ABSTRACTS

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METABOLIC EFFECTS ON CIRCULATION


The intravenous administration to 20 patients of synthetic angiotensin II had 10 times the effect of norepinephrine on the arterial blood pressure. Following discontinuation of the infusion, postural hypotension occurred in six subjects and lasted 18 to 24 hours. Discontinuation of an infusion of norepinephrine was followed by postural hypotension in four patients, which lasted 4 to 6 hours. Both agents elicited bradycardia in normal individuals and a diminished bradyerotic response in arteriosclerotic subjects. Angiotensin II caused a decrease in cardiac index, a marked increase in peripheral resistance, and an increase in venous pressure, half of that caused by norepinephrine. There was no demonstrable effect on serum sodium, potassium, plasma volume, or red cell mass. The infusion of equivalent amounts of angiotensin II and epinephrine caused a striking increase in cardiac output and a slight fall in arterial pressure and peripheral resistance from the elevated values associated with infusion of angiotensin II alone. A 24-hour infusion of angiotensin II caused a diminution in effective renal plasma flow, reduction in both inulin and PAH clearances, the latter larger than the former, and a slight decrease in urinary output. Angiotensin II was administered therapeutically to patients in shock, eliciting an increase in urinary output following the first 24 hours of therapy, but no evidence for tachyphylaxis or cardiac arrhythmias. Its potency in this clinical situation appeared to be two to three times that of norepinephrine. There was no tissue slough following inadvertent subcutaneous infiltration in eight instances.

Ross


Intravenous phenmetrazine produces a pressor effect in normotensive individuals about one fifth as potent as that noted with dextroamphetamine. There is no cardio-acceleration or cardiac irritability noted. In several hypertensive subjects tested there was a stepwise elevation in blood pressure with repeated doses. This is in contrast to the tachyphylaxis demonstrated with this preparation in the dog. Long-term oral administration in a dosage of 25 mg. three times daily did not produce significant change in the blood pressure of the hypertensive group. There was decrease in appetite with resulting weight loss. The authors advise that the administration of phenmetrazine to obese hypertensive patients is a useful adjunct to the therapeutic regimen, when weight loss is desired.

Shefs


An explanation for the apnea, bradycardia, and systemic hypotension following injections of
hypertonic saline was sought in 25 anesthetized, closed-chest dogs. Bradycardia and apnea appeared after 5 to 10 ml of 20 per cent sodium chloride were injected into the inferior vena cava or pulmonary artery, but not after injection into the left heart. Normal saline or 50 per cent dextrose had no effect. Vagotomy prevented both responses. Two successive phases of systemic hypotension were noted after hypertonic saline injection into the right or left cardiac chamber. Only an early phase followed injection into the coronary artery and a single later phase followed injection into the distal part of the aorta. The two drops thus appeared to be central and peripheral in origin, respectively. On the electrocardiogram, ST-segment and T-wave changes were almost simultaneous with the first period of hypotension, appeared immediately after the intracoronary injection and several seconds after the intraventricular and intrapulmonary injections. The initial hypotensive dip therefore seemed to be due to transient electrolyte imbalance and myocardial failure. The mechanism of the second blood pressure fall remained unexplained.

White


Evidence that catecholamines are important to ventricular rhythmicity was obtained in cats depleted of these compounds by reserpine. During anesthesia with Dial urethan or after spinal cord section at the first cervical vertebra, the right vagus nerve was stimulated electrically, producing bradycardia to the point of ventricular escape. Reserpine-treated cats in each group fell to a slower sinus rate than controls before ventricular escape occurred and maintained a slower ventricular rate afterwards. Asystole lasting longer than 5 seconds was more common in reserpine-treated cats, and their average duration of asystole was longer. Untreated animals responded the same whether they were cord sectioned or anesthetized, indicating no primary effect of sympathetic tone on ventricular escape. Convulsions during asystole usually coincided with ventricular escape in reserpine-treated animals, suggesting that some metabolic feature of anoxia provoked the escape. Mobilization of catecholamines from the adrenal glands did not appear important, since bilateral adrenalectomy after reserpine treatment did not further diminish the ability of the ventricles to escape vagal suppression, at least in one anesthetized cat and in two with cord section. Norepinephrine infusions after reserpine treatment prevented the development of long asystolic periods during vagal stimulation and permitted ventricular escape with much less slowing of the sinus rate. This reversal of reserpine effect by norepinephrine implies that reduction of ventricular rhythmicity by reserpine is the result of catecholamine depletion.

