ABSTRACTS

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HYPERTENSION


Serum from patients with severe essential hypertension has been previously shown to have a cardiotonic action on the isolated frog heart. A system of 3 proteins in plasma responsible for this activity has been characterized within the globulin group. One component, termed L protein, became strongly bound to the bioassay frog heart but the other 2 components comprised a washable fraction. Calcium was bound to the O-17 washable fraction and the calcium could be released by the addition of the L component to the system. The protein system described caused contracture of frog heart muscle in the absence of ionic calcium, in contrast to other contracture-causing agents such as strophanthidin and digitonin, which required free calcium for activity. The authors suggested that the biological activity of the protein system on the frog heart may be achieved by delivering calcium from component O-17 to the contractile mechanism.

Paul

METABOLIC EFFECT ON CIRCULATION


Various purine and pyrimidine ribosides (cytidine, uridine, thymidine, guanosine, and inosine) with the exception of adenosine were reported to exhibit a positive inotropic effect on an isolated strip of frog ventricle. In a preparation already responding maximally to 1 test compound, the addition of a second compound led to a further increase in tension. The authors suggested from the findings that the various ribosides acted, at least in part, through independent mechanisms. These compounds probably participated as co-factor precursors in a variety of enzymatic reactions. The gradual mechanical failure of the isolated ventricle strip preparation may result from depletion of the various quantitatively lesser nucleotide co-factors. The failure of adenosine to exhibit a positive inotropic effect may result from the abundance of adenosine nucleotide in the cell.

Paul


The effects of 3, 3', 5-triiodo-L-thyronine (T-3) upon the metabolism and circulation were measured in rats and mice. During the oral administration of T-3 there was a marked and sustained rise in metabolism, which disappeared when the T-3 was discontinued. The heart rates of both the rats and mice given T-3 were greater than those of the control animals. This increment in weight was not due to an increase in water content of the hearts. In the rat, following the removal of the T-3 in the drinking water, there was a return of the heart to approximately normal size. There were no abnormal electrocardiographic findings during the hypermetabolic state.

Kayden

Specific replacement therapy in hypothyroidism often gives rise to cardiac complications. Such complications are more related to initial vigorous treatment than to total thyroid dosage. Arteriosclerotic heart disease increases the risk, and the presence of this disease may be implied by evidence of arteriosclerosis in other sites. Thyroid therapy reverses anatomic changes that have occurred in the heart in hypothyroidism and may call upon an enlarged heart for function above its physiologic capacity. Therapy in patients with possible heart disease and hypothyroidism should be instituted with low doses and gradual increments.

Kitchell

PATHOLOGY


Histologic examination of sections of the aorta proximal and distal to the site of coarctation was performed in 9 patients. No structural changes in the elastic tissue ascribable to inactivity could be found. On this basis it was concluded that, although the blood pressure in the aorta distal to the coarctation was relatively decreased, the absolute level of mean pressure present in this segment of the aorta must have been high enough to maintain the normal configuration of aortic elastic tissue.

Sagall


The authors described the early ultrastructural changes observed in the ischemic rat myocardium following ligation of the anterior descending branch of the left coronary artery. Although light microscopy could not detect histologic abnormalities in infarcts of 5 hours or less duration, electron microscopy showed striking changes after 1 hour. These early changes consisted mainly of swelling of the mitochondria and the sarcoplasmic reticulum followed by an increase in lipid droplets. The abnormalities in the ultrastructure of the myofiber were believed to reflect the hyperosmolarity that resulted from anoxia.

Paul

PHARMACOLOGY


The effects of a previously described derivative of chlorpromazine, methoxyprazin (Mopazine) on the cardiovascular and autonomic nervous systems was investigated in the dog. The usual dose was 3 mg./Kg. Unlike chlorpromazine, methoxyprazin did not accelerate the heart rate; transient acceleration was noted only as a brief compensatory reaction to the hypotension produced in the unanesthetized animal. With chloralose anesthesia, on the other hand, a profound hypotension was observed, the result of the peripheral vasodilator effect of the drug. This effect was confirmed following destruction of the spinal cord and also by peripheral flow measurements following intrarterial injection. Like chlorpromazine, methoxyprazin suppresses hypertension induced by epinephrine. The reasons for the different action in the anesthetized animal are discussed.

Brachfeld


In the isolated frog heart, acetazolamide was found to have diphasic, inotropic, and chronotropic effects. On mammalian atria the drug mainly produced a negative chronotropic effect. It was concluded that the drug is basically a cardiac depressant.

Brachfeld


The properties of the l- and d-isomers of isoprenaline were compared in 3 normal volunteers by measuring the response of the heart rate and the pulse pressure to an intravenous infusion. The l-isomer was almost 50 times as potent. The subjective effects corresponded with the objective measurements and the local effects were qualitatively similar. Nevertheless, a suitable subeutaneous dose of the d-isomer had a clear-cut bronchodilator effect in a patient in status asthmaticus.

Kurland
ABSTRACTS


The duration of isometric and ejection periods was measured in healthy young males by means of combined tracings of the electrocardiogram, carotid pulse and phono-cardiogram. Following the recording of normal values, the effect of carotid sinus pressure, epinephrine and norepinephrine, atropine and the upright position was recorded. It was concluded that in the normal heart the duration of isometric contraction of the left ventricle is shortened by adrenergic and lengthened by cholinergic inotropic action. It remains nearly unaffected by changes of pulse rate or peripheral resistance. The elimination of the cholinergic factor by atropinization permitted indirect estimation of this factor. An adrenergic pattern was noted under emotional tension and during epinephrine infusion; the cholinergic pattern appeared during carotid sinus compression. Infusions of norepinephrine produced predominantly cholinergic effects due to secondary reflex stimulation. Atropinization uncovered the primary, specifically adrenergic action of norepinephrine.

