ABSTRACTS

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ATHEROSCLEROSIS


It is widely believed that the more severe complications of atherosclerosis such as cerebral and coronary thrombosis are rare among the Bantu. Three hundred consecutive necropsies in Bantu over the age of 19, excluding cases of syphilis and diabetes, indicate that aortic atherosclerosis was prevalent even in younger age groups and its degree and extent increased steadily with age. In 2,000 consecutive necropsies in Bantu patients cerebral hemorrhage or thrombosis was found in 10 men and 21 women. Up to the age of 55, there was no sex difference. Thereafter, women were more prone to cerebral vascular disease with and without hypertension. These findings are presented as evidence refuting the view that the Bantu enjoy any relative freedom from atherosclerosis or its cerebral complications. The high prevalence in Bantu women is contrary to the findings in people of European descent.

Kurland


The incidence of coronary atherosclerosis has been found to be remarkably low in native Africans. Since atherosclerosis has been associated with an elevation of serum betalipoprotein, the levels of this lipid were measured in several groups of Bantu and the results correlated with dietary habits and clinical data. The adult male and female Bantu were found to have levels of serum betalipoprotein of the S, 12-100 class that were significantly lower than those of white New York City individuals. The female Bantu had a higher level of the betalipoprotein than the male. The lower intake of dietary fat to levels of 20 per cent of the calorie needs in the Bantu has been regarded as an important factor in producing the low levels of atherogenic serum lipids. Other conditioning factors may be the high carbohydrate intake, exercise, ethnic considerations, liver disease, and the possible increased content of unsaturated fatty acids in their diets.

Shuman


The authors report the effects upon the serum lipids of the administration of 10 micrograms daily of ethinyl estradiol to 26 postmenopausal women who had sustained at least 1 myocardial infarction. It was noted that there was a fall in serum cholesterol, a rise in phospholipid, and a fall in cholesterol-phospholipid ratio of the same magnitude as reported by other investigators using very large doses. These lipid changes were progressive during the first 6 or 7 months of estrogen therapy and then remained at constant levels despite continued treatment. The effect of estrogen upon the blood lipids was found to be dependent upon the pretreatment pattern. Little or no effect was found when the lipids initially were normal, and the greater the initial lipid abnormality the greater were the changes found.

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under treatment. These observations suggest that estrogen may have a homeostatic effect upon the serum lipid levels.

SAGALL


Corn oil was given to 23 patients with coronary atherosclerosis in amounts of 30 to 45 ml. before each meal with minor dietary restrictions in order to appraise its influence upon serum cholesterol and phospholipid levels. The pretreatment cholesterol level averaged 271 mg. per cent. Seventy per cent of the patients had a 15 per cent decrease in serum cholesterol averaging 208 mg. per cent after a period of corn oil feeding. Another 26 per cent of the patients had smaller decreases in serum cholesterol. Corresponding decrements in the level of phospholipids were noted. The drop in serum cholesterol was maintained during a year of corn oil ingestion. None of these patients experienced any exacerbation of anginal symptoms while taking corn oil.

SHUMAN


The intravenous administration of lipid mobilizer (LM) produced a hyperlipemic response in each of 7 test subjects in the fasting state. Two forms of LM were employed in the study: a dialysate of plasma of cortisone treated horses, and a pure crystalline substance derived from the dialysate. The plasma lipid fractions measured included cholesterol, phospholipid, and total fatty acid. Each of these lipid fractions exhibited a 2- to 3-fold rise promptly after LM administration. Prefeeding of the subjects with glucose or cream blocked the hyperlipemic response. However, after amino-acid feeding a rise in plasma lipids could be evoked by LM. The role of the liver in the metabolism of the triglycerides mobilized by LM may govern the rate at which the lipids enter the systemic circulation. Evidence is cited to support the view that the damaged liver fails to metabolize fats in a normal fashion. The prefeeding of glucose may provide glycogen or other factors for improving fat utilization by the liver thereby preventing peripheral hyperlipemia. The prefeeding of fat may activate a clearing mechanism within the liver for the removal of lipids mobilized by LM. Attention is called to the finding that as little as 1.2 μg. of the crystalline LM was capable of inducing hyperlipemia. Further studies with this substance are in progress.

SHUMAN


Following a period of administration of a low-fat (50 Gm. daily) diet for a prolonged period 21 male patients with proved atherosclerosis were given alternating courses of beta-sitosterols and placebo lipid suspensions. The weight curves and diets remained constant throughout the period of study. Lipoprotein and cholesterol determinations were made serially during the various phases of the investigation. The effect of the agent upon serum lipoprotein levels parallels the action of the low-fat dietary regimen when given over an 8-week period. There was a considerable variation in the individual response to the drug, but, in general, significant reductions were recorded in mean levels of the S₇ 0-12 and 12-20 classes of serum lipoproteins. Changes in S₇ 20-400 lipoprotein and serum cholesterol were not significant. The changes induced by the drug were to some extent additive to those of the low-fat diet. No toxic effects were observed from an oral dose of 10 Gm. of beta-sitosterol over an 8-week period.

BLOOD COAGULATION AND THROMBOEMBOLISM


Using the isolated guinea pig tracheal chain technic, a method which correlates well with clinical bronchodilator responses in pharmacologic studies, the administration of warfarin sodium was compared with aminophylline. Under the conditions of the experiment described, warfarin sodium possessed about half the bronchodilator activity of aminophylline. This effect was not influenced by the simultaneous presence of heparin. The authors state that if the dilator effect as seen in this study is reflected in the corresponding bronchodilatation in man, it may be possible that the initial injection of warfarin sodium may produce some immediate bronchodilatation as well as initiating the slower anticoagulant activity. Studies are being extended to determine whether this activity is a general property of the 4-hydroxycoumarin anticoagulants.

In a 10-year period, 511 patients having clinical evidence of deep leg vein thrombosis (359) or pulmonary embolism (152) were treated initially with heparin in combination and then with an antiprothrombin drug alone, usually for a total of 10 to 21 days. The desired prothrombin depression of 10 to 29 per cent (Quick activity) was obtained on a minority of treatment days. Thromboembolic complications during or within 12 weeks after therapy were noted in 71 patients and were not demonstrably related to the degree of prothrombinopenia. Similarly, therapeutic results could not be related to the earliness of beginning treatment nor to its duration. Nonetheless, the conclusion was reached that anticoagulation can reduce significantly both morbidity and mortality from these 2 types of thromboembolism. Complicating hemorrhage was seen in minor form in 81 instances and in major form in 13, but all were controllable.

ROGERS


In a 3-year period, the authors encountered 10 patients who developed peripheral arterial embolism while receiving heparin. The clinical picture, gross appearance of the emboli, and the autopsy findings suggest a direct relationship to heparin effect on pre-existing, unsuspected, mural, aortic fibrin-platelet thrombi. All the patients had some clinical evidence of cardiovascular disease. Their ages ranged from 46 to 86 years, with a mean of 64 years. The period of heparin therapy preceding an embolic event ranged from 7 to 15 days. The heparin was administered either intravenously or intramuscularly at 6- to 8-hour intervals with the dose controlled by the clotting time as determined by the Lee-White method. A clotting time of 30 to 40 minutes was considered optimal and the daily dose varied from 150 to 500 mg. In 9 patients the emboli were multiple. All of the patients were treated by embolectomy. Six patients died.

Fresh emboli extracted at operation were strikingly similar, pale, soft, salmon-colored clots. Histologically these emboli were comprised mostly of fibrin, platelets, and leukocytes; red cells were rare. These histologic and gross appearances were thought to be consistent with platelet and fibrin precipitation over a prolonged period of time and in a location of rapid blood flow such as the aorta. Three case histories are presented in detail and are representative of the entire group. Although the authors continue to use heparin they are aware of the risk of embolization in susceptible persons and have decreased the dose of heparin that they previously thought was desirable. They no longer believe it wise or desirable to establish clotting times more than 2 or 3 times normal.