White


Hegglin designated appearance of the second heart sound more than 0.04 second earlier than the end of the T wave as "energetic-dynamic cardiac insufficiency," and found this condition especially in potassium deficiency. In the present study, however, this condition was not present in any of 11 patients with a serum potassium of less than 3.2 mEq./L. In 19 rats raised on a potassium-free diet the second heart sound did not appear earlier with respect to the T wave than in 40 rats on a normal diet. This observation is related to the finding that in potassium-deficient rats the intracellular potassium content of skeletal muscle decreased parallel to the decrease of serum potassium, but that of cardiac muscle remained practically unchanged. In rats exercised until exhaustion, the intracellular potassium in skeletal muscle also decreased considerably, whereas that of cardiac muscle remained unchanged or increased. The capacity of heart muscle to retain potassium can be due to its better vascularization or to its capacity to utilize products of anaerobic carbohydrate metabolism. The conclusion is made that signs of energetic-dynamic cardiac insufficiency appear only when there is los of intracellular potassium.

Lepeschkin

PATHOLOGY


The right common carotid artery in 62 rats was ligated in two places. The segments of artery between the ligatures and proximal and distal to them were studied with the electron and light microscopes. Clotting of blood within the ligated segment generally did not occur and hence did not influence the proliferation of the intimal cells. Within 48 hours after surgery, the entire endothelium was necrotic, with subsequent appearance of macrophage-like cells adherent to the necrotic layer. These macrophages were probably derived from monocytes in the

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blood contained in the ligated segment. Ten to 14 days following the carotid ligation, splitting of the internal elastic lamina occurred, with concomitant appearance of nests of smooth muscle-like cells lying inside the lamina. These cells appeared to have migrated from the media. The subsequent growth of these "myo-intimal" cells was responsible for the intimal hyperplasia and reduction in size or obliteration of the arterial lumen. There was no change in the endothelial cells themselves during this time, the endothelial layer remaining one cell thick. Eventually the endothelial cells were pushed to the center as the lumen was gradually obliterated. There cells were identified by their phagocytized particles of thorium dioxide, which had been injected just prior to the arterial ligation. The medial layer of the artery exhibited no consistent change.

Ross


The grossly normal heart of an 8-year-old child was examined microscopically for nerve fibers. After fixation in Bouin's solution, the left ventricle and part of the septum were serially sectioned and stained by Gomori's trichrome method. After reading, the Gomori stain was removed and the slide read again after restaining by Bodian's silver reduction method. A generous supply of fibers followed the coronary arteries into the cardiac muscle. Sympathetic and parasympathetic fibers intermingled and could not be specifically identified. Large and small rounded nerve trunks contained myelinated and nonmyelinated fibers, some becoming flat structures toward the endocardium at the arterial level. Certain fibers, presumably vagal, ended in a bulbous tip or a bunch-like terminus amid the myocardial synectium. The bulbous tips appeared to be sensory receptors. Nodose thickenings of cardiac nerves seen with methylene blue stains appeared as interrupted broad flat segments in this study. Some large and small nerve trunks entered the myocardium directly, not in association with branches of coronary arteries. After penetrating the myocardium, they had a scanty perineurium, divided dichotomously, and reached muscle tissue near the endocardium. No myoneural plates were seen. Related and similar studies in experimental animals were extensively reviewed.

White


A pathologic method demonstrating myocardial infarction especially in its early stages is described, combining the injection of the coronary system with contrasting material, and the so-called dehydrogenase maeroaction in the myocardium. This simultaneously enables determination of the state of the coronary system and the extent and localization of ischemic changes in the myocardium. The dehydrogenase reaction can demonstrate ischemic changes in the myocardium within 5 hours after the ligation of the coronary artery. The results of the reaction are particularly suitable for electrocardiographic correlation.

Brachfeld


The media of 10 arteriosclerotic human aortas were studied with the interference microscope for the site of calcific deposits and for quantitative characteristics of ground substance and elastic fibers. Sections through an atheromatous plaque were compared with sections through an adjoining area at the same level presenting no gross intimal lesion. No striking quantitative differences were noted between the two groups. Fat droplets in the ground substance and certain cells increased progressively toward the innermost interlamellar space. Calcium deposits progressed similarly, also located in the interlamellar spaces. No calcium deposits were found in the elastic fiber themselves, contrary to other reports. The refractive index of fibers of both groups was the same before and after fat extraction except for a reduction in thickness of the innermost laminas of the atherosclerotic group. The refractive index of ground substance was unchanged after fat extraction in both groups, but reduced thickness of the ground substance was observed in the inner third of the media of the atherosclerotic group and adjoining the innermost lamina in the nonatherosclerotic group. Calculations indicated that fat constituted 32 per cent of the mass of ground substance in the inner layer of the atherosclerotic group and 46 per cent of that in the innermost interlamellar space of the nonatherosclerotic group.

White


An anatomic basis was sought for pulmonary arterial hypertension associated with arterial hypoxemia. A quantitative histologic study was made from necropsy material of pulmonary ves-
sels of two groups of persons who had chronic hypoxemia but were free of intrinsic pulmonary parenchymal disease. A group having lived a lifetime at high altitude was compared with another having long-standing extreme obesity. In both, the smaller pulmonary arteries showed striking medial smooth-muscle hypertrophy without other structural abnormalities. Arterial and capillary beds were found to be dilated. Sclerosis of the arterial wall was absent, although an increase with age in the area of the intima plus internal elastic membranes of pulmonary arteries of all sizes was evident in both groups and in controls. The probably different blood carbon dioxide tensions between the obese subjects and those living at high altitude suggest hypoxemia rather than hypereapnia as the basis for the anatomic changes.