Brachfeld


Coronary flow and changes in heart contractions were recorded simultaneously in the isolated rabbit heart, using a modified Langendorff technic previously described. Injections of 0.025 to 2.5 mg. of magnesium chloride into the perfusing fluid, close to the heart, produced "primary" coronary vasodilatation without any apparent change in heart contractions. Larger doses (25-250 mg.) temporarily depressed the amplitude of the contractions so that the concomitant intense coronary dilatation might have been partly secondary to the associated decreased extravascular depression. Continuous perfusions with increasing concentrations (0.009-0.364 mg. Mg**/ml. in Locke's solution) were associated with increasing degrees of coronary dilatation without significant change in heart action (amplitude or rate). At lower perfusion concentrations of magnesium, a small dose of epinephrine (10 μg.) induced greater vasodilatation than during control, and a larger dose (100 μg.) induced the expected greater effect whereas such a dose-response relationship was lacking with norepinephrine. It was concluded that magnesium can alter coronary flow independently of heart rate and contraction and that the ion elicits different responses to epinephrine and norepinephrine by the isolated heart.

Brachfeld


This report deals with the characterization of the adrenergic blocking action of tetrazotized diorthoanisidine (TDA). This compound combined with epinephrine, norepinephrine, and isoproterenol in vitro to produce substances that had little or no effect on blood pressure. Intravenous administration of TDA produced typical adrenergic blockade that was also apparent in isolated dog carotid and rabbit aortic strips. The positive chronotropic action of sympathomimetics was not blocked by TDA. The pressor responses to carotid occlusion and asphyxia were not blocked.

Rinzler


This report compares the renal vascular effects of all commercially available sympathomimetic drugs. This was done in anesthetized dogs by inserting a rotameter in the renal artery. Four types of responses were found. The following drugs constricted the renal vessels when injected into the renal artery and intravenously: levarterenol, epinephrine, phenylephrine, metaraminol, methoxamine, and naphazoline. The following drugs constricted the renal vessels when injected into the renal artery but produced variable effects when injected intravenously: epinephrine, phylpropanolamine, hydroxyamphetamine, and compound 45-50 [eta-hydroxy-beta- (2, 5-diethoxyphenyl) isopropylamine]. The following drugs had no important effect on renal vessels when injected into the renal artery; when given by vein, renal blood flow was increased as a result of their systemic pressor effect: methamphetamine, pseudoephedrine, amphetamine, pholedrine, methylamineheptane, tuaminopheptane, mephentermine, and phenylpropylmethylamine. The following drugs had a local dilator action when given by renal artery; when given by vein, the renal blood flow was decreased as a result of their arterial depressor effect: isoproterenol, nylidrin, isoprophenamine, methoxyphenamine, and cyclopentamine.

Rinzler

The use of levarterenol (Levophed) is occasionally marked by the occurrence of ischemia and subsequent necrosis in an area in which the drug has infiltrated. This sequence of events can occur even in the absence of infiltration with the needle perfectly in place and the infusion running well. It has previously been established that both phenolamine (Regitine) and piperoxan (Benodaine) can reverse the ischemia if infiltrated by multiple punctures into the ischemic area. The efficacy of several agents in the prevention of necrosis from Levophed was studied in adult rabbits in whom the intracutaneous injection of 1 ml of Levophed (1 mg./ml) invariably produced an ischemic area and subsequent necrosis. It was found that secondary injection with Regitine or Benodaine not later than 18 hours after the Levophed injection would prevent necrosis in each instance. Similar administration of novocaine in no instance prevented necrosis. The admixture of Meticortelone or Solu-Cortef to the Levophed enhanced the ischemia and necrosis occurred more rapidly. The admixture of heparin, however, prevented necrosis. When heparin and Meticortelone were both added to a solution of Levophed, no ischemia or necrosis ensued. The authors suggest that by the addition of 10 mg of heparin to a solution of levarterenol being administered intravenously, ischemic necrosis might be prevented. However, they caution that in post-operative shock, even this small amount of heparin might increase the probability of bleeding and therefore should not be used.

Sheps


This report presents evidence that a dichloro analogue of isoproterenol (DCI) blocks the inhibitory, but not the excitatory, effects of sympathomimetic amines and selectively blocks the positive inotropic and chronotropic effects of adrenergic stimuli in dogs with intact circulatory systems and in isolated hearts of rabbits. In dogs complete blockade of the cardiac positive inotropic effects of small doses of epinephrine, norepinephrine, and isoproterenol and of supranormal stimulation of the cardiac sympathetic nerves was obtained with cumulative doses of DCI of 3 mg./Kg. and greater. Depression of contractile force was frequently observed in response to sympathomimetic amines and to sympathetic nerve stimulation after administration of large doses of DCI. No inhibition of the positive inotropic effects of digoxin, theophylline, or calcium chloride was observed. In dogs blockade of the positive chronotropic effects of isoproterenol but not of theophylline was obtained with DCI. In isolated rabbit hearts DCI had qualitatively the same blocking action on the effects of the maines but not on those of calcium, theophylline, or ouabain. The dichloro analogues of epinephrine (DCE) and norepinephrine (DCNE) had similar blocking actions to those of DCI but were less potent. DCI, in both dog and rabbit heart, initially stimulated the heart but with subsequent doses depressed it. DCNE had similar effects in the dog, but in the rabbit heart it produced only depression as did DCE. The cardiac depressant effects were not antagonized by atropine. Ephedrine, which also produced initial cardiac stimulation and subsequent depression with high doses in the dog, did not inhibit the cardiac stimulation actions of other sympathomimetic amines. The vasopressor effect of epinephrine in dogs was potentiated by DCI, that of norepinephrine was relatively unchanged, while that of cardine sympathetic nerve stimulation was blocked, presumably due to the cardiac blockade. The vasodepressor effect of isoproterenol was completely blocked, but not reversed, by DCI in the dog. DCI, on intravenous administration, transiently lowered blood pressure, while DCNE produced a prolonged rise. DCNE did not appear to inhibit the vasopressor actions of epinephrine and norepinephrine or the vasodepressor action of isoproterenol.

