ABSTRACTS

Editor: Stanford Wessler, M.D.

Abstracters

Jonas Brachfeld, M.D., Philadelphia
Massimo Calabresi, M.D., West Haven
Irwin Freedberg, M.D., Boston
Harold Karzman, M.D., Los Angeles
Herbert J. Kayden, M.D., New York
J. Roderick Kitchell, M.D., Pittsburgh
Seymour Krause, M.D., Pittsburgh
George S. Kurland, M.D., Boston
Eugene Lepeschkin, M.D., Burlington
Julian P. Levinson, M.D., Pittsburgh
Morton H. Maxwell, M.D., Los Angeles
Milton H. Paul, M.D., Chicago
Seymour H. Rinzler, M.D., New York
Wayne R. Rogers, M.D., Portland
Elliot L. Sagall, M.D., Boston
Sheldon Sheps, M.D., Winnipeg

ELECTROCARDIOGRAPHY, VECTORCARDIOGRAPHY, BALLISTOCARDIOGRAPHY, AND OTHER GRAPHIC TECHNIQUES


In 20 dogs the intravenous injection of lyceodipodium seeds or constriction of the pulmonary artery caused inconstant changes in the P-R interval, slight prolongation of the Q-T interval, increase in the R wave, decrease in the S wave and sometimes the appearance of an R wave in the right endocardial leads. The T wave became more positive in right ventricular epicardial leads and usually more negative in left epicardial leads. The S-T segment showed elevation in right ventricular endocardial and epicardial leads, no change in left endocardial leads, and often depression in left epicardial leads. Trans-septal leads usually showed no change in the S-T segment. The conclusion was drawn that acute cor pulmonale caused injury in the lateral wall of the right ventricle, but not in its septal wall, and that in many instances subendocardial injury in the lateral wall of the left ventricle appeared; this was attributed to decreased coronary flow as a result of increased coronary venous pressure.

Lepeschkin


Ventricular ectopic beats coupled with preceding normal beats occurred during the delivery of direct current when the anode or cathode was on the ventricular epicardium of the dog. These ectopic beats were induced within the T wave or immediately thereafter during the application of threshold direct current when the anode was on the epicardium. When anodal current was begun in the S-T segment of a given cycle, an ectopic beat was induced within or near the T wave of the same cycle. When the cathode was on the epicardium, coupled ventricular ectopic beats were induced within the P-R interval during the application of threshold current. Under these conditions, marked slowing of sinus rate by vagal stimulation did not alter the interval of coupling between the ectopic beat and the preceding normal beat. Thus, it was shown that abnormal ventricular beat, falling within the P-R interval, was ectopic and independent of the atrial impulse.

Kayden


Myocardial oxygen gradient was altered variously by means of gas mixture inhalation in acute coronary artery occlusion in the dog. This was correlated with the S-T segment elevation in electrocardiograms recorded in a bipolar subepicardial lead across the pink and cyanotic areas of the myocardium. The electrocardiograms revealed a positive relation between them, that is, the S-T segment increased in height with the increasing of the oxygen gradient and decreased in height with the decreasing of gradient.

Kayden

459 Circulation, Volume XX, September 1959

Catheterization through the exposed right common carotid artery was carried out in 17 patients, and the left ventricle was reached in all. Continuous pressure registration during retraction of the catheter enabled exact localization of the stenosis. Filling of the left ventricle with dye enabled good visualization of its outflow tract and the aortic valves, as well as recognition of mitral regurgitation. The only complication was hemiparesis in a patient with mitral stenosis. Ventricular arrhythmias caused by contact of the catheter with the left ventricular endocardium always could be terminated by withdrawing the catheter slightly.

Lepeschkin


A polyethylene catheter containing a fine steel wire was introduced through a trocar into the femoral artery, and the trocar then withdrawn. In order to prevent the catheter from entering the left subclavian artery the patient inclined his neck to the left. After passage of the aortic valves an intracavitary electrocardiogram was registered through the wire, and the latter withdrawn to enable dye injection, registration of pressures or oxymetry. The method allowed exact recognition of aortic disease and mitral regurgitation. It had the advantage of simplicity and good tolerance, but should not be carried out in old persons or those with vascular fragility, renal involvement, myocardial or coronary failure or active endocarditis. It may not succeed in persons with tortuous iliac arteries or marked coiling of the aorta. It should be carried out only if a surgical correction is contemplated.

Lepeschkin


A square rubber bag was completely encased in a metal box with adjustable walls. This fitted tightly against the radial artery where it crossed the carpal bones, accompanied by a tendon. The pressure in the bag was registered by means of a strain gage. The arm was completely immobile. This method minimized the loss of pulse pressure caused by tissue elasticity, so that registered pressures average 85 per cent of those measured according to Riva-Rocci on the same arm or by means of an intraarterial cannula on the other arm. The configuration of the pulse registered by the 2 methods was nearly identical. The pressure on the skin over the radial artery was tolerated well up to 3 hours.

Lepeschkin


In 5.6 per cent of all electrocardiograms a late R' wave in leads V1, V2, or V3R or with a wide S wave in leads I and V6 was registered. Of these 242 curves, the QRS duration exceeded 0.12 second (complete block) in 42, was 0.10-0.12 second (typical incomplete block) in 47, and less than 0.10 second (atypical incomplete block) in 153 patients. The percentage of men was 77, 68 and 73 in the 3 categories respectively. Patients with heart and circulatory disease were predominant in the first group, those with pulmonary disease in the second, and those without heart or lung disease in the third group. S-T displacement and A-V conduction disturbances were found practically only in the first 2 groups, while low voltage predominated in the third group. Patients under 30 years of age had a considerable predominance of "atypical incomplete block," while those over 50 years of age had definite predominance of "complete block." It was concluded that "complete block" was clinically most significant while "atypical incomplete block" was least significant.