White


Injections of hyaluronidase daily for 50 days into weanling rats led to histologic evidence of medio-necrosis of the aorta. The changes were even more striking than those found in lathyrism rats, treated for the same period with amino-acetonitrile (AAN). Swollen and fragmented elastic fibers, edema, and cystic lesions appeared in the aortic media. Bone changes were unimpressive in the AAN rats but hyaluronidase caused gross kyphoscoliosis and microscopic elongation of the zone of proliferating cells in epiphyseal cartilage. Changes in bony trabeculae resembled osteogenesis imperfecta. Thin, elastic skin was noted in both hyaluronidase and AAN groups on palpation but no marked changes were seen histologically. No ocular or electrocardiographic effects were found. Addition of chondroitin sulfate or vitamin E to the hyaluronidase regimen had a protective effect on bone and aorta. The damage caused by hyaluronidase was therefore attributed to destruction of mesodermal hyaluronic acid and chondroitin sulfate. Evidence is discussed that lathyrysm and the Marfan syndrome are similar pathologic conditions.

White

PHARMACOLOGY


The direct effects of two digitalis preparations on the contractile force of the heart were studied by means of the Walton-Brodie strain-gage arch in 21 patients who had never experienced congestive heart failure. In 14 patients with either atrial septal defect or pulmonic stenosis, acetylstrophanthidin (0.026 mg. per Kg. of body weight) was given during cardiopulmonary bypass. This resulted in an increase in contractile force ranging from 16 to 327 per cent and averaging 89 per cent of the contractile force measurement prior to digitalization. In three patients who received an average dose of 0.022 mg. per Kg. of lanatoside C during cardiopulmonary bypass, the right ventricular contractile force increased by an average of 31 per cent of control levels. The response of the left ventricle immediately after mitral valvulotomy was studied before and after digitalization. Acetylstrophanthidin increased contractile force by an average of 24 per cent of the control levels. The administration of digitalis to patients on cardiopulmonary bypass at a constant perfusion rate permitted study of the direct effects of these drugs on systemic vascular resistance. Acetylstrophanthidin resulted in a brief increase in systemic vascular resistance which averaged 23 per cent, and lanatoside C resulted in an average increase of 14 per cent of the control levels. It is concluded that these digitalis preparations augment the contractile force of the nonfailing human heart and constrict the systemic vascular bed.

Kayden


The naturally occurring purine and pyrimidine bases, guanine, hypoxanthine, thymine, and uracil, had a positive inotropic effect similar to that reported for their corresponding nucleosides on the acutely overloaded, failing left ventricle of the isolated dog heart. The nucleosides guanosine, inosine, uridine, and their respective bases were positively inotropic, and adenosine and cytidine and their bases were negatively inotropic for both failing and nonfailing rabbit hearts. Thymidine was positively inotropic for the failing heart and had a variable effect in the nonfailing heart, whereas thymine, its base, was positively inotropic for both preparations. Of the substituted purines and pyrimidines tested, only caffeine and orotic acid were positively in-
ototropic, and only xanthine, 6-chloropurine, alloxan, and 4-carboxypuridine were negatively inotropic, on the nonfailing rabbit heart. It was therefore concluded that substitution of hydroxyl groups, in addition to the one already present in the six position, did not enhance the inotropic effect of purine or pyrimidine bases. Conversely, substitution of other groups in the six position of the purine or pyrimidine ring led to a loss of inotropic effect. Of the parent ring structures, only pyrimidine was positively inotropic, despite absence of a hydroxyl group at the six position.

Ross


Current views of the circulatory effects of anesthesia from diethyl ether, halothane, thiopental, cyclopropane, and intraspinal agents were described. Little evidence was found that any of these significantly depressed cardiac function until a deep level of anesthesia was reached. The tendency of diethyl ether to depress myocardial action was considered to be largely counteracted by a concomitant increase in adrenergic activity. However, reserpine administration often depletes the myocardium of norepinephrine, in which case anesthesia, especially from ether, may be attended by hypotension. Cardiac function was believed to be only indirectly affected by spinal anesthesia, which produces principally a relaxation of the postarteriolar capillary bed. Arrhythmias occurring chiefly during deep levels of cyclopropane anesthesia were related to increased arterial pCO2 levels resulting from alveolar hypoventilation. The authors consider this agent to be contraindicated only when there is complete heart block. The choice of anesthesia in general should be based on the evaluation of the individual patient and on the ability of the anesthesiologist.