Rinzler

Physiology


A study was made of the effect of cigarette smoke on the time course of hemodynamic changes in the myocardium including cardiac work, coronary blood flow, and oxygen metabolism, using the anesthetized open-chest dog. There was a lack of correlation between the onset of the electrocardiographic effects and the change in cardiac work. Coronary blood flow increased and appeared to follow the changes in blood pressure and cardiac output. A marked decrease in the oxygen consumption of the heart occurred in a close time relationship to the electrocardiographic disturbances. The effects of cigarette smoke were duplicated by the intravenous injection of nicotine alkaloid.

Rinzler

The fundamental arterial wave was defined by its length, equal to the velocity of the pulse wave multiplied by the duration of the standing wave; the duration of the standing wave was given by the interval between the systolic peak and the diastolic wave; the velocity of the pulse wave was measured by direct recording of the pulse pressure curves in the carotid and femoral arteries. The effective length of the arterial system was a constant fraction of the length of the fundamental wave. Measurements were made in 14 dogs, modifying the hemodynamic parameters of cardiac rate, blood pressure, and blood volume by vagal stimulation, by bleeding and infusion, and by intravenous or intraarterial administration of drugs. The drugs used included: agents acting directly on the arterial wall (acetylcysteine, carbaminoxycholine, amyl nitrite, papaverine, histamine); blockers of the nervous control (regitine, procaine, tetraethylammonium bromide, hexamethonium bromide); vasopressors (noradrenaline, vasopressin). Evidence was presented to prove that the length of the fundamental wave was in fact a physical constant of the arterial system, provided the regulation of the circulation was not impaired. Drugs increasing the blood pressure enhanced the fundamental wave. Drugs acting on the wall of the arteries, directly or through the nervous control, prolonged the duration of the wave; carbaminoxycholine, regitine, and the ganglion blockers were the most active of the drugs tested; in higher dosage all these drugs obliterated the fundamental wave; this may result from marked decrease of the peripheral resistance and of the mean arterial pressure. The fundamental wave should not be considered an unavoidable imperfection of the arterial system; its hemodynamic significance is stressed.

Calabresi


Reflex changes in mean pulmonary blood flow that occurred in response to alterations in carotid sinus pressure were studied in the dog. Heparinized dog’s blood was perfused through innervated carotid sinuses that were isolated from the circulation. Pulmonary lobar blood flow, total pulmonary blood flow, and combined blood flow through the superior and inferior venae cavae were measured by means of a rotameter flow meter. Occlusion of the common carotid arteries produced tachycardia, a rise in systemic and pulmonary arterial blood pressure, and an increase in pulmonary blood flow; these effects were enhanced by division of the cervical vagosympathetic nerves. Stimulation of the baroreceptors by raising the perfusion pressure of the carotid sinus produced bradycardia, a fall in systemic and pulmonary arterial blood pressure, and a decrease in pulmonary blood flow and volume. The pulmonary arterial pressure and blood flow partly recovered despite continuous increased carotid sinus pressure, and there was an after-rise in these values when the sinus pressure was released. The authors suggested that the reduction of the pulmonary flow and pulmonary arterial pressure on stimulation of the carotid sinus baroreceptors was due to reflex bradycardia and hemodynamic events occurring in the peripheral circulation. Distention of the carotid sinus also produced a decrease in total peripheral vascular reflexes, a small increase in pulmonary vascular resistance, and a decrease in the stroke work of both ventricles. The changes in the left and right atrial pressures were small and quite variable.

Karpman


A constant output arterial pump was used to perfuse blood from a donor rat through an innervated, but otherwise isolated, hind limb of a recipient rat. The use of this technic made it possible to distinguish changes in vascular tone due to nervous factors from those due to humoral factors. Blood was then withdrawn from the carotid artery of the recipient animal until its blood pressure was reduced to 30 mm. Hg. In 8 experiments it was evident that acute blood loss did not result in any nervous responses causing appreciable compensatory changes in the blood vessels of the hind limb. In fact, repeated acute blood loss resulted in increasing vasodilatation in the perfused limbs. In the second group of experiments the hind-limb vessels were cannulated, all vessels and nerves were ligated, and the animals were then killed. The first acute blood loss in the donor rat resulted in a slight rise in perfusion pressure in the hind limb and repeated episodes of acute blood loss produced pressor responses of increasing magnitude. No marked increase of reactivity in these limbs to norepinephrine or to pitressin was noted. Experiments in which the kidneys or the adrenal glands, or both, were removed suggested that a vaso-
constitutor substance which came from neither the kidney nor the adrenal gland, was released or activated during blood loss. There was some suggestion that the presence of the adrenal gland decreased the vasoconstrictor response and the presence of the kidney tended to increase it.

**Karpman**


Respiratory movements, intraarterial blood pressure and forearm blood flow (by venous occlusion plethysmography) were measured in 4 healthy, young adults. Hypoxia produced by breathing 5-10 per cent oxygen in hydrogen produced a large increase in ventilation, heart rate, and forearm blood flow. There was relatively little change in mean arterial or venous pressure, so that the vascular resistance (calculated by dividing mean perfusion pressure by mean flow) was considerably reduced. When excess of carbon dioxide was breathed, the mean arterial pressure increased, the blood flow fell slightly, and the vascular resistance was increased. The vascular resistance in the nerve-blocked forearm was reduced by hypoxia and it was therefore postulated that forearm vasodilatation with hypoxia was due to humoral rather than neurogenic factors. When carbon dioxide was added to the oxygen-poor gas mixture in order to produce a relatively constant partial pressure of carbon dioxide in the hypoxic patient, the vascular resistance was not appreciably altered. This indicated that the fall in vascular resistance in the forearm during hypoxia was due more to the hypoeapnia resulting from the hypopnea than directly to the hypoxia itself.

