography, iodine value determination and fatty acid analysis. The fatty acids esterified with cholesterol (CFA) in plasma had a higher iodine value and a lower saturated acid content than the CFA from aortas. There were no significant differences in the esters from aortic plaques and from residual aortic wall or

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from coronary arteries. Studies of plasma CFA demonstrated the iodine value to be chiefly influenced by the linoleic and arachidonic acid content. There was an inverse relation between CFA iodine value and total plasma cholesterol level. Current evidence indicates that neither the extent of atherosclerosis nor the presence of coronary infarction is associated with a relative deficiency of essential fatty acids in CFA.

Kurland


Heparin was administered intravenously to adult healthy mongrel dogs and serial protamine titrations were carried out at hourly intervals. The level of heparin thus measured decreased by approximately 50 per cent per hour. Protamine in doses of 75 per cent or more by weight of the heparin invariably produced complete neutralization when given 15 minutes after the heparin. At longer intervals, proportionally less protamine was required to neutralize the residual active heparin. With larger doses of protamine there was an irregular, but definite inedence of protamine inhibition of clotting. There was no direct relationship between the relative amount of protamine given and the degree of inhibition of clotting. The increase in coagulation time above normal was usually small, rarely exceeding 15 minutes. There was no evidence found for a "heparin rebound," in the sense of a secondary or delayed rise in the level of active heparin. The possibility of protamine inhibition of coagulation being incorrectly interpreted as "heparin rebound" is discussed.

Sheps


The present paper reports a method that is rapid and reproducible for the quantitative assay of labile fibrinolytic activity of whole blood within a few hours. The rate of lysis is followed by means of hourly estimation of the hemoglobin content of the clot; 50 per cent lysis time is determined. Tests were carried out on 17 normal subjects and on 36 patients suffering from a variety of diseases including coronary occlusion, diabetes mellitus, cancer, and myxedema. Diurnal variation at least partly dependent on physical activity was demonstrated but comparatively little variation from one day to another. In most subjects, fibrinolysis times were significantly longer 2 hours after a fatty meal. There was a positive correlation between lipemia and lysis times. At 4 hours there was no significant effect. Experiments on the effect of exercise and fat feeding indicated that exercise has a considerable transient effect on accelerating fibrinolytic activity. Exercise after a fatty meal abolished the inhibiting action of fat on fibrinolysis. Studies of stypten clotting times were also made and showed shortening of clotting time after butter meals, but exercise had no effect on this finding.

Kurland


Latex particles with diameters of 0.14 μ have been shown to be partially effective in the absence of platelets or phospholipids in the thromboplastin generation test. The author concludes that the function of platelets in the coagulation of blood may be due partially to their particle size and that the action of the "intact platelet" is not completely replaced by "lyophilized platelets" or purified phospholipid fractions.

Karpman


The rationale of human fibrinolysin (plasmin) therapy is summarized, and some results obtained in over 300 patients with thromboembolic disease are described. Treatment begun early, before the clot organized (5 to 7 days), was more often efficacious. For example, 83 per cent of cases of phlebothrombosis treated within 5 days responded well, whereas 62 per cent of those treated later did so. Similar results were observed in pulmonary embolism. Doses of fibrinolysin above 50,000 units daily were found to be significantly better than smaller ones. The major side effect of treatment was fever, 29 per cent of patients having febrile responses higher than 102 F. The mechanism of fever production was uncertain, but it was short-lived. Fibrinolysin, unlike trypsin or papain, does not produce gross coagulation defects, although slight fibrinogenopenia may follow its use. The authors consider the therapeutic effectiveness of fibrinolysin to be established in phlebothrombosis, thrombophlebitis, and pulmonary embolism, and to be promising in many other types of thromboembolism.

Rogers

Review of the protocols of all autopsies done at the University of Michigan Hospital during 1945 to 1954 disclosed that pulmonary thrombotic emboli were found in 606, an incidence of 13.8 per cent, and pulmonary infarction was associated in 356. In two thirds of the 606, the embolization was significant in that it caused or contributed to the patient's death. Symptoms recorded for the latter group included by per cent dyspnea in 58, shock in 28, chest pain in 22, hemoptysis in 11; physical signs were noted in 6; and there was no sign or symptom in 27 per cent. Of the whole embolism group, 19 per cent had evidence of deep venous thrombosis in the leg. A clinical diagnosis of pulmonary embolism was made in 7.1 per cent of the entire embolism group, and in 9.3 per cent of those in whom the embolism was clinically significant. In an additional 4.1 per cent of the latter group this diagnosis was suspected. Chest roentgenograms in 60 patients were suggestive of infarction in 19. Electrocardiograms were made soon after infarction in 5 patients, and evidence of "acute cor pulmonale" was found in 4. In view of the poor ability to diagnose both pulmonary embolism and thrombotic disease of the lower half of the body, a plea is given for greater clinical awareness of these disorders and for readiness to treat or to give anticoagulants prophylactically.