BROTHEL


The effects of heparin administration in 75 patients having mainly thrombophlebitis and in 15 normal persons are described with emphasis on the technieal aspects. The subcutaneous route, employing 0.5 to 1.5 mg. of concentrated heparin per pound of body weight every 6 or 12 hours, was used in 52 patients for an average of 12 days with satisfactory therapeutic results in 44. However, significant bleeding or other complications developed in 15 of the 52. Most of these difficulties occurred during the first week of therapy and despite daily checking of the coagulation time, which was considered to be in a therapeutic range in the majority. Blood viscosity studies, although roughly inversely paralleling the coagulation time, appeared to be of little additional assistance in guiding therapy. In acute or postoperative thromboembolic conditions, the intermittent intravenous method of heparin administration through an indwelling polyethylene catheter was thought to be more effective and safer, thus leaving the subcutaneous technique for use in the more chronic conditions, including ambulatory patients.

ROGERS


Generalized or localized pulmonary embolism to the point of fatality was produced in anesthetized dogs by the injection of a starch suspension or of glass beads 100 microns in diameter. A large volume of either type of embolus evoked a similar response consisting of increasing tachypnea, bradycardia, aortic hypotension, and pulmonary arterial hypertension ending in hypotension with right ventricular failure and death. This response was not significantly altered by previous surgical or pharmacologic autonomic nerve interruption. Furthermore, when the arterial pressure was raised in one lung by selectively embo- lizing it, the pressure in the other lung, which was being maintained by artifical perfusion, did
ABSTRACTS

not change. Thus it was concluded that in this experimental setting no evidence of important reflex phenomena could be found and that these pulmonary emboli produced ill effects by mechanically obstructing the pulmonary vasculature.

ROGERS

CONGENITAL ANOMALIES


A method is presented for the experimental production of cardiac malformations. This consists of timed exposures of pregnant rats to increased carbon dioxide tension, with normal or decreased oxygen tension in the respiratory atmosphere. In this paper the histologic findings in the first 40 serially sectioned hearts of the abnormal offspring are reported. All the hearts obtained from treated animals were found to be abnormal. The following anomalies were observed: generalized marked myocardial thickening, 19 hearts; predominantly right ventricular thickening with narrowing of the pulmonary outflow tract, 9 hearts; left ventricular thickening with narrowing of the aortic outflow tract, 11 hearts; incomplete ventricular septation, 5 hearts; incomplete atrial septation, 13 hearts; and aortic arch anomalies, including persistent patency of the ductus arteriosus, 10 hearts. In some of the hearts a combination of developmental anomalies of the cardiovascular septum was observed. None of the 15 control hearts showed any of the above anomalies.

MAXWELL


This paper presents detailed hemodynamic observations during leg exercise in the supine position in 30 patients with single congenital anomalies. The subjects were subdivided into one group, in which the pulmonary artery systolic pressure exceeded 16 mm. Hg at rest, and another, in which the pressure was below this value. The first group consisted of 7 patients with atrial septal defects, 6 with ventricular septal defects, and 3 with a patent ductus arteriosus. The second group was composed of 7 subjects with atrial and 2 with ventricular septal defects and 5 with patent ductus arteriosus. It was found that in patients with pulmonary hypertension (the first group) the pulmonary blood flow was found to change only slightly during exercise, regardless of the magnitude of the vascular shunt. The pulmonary artery pressure and the pulmonary resistance were increased. On the other hand, there was no consistent increase in pulmonary resistance during exercise in the group without pulmonary hypertension, although there was a definite increase in pulmonary blood flow. Patients with large left-to-right shunts may adapt to the circulatory needs of exercise without major changes in vascular dynamics. The demands on the heart for an increase in systemic blood flow to meet exercise requirements can be met without a concomitant increase in "stress on those portions of the central circulation already overburdened by the presence of the abnormal shunt."

WAIFE


Of 55 patients with persistent ductus 24 showed increased pulmonary arterial resistance; in these, the systolic pulmonary artery pressure exceeded 30 mm. Hg in 13 and 50 mm. Hg in 9. Histologic study of pulmonary biopsies obtained during operation disclosed intimate correlation between pathologic changes in pulmonary vessels and the mean pulmonary arterial pressure. These changes are attributed to increased pulmonary flow, as all cases with pulmonary hypertension decreased the shunt. The electrocardiogram showed high voltage in $V_{1}-V_{6}$ in 29 per cent, but right ventricular "strain" only in patients with pulmonary hypertension. Forty-four patients with ventricular septal defect also showed a first phase with low pulmonary resistance and large left-to-right shunt, a second phase with equalization of pulmonary and aortic pressures (after the sixth to twelfth month), and a third phase with high pulmonary pressure and shunt reversal (after the second to tenth year). In 61 patients with atrial septal defects the shunt was smaller than in those with interventricular or aortico-pulmonary communications before development of pulmonary hypertension, as the atrial pressure difference was small. The third phase of pulmonary hypertension therefore usually does not appear until after the third decade of life, and is always accompanied by morphologic changes in the pulmonary vessels. These changes in all 3 types of heart disease disappear or show considerable regression after operative treatment, if this is undertaken before development of the third phase.

LEFESCHKIN

Cardiac catheterization in a 25-year-old man disclosed a pulmonary systolic arterial pressure of 160/80 mm. Hg; the catheter penetrated into the descending aorta. The right-to-left shunt was about 0.5 liter per minute while the phonocardiogram showed only a holosystolic murmur. Blood gas studies showed entry of a pulmonary vein into the persisting left superior vena cava, and this, together with congenital increase in the pulmonary resistance contributed to the pulmonary hypertension. In this patient ligation of the ductus was not indicated.

Lepeschkin


All of 162 hearts with congenital cardiovascular abnormalities subjected to this study showed a serous endocarditis of the valves and endocardium, which led to the formation of scar tissue and could have been the cause of valvular or infundibular stenosis and atresia. The progressive course of the disease was due partly to failure of the stenotic part to grow with the rest of the heart, but partly to increase of the stenosis due to active serous endocarditis. Prenatal serous endocarditis leading to valvular stenosis or atresia can alone be responsible for the development of a trilogy or tetrology of Fallot. Primary isthmic stenosis of the aorta may lead to secondary perforation of the interventricular septum.

Lepeschkin

CONGESTIVE HEART FAILURE


Prednisone was given orally in doses of 5 mg. 4 times daily for 1 week and then 10 mg. 4 times daily to 11 patients with varying degrees of congestive heart failure. The effect of this therapy was favorable in 5 patients who experienced a decrease in dyspnea; a decrease in weight was observed in 5, 1 had an increase in appetite with weight gain and a questionable increase in dyspnea. The administration of prednisone produced a decrease in 17-ketosteroids in 8 patients probably due to suppression of endogenous ACTH secretion. An increase in the urinary excretion of sodium was noted in 7 patients, a decrease in 2, and a variable response in 2. The effect on the excretion of potassium was similar to that of sodium. The mechanism of action of prednisone in congestive heart failure may be that of counteraction of aldosterone production by the adrenal cortex. Secondary aldosteronism may occur in heart failure because of impaired hormone metabolism in the congested liver or because of increased hormonal secretion stimulated by low sodium diets, rising serum potassium or relative dehydration. It is suggested that prednisone may aid in the correction of these defects and thereby ameliorate the cardiac status.