Lepeschkin


An analysis of 84 episodes of paroxysmal ventricular tachycardia in 60 patients is presented. There were 46 intermittent episodes with runs of 4 or more ectopic ventricular contractions of less than 30 seconds' duration recorded electrocardiographically and 38 persistent episodes with a continuous run of longer duration. No significant differences between the persistent and intermittent types were found in regard to age, sex, and race. In 6 patients there was no apparent heart disease. In 71 per cent there was atherosclerotic coronary ischemic heart disease with or without hypertensive cardiovascular dis-
ease and in 12 per cent rheumatic heart disease. Many of the patients, particularly those with persistent paroxysmal ventricular tachycardia, suffered acute myocardial infarction. Ten per cent of the patients showed definite evidence of digitalis intoxication and in another 17 per cent digitalis overdosage could not be excluded. The symptoms and signs in these patients could be arranged in 3 categories: (1) those of the underlying heart disease, such as acute myocardial infarction or congestive heart failure; (2) those due to precipitating factors, such as digitalis overdosage, and (3) those due to tachycardia itself. The therapeutic agents employed in this series were quinidine, procaine amide, and morphone, either individually or in various combinations. The prognosis of paroxysmal ventricular tachycardia was found to be influenced by many factors. The rhythm was especially serious when it complicated acute myocardial infarction. The prognosis in the intermittent type was somewhat better than in the persistent type. Five patients with persistent paroxysmal ventricular tachycardia died of the abnormal rhythm itself.


The electrocardiographic response to exercise (150 to 160 steps in place performed within a minute) was studied in 20 normal subjects and in 15 patients with angina. In both groups there was generally an acceleration of rate. The P waves and P-R intervals revealed little change but the T wave often became more prominent and caused a false S-T depression. The QRS interval tended to deviate to the right secondary to positional variations. Alterations of the S-T segment occurred in both groups and the distinction between normal and abnormal response had to be based on the degree of the deviation from the isoelectric line, on changes in its configuration, and particularly on the timing of these alterations. In none of the normal subjects was a modification of the S-T segment present 5 minutes after exercise. Elevation or lowering of the T-wave amplitude was common to both groups and not infrequently occurred without any other electrocardiographic alteration; however, in none of the normal subjects did a T-wave change persist after 5 minutes. The corrected Q-T interval varied in an irregular fashion: in the normal subjects there was a tendency to shortening during the tachycardia in contrast to the anginal group in which a significant prolongation of Q-T occurred.


Phonocardiographic and physiologic studies of the apical diastolic murmurs and sounds found in high-grade pure mitral insufficiency are reported. A short middiastolic murmur with its major components corresponding in time to the rapid-filling phase of ventricular diastole was found to be the most consistent and characteristic diastolic murmur in these patients. It was of maximal intensity at the apex, had dominant frequencies in the range of 75 to 150 cycles per second; and its intensity pattern corresponded to a small atrioventricular gradient developing during rapid ventricular filling. In 14 patients a third heart sound was found. It corresponded in timing to the trough of the ventricular pressure wave in early diastole and the peak of the rapid-filling wave of the apex cardiogram. In the presence of prolonged A-V conduction and sinus rhythm a fourth heart sound and presystolic murmur occurred with the development of an atrioventricular pressure gradient during atrial contraction. In 12 patients the high-frequency systolic murmur of mitral insufficiency persisted from 0.03 to 0.10 second after the major components of the aortic second sounds. The extension of this murmur with its decreasing intensity beyond the time of closure of the
semilunar valves to the onset of the rapid-filling murmur with mitral opening was coincident with the decreasing ventriculo-atrial gradient through isometric relaxation.

Sagall


The ultrasonic echo technic permits continuous recording of the motion of certain parts of the heart relative to the anterior chest wall. Records were obtained from hearts placed in a water bath after death. Tracings from the left atrium of normal subjects and of patients with mitral valvular disease were discussed. By means of recently developed electronic equipment, such tracings could be recorded with an oscillograph simultaneously with the electrocardiogram or any other monitoring parameter. Large thrombi or tumors of the left atrium, simulating mitral stenosis by a valve-like action, may be recognized by this method. Pericardial effusion yielded a pathognomonic tracing by altering the distances between the reflecting planes.

Brachfeld


In 15 patients with left bundle-branch block and in 15 control individuals both carotid pulses were recorded with the aid of a Marey capsule; the "global" neck pulse was recorded with the use of a pneumatic cuff placed around the neck and inflated to a pressure of 10 to 15 mm. Hg. The well-known delayed onset of arterial ejection in cases of left bundle-branch block was observed. The interval from the beginning of the QRS to the onset of arterial ejection at the neck was 0.15 to 0.26 seconds in patients with complete left bundle-branch block. These values agreed well with those found by others. The use of this approach to the elucidation of doubtful cases of conduction disturbances is stressed.

Brachfeld


In 320 subjects, alterations of the ballistocardiogram, pulse rate and arterial pressure were studied. The ballistocardiogram showed deterioration after smoking in 19 per cent of the subjects; the highest degree of such alterations was in the groups aged 30 to 60. Inhalation of the cigarette smoke caused an increase in pathologic alterations of the ballistocardiogram. The reaction of the ballistocardiogram to smoking was not dependent on the presmoking pattern. Pathologic alterations were observed equally in the ballistocardiogram of men and women. Repetition of the smoking test caused the same alterations in 89 per cent of the individuals. Pulse rate and arterial pressure changed significantly after smoking; decrease and increase of these parameters were observed to almost the same degree. The effect of nicotine is detectable with the use of the ballistocardiogram. This method seems more suitable for testing antinicotinic substances than the pulse rate or the arterial pressure.

Brachfeld

Hypertension


The results of sympathectomy in 212 patients suffering from hypertension were reported. The extent of the operative procedure used varied according to the recognized established procedures. In general more extensive procedures were used for the younger patients in whom symptoms were more evident, and the smaller operations were used for the older and less symptomatic patients. In 376 operations performed on the 212 patients there were 9 deaths within 6 weeks of the operation. The 10-year survival rate in this series was 66 per cent and the 5 year rate was 76 per cent. Reduction of the diastolic pressure by 15 to 45 mm. Hg after the procedure occurred in nearly all the patients for some weeks or months but only in 27 per cent was a reduction of more than 15 mm. Hg maintained. Retinal improvement resulted in 49 per cent with severe changes, and when there was no improvement in advanced retinal degeneration, death was not too long delayed. In general, sympathectomy resulted in symptomatic relief and gave many patients an increased expectation of a full and active life.