**Karpman**


This study of respiratory physiology was based on observations in 12 subjects with some anatomic basis for a pulmonary collateral circulation. These included subjects with prolonged obstruction of a pulmonary artery, unilateral pulmonary disease, so that 1 lung was perfused both by mixed venous blood and systemic arterial blood, and congenital absence of a normal pulmonary artery so that both lungs were perfused by systemic arterial blood. By a special adaptation of the Fick principle, it was found in subjects with bronchiectasis and cystic disease of the lungs that precapillary communications existed. Evidence of “effective” collateral blood flow was demonstrated in a subject with long-standing pulmonary arterial ligation. No effective collateral flow could be measured in subjects with either primary carcinoma of the lung or short-term pulmonary artery obstruction. Patients with atresia of the main pulmonary artery displayed large effective pulmonary collateral blood flows. These observations, discussed in detail in the text, emphasized the distinction between “effective” and total pulmonary collateral blood flow.

**Waife**


The diffusing capacity of the lungs for carbon monoxide was dependent not only on the thickness and the area of the membrane between alveoli and capillaries, but also on the volume of blood in the capillaries and the rate at which this blood can react with carbon monoxide. In this study, an estimate of the capillary blood volume and diffusing capacity of the pulmonary membrane in 19 normal subjects was studied. In addition, the effect of exercise and alterations in body position was examined. Under the conditions of the experiment described, both capillary blood volume and membrane diffusing capacity were significantly correlated with the weight, height, body surface area, vital capacity, and apparent diffusing capacity for carbon monoxide. The capillary blood volume appeared to be stable and reproducible over a long period of time (months) although the membrane-diffusing capacity was variable. In 4 subjects, these 2 parameters increased on mild exercise. Changing from the seated to the recumbent position caused changes in the capillary volume but not in the diffusing capacity. The observations seemed to fit in best with the hypothesis that the capillaries were incapable of dilatation and were either open or completely closed with only a small fraction of the alveolar capillaries open at any one time.

**Waife**


Clinical supraventricular tachycardia was simulated in 9 intact anesthetized dogs in whom catheters were introduced into the pulmonary artery,
coronary sinus, and right atrium while an indwelling needle was placed in the femoral artery. Tachycardia was induced by direct electric stimulation of the right atrial wall through a wired catheter, so that the average heart rate rose from 92 to 193 beats per minute. During the period of tachycardia, which averaged 25 minutes per animal, it was found that the cardiac output was unchanged and the measured parameters of general metabolism remained stable save for a slight rise in oxygen consumption. Pulmonary artery pressure and thus pulmonary artery resistance plus right ventricular work rose, although femoral artery pressure and its reflected left ventricular work were unchanged. During tachycardia the coronary blood flow per minute rose significantly, as did the cardiac metabolic rate, as measured by oxygen consumption and carbon dioxide production. Calculated myocardial efficiency fell during the period of stimulation and it was therefore assumed that at the faster rates energy was inadequately converted to useful work.

**Freedberg**

**PULMONARY DISEASES**


The findings were described in 19 patients in whom thrombosis of the major pulmonary arteries was confirmed at autopsy. There was a wide variety of predisposing illness and varied factors in pathogenesis. In 8 patients thrombosis was consequent on previous pulmonary embolism, in 9 the finding suggested that autochthonous thrombosis had occurred. In 2 patients the pathogenesis was not established with certainty. The clinical findings were extremely variable, at times minimal and at times those of sudden intractable right heart failure. The most frequent clinical course was that of repeated embolic episodes or of an overwhelming acute cor pulmonale. Only 1 patient showed a slowly progressive chronic cor pulmonale. The condition may first be suspected by roentgenogram. Examination of the chest may reveal right-sided heart enlargement, dilatation of the pulmonary artery proximal to the obstruction with alteration of the vessel contour and increased translucency of the lung fields distal to the obstruction. There may also be accentuation of the vessel outline due to diminished pulsations of the affected area. In the electrocardiogram the change from left-axis to right-axis deviation may be observed. By use of angiography, obstruction to the major arteries has been demonstrated. Because of the varied clinical picture thrombosis of the pulmonary arteries should be considered in the diagnosis of any case of acute, subacute, or chronic cor pulmonale.

**Krause**
RENAL AND ELECTROLYTE EFFECTS ON THE CIRCULATION


The intravenous infusion of isotonic saline produced a marked increase in the tubular repletion fractions for sodium and water. The glomerular filtration rate was slightly increased. The expansion of plasma volume produced by 6 per cent albumin in isotonic saline solution was less effective in producing a diuresis than a similar expansion of plasma volume by isotonic saline alone. These observations indicated that expansion of plasma volume alone cannot explain all the effects observed in saline diuresis. Bilateral vagotomy or bilateral severance of the cervical cardiac branches of the vagus did not significantly affect the diuretic response to intravenous isotonic saline.


The increased urinary sodium output induced by acetazolamide in water-loaded adrenalectomized rats was partially antagonized by the mineralocorticoid, deoxy cortisolone glucoside, the increased potassium excretion was augmented and urine volume was not affected. Intact rats subjected to the same treatment showed only a small rise in potassium excretion. The glucocorticoid, hydrocortisone hemisuccinate, under the same conditions, elevated sodium, potassium, and water excretion in the adrenalectomized rats receiving acetazolamide; intact rats showed an increase of sodium and water excretion with no significant change in potassium output. Hydrocortisone hemisuccinate (2.5 mg.) alone increased water excretion in adrenalectomized rats to a slightly greater extent than acetazolamide alone, with considerably less sodium loss.