Shuman


The response to chlorothiazide was studied in 24 edematous patients, of whom 17 had congestive failure. Thirteen had failed to improve on standard therapy including mersalyl. A daily dose of 2 Gm. produced good results in 14 patients. In patients who responded, chlorothiazide caused an approximately equimolar loss of chloride and sodium, usually maximum on the first day. As edema subsided sodium and water diuresis diminished. On the existing intake of sodium chloride, no changes in serum sodium, chloride, or bicarbonate levels were observed, but the serum-potassium level tended to fall, and there was increased loss of urinary potassium. Since potassium depletion may result, chlorothiazide should be supplemented with potassium chloride. A response to chlorothiazide may be evident in patients refractory to mersalyl or, when given with mersalyl, the diuresis may be greater than when either is given alone.

Kurland


In 16 patients with right ventricular failure the increase of venous pressure 30 seconds after exercise in the recumbent position, compared to the value at rest, was greater than in normal persons. After oral digitalization this increase was definitely smaller; the effect of a single injection of strophanthin was not as pronounced. The decrease of the increment of venous pressure can be used to assess the efficacy of digitalis treatment.

Lepeschkin
CORONARY ARTERY DISEASE


A study was made of 489 patients who survived an acute myocardial infarction for at least 2 months to determine the incidence of cardiac enlargement during the postinfarction period. Only those patients were included who had normal-sized hearts and in whom the onset of infarction could be determined with certainty. Serial fluoroscopic examinations or telerontgenograms were used to determine heart size. The observations extend over a period of 1 to 10 years. The incidence of cardiac enlargement due solely to myocardial infarction was 2 per cent of the group. Congestive heart failure was present in each of those exhibiting enlargement of the heart. Other factors causing cardiac hypertrophy, such as hypertension, valvular heart disease or eor pulmonale, were not present. The anatomic factors involved in cardiac enlargement were not determined except in 1 necropsied case in which left ventricular hypertrophy was found. Multiple infarctions did not cause cardiac hypertrophy in the absence of congestive failure. The opinion is expressed that myocardial fibrosis or aneurysm may develop over a period of time, leading to congestive failure, which by unexplained mechanisms leads to cardiac hypertrophy.

SHUMAN


An analysis of 68 cases of acute myocardial infarction complicated by high degrees of atrioventricular heart block is presented. This phenomenon was found more frequently with acute posterior than with acute anterior wall myocardial infarction. The immediate mortality rate of infarction in this series was found to be higher than that of myocardial infarction in general. The mortality rate was higher when the atrioventricular block complicated infarction of the anterior wall, or was due to necrosis of the ventricular septum, and increased with the severity of the block. The immediate prognosis of myocardial infarction complicated by atrioventricular block was further aggravated by the factors known to be of importance in determining the immediate mortality rate of infarction in general. The long-term prognosis, however, is those patients surviving the initial episode was not found to be affected by persistence of atrioventricular block.

SAGALL


Twenty-five male patients with myocardial infarction were treated with ACTH or cortisone to study the effect of these agents on the general course of the inflammatory reaction associated with the infarct. Frequent determinations were made of the temperature, leukocyte count, fasting blood sugar, sedimentation rate, erythrocyte count, and serum iron. The results were compared with those obtained in a like manner from a control group of 25 males with myocardial infarction who were not given steroids. In the patients treated with ACTH or cortisone, the average leukocyte count was higher than in the control group. Aside from this, none of the reactions studied was significantly influenced by the administration of the hormones.

BROTHERS


The action of Iproniazid has been studied in 41 patients with severe intractable angina pectoris. The drug has been given in doses of 150 mg per day, divided in 3 equal doses. Any other medication used for the treatment of angina was interrupted. No hypotensive agent was used. In all patients the clinical manifestations of angina completely disappeared within 4 to 12 days. If the administration of Iproniazid was interrupted, or if the dose was decreased the symptoms reappeared within 3 to 8 days. During the Iproniazid treatment the electrocardiogram showed changes toward normal. In 26 cases the electrocardiographic exercise test became normal. Collateral and toxic effects noted were: mouth dryness, meteorism, constipation, dysuria, euphoria, somnolence, vertigo, and tremors. These effects were usually not severe; they might however become limiting factors in the use of the drug. The author believes it is unlikely that Iproniazid acts as a vasodilator or as an analgesic. The opinion is advanced that the drug counteracts other substances increasing the oxygen consumption of the myocardium; it is also possible that Iproniazid increases the efficiency of the cardiac muscle. It is concluded that Iproniazid is a new specific agent for the treatment of angina pectoris. It is hoped that the study of its mechanism of action will lead to a better understanding of the pathogenesis of this syndrome.

CALABRESI

Of 70 patients with ventricular aneurysm, 67 had myocardial infarction, and 30 of these continued physical work on the first day of infarction while 3 continued it throughout. Of 7 dogs submitted to exercise in the treadmill 2 days after ligation of the descending branch of the left coronary artery, ventricular aneurysm developed in 5.

LEPESCHKIN


Electrocardiographic Master 2-step exercise tests were performed on 213 volunteer students with no evidence of coronary artery disease and compared with those found in 30 patients with a clinical diagnosis of coronary artery disease. False-positive exercise tests were found in 26 per cent of the normal group with the criteria recommended by Master. This figure was reduced to 16 per cent when Master's criteria were modified to permit recognition of false ST-segment depression caused by superimposition of the Tₚ and U waves in the ST-segment junction. With these new criteria all the true-positive tests of the coronary disease group still remained positive. Comparison of the 37 persons still showing false-positive tests even with the new criteria with the 30 true-positive group revealed that false-positive tests occurred most commonly in women over 40 years old and in individuals with past or present hypertension. Further study of these 2 groups indicated that the combination of criteria for a positive test with the least amount of overlapping, being present in 94 per cent of the true and in only 23 per cent of the false tests was as follows: inversion of the T wave in lead I or depression of the ST-segment junction beyond the continuation of a P-R interval of 0.75 mm. or more, the return of the S-T segment to the base line at this time taking place in the second half of the Q-T interval, and ST-segment depression of 0.5 mm. or more lasting for 2 minutes or more.

SAGALL


One hundred and sixty-four patients with typical clinical signs of angina pectoris but with normal electrocardiograms at rest were subjected to inhalation of 9 per cent oxygen in nitrogen for 10 minutes. Thirty five per cent of these had a positive response according to Levy; the electrocardiographic changes had a "subepicardial localization" in 5.5 per cent and were accompanied by pain in 3.7 per cent. Simultaneous registration of peripheral blood oxygen saturation showed that S-T depression appeared at saturations from 60 per cent to 80 per cent. After resumption of air breathing the saturation becomes nearly normal within 1-2 minutes; because of this rapid normalization, the test is considered safer than the exercise test. The hypoxia test can also be given to patients who cannot or will not execute the proper amount of exercise. Thirty patients were submitted to the Master 2-step exercise test some time after the hypoxia test, and 43 per cent showed a positive response, accompanied by pain in 30 per cent. Only 1 patient showed a negative response both to the hypoxia and the exercise test.

LEPESCHKIN


Microscopically identifiable atrial infarction was found in 8 of 768 autopsies of cardiac patients; among whom 198 also had ventricular myocardial infarction. In 5 patients infarction involved the right atrium; in 3, the left. Among 136 published cases the right atrium was involved in 83 per cent, the left in 13 per cent, and both in 4 per cent. The atrial appendage was involved predominantly in 59 per cent. In 4 patients biventricular posteroseptal, in 1 patient biventricular apical, and in 2 patients left ventricular posterior infarction was present in addition to atrial infarction. In 1 patient with mitral disease, atrial infarction was the only finding. Electrocardiographic signs suggestive of atrial infarction were atrioventricular block, atrial ectopic rhythms, inversion of the P wave in leads II and III, and notching of the P wave. Displacement of the P-R segment was diagnostic only if it occurred in the same direction as the P wave, but this finding was very rare.