Krause


The primary object in treating the hypertensive patient is to lower the blood pressure by the simplest means possible to levels as near normal as can be well tolerated. The vascular deterioration, especially of the kidney, which progresses in the presence of sustained hyper-
tension is well illustrated and provides the rationale for antihypertensive therapy. In mild to moderate cases, the authors began treatment with chlorothiazide 1 to 2 Gm. per day. For a more potent hypertensive effect a Rauwolfia preparation was added; and, if needed, hydralazine was added in doses up to 400 mg. daily. In severe hypertensive patients, with diastolic pressures of over 140 mm. Hg or over 120 mm. Hg in the presence of vascular complications, a ganglionic-blocking agent was promptly “titrated” in the patient who was receiving a baseline therapy of chlorothiazide plus Rauwolfia. Reserpine or resminamine (2.5 to 5 mg. intramuscularly every 6 hours) was used in emergencies. The roles of emotional factors, sodium restriction, and of other agents were described in presenting the broad view required in the proper management of the hypertensive patient.

Rogers


The authors describe their experiences with 78 severely hypertensive patients treated with pentolinium and mecamylamine over a 4-year period. The ability to lower blood pressure was not the only criterion by which these drugs were evaluated. The following factors were also considered: subjective improvement, production of side effects, reversal of eye-ground changes, and the survival period. Side effects, which occurred with both preparations, were more numerous with mecamylamine and in the authors' opinion these effects outweighed the advantage of its more constant absorption. In many patients the concomitant use of reserpine permitted the dose of the ganglionic-blocking agents to be reduced, with resultant decrease in the severity of side effects. In general both drugs (pentolinium and mecamylamine) were valuable in the treatment of severe hypertension and participated in prolonging life and restoring or preserving sight.

Krause


A plan is outlined for the management of the toxemia of pregnancy based upon its degree of severity. The combination of parenteral hydralazine and reserpine is most popular in severe cases. Protopiveratrine is held in reserve if the desired effect is not obtained with this combination. In milder cases, the combination of reserpine and chlorothiazide is recommended. Gener-

ally the vasodepressor drugs initially decrease the output of urine. This situation becomes serious only when it results in progressive retention of nitrogenous products or renal failure. The decrease in urinary output is secondary to increased reabsorption of water by the renal tubules. As a rule it is temporary and is soon followed by polyuria. If a patient is unusually sensitive to the action of hypertensive drugs, it is important to be aware of a method to combat a true hypertensive state of shock. Norepinephrine in such instances will usually promptly return the blood pressure to normal. A word of caution relative to the use of barbiturates in eclampsia or severe preeclampsia is added. These drugs depress the higher centers and may further reduce cerebral blood flow, which is already compromised by cerebral vasocstriction. The ultimate effect is an even greater decrease in oxygen consumption by the brain. The author suggests the immediate use of intravenous hydralazine during a convulsion rather than the use of a barbiturate.

Krause


The concomitant use of chlorothiazide allows lower and less toxic dosages of other hypertensive agents in controlling blood pressure. The drug does not reduce blood pressure in normotensive subjects although it induces the same increase in salt excretion as in hypertensive patients. In adding chlorothiazide to the regimen of a patient taking ganglionic-blocking agents the dosage of the latter must be reduced, usually by half. Patient responsiveness is so increased by chlorothiazide that in full dosage a severe hypotension including postural collapse may occur. The complications of chlorothiazide therapy are not common but awareness will aid in their prevention: the value of this drug far outweighs its harm. The so-called toxic reactions to chlorothiazide are extensions of its fundamental saluretic and kaluretic actions. Hypopotassemia is frequent, and potassium supplements should be used when this develops.

Kitchell


The functional importance of an increased wall to lumen ratio due to renal hypertrophy of the resistance vessels in hypertensive disease was evaluated by comparing the vascular resist-
ance in 25 normal and 34 hypertensive subjects when the vessels were brought to an absolutely maximal dilatation. This was accomplished by increasing the ischemia of the vessels of the forearm by means of a venous occlusion plethysmograph which measured blood flow and occluded the vessels by a proposed pressure. Increasing amounts of work on the forearm muscles during the last minute of ischemia were also used. Lastly, to augment the dilator influence, the plethysmograph permitted the circulation of warm water at a temperature of 43 °C., which was maintained by means of a hot-air stream from an electric fan. Six of the 25 normotensive subjects were studied when brought to a state of acute hypertension by means of a steady intravenous infusion of norepinephrine in amounts sufficient to raise the mean blood pressure about 30 per cent. It was found that the vessels promptly dilate both in normotensive and hypertensive subjects and an almost maximum dilatation was reached after only 5 minutes of ischemia in both groups. The resistance to flow for the 5 normotensive subjects during acute hypertension was found to be the same at the 2 perfusion pressure levels. It is believed by the authors that a given level of smooth muscle tone will probably result in a higher flow resistance in hypertensive disease, where hypertrophy of the vascular wall has taken place but that this rise in vascular tone may be due to local influences on the resistance vessels.

Rinzler


A number of aspects of sodium chloride metabolism in patients with essential hypertension are reviewed. It is suggested that the increased content of sodium and water found in the arterial wall of hypertensive patients and animals with experimental hypertension may be responsible for the elevation of blood pressure either by narrowing the arteriolar lumen or by increasing the reactivity of its smooth muscle. The effects of chlorothiazide in the treatment of edema and hypertension are discussed. It is suggested that chlorothiazide may reduce blood pressure in some instances by depleting plasma and extracellular fluid volume and, in others, by a redistribution of body sodium and water. The major effect of chlorothiazide may be to reduce the increased sodium and water content of the vascular smooth muscle in the hypertensive patient. This would decrease peripheral resistance and produce a fall in blood pressure without any change in extracellular fluid volume.

Kayden


The arterial bed of the small intestine was studied by means of postmortem arteriography with a bismuth gelatin suspension. Complete filling of the submucosal arteries down to 0.03 mm. was obtained in 6 cases of hypertension and 6 control specimens. A decreased number of vessels in the intestinal wall and more abrupt tapering of the lumen were demonstrated in 4 of the 6 hypertensive patients. Histologic examination showed only infrequent slight intimal thickening in the submucosal arteries and no definite medial hypertrophy. It is suggested that in established hypertension the submucosal arteries of the small intestine are in a state of diffuse structural narrowing.