Unilateral renal disease was induced in dogs by producing total unilateral renal ischemia for 30 minutes followed by perfusion for a 10-minute period with 100 ml. of isotonic saline containing an aminonucleoside (6-dimethylaminopurine-3'-amino-D-ribose), which was prevented from entering the systemic circulation by draining the renal vein. Split function studies were done before and after the procedure, facilitated by a preliminary bladder splitting surgical procedure with catheter drains to the outside from each hemilbladder. A moderate to severe decrease in function of the experimental kidney was noted in all the animals. Depression of renal function was maximal in the period immediately following the experimental procedure followed by a limited increase in function over a period of 6 to 8 weeks, after which clearance values tended to stabilize at levels appreciably below the control values. There was no persistent proteinuria, indicating that the lesion produced was different from the nephrotic syndrome that can be induced in rats by the subcutaneous administration of this agent. Anatomically, decrease in renal mass occurred and microscopically dilatation and atrophy of tubules, tubular luminal casts, interstitial fibrosis, decrease in size of glomerular tufts, dilatation of Bowman’s space, and thickening of the glomerular capsular epithelium and basement membranes were noted. The contralateral kidney remained normal and only minimal elevation of plasma urea and creatinine levels was seen to occur.


The diameter of the renal arteries was measured from translumbar aortograms in more than 59 patients having a variety of urologic conditions. A normal value (6.6 mm.) was found in advanced hydronephrosis due to acute ureteral obstruction, in some instances of intermittent hydronephrosis and infrequently in other disorders. However, renal artery narrowing was regularly associated with reduced function of that kidney, and this was corroborated by pallor or absence of the instantaneous nephrogram. In prolonged hydronephrosis the narrowing consisted principally of intimal proliferation. This method was advocated for evaluating the function of each kidney when retrograde pyelography was not possible or feasible and in certain other situations involving bilateral renal damage.


The properties of chlorothiazide and the mechanisms by which it affects urinary electrolyte and water excretion in man were studied in
16 hospitalized patients, 19 out patients, and 1 normal control subject. Natruresis was maximal within the first 2 hours after 1,000 mg. and lasted from 8 to 10 hours. The loss of chloride in the urine followed that of sodium; potassium excretion was much smaller. Bicarbonate excretion, measure of carbonic anhydrase-inhibiting activity of chlorothiazide, delayed in onset and gradually increased with dosage but was minimal at all doses. Three diuretics were compared with regard to their effect on the urinary electrolyte picture induced by α-fluorohydrocortisone. The mercurial produced a urine of greater volume which was more hypotonic with respect to sodium. There was a prompt but only partial reversal of the salt-retaining effect of the steroid by chlorothiazide as well as the others. The ionic pattern of excretion of chlorothiazide fell between that of acetazolamide and meralluride. In 3 edematous patients, the addition of acetazolamide potentiated the diuretic effect of chlorothiazide. Diuretic effects were shown in congestive heart failure, premenstrual edema, nephrosis, and cirrhosis. In the latter, an increase in blood ammonia may be a complication.

KURLAND


The renal response to an infusion of 800 ml. of 3 per cent sodium chloride was studied in 17 nonpregnant women, 11 normal pregnant women, 13 women with pre-eclampsia, and 12 with essential hypertension. The mean inulin clearance of normal pregnant women was higher than that of nonpregnant women; the inulin clearance in pre-eclampsia was depressed compared to normal pregnancy. The average filtration rates were not changed significantly during and after infusion of hypertonic saline. In the first 2 hours following saline infusion, the sodium excretion in pre-eclamptic women was significantly depressed compared to normal pregnancy. The sodium clearances in nonpregnant and normal pregnant women did not differ before or after salt loading; those of pre-eclamptic women were significantly lower in control periods and during and after salt loading. At comparable filtered loads, sodium clearance was markedly lower in pre-eclamptic and hypertensive women as compared to normal subjects. A larger percentage of filtered sodium was reabsorbed in women with pre-eclampsia than in normal women. It was concluded that renal tubular activity was markedly altered in women with pre-eclampsia and, in lesser degree, in pregnant women with hypertensive disease.

KURLAND

RHEUMATIC FEVER


The endomyocardial changes seen at autopsy in patients who had rheumatic disease and had been treated with cortisone have been described in a previous article. The changes found in other organs frequently involved in rheumatic disease are reported. The incidence of fibrinous pericarditis was not influenced by the treatment; necrosis was more frequent and more extensive; the healing process was slow, the fibroblastic reaction more intense, the newly formed connective tissue was looser. The inflammatory infiltrates of lymphoid cells, in the heart and also in other organs, were not influenced by cortisone. Rheumatic pneumonitis was found more frequently in patients treated with corticoids (37 per cent versus 11 per cent in patients not treated with corticoids); the fibrinoid necrosis of the alveolar septa was more extensive and the organization of the exudate was slow. Only 1 instance of rheumatic encephalopathy was found in this series of 30 patients; no detailed study of the cerebral pathology was therefore presented, and it was tentatively concluded that cortisone had a favorable effect on this localization, as on the polyarthritic manifestations of the rheumatic disease. Renal lesions were described in 4 patients, mild in 2, moderate in 1, and severe in 1; similar changes have not been found in other instances of rheumatic fever; it was inferred that these changes were due to the rheumatic process, and were made manifest by the corticoid treatment.

CALABRESI

ROENTGENOLOGY


In 17 patients 4 to 53 years old the left ventricle was catheterized through the right common carotid artery with a fairly stiff catheter guided carefully through the aortic valves in systole, under control of the fluoroscopic image amplifier.
Location of the catheter tip in the free lumen of the ventricle was verified by the contour of the intraventricular pressure pulse and the absence of ventricular extrasystoles. Injection of up to 60 ml. Triopaque 400 (1 ml./Kg.) in 1 to 2 seconds allowed exact visualization of the aorta, the left ventricle and its valves, and the coronary arteries, and exact determination of mitral regurgitation and left-to-right shunts. Pressure recording while the catheter was pulled back from the ventricle revealed tracings typical for various types of aortic valvular disease. Only one complication (cerebral embolism with hemiparesis) was observed; but as the patient had mitral disease, this was not necessarily caused by the catheterization.