Rogers


Quinidine gluconate was administered intravenously to anesthetized dogs at dosage levels of from 2 to 4 mg. per Kg. of body weight to 15 mg. per Kg. of body weight. Measurements of quinidine concentration were made of the arterial, venous, and coronary sinus blood from 1 to 30 minutes after injection. At the lower dosage levels a peak arterial value was reached in 1 minute with a rapid decline within 3 to 5 minutes. In three of six dogs, the quinidine level in the coronary sinus transiently exceeded that in arterial blood following the 1-minute specimen. With higher doses, the quinidine level in the coronary sinus usually exceeded the arterial level after the first minute. The myocardial concentration of quinidine following examination of biopsy specimens taken serially in the same animal exceeded the concentration in the blood from four to 10 fold. It is suggested that quinidine is pooled transiently or bound in the myocardium and is subsequently washed into the coronary sinus.

Kayden


A definite central component of the hypotensive action of chlorpromazine has been demonstrated by a variety of procedures by which the peripheral adrenergic blocking action of this drug was eliminated. Pressor response to intravenous norepinephrine was used as a test for adrenergic blockade throughout the study. In the dog, intracerebroventricular injection of chlorpromazine induced hypotension and inhibition of centrally mediated vasomotor reflexes. Injection of this agent into the vertebral artery in a neurogenic hypertensive dog produced a marked fall in blood pressure and inhibition of vasomotor response to centripetal vagal stimulation. In the intact cat, intravenous injection of chlorpromazine (in a dose inadequate to produce adrenergic blockade) inhibited vasomotor responses evoked by electrical stimulation of the medullary vasomotor center. This inhibition was abolished soon after midcollicular transection (which excluded the hypothalamus). Furthermore, intravenous chlorpromazine did not produce any effect on medullary vasomotor responses in de cerebrate cats. No action of the drug was demonstrable on the spinal vasomotor loe. The locus of central hypotensive action of chlorpromazine seems to be the hypothalamus.

Brachfeld

PHYSICAL SIGNS


The author points out that the improved forms of therapy now available for children with congenital and acquired heart disease make the differentiation between innocent and organic
heart murmurs exceedingly important. He reviewed the literature and presented a study of 231 children referred to a pediatric cardiac clinic. He found that the innocent systolic murmur was the most common murmur encountered in childhood and that it could be classified into 3 types in the following order of frequency: the vibratory parasternal precordial murmur, the blowing pulmonic systolic murmur, and the cardiorespiratory murmur. The clinical characteristics, causes, and significance of each type are discussed in detail.

**SAGALL**

**Henke, R. P., March, H. W., and Hultgren, H. N.:**

An Aid to Identification of the Murmur of Aortic Stenosis with Atypical Localization.


At times, the differential diagnosis between aortic stenosis and mitral insufficiency is difficult, particularly when the aortic murmur is faint at the base and louder at the apex, or when it is exclusively heard at the cardiac apex. Proper diagnosis sometimes can be made when the apical systolic murmur retains the diamond-shaped characteristics of the murmur of aortic stenosis. In six patients with aortic stenosis and atrial fibrillation, phonocardiographic studies showed that the intensity of the murmur varied with the preceding cycle length, being more intense after long diastoles. In contrast, patients with mitral insufficiency had apical systolic murmurs that did not vary significantly with cycle length. On this basis it is suggested that this specific property of the murmur of aortic stenosis can be helpful in the diagnosis of systolic murmurs heard maximally or exclusively at the cardiac apex.

**SAGALL**

**Hubbard, T. F., and Neis, D. D.:**

The Sounds at the Base of the Heart in Cases of Patent Ductus Arteriosus.


Data are presented on 30 patients with patent ductus arteriosus on whom at least one phonocardiographic study and routine right heart catheterization had been performed. In 10 patients, simultaneous right heart catheterization and phonocardiographic determinations were made. In 12, direct surface phonocardiography was obtained simultaneously with direct puncture aortic and pulmonary pressure records. Typical continuous murmurs were found in all but five patients, all under 3 years of age. With shunts greater than 30 per cent various additional abnormalities of the heart sounds were detected. A single systolic ejection sound was found usually to be indicative of some dilatation of the pulmonary trunk. Double or triple ejection sounds were always associated with large left-to-right shunts. In older children and adults the degree of paradoxical splitting of the second sound proved to be a rough guide to the volume of the left-to-right shunt. This phenomenon, however, was less consistent in infants and small children. Normal splitting of the second sound with a normal respiratory effect in a patient over 12 years of age usually indicated a small to moderate shunt. With the largest shunt volumes, well-defined eddy sounds were present. Observation of these heart sounds may enable a diagnosis of patent ductus arteriosus in infants and small children in the absence of the typical continuous murmur.

**SAGALL**

**Runco, R., Molnar, W., Meckstroth, C. V., and Ryna J. M.:**

The Graham Steell Murmur versus Aortic Regurgitation in Rheumatic Heart Disease. Results of Aortic Valvulography.