LEPESCHKIN

ELECTROCARDIOGRAPHY, VECTORCARDIOGRAPHY, BALLISTOCARDIOGRAPHY, AND OTHER GRAPHIC TECHNICS

Braunwald, E., and Morrow, A. G.: Sequence of Ventricular Contraction in Human Bundle

The validity of the classic concept of bundle-branch block was re-examined critically by simultaneous catheterization of both ventricles permitting determination of the temporal relation between the onset of contraction of the ventricles in 7 patients with normal intraventricular conduction, in 5 with electrocardiographic patterns of left bundle-branch block, and in 10 with right bundle-branch block. None of the patients with the electrocardiographic configuration of left bundle-branch block had a significant delay in the onset of left ventricular contraction. Six of 10 patients with right bundle-branch block showed no abnormal delay in the onset of right ventricular contraction. The absence of abnormal ventricular contraction in patients with complete bundle-branch block is not compatible with the concept of a complete interruption of conduction in a main bundle branch.

KURLAND


Four cases with paroxysmal atrioventricular nodal tachycardia were studied by intracardiac leads during the attack and following intravenous injection of 250 to 1000 mg. of procaine amide. The morphology of the atrial deflection and its temporal relation to the ventricular complexes permitted a precise location of the impulse origin in the upper, middle, or lower parts of the atrioventricular node. Procaine amide suppressed the ectopic rhythm in all 4 instances. One effect was a depression of the rhythmicity of the ectopic focus manifested by gradual slowing of its discharge. In 1 case this was initiated by transient alternation of the cycle length and in another by shifting of the pacemaker within the atrioventricular node. A second effect was prolongation of intraatrial conduction manifested by a delay of atrial depolarization and widening of the atrial complex. Finally procaine amide produced depression of forward and retrograde atrioventricular conduction manifested, respectively, by prolongation of the R-P intervals and dropped ventricular complexes. Disorders of intraventricular conduction occurred in 2 cases before treatment as a consequence of the tachycardia and were induced in 1 by the medication. In all, the ventricular complexes became normal with slowing of the ventricular rate.

PICK


The lowest values of contact potentials and polarization potentials are obtained with silver electrodes and a paste containing 27 per cent sodium soap, 7 per cent ammonium chloride, and 7 per cent glycerin, or with tin electrodes and a paste containing 7 per cent starch, 7 per cent glycerin, and 7 per cent stannic chloride. Both pastes contain also 36 per cent pumice and a bacteriostatic substance. Use of gold, nickel, or stainless steel electrodes leads to higher contact or polarization potentials.

LEFESCHKIN


The authors report electrokymographic studies performed in 62 normal individuals and 230 patients with various types of heart disease, with special attention to dynamics of the right atrium and the great veins. Th: method of choice for an analysis of systemic venous pulsations is an electrokymogram of the right diaphragm which, in contrast to the electrokymogram of the superior and inferior venae cavae, is easy to perform and provides dependable tracings with constant features under normal conditions. In 16 of the cardiac patients who had in common prominent features of right heart failure, the following characteristic combination was found; an atrial contraction wave of increased duration (0.10 to 0.18 second) and of large amplitude averaging in the different atrial points, recorded in the same individual, 50 to 100 per cent of the total height of the tracing, and abnormal presystolic “a” waves in electrokymograms from the venae cavae and the right diaphragm. This was found in 3 patients with tricuspid valve disease, in 1 instance of rupture of an aneurysm of the sinus of Valsalva into the right ventricle, in 3 patients with old infarction of the ventricular septum, and in 4 patients with constrictive pericarditis. It would appear that in all these instances the particular electrokymographic pattern was caused by mechanical factors compromising right atrial outflow.

PICK

In a patient with complete atrioventricular block on the basis of posterior myocardial infarction, the idioventricular rhythm originated in the left bundle branch on 25 occasions during the subsequent 5 years; the rate of this rhythm was slow when inversion of the T wave in leads II and III was greatest. Origin in the right bundle branch was observed on 8 occasions, and the rate was slower when inversion of the T wave in the left precordial leads was greatest. Origin in the common branch was seldom seen.

Lepeschkin


Of 15 patients with the Wolff-Parkinson-White syndrome, 9 showed Type A (QRS area vector between +38° and +112°, upright QRS in V3); this type is attributed to pre-excitation of the left ventricle. The axis of T was within normal limits and its deviation from the QRS axis was counterclockwise in this group. Six patients showed type B (QRS axis from -21° to -57°, QS in V3 in all except 2 cases, which were called “BA”). In this group, which is attributed to pre-excitation of the right ventricle, the axis of T always showed a deviation of 65° to 154° clockwise from the QRS axis as in the pattern of left bundle-branch block.

Lepeschkin


Of 4,000 routine electrocardiograms, 106 showed a maximal voltage of the RS defection of less than 0.7 millivolt. Of 100 cases studied in detail, 80 had had a systolic blood pressure of less than 80 mm. In 25 patients the ratio of the highest voltage of RS in the limb and the precordial leads was less than 0.35, the lowest value found in 100 normal persons; these patients were said to have absolute low voltage. In this group pulmonary disease was present in 36 per cent, pericardial disease in 24 per cent, myxedema in 12 per cent, myocardial infarction in 8 per cent, and psoriasis in 4 per cent. Seventy five patients had a ratio of more than 0.35, and were said to have absolute relative low voltage; women tended to have higher ratios than men. In this group pulmonary or pleural disease was present in 76 per cent, pericardial disease in 5 per cent, myxedema in 2 per cent, cachexia in 2 per cent, obesity in 9 per cent, and asthenic body build in 8 per cent. A ratio of more than 1 (“paradoxic low voltage”) was found in 1 man with extensive myocardial infarction and 2 women with obesity. Various causal factors are discussed in detail in reference to the 3 types of low voltage.

Lepeschkin


An electrocardiographic study is presented of 44 patients with interatrial septal defects proved by cardiac catheterization and surgery. It is concluded that RSR’ or RSR’S’ patterns in lead V1 in this condition do not mean disturbance in conduction of the right branch of the bundle of His but arise from a delay in the activation of the basal portions of the right ventricle and of the higher parts of the interventricular septum because of hypertrophy and dilatation of these structures. This pattern appeared mostly in those anomalies that produced a diastolic overloading of the right ventricle. In uncomplicated interatrial defect the fundamental hemodynamic change is an increase in blood volume-work without significant increase in pressure in the right ventricular chamber. In the author’s opinion there is a definite correlation between the morphology of the QRS complex in V1 and the magnitude of the shunt flow. In the same way, the morphology of the P wave in the right precordial leads bears some relationship to the magnitude of this flow.

Sagall


Phonocardiographic studies of the heart sounds in dogs and man are reported and conclusions regarding the mechanism of the heart sounds are presented. The first heart sound is made of 3 phases: a low-pitched beginning due to myocardial tension; a higher-pitched central phase due to valvular events; and a low-pitched final phase due to vascular phenomena. The central phase contains at least 4 vibrations corresponding to the motion of the heart valves in the following sequence: mitral closure, tricuspid closure, pulmonic opening, and aortic opening. The second heart sound is made of 3 phases: a low-pitched beginning due to eddies preceding the valvular closure; a higher-pitched central phase due to closure of the semilunar valves; and a low-pitched final phase due to final vibrations plus opening of the A-V valves. The central and final phases correspond first to the closure of the semilunar valves and, then, to the opening of the A-V
ABSTRACTS

Sagall


The P waves of the electrocardiograms of 20 patients with rheumatic heart disease and mitral stenosis were studied with reference to abnormalities in contour in relation to the volume of the left atrium. The combined technic of cardiac catheterization and biplane stereoscopic angiocardiography was employed for evaluation of intracardiac volumes and flow velocities. Notching, amplitude, or duration of the P wave could not be correlated with the degree of left atrial enlargement demonstrated. Notching of the P wave was commonly observed while high amplitude was the least frequent abnormality in patients with mitral stenosis. For any given amplitude of P wave, the left atrial volume varied greatly. The electric axis of the P wave was usually semivertical, occasionally vertical, and rarely horizontal. In lead V1, the qR complex was unrelated to left atrial enlargement but was associated with cardiac hypertrophy, right atrial enlargement, and pulmonary hypertension. The enlargement of left atrium showed a tendency to rightward deviation of the P wave but was best correlated with rightward deviation of QRS.