ROGERS

BLOOD COAGULATION AND THROMBOEMBOLISM


Many remarkable findings during routine hematologic and coagulation studies on 8 mammalian and 2 avian species are described. Large thrombocytes, instead of platelets, were found in chickens and ducks. These were nucleated cells, with a high glycogen content and tendency to clump, as in mammalian platelets. Clot retraction was negligible in fowls, and differences were also negligible between clotting times in glass and silicone tubes. The blood of fowls showed also low levels of prothrombin, proconvertin, and procecelerin, and a complete lack of plasma thromboplastin component, Hageman factor activity, and "glass factor" activity. In opossum, sheep, and cow, prothrombin and proconvertin levels were also low, but in these and all other mammals studied (rhesus monkey, dog, cat, rabbit, and raccoon), levels of procecelerin were far higher than in human beings. Mammalian Hageman factor was generally similar to human. Antihemophilic factor levels were very high in cow and sheep plasmas. Brain tissue thromboplastin showed a definite species specificity only in the opossum, chicken, and duck. Erythrocyte sedimentation time was slow in all but the dog and cat. The importance of using homologous species systems in the study of blood coagulation mechanisms is emphasized.

MAXWELL


The authors report 3 patients with chronic cor pulmonale secondary to thromboembolism involving the pulmonary artery. All 3 patients were young, previously healthy men with evidence of peripheral thrombotic phenomena preceding the pulmonary emboli. Exerese tolerance was low, but the pulmonary function studies including the tests of gaseous diffusion were normal. Pulmonary blood shunting occurred as indicated by an increased venous admixture in all of the patients. Pulmonary and alveolar ventilation was increased at rest and at work. Increased vascular resistance occurred, which resulted in elevated pulmonary artery pressures and subsequent right heart strain. Both the stroke volumes and the cardiac outputs were diminished in 2 patients. The authors emphasize that the diagnosis of chronic cor pulmonale following thromboembolism of the pulmonary artery should be suspected in patients with dyspnea who have normal pulmonary function studies and no evidence of primary heart disease, and especially if there is a history of peripheral thrombosis.

KARPMAN


Long-term anticoagulation is being used with increasing frequency but statistics on its relative safety remains uncertain. This paper is primarily concerned with the hemorrhagic complications of phenindione therapy in 217 patients treated for periods up to 3 years. The therapeutic goal was to lengthen the 1-stage clotting time to twice that of the control, the prothrombin concentration then being 12-15 per cent. Twenty-one patients died while under treatment; in 2 fatalities anticoagulant therapy undoubtedly played a part. In
18 patients, anticoagulants were withdrawn. In 7 of these, this was done because of bleeding; in 5, because of lack of intelligence or cooperation. Of the 217 cases, 165 had 194 hemorrhagic episodes, 24 severe, 31 moderate, and 139 mild. The data suggest that 1 patient in 3 will have some sort of hemorrhagic episode during the first 3 months of treatment and that thereafter the incidence of bleeding is halved. Severe bleeding occurred in 22 patients leading to 2 and possibly 3 deaths. An unduly prolonged clotting time may be revealed by a minor bruise, but it may also herald a fatal hemorrhage. Therefore, any sign of bleeding is serious. Anticoagulant therapy is best reserved for cooperative, intelligent patients. Some hemorrhagic complications are inevitable.

KURLAND


The Tromexan level in specimens of human milk were estimated at variable intervals after the administration of Tromexan. There was no correlation between the concentration in the milk and the dosage or time of administration of Tromexan to the mother. Babies receiving breast milk showed no adverse effects, but no prothrombin-time estimations or liver-function tests were carried out on the babies. However, the small quantities of drug found in the milk would indicate that the administration of Tromexan to a lactating woman is not dangerous to the baby.

Sheps


An alternate case study is reported on 100 postoperative patients, half of whom received alpha-tocopherol for 2 weeks. The clotting time, prothrombin time, and prethrombotic index of Kay were determined from the preoperative period to the end of the second postoperative week. There was no significant difference in the clotting time and prothrombin time, but the prethrombotic index reached a “dangerous” level in 6 cases of the treatment group as compared with 22 cases of the control group. Two of the latter patients developed thrombophlebitis. The addition of intravenous calcium gluconate to certain members of the treatment group did not produce any significant differences. A further 28 cases of venous thrombosis were treated with alpha-tocopherol. Seventeen cases were “successfully treated,” 8 showed some effect, and 3 “failed” in the treatment. Acute and subacute cases were treated more effectively than were chronic cases. The criteria for these statements are not given. In 4 cases of thrombophlebitis the clearance of radioactive saline injected intramuscularly was compared before and after treatment. These patients showed a definite improvement in clearance; however, the time relationships and other clinical data are lacking. The author suggests that alpha-tocopherol can control the high blood coagulability that occurs in patients with operations and therefore can prevent the development of postoperative thrombosis.