Aortic valvulography was performed in 25 patients with mitral stenosis in whom the diagnosis of a Graham Steell murmur was entertained. Eighteen were shown to have aortic regurgitation in spite of clinical findings favoring pulmonic insufficiency. No attempt was made to evaluate the presence of pulmonic insufficiency. The results seem to indicate that the incidence of a Graham Steell murmur in rheumatic heart disease has been greatly overestimated.

**KALMANSOHN**

**PHYSIOLOGY**

**Bickelmann, A. G., Lippshutz, E. J., and Brunjes, C. F.:**

Hemodynamics of Idiopathic Orthostatic Hypotension.


The syndrome of idiopathic postural hypotension is described in two subjects with a report of hemodynamic studies. Elevation on the tilt table resulted in an impressive fall in both systolic and diastolic blood pressure, which was quickly reversed by returning to the horizontal position. Acceleration of the pulse was not appropriate to the remarkable degree of hypotension. Following 25 mg. of Metaraminol orally, progressive increase in blood pressure was noted, and orthostatic hypotension was no longer present. In the second subject, the eardial output in recumbency was also extremely low, and the calculated peripheral vascular resistance was extremely high. When the patient was tilted to
45°, the mean arterial pressure fell to almost half of the control value. No significant change occurred in cardiac output, and the calculated resistance to flow diminished profoundly. It is contended that this disease is the result of a basic defect of cardiovascular regulation manifest in the standing and recumbent positions. Autonomic nervous system dysfunction may be consistently demonstrated, and is an essential feature of the disease. But it is suggested that some other unidentified regulatory mechanism may also be deficient.

KURLAND


Vasovagal reactions occurred in two patients during cardiac catheterization, after control data had already been obtained. Both patients experienced an abrupt decrease in systemic and pulmonary arterial pressure, heart rate, cardiac index, and stroke volume, with an increase in systemic arterial resistance. The patient with severe hypertensive heart disease and congestive heart failure experienced, in addition, a fall to normal levels of pulmonary arterial and right ventricular diastolic pressures, with a concomitant marked decrease in central blood volume and pulmonary vascular resistance. The heart rate reverted to normal 27 minutes following the vasovagal reaction. However, the other parameters approached, but did not attain control values during the 45 minutes subsequent to the reaction. In the mildly hypertensive patient the pulmonary vascular resistance increased during the reaction. The heart rate rose to a normal value, with a diminution in stroke volume, 50 minutes following the reaction. The other parameters exhibited little change during this time. Since hypotension persisted for 95 minutes after the vasovagal reaction, 0.4 mg. of atropine was injected into the pulmonary artery. There was an immediate increase in heart rate above that of the control level, with a slight rise toward normal of systemic arterial pressure. The other parameters did not change initially. Systemic arterial pressure and resistance and cardiac index returned to control levels 45 minutes following the atropine injection. Possible physiologic mechanisms responsible for the observed hemodynamic changes are discussed.

Ross


Measurements of venous return were made in open-chest dogs under combined general and spinal anesthesia, thereby abolishing circulatory reflexes. Hematocrit levels ranging from 9.5 to 65 per cent were produced by bleeding with replacement by either Tyrode’s solution or packed red cells. Venous return varied inversely with the hematocrit, with 36 per cent average increase in anemia, and 37 per cent average decrease in polycythemia. Both anemia and polycythemia caused a decreased “minute flow of red cells,” increased venous return not compensating for the decreased red cell mass in the former, and increased red cell mass not compensating for the decreased venous return in the latter. The curve for peripheral resistance, which varied directly with the hematocrit value, was similar to a curve representing changes in peripheral resistance due to variation in viscosity alone. It was concluded that there is a general correspondence between increased viscosity and decreased venous return, cardiovascular reflexes and tissue oxygen having been negated as influential factors in the experimental data. The effect of the hematocrit level on the venous return and cardiac output of the weakened heart was negligible. The venous return curves, representing various hematocrit levels approached each other at elevated right atrial pressures. It is suggested that increased cardiac output in anemia is due primarily to decreased viscosity of the blood. Local variation in vascular resistance due to diminished availability of oxygen was considered a possible contributing factor to the increased output. The reasons for variations in man that differ from the experimental data for polycythemia are also discussed.


An improved conductivity method for determining cardiac output permitted measurement at short intervals in lightly anesthetized dogs accelerated on a centrifuge. Blood pressure and heart rate were measured and stroke volume and peripheral resistance calculated. Headward acceleration reduced cardiac output and stroke volume and increased peripheral resistance. Transverse acceleration did not affect stroke volume, left cardiac output was the same or slightly increased, and peripheral resistance was reduced. The measurements confirmed clinical observations that circulatory adjustments are more favorable during transverse than headward acceleration.