Shuman


In patients with sinus arrhythmia, atrial extrasystoles or atrial fibrillation, the U wave usually shows greater voltage after long diastolic pauses. This applies to positive as well as to negative U waves. As the configuration of QRS remains unchanged, the U-wave changes must be considered as primary; they are attributed to accumulation of blood in the atria and the resulting greater diastolic distention of the ventricle. The T wave often shows changes opposite to those of the U wave. In cases that show no change of U, this wave is usually very small. In some patients with atrioventricular dissociation due to complete block or to sinus bradycardia with nodal escape rhythm, the U wave was taller in ventricular complexes in which the P wave was superimposed on the QRS complex or S-T segment than in those preceded by the P wave, although the preceding diastolic pause remained unchanged. The only explanation applicable to these cases is that coincidence of atrial and ventricular contraction prevents proper emptying of the atria, and the filling of the ventricle at the beginning of the following diastole is more forceful. In 1 patient with pulsus alternans the U wave also appeared to show alternation. The conclusion is made that the U wave must result at least in part from the mechanical effect of ventricular filling.


In 217 consecutive patients, admitted to the Contagious Diseases Hospital, Stockholm, for various acute infectious diseases, standard, unipolar extremity and chest leads were taken concurrently once weekly for at least 3 to 5 weeks. Electrocardiographic signs suggestive of myocardial lesions were observed in 11 patients. In 4 of these, abnormal changes were demonstrated only with chest leads, the extremity leads either being normal or showing only slight or ambiguous changes. At the same hospital, abnormal electrocardiographic changes were observed to occur in the serial standard leads taken routinely in 210 out of 2,310 patients with acute infectious diseases. Most of the abnormalities consisted of T-wave changes. Chest leads were also obtained on these patients. In most instances it was possible to localize the electrocardiographic changes in this series to one or more leads corresponding to the right ventricle, apical region, or left ventricle. In children, changes were more frequently localized to the right ventricle, while signs of left ventricular involvement were more frequent in adults. Chest leads showed the most pronounced changes and were diagnostically significant more often than the unipolar extremity or standard leads. The author believes this study demonstrates that a full set of chest leads greatly enhances the possibility of making a diagnosis of myocarditis.

Brotters

In a group of 98 patients with a variety of acute infectious diseases, changes had taken place in their resting electrocardiograms. After the resting electrocardiograms of these patients had returned to a normal, or almost normal, pattern, exercise electrocardiograms were done and were interpreted as being abnormal in more than 40 per cent. In the majority of patients, the principal change consisted in abnormalities of the ST-T complex. Disturbances of rhythm, chiefly extrasystoles, were also common and were encountered in adults more frequently than in children. Patients who had earlier shown disturbances of rhythm on the resting electrocardiograms presented abnormal exercise electrocardiograms to a greater extent than those with changes mainly in the ST-T complex or the P-Q interval. The changes sometimes appeared both during and after exercise but often only during exercise. Chest leads taken at 3 to 4 minutes after exercise disclosed abnormal findings in more than 40 per cent of all the cases investigated and by comparison with the standard leads and lead aVR, were much more valuable in detecting electrocardiographic abnormalities. Chest lead abnormalities occurred more often in children than in adults. As in an earlier investigation with resting electrocardiograms, changes corresponding to the right ventricle were seen more frequently in children than in adults, whereas changes corresponding to the left ventricle were more common in adults than in children.

BROTHERS


In 1 patient, each series of 2 to 3 sinus beats with a P-R interval of 0.33 second and right bundle-branch block (Type V) was terminated by a blocked P wave; the following complex always showed a P-R of 0.22-0.24 second and a "paradoxical" left bundle-branch block. To explain this pattern, the assumption is made that the right bundle-branch shows a variable conduction disturbance dependent on the preceding pause, while the left branch shows a considerable conduction delay independent of the preceding pause. The diagnosis of a bilateral bundle-branch block can accordingly be made only if alternation between right and left bundle-branch block is always accompanied by a corresponding change in the P-R interval. In the case of 1 patient with such alternation and complete atrioventricular block, and of 2 patients with delayed intrinscocid deflection in right as well as left preconcurrenceal block, this diagnosis could not be made with certainty. These patterns can result also from unilateral block combined with a conduction disturbance in the atrioventricular node, peri-infarction block, left ventricular hypertrophy, or left intraventricular block.

LEPESCHKIN


Of 4,320 patients subjected to electrocardiographic study during a single year, 5.9 per cent showed a QRS amplitude less than 0.5 mV in the limb leads. The average age in this group was significantly higher. Sixty-five per cent had pulmonary emphysema, 5 per cent hepatic cirrhosis or neoplasms, 14 per cent heart disease, and 6.5 per cent peripheral edema. Low voltage in precordial leads was found in only 9 per cent. Other electrocardiographic abnormalities were found in 48 per cent. The incidence of low voltage in pulmonary emphysema was 14 per cent, whereas in marked emphysema it was 39 per cent; the higher incidence in emphysema is statistically significant. The incidence in malignant neoplasms was 13 per cent, in hepatic cirrhosis 14 per cent, and in adrenal insufficiency 10 per cent; in these groups the increased incidence was not significant statistically. In myxedema the incidence was 47 per cent. In patients with hepatic cirrhosis there was no relation between the incidence of low voltage and that of increased serum globulins. The results emphasize the significance of extracardiac factors in the genesis of low voltage.

LEPESCHKIN


Of 12 patients with atrial septal defects, 8 showed middiastolic or presystolic murmurs only in the esophageal phonocardiogram, registered through a catheter having a window with a rubber membrane, but not in the precordial phonocardiogram. These murmurs were attributed to a relative tricuspid stenosis caused by the increased blood flow through this orifice. In 2 patients isolated early diastolic murmurs appeared in the esophageal as well as the precordial phonocardiogram.

A light source having a wavelength of 620 mμ and a small selenium photocell are placed at the tip of a no. 9 cardiac catheter, separated by a slit accessible to intracardiac blood. Blood samples used in calibration of the catheter can be taken through an opening in the side of the catheter next to the photocell. Intracardiac pressures can also be registered through this opening. The entire assembly is only slightly larger than the diameter of the catheter, and is now manufactured by the Rüsch Company, Rommelshausen/Stuttgart. The advantage of the method is that the oxygen saturation in any position of the catheter can be registered immediately, without loss of blood. In 1 patient a sudden change in oxygen saturation at the boundary between right atrium and superior vena cava could be demonstrated repeatedly. In this way the site of a left-to-right shunt can be located much more accurately than with other methods.

LEPESCHKIN


Synchronized registration of curves from many points of the ventricular border shows that each electrokyrogram is the resultant of changes in volume, configuration, and pendular movements. The latter are caused by systolic movement of the ventricular apex into a position perpendicular to the valvular plane, and are least pronounced at the base of the heart. Separation of 2 of these components is possible if one of them can be determined approximately. The time of appearance of different points on the resultant curve does not coincide with corresponding points on the component curves. The isometric period of contraction can therefore not be measured accurately on either the ventricular or the aortic curve, but the beginning of the rapid rise of ventricular pressure can be determined in most ventricular curves.