**LEFESCHKIN**


Mediastinal tumors can now be operated upon with a low mortality. The most common cause of mediastinal enlargement by large vessels was long thought to be due to aneurysm of the aorta or aortitis. Now it appeared that coarctation and kinking of the aorta (pseudo-coarctation) also enlarged the mediastinal shadow. Three cases of dilatation and elongation of the thoracic aorta causing rounded mediastinal shadows were presented. A diagnosis of mediastinal tumor was seriously considered in all 3. Conventional roentgenographic procedures were carried out, but of these studies posteroanterior roentgenography with higher voltages and laminography was most helpful in establishing that the aorta caused the abnormal shadows. It appeared that attention should be paid to possible blood vessel abnormalities when interpreting mediastinal masses on conventional roentgenograms.

**KITCHELL**


This investigation indicates that the injection of large doses (40-80 ml.) of contrast medium (Urografin 60 per cent, Miokon 50 per cent) into the aorta of anesthetized, healthy dogs just above the origin of the renal arteries does not cause any renal abnormalities. Renal function was tested by means of inulin and PAH clearances several days before and after the contrast material injection, and the kidneys were also examined histologically. The volume of contrast medium injected was relatively 5 times as large as that injected into the human aorta, and the authors concluded that properly performed aortography will not damage healthy kidneys in human subjects. The renal damage that has been described in the literature was attributed to the injection of an aortic dose of contrast medium directly into a renal artery, and to the performance of aortography in patients with impaired kidney function.

**PAUL**


Although angiography is a well-accepted procedure, selective angiography is still in the process of evaluation. Clinical and experimental evidence presented here gave no support to apprehensions concerning this procedure. The methods, difficulties, and cautions in performing selective angiography were discussed. The newer contrast media employed seemed less toxic than previous materials used. Radiation damage was not remarkable. The procedure was a reproducible one with diagnostic and surgical promise and the authors reported 159 human cases performed without fatality or significant sequelae.

**KITCHELL**


Experience with the dynapulse method of ultra-fast roentgen-ray timing, with exposures as short as 1/1000 second, showed that this method was of practical value for the production of sharp roentgenograms in pediatric roentgenography, especially in angiography. Such milliseconds exposures stopped motion of 80 cm. per second, which approached the estimated maximal rate of blood flow. Dynapulse timing, however, revealed no diagnostic superiority over rapid impulse timing in pediatric chest roentgenography, in cerebral angiography, and in angiography in normal dogs.

**KITCHELL**


Roentgen studies over the last 20 years have resulted in considerable data regarding the sub-
clavian arteries in health and disease. Following angiocardiography all vascular trunks arising from the aortic arch are opacified. The right subclavian artery was seen in its entirety in the frontal projection while the first portion of the left subclavian artery was best seen in the left anterior oblique view. Such conditions as anomalous origin, congenital subclavian arteriovenous fistula and aneurysm, subclavian buckling, occlusion (Takayasu’s disease), tumor involvement and aneurysm were demonstrated. Conditions caused by the presence of coarctation of the aorta, the thoracic inlet syndrome, and kyphoscoliosis can be discovered. The authors seek to establish normal standards of caliber and length for the subclavian arteries and present data of academic and practical significance concerning the subclavian arteries in health and disease.


A series of 23 patients who had surgical treatment of the aortic valve under direct vision using hypothermia and inflow occlusion was presented. All the patients (except those with congenital aortic stenosis) had significant cardiac symptoms placing them in class III or class IV. The ages of the patients ranged from 5 to 56 years. In 18 patients with calcific stenosis, 9 have shown considerable improvement and 4 died—3 operative deaths and 1 late death. Of the 5 congenital cases it was more difficult to evaluate improvement; none in this group died.

Sagall


With improved control of infection, toxemia of pregnancy and hemorrhage, heart disease has gained a prominent place as a primary cause of death of the parturient woman. With rapid advances noted in the field of cardiac surgery, it is important that specific correctible cardiac lesions be recognized early so that more of these patients may be salvaged and the maternal mortality due to heart disease be reduced. Among the 37 patients included in this report 8 were pregnant at the time of operation, 2 had coarctation of the aorta, and 6 had mitral stenosis. Those with coarctation were delivered of normal infants without difficulty following repair of the lesion. Of those undergoing mitral commissurotomy, 1 died during operation, 1 had a premature delivery 9 weeks after operation, and 1 delivered a mongoloid infant. Operation prior to the twenty-eighth week of pregnancy was advised in selected cases of mitral stenosis and in coarctation of the aorta. Pregnancy was not considered a contraindication for surgery and did not appear to affect the fetus adversely or to increase the incidence of prematurity under the protective influence of progesterational hormone therapy. Therapeutic abortion for pregnant patients with mitral stenosis is becoming an obsolete method of management as a result of the success noted with mitral commissurotomy in indicated cases and conservative management in the remainder.

E. Shuman

VALVULAR HEART DISEASE


In a group of young women between the ages of 26 and 45, operated upon for mitral stenosis, an unusually high incidence of gallstones was found. In many this was evidenced by attacks of cholecystitis occurring in the immediate postoperative period following commissurotomy. Because of this high frequency of the 2 conditions in young women and also because of the problems in differential diagnosis that may arise in the postoperative period between acute cholecystitis and right heart failure in these patients, the
authors have formulated a policy of instituting x-ray studies of the gallbladder in all sick patients prior to mitral surgery, even in the absence of symptoms referable to the biliary tract. They further believe that unless the indications for the surgical correction of the mitral stenosis are most urgent biliary tract disease if present should be operated upon first. In their experience cholecystectomy alone or combined with common duct exploration has been well tolerated by patients with moderately severe mitral stenosis and the mitral lesion can then be corrected in 3 weeks or more.

SAGALL


A group of 154 patients with mitral stenosis who were between the ages of 50 and 70 at the time of operative correction of the lesion were compared with a larger group of younger patients. As would be expected a higher percentage of the older patients were in an advanced stage of their disease (group IV cases). Similarly, preoperative arterial embolization, associated arteriosclerotic heart disease, and elevated blood pressure were all significantly more common in the older age group. Despite these adverse factors, no significant increase in operative risk was found with advancing age when similar stages of the disease were compared. Evaluation after an average of 25.7 months further revealed in this comparison that the frequency of late death and the percentage of improvement after operation in the group of older patients was practically identical with that found at younger ages. On the basis of these observations the authors conclude that the properly selected patient over the age of 50 who has mitral stenosis should be offered surgical relief with the same assurance that is justified at an earlier age.