Kurland

METABOLIC EFFECTS ON CIRCULATION


The metabolism of the acutely failing rat heart, produced by constricting the ascending aorta, was studied. The changes in cardiac metabolism were characterized by impairment of energy production and were similar to those of acute anoxia. The synthesis of high-energy phosphates was decreased; oxidative as well as anerobic processes involved in energy production were found to be depressed. It seems possible that myocardial anoxia (probably of the stagnant type) is also responsible for the disturbance in cardiac energy production in cases of experimental heart failure.

Brachfeld


Hyperthyroidism should always be suspected when atrial fibrillation is present, particularly if a rheumatic, coronary, or hypertensive etiology is not apparent. A clue to the diagnosis is the inability to slow the ventricular response with digitalis, particularly in the older age groups. An increased pulse pressure is an additional valuable clue to the diagnosis of hyperthyroidism. The treatment for failure with fibrillation
is the use of digitalis and diuretics combined with an antithyroid drug. After several weeks, if sinus rhythm has not returned, the use of quinidine may convert the fibrillation to a normal sinus mechanism. The clinical expression and the cardiac and electrocardiographic signs of myxedema are in many ways the antithesis of hyperthyroidism. The characteristic electrocardiogram shows a slow, low voltage, and a flattening of the T waves. Exceptions naturally occur; for example, a previously hypertensive patient (now myxedematous) may have an electrocardiogram with left ventricular hypertrophy. In general the myxedema electrocardiogram shows changes in all leads. In the roentgenologic appearance of the myxedema heart it is probably true that enlargement is almost always due to pericardial effusion. This "enlargement" usually disappears with proper thyroid therapy.

Krause


Various causes of intractable heart failure are discussed and several methods to reverse the refractory state are presented. When factors other than those directly related to heart failure are eliminated and the usual methods to control the failure have failed, the use of steroids has been suggested. The neurohypophysis and the aldosterone-producing adrenal glands play a major role in this failure of the homeostatic adjustment mechanisms. This failure results in the extracellular fluid electrolytes. Ten patients with cardiac edema and normal serum electrolytes became unresponsive to the commonly used diuretic measures, including mercurials, and attempts to produce hyperchloremia and acidosis. In 8 patients the refractoriness was reversed by the use of prednisone in a specified manner and dosage. This was probably accomplished by the promotion of transcellular and trans compartmental shifts of electrolytes from an electrolyte pool.

Krause


Adrenal vein plasma concentration of aldosterone, corticosterone and Porter-Silber steroids was studied in dogs subjected to acute constriction of either the thoracic or the abdominal vena cava. Within 30 minutes after a ligature previously placed around the thoracic or the abdominal vena cava had been tightened, aldosterone secretion in adrenal vein plasma reached levels 2 to 4 times greater than control values, while corticosterone and Porter-Silber reacting steroid output decreased in 3 of the 4 animals studied. During the period of time that the ligature was in place, inferior vena caval pressure rose 8 to 13 cm. of water while arterial pressure, adrenal blood flow and plasma volume fell without any consistent change being observed in plasma sodium or potassium concentration. When dextran was infused into 3 similarly prepared dogs at a rate which increased the plasma volume 44 to 330 per cent, a comparable increase in aldosterone secretion rate was noted. In 4 animals the abdominal vena cava was constricted at a level above the adrenal veins and in 2 of these dogs the aldosterone output rose when the pressure in the vena cava increased to levels greater than 14 cm. of water above control value. When the pressure elevation was not sustained at a high level, the aldosterone output either remained unchanged or decreased. The levels of corticosterone and Porter-Silber steroids did not show consistent changes. The authors believe that the data presented demonstrate the acuteness of adrenal cortical response with reference particularly to aldosterone secretion following an alteration in cardiovascular function. The mechanism responsible for the changes however remains obscure. Since corticosterone output decreased as aldosterone output increased, it was thought that increased ACTH secretion was not involved, while the dextran experiments indicated that loss of vascular volume alone was not responsible.

Freedberg


Preoperative and postoperative determinations of serum glutamic oxalacetic transaminase, serum lactic dehydrogenase, and serum glutamic pyruvic transaminase were performed in 21 surgical patients. No significant changes were found. This limited series thus indicates that surgical procedures by themselves, including major operations with skeletal muscle incision and dissection, will not cause sufficient elevations of these serum enzymes to mask the characteristic curve of myocardial infarction when it complicates the operative or postoperative course.

Sagall
PATHOLOGY


Detailed histologic observations on the pulmonary vascular changes that occurred in 4 patients with Eisenmenger's complex are presented. The primary vascular changes were medial hypertrophy of the small muscular pulmonary arteries, the development of a distinct muscular media between the internal and external elastic lamina in vessels less than 100 micra in diameter, and fibroelastosis of the intima causing thickening or complete occlusions. Secondary compensatory changes, which presumably maintained an adequate blood flow through the pulmonary capillaries, were the formation of thin-walled dilated branches of the muscular pulmonary arteries; these branches arise proximal to the sites of arterial obstruction and end as capillaries in the alveolar walls. In 1 patient there were many demonstrable anastomoses between the pulmonary arteries and the bronchial circulation and also between the pulmonary arteries and the pulmonary veins. No significant degree of hemosiderosis was seen, probably because the pulmonary venous pressure was not elevated in these patients.

KARPMAN


Two groups of necrotizing angitis entirely or chiefly limited to the skin were investigated by histologic examinations. One group of cutaneous eruptions known clinically as arteriolitis allergica cutis was distinguished by exudative vascular reactions (all of approximately the same age) associated with swelling of the endothelial cells, fibrinoid changes in the vessel wall, and inflammatory infiltrates. The cutaneous type of periarteritis nodosa revealed fibrinoid swelling of the intima and fibrinoid necrosis in addition to inflammatory infiltrates: simultaneous exudative and reparative processes were often seen in a single section. Allergy in the personal or family history was often present in patients with arteriolitis allergica cutis but not in those with periarteritis nodosa. This may be a significant observation, for it was noted that eosinophils were lacking in most cases of cutaneous periarteritis nodosa whereas they were seldom absent in arteriolitis allergica cutis.