LEPESCHKIN


Study of the cxfe-system vectorcardiogram in 140 patients with anterior infarction and a QRS duration of 0.10 second or less showed that anteroseptal infarction was characterized by indentation of the Q portion of the vector loop, anterolateral infarction by indentation of the R portion of the loop and extrusion of the S portion, while large anterior infarction combined both these characteristics. Absence of the R wave in leads V_1-V_2 in left ventricular hypertrophy was usually accompanied by a smooth QRS loop while the same pattern in anteroseptal infarction usually was accompanied by typical indentation in the Q portion of the loop. If infarction is accompanied by considerable cardiac enlargement the area of infarction may no longer face any of the standard precordial leads, which show only low voltage of R, but the vector loop still shows typical indentation in the Q portion; in the limb leads these changes may appear only as a notch preceding R. Fresh infarction is characterized by displacement of the S-T vectors forward, downward and to the left, while in the healing phase T vectors show displacement backward, upward, and to the right.

LEPESCHKIN


Detailed serial studies in 2 patients with anterior myocardial infarction showed deviation of the gradient to the right of the QRS axis, while in 3 patients with posterior infarction it deviated to the left. One patient with an apparently normal resting electrocardiogram showed deviation of the gradient 28° to the right of QRS, and this was considered to indicate left ventricular ischemia.

LEPESCHKIN

ENDOCARDITIS, MYOCARDITIS, AND PERICARDITIS


Twenty-nine patients with subacute bacterial endocarditis were treated with penicillin from 1946 to 1954. Eleven (38 per cent) died, 11 (38 per cent) were worse than before their illness, and only 7 (24 per cent) did not appear to have deteriorated. Eight patients died of congestive heart failure within 2 years of the start of treatment. The prognosis was not affected by the organism, but the site of valve disease was important. Ten patients had predominant aortic incompetence. Six of these died from heart failure, and the other 4 were worse than before their illness. In general, the mortality tended to be higher in the patients who had been ill the longest. Congestive heart failure, cardiac enlargement, and atrial fibrillation were associated with a poor prognosis.

KURLAND

In order to determine whether myocardial atrophy actually occurred in constrictive pericarditis, the authors used micrometer measurements of the diameter of the myocardial fibers. Eleven cases of constrictive pericarditis were studied in regard to the thickness of their myocardial fibers. These measurements were then compared to those obtained in normal hearts and also cases of chronic exudative pericarditis and chronic pericardial effusion. In each of the 11 hearts from patients with chronic constrictive pericarditis, myocardial atrophy was seen. This atrophy appeared uniformly in both ventricles. In those cases of exudative pericarditis, atrophy was only seen in the area of myocardium adjacent to the inflammatory process in the epicardium. In 2 cases of chronic pericardial effusion, there was evidence of myocardial atrophy similar to the atrophy in constrictive pericarditis possibly due to the long duration of the compression.

Krause


One hundred and twelve patients with cardiovascular syphilis were treated with penicillin only. No fatal complications definitely attributable to penicillin occurred. A follow-up study of 54 patients who received their therapy 5 or more years earlier, disclosed that only 23 (42.6 per cent) were living 5 years after treatment. The prognosis in this group as well as in the full series was significantly better in women. The total penicillin dosage did not appear to influence the prognosis, for there was no demonstrable difference in this respect between those receiving less than 10 million units and those receiving 10 million units or more. Grouped on the basis of functional capacity according to the classification of the New York Heart Association, it was clearly evident that the greater the functional impairment at the time of treatment, the poorer was the prognosis. Of the patients falling into Class I and II, 60.8 per cent were living 5 years later, whereas for those falling into Class III and IV only 9.0 per cent survived 5 years. Four of the 23 patients surviving for 5 years, died during the sixth year leaving 19 available for a follow-up examination, to which 14 responded. Thirteen of these were originally designated as being in functional class I or II. Ten patients were working.

ABSTRACTS


The authors discuss the treatment of bacterial endocarditis from the year 1945 to the end of 1956. A total of 82 patients were included in the survey. The immediate mortality was about 25 per cent. A delay in diagnosis was demonstrated in a high percentage of patients and this was particularly true when features less typical of endocarditis dominated the clinical course. Precipitating factors were also investigated, and the extraction of infected teeth without antibiotic coverage was responsible for the infection in 11 patients. As reported in the literature, streptococcus viridans was by far the most common organism found. When blood cultures were positive, it was usually the first blood culture that helped identify the organism. Fifteen of the group were diagnosed as having 2 attacks of endocarditis apparently due to inadequate antibiotic treatment. When the infections seemed resistant to penicillin, increased dosage of the drug and the addition of streptomycin usually proved to be successful. The disease has its greatest mortality and is more often missed among the older age groups.

Krause

HYPERTENSION


The fact that experimental hypertension can be produced by partial occlusion of a renal artery and the demonstration of the renal pressor system led the authors to study certain hypertensive patients by means of aortography. This method of study was not used routinely but was performed on 4 classes of hypertensive patients: (1) those with unexplained disparity of the size or function of the kidneys by intravenous urography; (2) those young patients who do not seem to have essential hypertension; (3) those elderly hypertensive patients who suddenly develop accelerated or malignant forms of the dis-
ease; (4) those individuals of any age with long-standing essential hypertension when the disease abruptly becomes more serious. One hundred four patients were studied and 30 were found to have focal renal artery disease. Nineteen of these 30 were subjected to various surgical procedures, ranging from endarterectomy through renal artery grafting to nephrectomy. Nephrectomy is the choice when there is unilateral disease with atrophy and reduced function of the involved kidney. Of the 19 operated on, 5 have normal blood pressure, 2 have had reversal of malignant hypertensive syndrome even though they still have hypertension. These have been followed more than a year. In patients followed less than 1 year, blood pressure returned to normal in 6. Death has occurred in 2 patients postoperatively (1 from renal failure and the other from hemorrhage).

Kitchell


This is the third recorded report of a phaeochromocytoma of the urinary bladder. The tumor produced pressor amines and gave rise to a recognizable striking clinical picture. Typical attacks consisted of palpitations, headache, pallor, and sweating commencing as soon as the bladder was emptied, lasting a few minutes, occurring only in the summer. Remission occurred from menarche at 15 to age 41. Urine contained 0.8 mg. norepinephrine per ml. When cystoscopy revealed a bladder tumor, operation was performed. The tumor contained epinephrine and norepinephrine. The urinary output of catechol fell postoperatively, but the blood pressure remained 190/100 mm. Hg although the patient was asymptomatic.

Kurland


A solution of the essential oil of Nardostachys jatamansi in Tween 80, beta alcohol, and propylene glycol was injected in the femoral vein of dogs. A prolonged and marked hypotensive effect was produced. In moderate doses the drug did not cause electrocardiographic changes; it had a negative inotropic effect; it did not block ganglionic transmission; it had some adrenolytic action; it did not depress the vasomotor center, but it blocked the proprioceptive blood pressure-regulating reflexes. Although these effects may contribute to the hypotensive action of the drug, it appears that this is primarily due to a direct peripheral vasodilator effect. The "therapeutic ratio" of this drug is very high; although there are no controlled clinical observations, clinical trial of this preparation in selected cases of hypertension and of peripheral vascular diseases appears justified.

Calabresi


In rabbits under urethane anesthesia and artificial respiration, after bilateral vagotomy and intravenous atropine sulfate, intravenous injections of epinephrine or norepinephrine in adequate dosage caused a reproducible hypertensive effect. To study the influence of adrenolytic drugs on this hypertensive effect, gradually increasing doses of the following agents were administered by intravenous injections: Prosympal and Benodrame (both benzodioxane derivatives); Priscol and Regitine (imidazoline derivatives); Dibenzyline; Ilidar; Dihydroergotamine. Each animal was tested with only 1 of these drugs. Previous investigators have found it difficult to obtain blockade or reversal of hypertension, particularly after norepinephrine. In these experiments 3 different results have been noted, varying with the inhibiting agent used and with its dosage: blockade of the hypertensive effect; diphasic reaction (hypotension followed by hypertension); reversal of the hypertensive response. No qualitative difference has been noted in the influence of these drugs on the hypertensive response to epinephrine or norepinephrine, although frequently higher doses were necessary to elicit the inhibitory effect when norepinephrine was used as the hypertensive agent.