SAGALL


Simultaneous left and right heart catheterization was performed to measure pressure-flow relationships in 37 patients with clinically pure aortic stenosis. The most constant physiologic abnormality was a pressure gradient between the left ventricle and the aorta. This gradient was dependent not only upon the degree of obstruction but upon the rate of flow. No correlation could be made between the contour of the tracheal artery pressure tracing and the degree of obstruction. In all patients, the aortic orifice was below 1.1 cm.² Left ventricular function was altered with reduction generally of cardiac output. Systolic and end-diastolic pressures in the left ventricle were elevated and total work was increased. The mean left atrial pressure was elevated, reflecting the high left ventricular diastolic pressure, possibly a result of myocardial failure or the decreased distensibility of hypertrophy.

KURLAND


Mural calcification of the left atrium was found in 4 of 180 patients with mitral stenosis; this was most clearly seen in the oblique view, in roentgenograms and especially in tomograms. In agreement with 38 cases from the literature, it was seen only in mitral stenosis of long duration with atrial fibrillation, accompanied by significant mitral insufficiency and multivalvular involvement. In most cases this finding constitutes a contraindication to mitral valvulotomy.

LEFESCHEIN

VASCULAR DISEASE


Primary Raynaud’s disease implies intermittent attacks of digital pallor or cyanosis with no known local cause or associated systemic disease. Twenty-one patients with this disease were discussed. In 16 of the 20 patients in whom a complete family history was available a history of similar attacks was present in one or both parents. It was reasonable to assume an inheritable predisposition, although the nature of the inherited defect remained unknown. In 8 patients symptoms arose within 6 months of childbirth; in 6 patients digital symptoms appeared after the onset of menopause; and in 7 patients the symptoms followed a period of prolonged and severe mental stress. This group of 21 cases represented 50 per cent of a larger series in the remainder of which no such etiologic factor could be detected.

KRAUSE


An analysis of the surgical treatment of 803 cases of occlusive disease of the aorta and fem-
oral arteries was presented. This series thoroughly established the concept that in chronic arteriosclerotic occlusive disease of the lower extremities the obstructing lesion was usually well localized and segmental in nature with a relatively patent lumen above and below the occluding lesion. The cases could be classified into 2 major groups, namely, aorto-iliac occlusion and femoral occlusion. The series of aorto-iliac occlusion comprised 448 patients of whom 100 (44 per cent) showed complete aortic occlusion and 249 (56 per cent) an incomplete aortic occlusion. Associated occlusive disease of the peripheral arterial bed was found in 18 per cent. Three types of surgical procedures were employed in these patients depending on the location, extent, and nature of the occlusive process as well as certain systemic factors. These consisted of thromboendarterectomy, excision with graft replacement, and bypass graft. With associated peripheral disease lumbar sympathectomy was considered a desirable supplemental procedure. In about 95 per cent of the patients a pulsatile circulation through the major arterial channel was restored by employing the technic indicated in that case. The operative mortality was 2.7 per cent and resulted primarily from associated cardiac and renal disease. Nine late deaths, due primarily to cardiac disease, occurred from 1 to 30 months after discharge from the hospital. Recurrent occlusion occurred in only 8 patients after varying periods following operation ranging from 3 to 27 months. With occlusive disease of the femoro-popliteal region wide variations in the nature and extent of the pathologic features of the occlusive process were found, but the cases could be classified into 3 main groups: (1) those with a discrete localized occlusive lesion with relatively normal arteries above and below the occlusion, (2) those with more extensive involvement of the femoral artery but with patency of the popliteal and distal arterial bed, and (3) those with still more extensive and diffuse obliterative disease extending well down into the smaller vessels of the calf. Preoperative arteriographic studies were necessary to determine the form of the occlusion and the application of the appropriate surgical procedure. Only those patients in the first 2 groups could be helped by surgical procedures which aimed at restoring normal circulation while those in the third group were best treated by lumbar sympathectomy. Of the 353 cases of occlusive disease of the femoral artery in this series 90 per cent were treated by means of bypass graft. Endarterectomy was still considered a desirable procedure but its use was limited only to those patients in the first group. In 84 per cent of all the treated cases a normal pulsatile circulation was restored. Recurrent occlusion was observed in only 14 per cent of cases ranging over a period of 3 weeks to 38 months after discharge from the hospital.

SAGALL


The clinical syndrome of carotid artery thrombosis is well recognized. However, obstruction of the carotid artery without occlusion is more common and is generally unrecognized. Such occlusion produces localized carotid murmurs which can be detected by auscultation of the head and neck. In unselected hospital patients, 7 per cent showed carotid systolic murmurs and 2 per cent showed continuous murmurs indicative of partial occlusion of the carotid artery. A continuous murmur over the carotid bulb is a valuable sign of carotid artery insufficiency and may be found in completely asymptomatic patients with unsuspected carotid artery insufficiency as well as in patients in whom the diagnosis of "cerebral thrombosis" has been entertained. It also may be found in patients in whom transient neurologic symptoms have appeared, usually in relation to changes in blood pressure. Carotid artery insufficiency is treatable by both surgery and anticoagulant therapy and its early recognition and treatment before a complete thrombosis occurs are important.

KITCHELL


The value of vitamin E in the treatment of peripheral vascular disease was studied in 40 nondiabetic male patients with obliterative vascular disease who complained of intermittent claudication. Patient evaluation and exercise tolerance were measured in 20 patients treated with vitamin E and in 20 with placebo. Thirteen treated patients showed subjective and objective improvement as compared with only 2 in the control group. No criteria were formed for selection of suitable cases for vitamin E therapy, but large doses over long periods were necessary, for there was a considerable delay before any response.