KARPMAN

PHARMACOLOGY


This article reports the effects of 2 cardiac glycosides, crystalline ouabain U.S.P. and dihydro-ouabain, and 3 nonsteroid lactones, β-angelicalactone, patulin, and pulvinic acid dilactone on the function and the potassium balance of the isolated, perfused guinea pig ventricle preparation. Ouabain and dihydro-ouabain produced positive inotropic effects in all concentrations used. Patulin in sufficiently high concentrations caused a brief increase in contraction height followed by a return to the hypodynamic level. In lesser concentrations it did not alter contraction height. Alpha-angelicalactone and pulvinic acid dilactone in sufficiently high concentrations caused only negative inotropic effects. All the lactones caused contracture, the extent of which varied with the concentration. In the case of the steroid lactones, contracture occurred only with concentrations higher than those necessary to restore contraction height to normal, while the nonsteroid lactones caused contracture in concentrations that did not alter the height of contraction. All the lactones caused the ventricles to lose potassium to the perfusate. Small concentrations of dihydro-ouabain caused only an initial loss, after which the ventricles were in potassium balance.

RINZLER


Chlorazanil (Daquin, Orpidan, Neo-Urofort) is a triazine derivative, the diuretic potency of which depends on an N = C - N group. The present study of its pharmacologic value in dogs and in man gave results similar to those previously obtained. Given orally in a dose of 300 to 600 mg, its action was evident within 2 hours and continued for approximately 18 hours. Urinary excretion of water, sodium, chloride, bicarbonate, and potassium were increased in descending order of magnitude. The potency of 600 mg. of the drug, in terms of natriuresis, was equivalent to that of 1 ml. of meralluride. Its action was not appreciably altered by the concomitant administration of theophylline in dogs. Repeated doses were effective and, after
5 days of therapy, serum electrolyte levels had not changed significantly. However, in some patients chronic therapy was associated with evidence of diminution in glomerular filtration rate. Although the mechanism of action of chlorazanil was not clear, it appeared to differ from that of acetazolamide or of organomercurial agents.


A single intravenous injection of 0.25 mg. of strophanthidin K or 0.5 mg. of digoxin in 23 patients with mitral stenosis and sinus rhythm led in all instances to an increase in the interval between the second sound and the mitral opening snap. This increase averaged 33 per cent and was greater in uncompensated than in compensated patients. It showed no correlation with the changes in heart rate, cardiac output or venous pressure. At the same time, the interval from QRS to the first heart sound showed a progressive decrease. These changes were attributed to a decrease in left atrial pressure, and could be caused by a more forceful atrial contraction, or decreased pulmonary blood volume. These results, which were similar to those obtained in left ventricular failure, indicated that digitalis therapy had a favorable effect also on patients with mitral stenosis without heart failure.


The infusion of small doses (10 γ/min.) of serotonin into the brachial artery of the dog resulted in a decrease in total forelimb resistance when the resistance was high, no change when the resistance was intermediate, and an increase when the resistance was low. The vascular tone was varied by denervation of the forelimbs or by bilateral vagotomy. The bidirectional responses to serotonin resulted from the fact that neurogenic factors changed small vessel calibers without altering the caliber of large vessels and serotonin dilated small vessels at the same time that it constricted large vessels. When vascular tone was varied by humoral agents, including intraarterial infusion of methacholine or levarterenol, the bidirectional response to serotonin was difficult to demonstrate.


The authors demonstrate that the heart-rate-increasing effect of a challenging dose of 3 mg. of reserpine given to the heart-lung preparation of the dog is a reliable measure of the cardiac content of intrinsic sympathomimetic amines, especially norepinephrine. Hexamethonium does not prevent the release of norepinephrine in the heart-lung preparation. In a single intraperitoneal dose of 100 µg./Kg. reserpine can deplete the heart of norepinephrine in 24 hours with no side effects. By 10 to 20 days normal stores of norepinephrine are found. Some accumulation has begun by the sixth day.

**Rinzler**


This study was designed to explore the concept that the mechanism of action of certain diuretics are either competitive or noncompetitive when administered simultaneously. Subjects were men with well-controlled congestive heart failure due to hypertensive cardiovascular disease who were edema free at the time of the study. The patients were given an initial water load, drank a stated volume of water throughout the study period, and were given intravenous isotonic saline throughout the study period. Meralluride, acetazolamide, and chlorothiazide were the 3 diuretic agents studied and all were administered intravenously. When given in combination, doses of equal potency in terms of sodium excretion were used. It was found that sodium excretion, which was increased by the administration of meralluride, could be further enhanced by the subsequent administration of acetazolamide. Conversely, natriuresis was produced with the initial administration of acetazolamide and increased with the subsequent administration of meralluride. When meralluride was followed by chlorothiazide, the initial response to the first agent was increased by the second, but when the order was reversed so that chlorothiazide was given first, no further natriuresis could be induced by the administration of meralluride. Similarly, administration of acetazolamide first followed by chlorothiazide resulted in an increased sodium excretion both after the first and second agents, whereas, when chlorothiazide preceded the acet-
zolamide, sodium excretion was not increased by the second agent. In another study when meraluride and acetazolamide were given initially, producing sodium excretion greater than either of the 2 agents alone, the addition of chlorothiazide resulted in an even greater sodium excretion.

Maxwell


This study deals with the effects of 10 rauwolfia preparations on the heart rate, the functional refractory period of atrioventricular transmission and the A-V propagation time. The heart-lung preparation of the dog was used and a comparative study was made of the action of the different types of rauwolfia alkaloids on normal and reserpine-pretreated dog. Two distinct groups were found. The first, consisting of ajmaline, serpentine, aricine, reserpine and α-yohimbine, caused a decrease in heart rate and a prolongation of the functional refractory period of A-V transmission and of the A-V propagation time. The second, consisting of ajmalicine, isorauvenicine, deserpidine, reserpine and rescinnamine, at first increased the heart rate and shortened the functional refractory period and the A-V propagation time. After 1½ to 2½ hours, with a dose equivalent in effect to 3 mg. of reserpine, the heart rate slowed while the other 2 modalities returned toward their control duration or were frequently further prolonged. When the heart-lung preparation was first depleted of intrinsic sympathomimetic amines by previous treatment with reserpine, the drugs in the second group lacked this transient cardioaccelerator action and facilitating action on A-V transmission.