Calabresi


Determinations of cardiac stroke volume according to Wezler and Böger were carried out in 2,833 patients; of 1,355 patients with hypertension 25 per cent showed a stroke volume exceeding 100 ml. Persons without hypertension showed such values in only 7 per cent. In 3 patients without hypertension who showed an elevated stroke volume and increased duration of the resonant oscillation of the arterial system,
arterial hypertension developed later. It is concluded that an increase in stroke volume is the cause of hypertension in some of the patients.

Lepeschkin


One hour after meals the blood pressure shows a decrease parallel in its magnitude to the initial pressure level; this decrease does not appear after ingestion of barium sulfate and must therefore be attributed to digestive activity. It is caused by a decrease in the peripheral resistance, while the heart output remains essentially unchanged. It does not appear after previous medication with neprosil, since this drug acts primarily on the peripheral resistance. On the other hand, it is not influenced by previous medication with Serpasil, since this substance acts primarily on the cardiac output.

Lepeschkin


Treatment with sleep induced by means of barbituates and conditioned reflexes in 73 patients with ulcers caused improvement immediately in 37 and after 4 to 6 months in 63 persons. The same treatment in 40 patients with hypertension caused improvement immediately in 22 and after 4 to 6 months in 9 persons. Basal metabolism and blood sugar were usually more normal after treatment. Patients with ulcers usually showed predominantly inversion of the skin temperature reaction to heat, while those with hypertension showed predominantly inversion of the blood pressure reaction to cold. After treatment the reaction least affected before treatment usually became more normal.

Lepeschkin

PATHOLOGY


The authors report detailed anatomic studies of the specialized conduction tissues in 15 human hearts with high interventricular defects. In all cases there were additional cardiac anomalies, but no cardiac arrhythmias. Ten specimens were studied in microscopic serial sections, and 5 were studied grossly with the aid of a dissection microscope. The conducting tissues were readily identified by Masson stain in the microscopic sections, and by their pale appearance in the gross specimens. In 12 of the 15 specimens the common bundle as well as the left and right bundle branches were found to be in the postero-inferior margin of the septal defect. This corroborates the presumed location previously reported by Kirklin. In 7 of 10 microscopic specimens early rami (Mahaim's fibers) were demonstrated. These arise above the bifurcation of the bundle and pass directly into the septal myocardium. Another unexpected finding was the presence of accessory pathways (bundles of Kent) connecting the common bundle above the fibrous ring with the septal myocardium below. The latter 2 accessory pathways may become very important in cases where the common bundle is injured in the course of surgical repair. Hemorrhage of unexplained origin was found in the conducting system in 6 cases.

Enselberg


The case of a 57-year-old woman with known complete heart block of at least 42 years' duration is presented with a detailed histopathologic study of the conduction system, the atria, and the ventricles. The atroventricular node was found to be absent or fibrosed and there was a complete lack of connection between the atrial musculature and the bundle of His. The atrial musculature was malformed and exhibited marked fibrosis, fatty infiltration, and calcification with areas of absent or replaced muscles. It was suggested that the atrial changes were due to a congenital malformation and that the patient had either congenital heart block or congenital heart disease with acquired heart block.

Sagall


In 20 patients with aortic stenosis and 50 normal individuals of a comparable age, aortic diameter and thickness of the aortic wall showed considerable individual variability in normal persons, so that absolute measurements could not be used in the diagnosis of stenosis. This could be made definitely if the ratio of the diameter of
the aortic ostium to that of the narrowest region of the aorta exceeded 1:0.40, for in all normal individuals the ratio was smaller. Some patients with stenosis had values between 1:0.40 and 1:0.60, but in these patients the difference between the ratios at the isthmus and the thoracic aorta was greater than 0.30. Hypertrophy or atrophy of the aortic wall or structural differences between the aorta proximal and distal from the point of stenosis could not be found, except in 1 patient with congenital aortic hypoplasia.

Lepeschkin

PHARMACOLOGY


Urea, once considered a satisfactory diuretic, is rarely used for this purpose today. In an attempt to re-evaluate this substance, the authors studied for varying periods of time ranging from 2 1/2 weeks to 7 years, 17 patients with chronic right ventricular failure and ascites. These patients were now refractory to mercurial diuretics. Fifteen grams of urea in 57 ml. of water or grapefruit juice were used 3 times daily after meals. There were 3 therapeutic failures: 1 patient had complete lack of response to the drug, 1 patient died before sufficient time elapsed for proper evaluation, and 1 refused to take further medication after 1 week. Urea as a diuretic does seem to have a place in the therapy of chronic congestive failure with edema. In 50 per cent of the patients a negative fluid balance was changed to a positive one. In those instances in which a negative fluid balance persisted, it was at least reduced in magnitude. As a matter of fact, urea may convert an intractable ease of congestive heart failure to a controlled case. Such patients have been able to continue with restricted physical activities for several years when the initial situation seemed hopeless. The chief disadvantage is that the drug is unpalatable and may cause vomiting and gastrointestinal irritation when administered in the required dose. Furthermore, although the blood urea nitrogen may rise with the administration of the drug, the presence of azotemia does not contraindicate its use.

Krause


Calcium and digitalis have been shown to have synergistic effects in enhancing cardiac irritability mediated by their influences upon cellular ionic permeability. It is probable that both inhibit the influx of potassium into the myocardial cells. The binding of serum calcium by ethylenediamine tetraacetic acid (EDTA) was found to terminate promptly the arrhythmias due to digitalis toxicity in 3 patients. EDTA did not lower circulating calcium levels but rapidly sequestered ionized calcium in a physiologically inert form. It was excreted in the urine with bound calcium over a 48-hour period. Both atrial and ventricular ectopic rhythms caused by digitalis were abolished. In 2 other patients, prior administration of sodium or magnesium salts of EDTA in doses of 600 mg. in 250 ml. of 5 per cent glucose in water intravenously over 15 to 30 minutes offered certain advantages over potassium therapy in treating digitalis toxicity. The effect of potassium is delayed and in large doses orally it may be poorly tolerated. Arrhythmias due to digitalis toxicity should be promptly corrected because of the possible development of fatal ventricular fibrillation and because heart failure is aggravated by the arrhythmias. The use of EDTA affords a means of rapidly overcoming digitalis toxicity.

Shuman


The authors studied the effect of nicotine on the atria of rabbits. Since nicotine is a ganglionic stimulant, it has an inhibitory action on the rate of the isolated heart. However, it also has a stimulant action that can be demonstrated when the atria are dissected from other tissues and suspended in a bath that contains atropine to exclude the inhibition. The stimulant action is probably due to the fact that nicotine releases norepinephrine and epinephrine from stores within the heart. When the rabbits were prepared with reserpine, the atrial depots of epinephrine and norepinephrine were depleted. The atria prepared in this way were not stimulated by the action of nicotine. The cardiac stores of epinephrine and norepinephrine normally exerted some effect and accelerated the spontaneous rate of the heart. The mean rate of atria from animals treated with reserpine was 112 and that of isolated atria from control animals was 142 per minute. If this data can be transferred to human subjects, smoking may liberate norepinephrine and epinephrine from cardiac depots, and thus produce acceleration and exaggerate ventricular arrhythmias. On this basis, smoking may be contraindicated in patients who have cardiac abnormalities.

Krause

Daucarin (an alcoholic extract of carrot seeds) definitely decreases smooth muscle tonus in animals. It was tested in 88 patients with angina pectoris in an oral dose of 20 mg. 3 to 5 times daily for 1 to 3 weeks, after a control period of 1 week. Sixty-six per cent of the patients showed definite improvement, 16 per cent questionable improvement, and 18 per cent no change. The improvement was greatest in persons with hypertension. No unpleasant side effects were observed.