White

In eight patients subject to orthostatic hypotension observations on cerebral blood flow, cerebral vascular resistance, cerebral arteriovenous oxygen difference, cerebral oxygen delivery, cerebral oxygen consumption, and mean arterial pressure were made in the supine and tilted (head up) positions. The observations in the latter position were made just before signs and symptoms of syncope appeared. Immediately prior to syncope there was a marked fall in mean arterial pressure, cerebral blood flow, oxygen delivery, and venous oxygen content. There was a widening of the arteriovenous oxygen difference, which was thought to be due entirely to a reduction in cerebral blood flow (based on previous studies in which the actual measurement of cerebral oxygen consumption was shown not to have undergone a demonstrable reduction during unconsciousness due to pharmacologically induced hypotension). The cerebral vascular resistance fell consistently. In half the patients there was some decrease in arterial carbon dioxide content, most likely due to hyperventilation preceding the syncope. Cerebral ischemia appeared consistently at cerebral blood flow rates of approximately 30 ml. per 100 Gm. of brain per minute. The blood pressure at which this occurred varied, depending upon cerebral vascular resistance. The finding of persistence of significant levels of oxygen in the cerebral venous blood during the period of cerebral ischemia indicated that the symptoms might be due primarily to oxygen deprivation maximal in relatively small brain areas. In some of these cases this may be related to hyperventilation, which may induce syncope because of marked reduction in cerebral blood flow. This latter may be superimposed upon acute hypotension.


The responses of systemic vascular volume, venous return, and distensibility of the venous bed to alterations in blood pressure mediated by the isolated carotid sinus or vasoactive drugs were studied. The preparations consisted of anesthetized open-chest dogs on cardiopulmonary bypass. Infusion of catecholamines caused a decrease in intravascular blood volume, manifested by a shift of blood to the oxygenator, and increased venous return and distensibility. Trimephapain (Arfonad) caused effects opposite to those of the catecholamines. That venous effects were primarily related to the drugs, and not secondary to arteriolar changes, was shown by administration of acetylcholine, which caused arteriolar dilatation with concomitant diminished intravascular volume and increased venous return and distensibility. Elevation of carotid sinus pressure caused a shift of blood back into the intravascular circuit, with diminution of venous return. Diminution of carotid sinus pressure elicited effects the reverse of those occurring during elevation of the carotid pressure. The changes in venous return necessitated modification of the rate at which the pump perfused the preparation analogous to alterations in cardiac output that would have occurred in an intact preparation. The integrative role of the baroreceptor mechanism in circulatory adjustment is discussed.


The validity of calculations of cardiac output from indicator-dilution curves obtained by use of ear oximeters is dependent mainly on accurate calibrations. The “venous end-tail” method supplies a single point low on the calibration curve, hence any error is multiplied over the whole range of the curve; other potential sources of inaccuracies include instability of the instruments, changes in the ear circulation, and vari-

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ations in arterial oxygen saturation. The authors describe an alternative method based on the assumption that by measuring the absorption of light by the ear in the red and infrared bands separately, and the increase in light absorption in the red band due to the presence of dye in the blood, the concentration of dye in the blood can be predicted. No sampling of blood is necessary to make the dilution curves quantitative, and the method can be applied irrespective of wide variations in ear thickness and pigmentation. Theoretical considerations, electronic circuitry, and calibration procedures are discussed in detail. In a trial of the method, 41 estimations of cardiac output were made in 15 subjects, using Coomassie blue as indicator. Results were compared with those obtained simultaneously by the "end-tail" venous calibration method. Owing to the systematically high values for output obtained by ear oximetry as compared with nearly simultaneous measurements by the direct-Fick method, all values for cardiac output in this study were adjusted using a factor of 0.79. Seven results were excluded owing to obvious inaccuracy of the "end-tail" method. In the remainder there was reasonable agreement, the standard deviation of the differences between simultaneous values by both methods being 14.4 per cent. In a further study, a similar comparison was made in 52 determinations from 17 subjects at rest and during exercise, and the standard deviation of the differences was 14.2 per cent.

MARSHALL


The authors described a method for testing the stimulating effectiveness of linearly rising current. Cardiac muscle, like nerve fibers, spinal neurons and skeletal muscle, has a minimal gradient requirement. Dog trabecular muscles showed great differences in their minimal gradients, even at the same temperature; but the requirements of individual muscles were rather constant. During hypothermia (24 to 27 C) there was a reduction in threshold to stimulation by a rectangular pulse and a great prolongation of the minimal gradient requirement for stimulation, as though a type of accommodative reaction present at normal temperatures had been suppressed. Determination of minimal gradient requirements by exponentially rising current gave the same result as obtained with linearly rising currents. Excitation occurred when the rheobasic strengths, as determined by rectangular pulses of long duration, were attained if stimuli satisfied the minimal gradient requirement.