Sheps


Prolonged anticoagulant therapy after vascular accidents is a well-recognized medical practice but it entails significant risks. Contraindications to anticoagulant therapy include renal disease, hepatic disease, shock, purpura, age of more than 70 years, diabetes, severe congestive heart failure, blood dyscrasias, recent neurosurgery, peptic ulcer, catheter or Wangensteen suction, hemotherax, positive reaction to fecal examination for occult blood, and persistent hemoptysis. Difficulties may be occasioned by failure of the patient to report for frequent examination or by occurrence of intermittent complications. The authors report 1 of the latter in a man who took 50 mg. of phenindione twice daily for 4 years. He was admitted to the hospital with nausea, vomiting, jaundice, and various hemorrhagic manifestations. Apparently the patient developed an acute viral hepatitis and this potentiated the therapeutic effect of phenindione. This case re-emphasizes the dangers of anticoagulant therapy in the presence of hepatic disease and emphasizes the need for careful observation of patients receiving prolonged therapy.

Kitchell


Antifibrinolytic activity was studied in patients with uncomplicated cirrhosis of the liver, in cirrhotic patients with hepatocarcinoma and in healthy volunteers. There was no difference in spontaneous fibrinolytic activity in patients with hepatocarcinoma and healthy controls but activity was significantly greater in the group with cirrhosis of the liver. Fibrinogen levels were higher in persons with hepatocarcinoma than in the con-
control subjects, and these were higher than in the cirrhotic patients. No significant change in fibrinolytic activity followed the injection of epinephrine in patients with hepatocarcinoma, whereas significant increases were encountered in the healthy control subjects and even greater increases in the cirrhotic patients. Both control groups responded to ischemia with increased fibrinolytic activity, but none was found in the tumor group. Four patients were studied before and after the development of hepatocarcinoma. The later results showed a reduction in fibrinolytic activity to normal and elimination of the response to epinephrine and ischemia. Significantly greater antifibrinolytic activity was found in the plasma of patients with hepatocarcinoma than in the controls. A saline extract of tumor exerted greater effect than normal liver. Since no increase in antiplasmin activity was found, it was concluded that the factor responsible for these phenomena did not act directly on plasmin but inhibited the activator that converts plasminogen to plasmin.

KURLAND


Estimation of prothrombin times in man before and after exposure to high environmental temperatures indicates an increase in prothrombin time after sweating. The study was conducted on 2 groups of patients. One group was on anticoagulant therapy for thrombotic disease, and the other was not on anticoagulant therapy. The average rise in prothrombin times following treatment combined with anticoagulant therapy was 93 seconds, and without anticoagulants the average rise was 10 seconds. The blood failed to coagulate after sweating in 5 subjects treated without anticoagulants.

MAXWELL


The blood fibrinolytic activity in 30 male patients with intermittent claudication as a manifestation of extensive arterial thrombosis was compared to the activity in the blood of 30 men who had no symptoms or signs of peripheral arterial disease. The fibrinolytic activity was significantly depressed in the patients with claudication. It is unknown whether this decreased activity is causally related to the disease or is a consequence of disturbed lipid metabolism.

KURLAND


A new method has been devised for the control of anticoagulant therapy. For maximum simplicity an “all-in-one-reagent” has been devised which contains cephalin, thromboplastin and substrate-plasma with a high and constant content of all clotting factors. Calcium chloride is added in optimal concentration. Lyophilized and vacuum-sealed, the reagent is stable for 12 months. When the patient’s blood or plasma is added, clotting time will depend only on the concentration of factors IX, VII, Stuart factor, and prothrombin. The high stability of the reagent makes possible the use of a standard dilution curve. The method provides good sensitivity; the therapeutic range is 10-30 per cent of normal. Sources of error lie in coagulation in capillary blood, contact activation of the test sample, inactivation of clotting factors, non-optimal calcium concentration, and the presence of heparin. The technic is simple; little equipment is needed; reliable results can be obtained with little experience.

KURLAND


Details are given on the use of the thrombelastograph. The normal thrombelastogram is described and the variations induced with heparin in vitro and in vivo are also outlined. Following the administration of “Dindeval,” there was no change in the thrombelastogram until the prothrombin time had been increased beyond twice the control value. Abnormalities are described in some cases of coronary thrombosis prior to the institution of anticoagulant therapy that suggest the presence of accelerated coagulation due to an autogenous anticoagulant with a heparin-like action. It is suggested that the thrombelastograph is a sensitive indicator of liability to either spontaneous thrombosis or hemorrhage. It suggested further that the thrombelastograph is a more sensitive indicator of hemorrhagic tendency than the prothrombin time estimation during the administration of anticoagulants.