KURLAND


In a total of 1,597 autopsy reports, 67 instances of thrombosis of the abdominal veins were found: 44 of these were limited to the pelvic vessels, 7
involved the iliac veins and did not extend to the visceral veins. Of the 16 remaining cases, 11 were cardiac patients; 6 of these also had thrombosis of the right cardiac chambers. Seven of these 16 patients were not suitable for detailed analysis and clinicopathologic correlation. Of the 9 specimens studied, 6 had unilateral or bilateral renal vein thrombosis, 2 had isolated splenic, 1 had splenic and portal, and 1 had isolated portal vein thrombosis. Three cases of acute renal vein thrombosis had evidence of a nephrotic syndrome; the 1 instance of chronic renal vein thrombosis also had nephrosis, recurrent abdominal pain, and late transitory arterial hypertension. While in children massive infarction and hematuria were noted, these patients had only moderate or noncharacteristic hematuria, and hemorrhagic infarction was not found at autopsy. None of the patients with portal or splenic thrombosis has had gastric hemorrhages; the patient with portal and splenic thrombosis had hemorrhagic infarction of the liver.

CALABRESI


Aneurysms of the splenic artery are uncommon. In a 47-year period, ending in December 1957, 46 aneurysms were found in the course of 28,512 postmortem examinations, an incidence of 0.16 per cent. Sixty-eight per cent occurred in women. Most of the lesions in both sexes afflicted persons in the sixth, seventh and eighth decades. Three (6 per cent) ruptured and were the cause of death. The spleen was enlarged in 11 patients. In 5 patients (21 per cent) aneurysms were found elsewhere in the body; 3 of these latter lesions affected intraabdominal arteries. Twenty-four aneurysms were asymptomatic and were not suspected clinically. Two of the aneurysms were mycotic and were associated with subacute bacterial endocarditis. Two dissecting aneurysms were restricted to the splenic artery. One of these had developed in continuity with acute hemorrhagic pancreatitis and the other was associated with multiple systemic embolization. Of the remaining 20 bland aneurysms, 11 were congenital and 7 of these were associated with secondary deposits of atheroma.

KRAUSE


Aortic thrombosis (Leriche's syndrome) was studied in 32 patients over a 4-year period. Although the autopsy incidence is approximately 0.12 to 0.15 per cent, the clinical incidence is closer to 0.61 per cent. The clinical diagnosis in all patients in this study was confirmed by aortography. There were 24 males and 8 females. The average age for the group was 51.3 years. Twenty patients had a gradual onset of symptoms and in 12 patients the onset was more rapid. The chief symptom was intermittent claudication and usually this was progressive in nature. In 50 per cent of the cases this was associated with a loss of power in the muscles of the legs and also wasting of these muscles. The most important sign of aortic thrombosis was the loss of palpable arterial pulsations below the block. However, the absence of femoral pulsations does not imply that these vessels must be occluded, for it has been proved by aortography that this can be due to the damping of the pulse where blood is carried by collateral vessels from the aorta to the femoral arteries. A less often observed sign of aortic thrombosis is vigorous pulsation above the site of block. A systolic murmur over the spinous processes of the lumbar vertebrae and lower abdomen due to the development of collateral circulation can occur. A plain roentgenogram of the involved site is of no help, and even the identification of calcification means little in the diagnosis of aortic thrombosis. The most helpful diagnostic air is aortography and a certain diagnosis includes the visualization of an abruptly ending column of contrast medium. Usually the block lies between the level of the renal arteries and the aortic bifurcation, and collateral blood vessels are often demonstrated. Although in this series there were practically no complications to the aortography, the authors recognize that the procedure is not innocuous. Furthermore, false positive x-rays may be due to subintimal injection of the dye stuff and also extension of the thrombosis, anuria, and paraplegia have been reported as complications. The chief differential diagnosis is that of bilateral iliac thrombosis, which can usually be accomplished by aortography. Hypertension when associated with aortic thrombosis may in fact be due to blockade of a renal artery by retrograde extension. Impotence due to inadequate blood flow to the corpora cavernosa through the internal pudendal artery does occur. This symptom often is reversible when adequate collateral blood flow to the corpora cavernosa develops. It is the feeling of the authors that the prognosis is not as poor as previously thought in either the untreated or the treated form. Even though major surgery is available for aortic thrombosis, careful clinical judgment must be used in deciding whether this should be attempted.

KRAUSE

Cerebral embolism occurred in 34 (20 per cent) of 172 patients with rheumatic heart disease. The right and left cerebral hemispheres were involved with almost equal frequency. Hemiparesis was the resultant major disability, being severe in 10, moderate in 16, and mild in 6 patients. Of 33 patients analyzed, less than one fifth died within 3 months. Two thirds of the patients made a virtually full clinical recovery. The average time to the beginning of recovery was 1 week, and to maximum recovery, it was 4 months. Based on this data, the authors emphasized a hopeful outlook for patients with this complication of rheumatic heart disease as regards neurologic recovery.

Krause

OTHER SUBJECTS


Fear, often associated with nausea, may cause syncope. The fear of the dental chair and the nausea produced by the use of apomorphine in alcoholics were used to study the dynamics of such syncope. Continuous circulatory measurements were made before and during nitrous oxide anesthesia for tooth extraction. Five out of 21 dental patients developed acute hypotension with vasodilatation of the forearm vessels; 4 of these before the anesthetic was given. Fear appeared to be the main cause, with a fall in arterial oxygen saturation as a possible minor factor. Apomorphine-induced nausea caused a fall in the effective filling pressure of the heart which preceded hypotension and syncope. The authors suggested that emotional stimulation of the heart beat and a fall in eardine filling pressure causes virtual emptying of a ventricular chamber during systole which fires the afferent mechanism of the faint reflex. Normally a person who faints, falls to the ground and the supine position increases the filling pressure of the heart with rapid recovery of consciousness. There is strong evidence that subjects with heart failure, whose ventricles are not easily emptied, do not faint.

Krause

REVIEWS IN CARDIOVASCULAR DISEASE