Kayden

PULMONARY DISEASES


In the first case of the Hamman-Rich syndrome (diffuse progressive interstitial pulmonary fibrosis) the diagnosis could be made at autopsy; in the second case, the gradual spontaneous development differentiated it from tuberculosis, pneumoconiosis, or secondary pulmonary fibrosis in collagenosis. The fact that the enlargement of hilar nodes appeared at the same time as the pulmonary process and showed no further development differentiated it from pulmonary sarcoidosis, while spirometric findings of reduced pulmonary elasticity without signs of pulmonary obstruction or emphysema differentiated it from a congenital cystic lung. In both cases the fibrosis was at first diffuse but later became concentrated in the upper lung fields due to shrinkage. Both cases showed spontaneous pneumothorax, which was described in only two other cases of the syndrome. The first case developed cor pulmonale and died of right-sided heart failure; the second case is still under observation.

LEPESCHKIN


Four cases of pulmonary hypertension are reported in which the elevated pulmonary pressure was thought to be caused by obstruction of innumerable small branches of the pulmonary artery by glomoid lesions arising within the pulmonary arterioles. Proximal to the glomoid lesions the vessels revealed profound sclerosis which seemed to be more intense in the older patients; that is, the intensity of sclerosis was apparently directly related to the duration of the pulmonary hypertension. Distal to the lesion the vessels were apparently normal and exhibited some of the anatomic characteristics of veins which eventually merged with the pulmonary capillaries. These lesions have never been observed in pulmonary hypertension secondary to acquired cardiac or pulmonary lesions, but rather in the overwhelming majority of cases, the lesions were associated with congenital car-
lesions were patients who had not yet developed cardiac failure. The results in 23 cardiac patients were compared with those in 71 patients who had no cardiac failure. Before cardiac failure, the pattern of ventilatory disturbance was typical of the findings in chronic bronchitis and emphysema with reduction in vital capacity, maximum breathing capacity, and a high residual lung volume, but there was no greater severity of ventilatory defect than in a group of 71 other patients with chest disease without heart failure. In contrast, the carbon dioxide tension and arterial oxygen saturation in 20 of the cardiac patients before heart failure was often more severely abnormal. Abnormal blood gas values existed for months or years before signs of heart failure were elicited, but worsened during the latter period. Studies before, during, and after heart failure revealed remarkably little fluctuation in ventilatory function. Carbon dioxide tension and oxygen saturation, however, were slightly less abnormal before the last recovery from heart failure. Electrocardiographic abnormalities were found in 13 of 17 patients examined before the onset of heart failure. A "P pulmonale" and an abnormal QRS complex in V1 preceded the development of heart failure. A normal mean glomerular filtration rate and a reduced renal plasma flow with a high normal filtration fraction were found in 11 patients before heart failure was present. These changes persisted during and after heart failure.

KURLAND

RENAL AND ELECTROLYTE EFFECTS ON THE CIRCULATION


Endocrine kidney operations were performed on rats by partially ligating the aorta between the 2 renal arteries. The left ureter was subsequently ligated and transected. When certain sodium salts, such as Na2HPO4, Na2SO4, or NaClO3 were given by stomach tube, massive and often fatal myocardial necrosis occurred. None of the sodium salts tested had any influence upon the myocardial hyalinization or periarteritis nodosa normally seen as a result of the endocrine kidney itself. Most of the non-sodium salts with the exception of KCI and CaCl2 are devoid of toxicity when applied conjointly with the endocrine kidney. The compounds known to protect the heart against the combined effect of electrolytes and steroids are completely inactive, if the myocardial lesions are produced by the endocrine kidney plus electrolytes.

KALMANSOHN


The diuretic and antihypertensive properties of the benzothiadiazine compounds (e.g., chlorothiazide) were separated by synthesizing 2,4-dichloronitrobenzene a compound devoid of the benzenoid sulfamyl group. The resulting 7-chloro-3-methyl-1,2,4-benzothiadiazine-1,1-dioxide was administered orally at a dose of 5 mg./Kg. per day to renal hypertensive dogs. Blood pressure fell gradually in 2 to 6 days and remained low for the duration of study (12 days) without evidence of diuresis. After withdrawal of the drug, blood pressure returned to pretreatment levels in 3 to 6 days. Similar effects were obtained in metacorticoid hypertensive rats and in clinical trials. The sulfamyl group appears to be intimately related to the diuretic but not the antihypertensive properties of this group of drugs.

WHITE

RHEUMATIC FEVER


The effectiveness of available therapeutic agents for the control of streptococcal infections has made possible the prevention of rheumatic fever and glomerulonephritis. The prevention of first attacks of rheumatic fever cannot be entirely successful because of the large numbers of asymptomatic infections, but it is hoped that this problem will ultimately be solved with the
development of an appropriate vaccine. Recurrent streptococcal infections in patients who have previously had rheumatic fever may be prevented by antibiotic therapy; the most effective prophylactic agent has been shown to be repository injections of benzathine penicillin, but, in addition, oral penicillin or sulfadiazine is also quite effective. Prophylactic antibiotics should be given to those patients with a clearly established history of rheumatic fever and should be continued for at least 3 years, and preferably 5 years after the acute episode; the use of continual prophylaxis appears to be preferable to identification and therapy of streptococcal infections as they occur. Prophylaxis is not required in the therapy of patients suffering from acute glomerulonephritis, since these patients are not susceptible to recurrences of the disease when reinfected with hemolytic streptococci. Subacute bacterial endocarditis may be prevented if bacteremia is avoided. Bacteremia most commonly occurs following dental manipulation, tonsillectomy, urethral manipulation, parturition, and following cardiac surgery; in these situations one of several antibiotic regimens (mainly utilizing penicillin) may be given for prophylaxis.