SHEPS


The experience gained with the use of a blood-drop test on 610 patients with known or
suspected venous thromboembolism is outlined. This test consists in timing the interval taken by 14 drops of blood to fall from the tip of a standardized test instrument. This is compared to a water-drop time standard and the ratio again compared with the hematocrit level. The author suggests that certain alterations in these measurements reflect a hypercoagulable state during which thrombosis may occur if there is concomitant vascular damage. This state may be temporary and not recur or may persist for years. It is further suggested that while these alterations persist, anticoagulants should be administered. In those patients who show no alteration in the blood-drop test from normal, and have superficial venous thrombosis or suspected venous thromboembolism, anticoagulants need not be given. They are treated with symptomatic anti-inflammatory measures. When the alteration is great to begin with, or persists for longer than 2 weeks, anticoagulant therapy with heparin and oral anticoagulants is begun. Between these extremes, intramuscular heparin alone is the treatment of choice. Deep venous ligation was undertaken when patients had recurrent (3 or more) pulmonary emboli, despite adequate anticoagulant therapy. Long saphenous vein ligations were carried out on patients who had superficial venous thrombosis in varicose veins. It is concluded that the blood-drop test isolates for concentrated attention those patients requiring prolonged meticulous treatment. In addition it is said to indicate the specific need for anticoagulant therapy.

SHEPS


The authors confirmed reports by others that nicotinic acid has fibrinolytic properties. They found that the intravenous injection of 1 to 2 mg. of nicotinic acid per Kg. produced in more than half of the subjects complete fibrinolysis as measured by thromboeleastographs. The action was usually transient and was no longer demonstrable 1 hour after the injection. After ingestion of 1.0 Gm. of nicotinic acid, longer lasting fibrinolysis was achieved. The incidence of thromboembolic phenomena was compared in 209 patients with hemiplegia, many of whom had not received nicotinic acid for varying periods. The frequency of thromboembolism was increased 4 fold during periods when the drug was not being given. The difference was even more striking in the group of patients with atrial fibrillation. Nicotinic acid had no effect on coagulation. The drug thus offers some of the advantages of anticoagulants without any of their dangers.

BRACHFIELD

CONGENITAL ANOMALIES


A 28-year-old woman with atrial septal defect and moderate pulmonary hypertension showed an intense systolic murmur continuing beyond the second component of a reduplicated second heart sound, into the mitral part of diastole; the murmur had maximal intensity in the second interspace in the left mediasternal line. After operative closure of the septal defect, the murmur disappeared completely, and the terminal portion of the vectorcardiographic QRS loop became directed less to the right. The murmur, which could not be distinguished from that characteristic for patent ductus arteriosus, is attributed to increased pulmonary flow.

LEPESCHKIN


The subject of persistence of the left superior vena cava was reviewed historically, embryologically, and clinically, emphasizing the authors' experience with 37 patients. The significance of this uncommon abnormality lies in its occasional interference with cardiac catheterization via the left arm, the need to occlude it during open-heart surgery and especially in its usual association with hemodynamically significant lesions, such as atrial septal defect, in 25 patients or anomalous pulmonary venous return in 15 patients. The diagnosis of persistent left superior vena cava could be strongly suspected in 86 per cent of the group by finding a significant widening of the vascular pedicle at the level of the third rib in a posteroanterior chest roentgenogram. Confirmation was obtained by angiography or by noting the course of a catheter as it passed along the vessel.

ROGERS


Fourteen cases of persistent foramen ovale, which were selected among 2,055 autopsy reports,
were studied. Clinical, radiologic, and electrocardiographic studies were reviewed. Six patients had rheumatic heart disease with a double mitral lesion; 3 had secondary hypertension; 1 had lupus erythematosus; 1 had syphilis aortitis with aortic regurgitation; 2 had atherosclerotic heart disease, and the last patient had an infectious pulmonary disorder. The patients were in heart failure and 7 had unquestionable clinical signs of arterial pulmonary hypertension. Nine had variable degrees of cardiomegaly. When the pressure in the right atrium increases for any reason, the foramen ovale may theoretically open and become functional, permitting a right-to-left shunt. The authors believe that the right atrial pressure must reach very high levels before overcoming the resistance presented by the valve of the foramen ovale, as the right atrium is capable of dilating markedly before elevating its pressure. One factor that prevented the right-to-left shunt was the presence of pathologic circumstances which tended, per se, to elevate the pressure within the left atrium simultaneously. Anatomic characteristics of the adult septum also preclude shunting. The electrocardiogram did not aid in the diagnosis of the presence of a patent foramen ovale. Of the 14 patients studied, 8, due to the peculiar conformation of the foramen ovale and its valve, probably could not become functional; in 5 patients a functional foramen ovale seemed possible and only 1 case was consistent with a true functional foramen ovale. In the authors' experience a functional foramen ovale is extremely rare.