Rinzler


In the year 1957, 32 episodes of paroxysmal atrial tachycardia with block were diagnosed electrocardiographically in 23 patients. In 24 episodes the etiologic factor was digitalis intoxication resulting from either overdosage of the drug, a mercurial-induced diuresis, or increased sensitivity to digitalis. The patients in whom this rhythm appeared were usually in an advanced state of chronic cardiac decompensation and had been subjected to a rigid sodium restriction. Often no striking change in symptoms developed in association with the arrhythmia and the abnormal rhythm was detected only by the electrocardiogram. The atrial rate in this series ranged from 138 to 250, with a mean of 176. The degree of atrioventricular block varied greatly. The atrial complex frequently was diminutive and difficult to distinguish except in the right precordial leads. When present in the limb leads, the P wave was invariably upright in lead II. Carotid sinus stimulation increased the degree of atrioventricular block but did not alter the atrial rate. The rhythm was most frequently confused with atrial flutter, but also simulated other rapid supraventricular rhythms. In 4 of the 24 episodes due to digitalis overdosage, a normal mechanism was restored simply by discontinuing digitalis and diuretic measures. Digitalis was continued in 2 patients and both died. In the remaining 18 patients additional measures were necessary; of this group 5 episodes were controlled by the oral or intravenous use of potassium, 10 by the combined use of potassium and procaine amide, and 3 by procaine amide alone.

Sagall


The tissue toxicity of Urokon 70 per cent and Hypaque-M 90 per cent was assessed in dogs. This was limited to an evaluation of their effect on the spinal cord and kidney, as damage to these organs has been the cause of over 50 per cent of the serious complications resulting from the clinical use of Urokon 70 per cent in abdominal aortography. These substances contain comparable amounts of iodine and are of the same radiopacity. The osmolarity and pH are also similar. Hypaque is somewhat less soluble and has to be warmed to body temperature before injection. Hypaque is significantly more viscous than Urokon. Urokon produced paraplegia in nearly all the animals tested, regardless of whether the medium was injected into the aorta or into the first pair of lumbar arteries caudad to the origin of the left renal artery. Hypaque on the other hand was not associated with any paraplegia in doses up to 15 times that used with Urokon. There was marked necrosis of the gray matter of spinal cord, but minimal evidence of vascular involvement in the form of thrombosis. Of the animals receiving intra-aortic Urokon, only 3 survived 48 hours. All 3 developed azotemia. No animal receiving Hypaque
became uremic. There was injury to the tubular epithelium but no evidence of thrombosis. These studies indicate that the mechanism of Urokon injury to the spinal cord and kidney is a direct cytotoxic effect. Hypaque-M 90 per cent exhibited much less neurotoxicity and nephrotoxicity than Urokon 70 per cent. However, the greater viscosity of Hypaque impairs its angiographic effectiveness when manually injected into the aorta through the small bore injection equipment used for translumbar aortography.

Sheps


The technic of "stop-flow" analysis has been used to compare proximal and distal tubular function in dogs before and after administration of chlorothiazide. After chlorothiazide the ability of the proximal tubule to reabsorb water during stopped flow was reduced. Proximal reabsorption of sodium and potassium was reduced in such amounts that the concentrations of these substances in the fluid reabsorbed from the proximal tubule during occlusion did not change but remained plasma-like. Chlorothiazide increased distal tubular potassium secretion. The data on distal potassium reabsorption were less clear-cut, but chlorothiazide appeared to have some inhibitory effect upon distal potassium reabsorption. Chlorothiazide exerted no effect on the distal capacity to lower sodium concentration during stopped flow.

Rinzler


Intravenous injections of chloroquine in doses of 0.2 to 1.5 mg. per Kg. are capable of terminatingaconitine-induced atrial fibrillation in the open-chest dog preparation. Intravenous chloroquine (2 mg. per Kg.) had little effect on the systemic blood pressure, despite its marked vasodilating action on intraarterial administration and a depressant effect on ventricular contraction. In contrast, comparable doses of quinidine produced a marked fall in systemic blood pressure. Chloroquine and quinidine were equally effective in depressing the resting excitability of the isolated cat papillary muscle; however, chloroquine, in contrast to quinidine, decreased conduction velocity very little. The muscle recovered from chloroquine-induced depression but showed little recovery from the quinidine effects. These attributes of chloroquine suggest its usefulness in the treatment of clinical arrhythmias.

Paul

Physical Signs


The diastolic gallop sound resulting from the summation of the third heart sound and the atrial sound was found in 14 per cent of all phonocardiograms, usually in the 35 and 70 c.p.s. range. It appeared when the P wave happened to begin 0-0.7 second after the end of the preceding T wave; this took place in sinus tachycardia, wandering pacemaker, supraventricular extrasystoles, and A-V block (complete, 2:1 or Wenckebach type). In some patients only the atrial sound of the third heart sound was present when this time relation was not met. The gallop sound was considered to originate when rapid ventricular filling in early diastole became even more rapid because atrial systole occurred at the same time. Appearance of the gallop in sinus tachycardia of adults usually indicated latent or manifest cardiac failure.

Lepeschkin


A cardiac murmur was often heard in the newborn during the first few hours of life. This murmur was usually crescendo, at the end of systole, and sometimes it continued through the second sound. It was probably due to flow through a persistent ductus arteriosus. A direct relationship to rectal temperature and to asphyxia at birth was demonstrated in the mature babies. In premature babies the incidence was equal to that of mature babies after birth asphyxia. The murmur accompanied dyspnea in premature babies and in severely breathless mature babies. When mature babies had suffered birth asphyxia a raised respiratory rate was evident though they appeared healthy. The murmur was present in 75 per cent. A reduction in rectal temperature seemed to result in relief of dyspnea and disappearance of murmur. Conversely, warming 3 babies shortly after birth brought about dyspnea as well as the murmur. These data complement the hypothesis that there may be changes in blood flow through the great vessels, consequent on temperature changes, which influence the genesis of the murmur.