LEPESCHKIN


The resistance of the capillary vessels of the skin to negative pressure was studied in female rats treated with intraperitoneal injections of reserpine in single doses of 1 or 3 mg. per Kg. of body weight. In another series of experiments the drug was administered for 10 or 21 days, daily or on alternate days. Adequate series of controls were also studied. These treatments caused marked depletion of platelet 5-hydroxytryptamine, but did not produce decrease in the capillary resistance. These experiments complement observations of other investigators, indicating that platelet 5-hydroxytryptamine depletion does not prolong the bleeding time; they do not support the theory that 5-hydroxytryptamine influences hemostasis.

CALABRESI


Quinidine, amethocaine, Trasentin, and atropine were tested for the ability of each to stop atrial fibrillation produced in a dog heart-lung preparation by stimulating the right atrium in the presence of acetyl choline and to decrease the maximum rate at which the rabbit atria would respond to electric stimuli. Atropine appeared to act by inhibiting acetyl choline, but the action of amethocaine and Trasentin was mainly quinidine-like. Amethocaine potentiated the effect of acetyl choline on the atria while both quinidine and Trasentin had some atropine-like influence.

ROGERS


The diuretic action of chlorothiazide was examined in 13 patients with edema of various etiologies including 10 with cardiac failure, 2 with cirrhosis, and 1 with nephrosis. Observations on the weight curves and serum electrolytes were conducted before and during the course of treatment with this agent. Favorable effects were noted in seven of the 10 cardiac patients and in the 2 cirrhotic patients. Several patients resistant to other diuretic agents responded well to chlorothiazide. A transient and asymptomatic lowering of serum potassium levels developed in 5 cases during treatment with this agent. The nephrotic patient was resistant to all therapy. Chlorothiazide has been employed on a weekly schedule of intermittent therapy, 4 days on and 3 days off.

SHUMAN


The authors report 4 cases of purpura related to quinidine toxicity. The hemorrhagic picture may vary from one of premonitory symptoms with scattered petechiae and ecchymoses to that of sudden onset of bleeding from multiple sites and systems. Usually most patients have had previous exposure to quinidine, but an occasional case of purpura has been observed in patients not aware of previous quinidine therapy. The diagnosis is made clinically and requires a high index of suspicion. The hematologic findings are those of acute thromboctopenia. On rare occasions a fatal case has been reported. Usually when quinidine therapy is discontinued after the diagnosis is correctly made, the prognosis for recovery is good.

KRAUSE


The hypothesis that the potentiation of sympathetic neurohormones by ganglionie-blocking agents is due to the elimination of the aortic arch and carotid sinus baroreceptors has been tested in atropinized dogs in sodium pentotal anesthesia; the carotid sinuses and the ganglia nodosa had been removed bilaterally, thereby eliminating also the afferent fibers from the aortic arch. Hexamethonium potentiation of epinephrine or norepinephrine was still obtained. Epinephrine
reversal by dibenamine was prevented by hexamethonium, but was not influenced by removal of the baro-and chemoreceptors. The relationship between the potentiating effect of hexamethonium and the results of sympathectomy and of in vitro oxidase inhibitors, and also the possible mechanisms of action of the ganglionic-blocking agent are briefly discussed.

**Eliakim, M., Rosenberg, S. Z., and Braun, K.:**

**Effect of Acetylcholine on the Pulmonary Artery Pressure in Anesthetized Dogs.** Arch. int. pharmacodyn. 113: 169 (Dec.), 1957.

In order to study the site and mechanism of action of the drug on the pulmonary artery pressure, the hemodynamic effects of injections of acetylcholine hydrochloride at various sites and in doses varying from 1 to 500 µg. per Kg. of body weight have been studied in anesthetized dogs. The pulmonary artery and left atrial pressures have been measured by means of right and left heart catheterization; catheters have also been passed into the abdominal aorta and inferior vena cava via the femoral vessels. The injection in the pulmonary artery causes a rise in pulmonary artery pressure and a fall in systemic arterial pressure. Aminophylline, in doses insufficient to affect the systemic arterial pressure, diminishes, but does not abolish, the rise in pulmonary pressure. This effect is interpreted as due to the bronchodilator effect of aminophylline; since large doses of this drug do not abolish the pulmonary artery hypertensive effect of acetylcholine, it is concluded that bronchospasm is only 1 of the factors responsible for the rise in pulmonary artery pressure. Following injection in the pulmonary artery, there is no significant change in left atrial pressure; the systemic arterial pressure falls, mainly due to the cardiac effect of the drug. Injection in the inferior vena cava has similar effects. Injection into the aorta causes a drop in the systemic pressure, due to peripheral vasoconstriction, and a late rise in pulmonary artery pressure, apparently secondary to an increase in venous return and in pulmonary artery flow. Injection in the portal vein has no effect on the systemic pressure and an insignificant effect on the pulmonary artery pressure, presumably because of the rapid enzymatic inactivation of the acetylcholine in the liver.

**Beck, I. T., and Beck, M.:**

**The Anti-fibrillatory Action of 2-Pentene 1-4-Olide (Alpha-beta Unsaturated Angelica Lactone) on the Electrically Induced Ventricular Fibrillation of the Cat’s Heart.** Arch. int. pharmacodyn. 113: 400 (Jan.), 1958.

Ventricular fibrillation was induced in cats under chloralose anesthesia and artificial respiration by direct electric stimulation. After 5 minutes of cardiac massage, 2-pentene 1-4-olide (alpha-beta unsaturated angelica lactone) was administered by intravenous or intracardiac injections in doses of 200 mg. per Kg. of body weight, with reversion to normal rhythm within 5 minutes or less. In 4 cats the same dose was also given before adequate electric stimulation, and either prevented or decreased the duration of ventricular fibrillation. In previous investigations it was seen that the drug may reverse ventricular arrhythmia due to digitalis or to barium chloride. It is suggested that this lactone be tested clinically for treatment of premature beats and of atrial or ventricular fibrillation.

**O’Meara, D., Shepherd, D. M., and West, G. B.:**

**The Vasodilator Action of Glucose Nitrates.** Arch. int. pharmacodyn. 113: 432 (Jan.), 1958.

The effect of a series of glucose nitrates on the blood pressure has been studied in dogs under sodium pentobarbitone anesthesia. The drugs were given by intravenous injections or by mouth. Mono- or dinitrates were found to be inactive; compounds containing 3 or 4 nitrate groups possessed depressor activity comparable with that of erythritol tetrinitrate. Data are given on the structure-activity relationship of these compounds. The need for further studies is indicated. No correlation has been found between the depressor effect and the amount of nitrate ion released in vitro by alkaline hydrolysis; the formation of nitrates in vivo has not been studied yet; it is known, however, that other vasodilator organic nitrates that liberate large amounts of nitrite on alkaline hydrolysis in vitro have very little effect on the blood nitrite level of dogs.

**O’Meara, D., Shepland, D. A., and West, G. B.:**

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**Prasad, B. N.:**

**Role of Prednisone in Acute Pulmonary Oedema.** Arch. int. pharmacodyn. 114: 146 (March), 1958.

Acute pulmonary edema was produced in guinea pigs by intravenous injection of 1 per cent chloropropic in hydroalcoholic base. The protective effect of various drugs, including phenergan, alcohol aerosol, morphine sulfate, and ACTH is reported. At the doses used ACTH protected 6 out of 10 animals; all the other drugs were less effective; cortisone and hydrocortisone were of little help. Prednisone protected all the animals tested, both when chloropropic was given in LD₅₀ and in LD₃₀ dose. The possible mechanism of action of the drug is briefly discussed.