BRACHFELD


The father of the family died at the age of 27 of heart failure, and a large atrial septal defect of the ostium primum type was found at autopsy. His daughter showed an atrial septal defect leading to death at 5 months, which was confirmed at autopsy. A brother and sister who had the same grandparents and great-grandparent as the first 2 patients showed an atrial and ventricular septal defect respectively, while their cousin showed an ostium primum type of atrial septal defect. The 3 patients died at an age of less than 4 months, and the diagnosis was confirmed at autopsy. In none of the patients was the mother exposed to virus infection, roentgen radiation, or metabolic disturbances, but in 1 patient the pregnancy was preceded by 3 abortions. These patients emphasize the importance of hereditary factors in the genesis of congenital cardiac anomalies and show also that a large atrial septal defect can lead to early cardiac failure through volume overload.

LEFESCHKIN


The typical triangular pulse configuration, which is observed in human aortic coarctation and appears also during local compression of the thoracic aorta in experimental animals, could be reproduced when an artificial pulse was sent through a rubber tube and the latter compressed in the middle. This led to decreased higher oscillatory harmonics in the central and peripheral segments of the tube, and caused both to resemble the response of a simple elastic reservoir. The pulse wave velocity remained unchanged.

LEFESCHKIN


A 28-year-old woman with pulmonary stenosis had 2 normal deliveries after an interval of 7 years. During the second delivery 3:2 atrioventricular block with high ventricular escape beats appeared; this could be provoked also after delivery by the erect position.

LEFESCHKIN


The preoperative and postoperative status of 12 patients whose ventricular septal defect appeared to have been completely repaired are described. Five of these additionally had pulmonic stenosis, which was corrected simultaneously. Of the pure septal defect group, 3 were asymptomatic before and all were asymptomatic after surgery. The grade III-IV harsh systolic murmur decreased or disappeared in all except 1. The heart increased slightly in size, and complete right bundle-branch block appeared in all patients. Four had moderate pulmonary hypertension which returned to normal after surgery. Of the septal defect plus pulmonic stenosis group, all were asymptomatic preoperatively, and 1 was cyanotic. The uniformly present grade I to IV left sternal border systolic murmur persisted but in lesser intensity postoperatively. Again, the heart size increased slightly and complete right bundle-branch block developed in all patients.
The moderately elevated ventricular pressure fell postoperatively in each instance, and in 3 it reached normal levels. Open-heart surgery when indicated was considered to be the treatment of choice for ventricular septal defect, with or without pulmonic stenosis.

**Rogers**


The heart sounds in 30 patients with confirmed atrial septal defect (ostium seconundum defect with left-to-right shunt) were examined phonocardiographically and by auscultation. The recording was performed simultaneously with 2 microphones at various sites of auscultation during breath holding, normal respiration, and cardiac catheterization. Simultaneous tracings were recorded of the electrocardiogram, respiration, pressure pulses from various cardiac chambers as well as carotid pulse curves. The first sound was split in 17 patients. An early systolic ejection click was noted in 2 patients, which was correlated with a marked widening of the pulmonary artery. In all patients, a spindle-shaped systolic ejection murmur was heard over the pulmonic area, with a maximum prior to mid systole and ending always before the aortic component of the second sound (relative pulmonary stenosis). The interval between the 2 components of the second sound (which was split in all patients) remained practically constant during respiration. In 2 patients, an early-diastolic, high-pitched, decrescendo murmur occurred over the pulmonary area as an expression of relative pulmonary insufficiency. A middiastolic murmur was heard in 19 patients. A presystolic murmur was noted in 9 patients. In 6 patients the rapid pulse rate did not permit differentiation between a middiastolic and presystolic murmurs or summation of these 2. In 6 patients, both murmurs could be demonstrated separately. On the basis of these findings it appeared possible to diagnose an atrial septal defect by means of phonocardiogram and auscultation. The combination of a systolic murmur over the pulmonary area, fixed splitting of the second sound, and a middiastolic murmur characterized an atrial septal defect.

**Brachfeld**

**CONGESTIVE HEART FAILURE**


Acute left ventricular failure was studied in the isolated dog heart exposed to elevated aortic resistance. Experiments in which only the left ventricle performed mechanical work showed that progressive changes in distensibility and contractility occurred. When exposure to the elevated resistance was prolonged, the failure became hemodynamically irreversible and there was a loss of responsiveness to increases in filling pressure. Experiments in which both ventricles worked under separately controllable hemodynamic conditions established that aortic failure did not develop in the adjacent right ventricle. The observations suggest that the unilateral ventricular failure involved a permanent alteration of the distensibility and contractility of the wall of the left ventricle as a result of a process that permitted the right ventricle to retain normal function.

**Kayden**


Liver-cell damage is associated with markedly increased levels of cyanobetalamin (vitamin B₁₂) in the blood due to the release of this vitamin from damaged hepatic cells. This report deals with observations on cyanobetalamin activity in the serum of patients with congestive heart failure and hepatomegaly. This vitamin was increased in 23 of 28 patients suffering from severe chronic congestive heart failure. In these patients the commonly used tests for hepatocellular function were usually normal. As the congestive heart failure was controlled, the levels of serum cyanobetalamin decreased considerably. The authors relate the increased release of this vitamin into the serum to anatomic changes in the hepatic architecture. These consist of centrilobular necrosis, resulting from hepatic anoxia and hemorrhages from the distended sinusoids due to the increase in venous pressure. The highest levels of serum vitamin B₁₂ were found in patients with long-standing heart failure.