Krause
PHYSIOLGY


Ventricular contractile force and arterial blood pressures were measured in anesthetized, vagotomized dogs rendered hypoxic by respiration with 100 per cent nitrogen. Marked increments in heart force and blood pressures were observed during brief nitrogen exposure and during the period of reoxygenation following substitution of room air for nitrogen. Experiments in animals subjected to bilateral adrenalectomy, thoracie sympathectomy, and total preganglionic sympathetic block indicated that the responses to acute oxygen lack were mainly due to stimulation of the sympathetic nervous system, while the responses to reoxygenation were dependent upon both the adrenal medulla and the sympathetic nerves.

Kayden


The ventilatory response to increasing carbon dioxide tension was studied by means of a rebreathing method in 20 cardiac patients. Compared to the findings in 11 normal subjects, there was a lowered critical threshold for carbon dioxide stimulation, whereas central respiratory responsiveness remained practically unchanged. Central responsiveness was determined by the slope of the carbon dioxide tension—ventilation curve. The 7 patients with predominant mitral stenosis in this group were characterized by a significant depression of central responsiveness. Their total ventilation was nevertheless higher than normal, because of the extreme lowering of the threshold for carbon dioxide stimulus.

Brachfeld


The cardiac output was calculated by the Fick principle in 245 adult dogs. The mean cardiac output was 2.36, and the range from 0.91 to 5.09 liters per minute. Determination of cardiac output using venous blood from the right atrium was not significantly different from the mean of all determinations. The 6 groups of dogs, based on different sources of arterial and venous blood, differed from each other in unpredictable ways, suggesting that the physiologic measurements obtained between 60 and 90 minutes after anesthesia were subject to great variation, but that cardiac output was no more variable at this time than other physiologic measurements. The cardiac output of these anesthetized dogs was found to have a low correlation with body weight.

Kayden


Pulmonary venous occlusion was shown to increase the activity of slowly adapting pulmonary stretch receptors by mechanical alterations within the lung parenchyma. Two types of response were evident: stimulation throughout the respiratory cycle and stimulation only during low lung volumes. Pulmonary arterial occlusion caused both significant increases and decreases in fiber activity. Two fibers demonstrated cardiac-triggered impulses superimposed upon a basic respiratory rhythm, an effect dependent upon pulsation of the pulmonary arterial tree. The results of this investigation indicated a 2-fold responsiveness of the pulmonary stretch receptors, i.e., to the volume of air in the lungs and, to a lesser extent, to the degree of distention of the pulmonary vasculature. The latter effect was suggested as an important factor in the decreased depth of respiration during pulmonary congestion.

Kayden


The myocardial uptake of Rb⁸⁶ was studied in dogs by measuring the extraction of Rb⁸⁶ from arterial plasma during 1 passage through the myocardium. The extraction of isotope by the myocardium was found to be logarithmically related to coronary plasma flow. The maximum extraction in very low coronary plasma flows approached 85 per cent rather than 100 per cent, and this observation was interpreted as supporting the concept that anatomic or functional shunts of plasma exist within the myocardium. It was suggested that estimates of the rate of coronary plasma flow can be made in man without cardiac catheterization, if myocardial radioactivity can be measured accurately with an external monitor.

Paul

The effect of various respiratory maneuvers on the heart rate was studied in normal young male subjects and in anesthetized cats and rats. A sinus arrhythmia was noted to occur normally in man with quiet respiration. During voluntary positive-pressure breath-holding the heart rate gradually increased (after an initial short period where the response was unpredictable) and then remained at that level during the rest of the breath-holding period. With a negative-pressure breath-holding maneuver, the heart rate fell below the initial value and then returned approximately to the starting rate. Correlations were derived between various positive intrapulmonary pressures and the heart rate; no correlation was found between the various negative intrapulmonary pressures and the heart rate. The response of the heart rate to passive variations of the intrapulmonary pressures in animals was completely different from that in man. It is suggested that the aortic baroreceptors represent the sensory area for the blood-flow heart rate reflex and that the variations in blood flow occur at the level of the pulmonary circulation and are brought about by respiratory maneuvers.

Karpman


The authors have investigated the nature and cause of delay in the propagation of excitation from atrium to ventricle. Multiple intracellular microelectrodes were used to obtain simultaneous records from single fibers of atrium, A-V node and His bundle in the rabbit heart. Measurements of conduction times demonstrated that the slow spread of the impulse near the atrial border of the A-V node caused the major portion of the atrioventricular delay. The conduction velocity fell from 0.8 to 1 M. per second outside this critical region to 0.05 to 0.02 M. per second at the border of the A-V node. Furthermore, in cells in this area, the recorded action potentials showed consistent differences and were characterized by a tendency to have a notched upstroke, slow rate depolarization, low amplitude, and a low resting potential. The authors suggested that conduction in the node was decremental, implying that the action potential appeared to diminish progressively in amplitude and rate of depolarization.


Observations of the electrical and mechanical events that follow the induction of ventricular tachycardia and ventricular fibrillation in the isolated guinea pig by aconitine are reported. Individual myocardial fibers were studied by the micropuncture technic. Ventricular fibrillation was characterized by irregular action potentials of varying amplitude. When the individual fibers were in close proximity there was a partial synchronism of these action potentials that was not evident when the fibers were at a distance. During ventricular tachycardia single fiber electrical alternans was frequently observed. This was associated with mechanical alternans, but mechanical alternans occasionally was seen without demonstrable single fiber electrical alternans. Further, in any 1 preparation not all of the cells participated in electrical alternation. These experimental results indicate that alternation of the heart, both electrical and mechanical, may be related to alternate variations in behavior of individual fiber membrane and contractile elements.

Sagall


Transmembrane recordings were obtained from fibers of the A-V node, in the rabbit heart during the action of acetylcholine. During total atrioventricular dissociation no block of conduction was noted at the junction between the A-V node and the bundle of His or within fibers of the atrium. Failure of impulse transmission did occur in fibers in the atrial margin of the A-V node. Acetylcholine blockade was associated with slow depolarization, a decreased amplitude in the action potentials, and fragmentation of the action potential into several asynchronous components. The results are believed to support the concept that transmission through the A-V node is decremental.