**Krause**


The action of hydrochlorothiazide was observed during periods up to 3 months in 4 hospitalized and 27 ambulatory patients with congestive failure due to acquired heart disease. All patients were previously under treatment including chlorothiazide, digitalis, and sodium chloride restriction to 4 to 6 Gm. daily. Therapeutic dosage was usually 50 to 100 mg. twice daily, the effectiveness of which was equal to that of 1 to 2 ml.
of mercurialuride. Thirteen patients responded further to hydrochlorothiazide in terms of weight reduction of 4 to 8 pounds. Several ceased to require mercurialurid diuretics. The diuretic response was prompt and included a nearly parallel increase in sodium and chloride output with lesser increases in elimination of magnesium and potassium. Few serum electrolyte imbalances were encountered, and only 1 instance of hypokalemia was noted. Side effects of therapy included dryness of the mouth, paresthesia of the face and hands, and gastrointestinal disturbances; but all were mild, and none required discontinuance of the drug. It was concluded that hydrochlorothiazide was more potent than chlorothiazide and caused fewer serum electrolyte disturbances.

ROGERS


Little is known about the physiology, psychology, and environmental circumstances associated with the initiation of congestive heart failure. In many patients precipitating factors are difficult to demonstrate. The literature dealing with the influence of emotional factors on certain aspects of cardiovascular function is reviewed briefly. In an attempt to understand better the frequently unexplained onset of congestive heart failure, a series of studies was designed to examine the effects of emotional stimuli on central venous pressure and peripheral venous tone, and to evaluate the significance of specific emotional experiences in relation to the symptoms of congestive heart failure. Central venous pressure (CVP) was measured by means of a catheter advanced to the central veins. Peripheral venous segment pressure (PVSP) was measured with the catheter tip in the forearm vein. CVP increased in response to physical stimuli, as lifting a 2 Kg. weight, to “neutral” and “stressful” rhetorical questions, and to repeated emotional stimuli in 25 studies of 22 patients, and to psychiatric interviews of 10 patients. The data justify these conclusions: experiences which a patient with heart disease considers emotionally “stressful” can be elicited and predicted with a fair degree of confidence during a short medical interview; in varying degrees of congestive failure, rhetorical questions, which a patient considers intellectually and emotionally, are associated with varying but definite CVP increases of as much as 45 cm. of water. Psychiatric studies of patients may explain poor responses in spite of superior medical regimens. PVSP in 6 healthy subjects was modified by emotional stimuli, and was of greater magnitude and duration than seen with physical stimuli. Disturbing life situations and the emotional reactions evoked may cause recurrent and cumulative increases in peripheral and central venous pressure.

MAXWELL

CORONARY ARTERY DISEASE


Aspirin was administered for 8 weeks to 5 men and 4 postmenopausal women with hypercholesteremia and angina pectoris in doses of 5 to 8 Gm. daily, yielding a serum salicylate level of about 40 mg./100 ml. The serum cholesterol was consistently reduced after 2 weeks of treatment. Although basal metabolism was increased, there was no increase in angina on effort nor any change in the electrocardiogram. A second study was made after administration of 3.3 Gm. and 5.0 Gm. of aspirin daily to 6 hypercholesteremic men and of 4 and 8 Gm. daily to 6 postmenopausal women. Doses less than 4 Gm. daily were ineffective. The group with the highest serum salicylate concentration showed the greatest decrease in serum cholesterol but the effect may not be directly related to an increase in metabolic rate.

KURLAND


Ventricular fibrillation is responsible for a great percentage of deaths following acute myocardial infarction. There have been successful attempts at defibrillation reported but acceptance has been slow because of technics involved and the feeling that successful defibrillation is rare unless the occlusion is first removed. The authors have reported here on their method of defibrillation in a series of 25 dogs in which myocardial infarction was produced experimentally by ligation of the anterior descending branch of the left coronary artery. Twenty-two of the 25 animals developed ventricular fibrillation within 2 to 25 minutes following ligation. Eighteen of the 22 dogs were successfully defibrillated. The method used was one of electrical countershock into the fibrillating ventricles of 1.5 to 3.0 amperes, with a duration of 0.15 second and an amplitude of 150 volts. The pulses can be given as often as 1 per second. Three rapid shots were given. If this was effective in restoring a beat then 100 mg. of pronestyl and 0.5 mg. of
onabain were given by intracardiac injection. The ligatures were left intact. If electrical countershock was ineffective after several attempts, pronestyl was injected and countershock attempted. With the return of an effective beat, ouabain was then given. In instances of refibrillation, electric defibrillation and massage were utilized. In those instances in which response was not obtained with the above measures, epinephrine and calcium were also utilized. All the animals that survived 10 hours to 60 days required only countershock, 100 mg. of pronestyl, and 0.5 mg. of ouabain for successful resuscitation. In all but 3 of these countershock alone was effective. No dog that required more than the above measures survived more than 3 hours in spite of increased ouabain, calcium, and epinephrine. Following ligation a large eanotic area of infarction developed in an area corresponding to distribution of the ligated vessel. This persisted in spite of return to an adequate beat. Immediately following ligation there was marked decrease in the peripheral coronary artery pressure and reduction in coronary backflow. In those animals surviving 60 days these values increased and with barium injection studies anastomotic channels were demonstrated. With this experiment and an analysis of the human cases of successful defibrillation reported it would appear that countershock would be the most effective weapon probably best applied through the open chest. Multiple countershocks appear to be necessary. Pronestyl is successful in combating multiple premature ventricular contractions and fibrillation. In these animals ouabain seemed to increase the effectiveness of cardiac contractions.

LEVINSON


Ten case reports of this unusual syndrome were presented. Each followed typical acute myocardial infarction by periods ranging from several hours to 3 weeks. The syndrome was characterized by evidences of pleurisy with or without effusion in all patients and by pericarditis in at least 9 with pericardial effusion in 3 or more of these. Pneumonitis was found in 2 instances, and cardiac tamponade was not observed. There was moderate but variable fever. Aside from electrocardiographic changes suggesting pericarditis (in 3 patients) and roentgenographic findings, laboratory data were of help only in a negative sense. Both the clinical picture and course were variable, the duration ranging up to 3 months. Recurrences were observed in 5 patients. In these and in previously described examples the disorder has been benign and its importance lay chiefly in distinguishing it from new myocardial infarction, pulmonary infarction, or sepsis. Treatment was symptomatic, although corticosteroid therapy was employed in 2 patients, both with dramatic effect. Anticoagulant therapy generally was considered to be contraindicated during pericarditis. The pathogenesis remained speculative; viral infection and hypersensitivity were thought possibly to be involved.

ROGERS


One hundred and eighty patients with angina pectoris, without associated hypertension or valvular lesions, were treated with L. 2329 (a benzofuran derivative) for periods varying from 7 months to 2 years. The daily doses varied from 75 mg. to 450 mg.; 300 mg. had a therapeutic result in most cases. In 77 per cent of cases, a good or excellent effect was observed, manifest by a substantial reduction in the number of painful attacks after effort or at rest, or in their total disappearance. In many cases, an objective improvement in the electrocardiographic tracing was observed; this normalization occurred immediately when L. 2329 was given intravenously but more slowly after rectal or oral administration. No side effects on heart rate or blood pressure or thyroid function or on the blood components were observed. Toxic phenomena were never seen, even after the intravenous administration of large doses (450 mg). Slight gastric intolerance occurred in 2 per cent of patients, after oral doses only. The onset of action of L. 2329 by mouth was much slower but of much longer duration than that of nitroglycerin.

BRACHFIELD


Nitroglycerin is the best medication to relieve the anginal distress of coronary insufficiency. Its chief disadvantage is its short duration of action, which limits its value as a prophylactic agent against anginal pain. For long-acting use the best drug seems to be pentaerythritol tetranitrate, and the authors tested the value of this chemical agent in timed-disintegration capsules. Twenty patients with coronary artery
insufficiency and angina pectoris showed an excellent improvement by the reduction of from 50 to 85 per cent in nitroglycerin requirements when treated with 2 such capsules daily 12 hours apart using a double-blind technic for 1 year. Using the single-blind technic 17 out of 20 patients showed an excellent response. Oscillographic readings were improved 62 per cent in double-blind study groups and 56 per cent in the single-blind group. The ability to walk greater distances was prominent in both groups. Twenty patients treated for 12 months on placebos were dissatisfied and unimproved until they were placed on the continuous release medication. This form of penterythritol tetranitrate has been shown to be remarkably more efficient for relieving angina for long periods of time than any other comparable medication.

Krause


Many surgical procedures have been devised in an attempt to increase the blood supply to the ischemic myocardium by the development of a collateral circulation. There is no evidence that any of these operations are effective in bringing a new blood supply to the heart. However, a simple procedure was adopted of ablating the parietal and visceral pericardium to produce a myocardial resection sufficiently brisk to improve the intercoronary anastomoses. Occasionally, internal mammary ligation was included. The indication for operation was progressive and incapacitating angina without cardiac enlargement or cardiac failure unresponsive to medical therapy. Preoperative assessment included clinical and laboratory evaluation and a standard exercise test under stable conditions. Ten patients are described with 1 death. The results were striking in 3 cases, good in 5 and slight in 1. Abrasion of the pericardium produces the electrocardiographic appearance of lateral wall infarction. Hence, postoperative assessment was mainly clinical. While the psychologic impact must be considerable, improvement in pain and effort dyspnea was greatest after 4 months when such effects might be expected to be waning.