Paul


An electronic system was built that provided a continuous plot of pressure versus volume on
the screen of a cathode ray oscilloscope. With this technic a study was made of isolated segments of human aortas which were being continuously expanded and contracted at a frequency and amplitude approximately that found under physiologic conditions. When the pressure-volume curves under dynamic conditions were compared with those static conditions, it was found that the aortic measurements showed a slight change in slope. When the volume of the aorta was changed rapidly and continuously in sinusoidal fashion with pulse pressure and pulse rates maintained in the physiologic range, the resulting pressure-volume curves showed slight but consistent increases in stiffness, compared to pressure-volume curves obtained on the same specimen when inflated stepwise.

Rinzler


Five patients without congestive heart failure were studied while at bedrest in the hospital in regard to the output of volume, work, and power by the right and left ventricles. It was found that in the tropical weather during midsummer in New Orleans there was a 37 per cent increase in the mean cardiac output over that in a comfortably cool air-conditioned atmosphere. The calculated time-course curves of the pressure-volume diagram, work, and power were proved to be better indices of cardiac work than the conventionally obtained mean volume of cardiac output. These observations indicate that when it is desired in treatment to maintain the heart at rest, the atmosphere of the patient’s room should be cool and comfortable.

Sagall


Pulmonary compliance, central venous pressure, and pulmonary vascular density were measured in normal subjects before and during inflation of a G suit and during body immersion in water. Within 30 seconds after suit inflation to 2 psi, compliance decreased, central venous pressure increased and pulmonary vascular density increased maximally. After these maxima were reached, changes in the opposite direction occurred throughout the remainder of the 2-minute period of G suit inflation in all of the parameters. Changes of similar magnitude and direction in pulmonary compliance occurred during immersion in water to the neck and to a greater extent during total body immersion. When peripheral arterial pressure was reduced by administration of hexamethonium there was a smaller increase in compliance with the G suit followed again by the rise toward normal. When the peripheral arterial blood pressure was raised with norepinephrine there was an increase in central venous pressure and a fall in compliance before inflation of the suit, which in turn enhanced these changes initially. The usual return toward normal was not observed in these subjects. Similar changes occurred with immersion of 1 arm in ice water during the studies.

Maxwell


This study was undertaken to resolve the divergent views on the effect of exercise on arterial blood gas tensions. The subjects were 14 young athletes 19 years of age and younger. The physical working capacity of each subject was assessed on an electrically braked bicycle ergometer. Resting, exercise, and postexercise electrocardiograms were taken. During the test arterial blood was taken by means of a polythene catheter introduced into the brachial artery. Samples were taken at rest and during muscular work of defined absolute and relative intensities. The oxygen tension of arterial blood was found to be lower during heavy work than at rest. Exhaustive work caused a further decrease in oxygen tension. Carbon dioxide tension tended to decrease during exhaustive work. The divergent results of other investigators may therefore be due to data obtained at different relative work loads.

Rinzler


When, under pentobarbital anesthesia, dogs were cooled in ice water to terminus, the incidence of ventricular fibrillation was found to be 96 per cent. Treatment with intravenous
potassium chloride, 150 to 250 mg. per Kg., reduced this incidence to 57 per cent. The administration of ethylene diamine tetracetic acid had only a slight effect on decreasing the incidence of fibrillation. By combining both drugs, the incidence was reduced to 50 per cent.

Rinzler

PULMONARY DISEASES


Ammonium acetate was infused intravenously into 7 anesthetized dogs, and the concentration of ammonium in the expired air was measured by nesslerization. Calculations of the partial pressure of ammonia in alveolar air and estimations of the theoretical partial pressure in arterial blood were made. The authors point out that demonstration of free ammonia in alveolar air may be taken to indicate that under special circumstances there are significant levels of circulating ammonium. The study of ammonia excretion by the lung may, therefore, make it possible to reassess the quantitative aspects of ammonium metabolism and its relation to hepatic coma.

Karpman


Experiments were performed on the isolated and perfused lungs of the cat in order to study the chemical control of pulmonary blood flow. Cannulae were introduced into the trachea, carotid arteries, pulmonary artery, and left atrium. The plastic tube to the pulmonary artery, was connected with a strain-gage manometer. Blood from the lungs passed a recording pH meter. Constriction of pulmonary vessels obtained by raising the carbon dioxide tension of the ventilating gas mixture was mediated by lowering the pH of the blood: a decrease of 0.01 corresponding to a rise in perfusion pressure of about 1 per cent. Ventilation with nitrogen sometimes led to a decrease or an increase in the perfusion pressure. Lactic acid was continuously released from the perfused lungs and this was enhanced by hypoxia. Injections of monoidoacetic acid abolished or reversed the pressure rise obtained during ventilation with nitrogen.

Rinzler

ROENTGENOLOGY


Cardiac size alone, with the exception of extreme cardiac enlargement, cannot be used in estimating cardiac efficiency. This is especially true of conditions causing increased cardiac filling, such as aortic insufficiency, intracardiac shunts, and arteriovenous aneurysms. In these cases appearance of pulmonary congestion or atrial enlargement is a more sensitive sign of cardiac failure than of left ventricular enlargement. The value of the appearance of pulmonary vessels, vena cava, and pleura in the diagnosis of right, left, or bilateral heart failure is demonstrated with numerous examples.

Lepeschkin


In 1 patient the catheter could not be made to enter the aorta in spite of repeated catheterizations from the pulmonary artery, but a ductus could be visualized by means of retrograde aortography. In another patient, whose ductus had been ligated previously, the catheter entered the descending aorta in a manner held typical for persistent ductus, but a wide aortico-pulmonary communication was found during operation. It is concluded that only direct visualization of the ductus by means of retrograde or transdental aortography can allow definite differentiation between persistent ductus and aortico-pulmonary communication or fistula.

Lepeschkin


Minute visualization of the cardiovascular congenital anomaly is of great importance for the surgeon; this can be carried out best by means of selective angiocardiography. The anomalies most commonly found in children are discussed in relation to the best method of angiocardiography, location of the catheter and choice of camera or film changer. The dangers of using the method unilaterally are illustrated in a patient with tricuspid stenosis who died in pulmonary edema 2 days after angiocardiography of the right ventricle; this complication could have been prevented by injecting the dye into the right atrium.

Lepeschkin
ABSTRACTS

Circulation. 1959;20:459-473
doi: 10.1161/01.CIR.20.3.459
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1959 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/20/3/459.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/