Kurland


All 206 adult patients with cardiac symptoms admitted to the Edendale Hospital in Natal during a 6-month period were included in a clinical study, which was complemented by analysis of a 12-month autopsy series of 243 patients aged 35 years and over. The presence of ischemic heart disease was suspected clinically in 3 patients with possible myocardial infarction, 8 with angina pectoris alone, and in 20 with angina plus congestive heart failure of undetermined cause. Anatomically, the coronary arteries appeared normal in 53 per cent of autopsies; 40 per cent showed slight arteriosclerosis, while severe stenosis or occlusion of 1 or more main coronary arteries was found in 7 per cent. Myocardial fibrosis was observed to a slight degree in 25 per cent, to a severe degree in 10 per cent and as a frank infarct in 1.7 per cent. It is suggested that the South African Bantu has no immunity to coronary atherosclerosis or to resultant heart disease but that he differs from Europeans who more commonly present with acute myocardial infarction. Instead, the Bantu tends to develop smaller myocardial scars with resultant "cryptogenic" heart failure.

Rogers


The development of a satisfactory technic for the production of gradual arterial occlusion is described. The final technic involved the use of a casein plastic sleeve encased in stainless steel. These produced gradual occlusion of arteries over reasonably predictable periods of time. This occlusion resulted from reduction in external vessel diameter due to luminal swelling of the plastic, fibroplastic response of the arterial walls at the site of the sleeve, and the development of intraluminal thrombi arising concentrically from the intima. If the occlusion was complete, there was a narrow zone of thrombotic material proximal and distal to the sleeve site. There was no evidence of embolization. These sleeves produced progressive myocardial ischemia and infarction in 12 dogs without complete anatomic occlusion of coronary arteries. The dogs died from 4 to 26 days after thoracotomy. In none of the animals studied were the arterial lumina completely occluded.
blood flow and the anemia in itself interferes with myocardial metabolism. Therefore, treatment consists of pressor amines in sufficient amounts to maintain the blood pressure and the use of blood transfusions in amounts equal to blood loss. In order to prevent myocardial damage, treatment should be prompt. Two case reports are presented.

KRAUSE


A group of 106 men with documented myocardial infarction were studied for a period of 3 to 20 months at an outpatient cardiac clinic. The patients were divided into 4 groups: 1 group was given no medication and 3 groups received oral synthetic estrogen therapy. The drugs were ethinyl estradiol, conjugated equine estrogens (Premarin) and SC6924 (Manvene), and were administered to the maximum tolerated dose for each patient. In four fifths of the patients feminization effects were noted, and in the remaining one fifth treatment had been given for only a short period of time. After 90 days of therapy the effects of estrogen on the serum lipids appeared to be maximal, and tended neither to increase nor decrease thereafter. The effects of the 3 estrogens appeared to be similar. Under estrogen therapy, initially high levels of serum cholesterol and the cholesterol to phospholipid ratio tended to fall, while initially low levels tended to remain unchanged or to rise. Untreated control patients showed little variation in their serum cholesterol levels. The changes in serum phospholipid levels in the treated group were qualitatively similar to the changes in serum cholesterol levels, but the phospholipid levels of the control group also showed changes, high values falling and low levels rising. The differences between the treated and untreated groups were not statistically significant. The effects upon serum lipids of men receiving estrogen are similar to those previously reported for estrogen therapy in postmenopausal women.

KAYDEN


A striking sex difference in the incidence of angina pectoris has long been recognized. A study was undertaken to determine whether a premature menopause was followed by a significant change in the incidence of coronary artery disease and in cholesterol levels. Since the peak incidence of coronary disease in women is about 15 years after the menopause, it was decided to investigate women who had had surgical removal of both ovaries, 20 or more years previously. These were compared to a group who had undergone only unilateral oophorectomy. Information was also sought about the incidence of coronary artery disease in a healthy population from a general practice in Edinburgh. During the 20 years since operation, features of coronary disease developed in 9 of 36 women who had bilateral operation and in 1 of 31 who had had unilateral ovariectomy. One woman in the bilateral ovariectomy group died from myocardial infarction before the study. There was no difference in the prevalence of diastolic hypertension or obesity between the groups. There was a significant elevation of serum cholesterol and the phospholipid ratio in the bilateral group compared to the unilateral group. Among the women with bilaterally oophorectomy, the serum lipids of those with coronary artery disease were not different from those without coronary disease. The findings indicate that clinical coronary artery disease and elevated serum cholesterol are more common in women who have had both ovaries removed prematurely than in those who have had only 1 ovary removed. It is suggested that where possible, complete removal of both ovaries be avoided and, if unavoidable, replacement therapy should be administered to the age of 50.

KURLAND
ABSTRACTS
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