KARPMAN


One hundred sixty-three patients who were referred with a diagnosis of acute or chronic rheumatic fever were studied. The diagnosis was substantiated in 144, or 88 per cent, according to the modified Jones criteria. In the other 19, or 12 per cent, diagnostic errors had been made. Eleven of them had minor self-limiting illnesses such as accentuation of a physiologic murmur during an infection that led the physician to interpret it as rheumatic cardiac involvement; sporadic elevations of sedimentation rate with ventricular premature contractions, misinterpretation of a rise in antistreptolysin titer as being diagnostic of rheumatic fever; sporadic elevated temperatures orally that vanished when rectal temperatures were taken; joint symptoms in emotionally disturbed children with no objective evidence clinically or on x-ray of arthritis; osteomyelitis mistaken for rheumatic fever; occasional low-grade fever with sporadic joint pains; and a change in the intensity of systolic murmurs after exercise, which is often seen in normal patients. Eight patients had major illnesses incorrectly diagnosed as rheumatic fever. These included congenital heart lesions with associated infections; bony inflammations especially of the distal part of long bones; subendocardial fibroelastoses; lupus erythematosus; acute and chronic glomerulonephritis; and subacute bacterial endocarditis. To eliminate these errors, the authors suggest not only a thorough knowledge of the Jones criteria, but proper application of them. Evidence of a preceding group-A streptococcal infection should be made a prerequisite to the diagnosis of rheumatic fever. Streptococcal evidence can often be obtained from an initial throat culture and an antistreptolysin-O titer. If these are initially negative, positive results can be sought by serial determinations. If serial studies fail to demonstrate a significant change in the antibodies, this is strong evidence against a preceding streptococcal infection and makes the diagnosis of rheumatic fever unlikely. If the public health authorities provided facilities for these tests and made them available to physicians this would help to decrease the errors in the diagnosis of rheumatic fever.

KRAUSE


Four hundred ninety-seven children (257 from the United States and 240 from the United Kingdom) under 16 years of age with rheumatic fever were divided into three groups for treatment and study over a 5-year period. One group was treated with aspirin, one with ACTH, and one with cortisone in an effort to determine which method of treatment, if any, was superior in preventing recurrence of rheumatic fever or rheumatic heart disease. Group A (at the beginning of treatment) included those children with no or questionable carditis but no pre-existing heart disease. Group B patients included those with carditis but no pre-existing heart disease. Also included in group B were patients with cardiac status ranging from grade I systolic murmurs to those having pericarditis or failure. Group C was composed of patients with pre-existing heart disease with or without failure or pericarditis at the start of treatment. Of the 497 children treated and studied, 445 were followed for the complete 5 years. At the end of the 5-year period the cardiae status of 426 was known. Sixteen or 3.2 per cent had died (14 from rheumatic heart disease). Thirty-six or 7.2 per cent of the original 497 cases were untraced. The prognosis was not influenced more by one drug than another. The most important determining factor relative to the occurrence of
Rheumatic heart disease at the end of the 5-year period was the cardiac status at the beginning of treatment. In cases without carditis initially, the prognosis was excellent, since in 96 per cent there was no residual heart disease. In cases with carditis initially, but without pre-existing heart disease, the proportion without residual heart disease decreased progressively from 82 per cent for those with only a grade-I apical systolic murmur to 30 per cent for those with failure or pericarditis. Thus, the cardiac status must be carefully evaluated and taken into account in attempting to evaluate treatment of acute rheumatic fever.

Krause

ROENTGENOLOGY


Of 2,400 translumbar aortograms performed in the Baylor University College of Medicine Affiliated Hospitals, only six deaths could be attributed to the procedure. No deaths occurred in the last 1,625 studies. During this latter period the procedure was standardized to no more than one injection of 30 ml. or less of 70 per cent Urokon sodium into that part of the aorta several centimeters proximal to the celiac axis, the patient being well hydrated during the procedure. Renal damage and aortic dissection comprised earlier complications. Occlusive disease in the aortoiliac region constituted the major indication for study, although renal hypertension and abdominal angina were receiving increasing attention. Abdominal aneurysms rarely required this study.

White


The authors collected and illustrated by case reports the various causes of a false-positive roentgen diagnosis of internal carotid artery occlusions. These include narrowing of the lumen caused by subintimal injection of the contrast agent or subintimal hematoma from the trauma of the puncture per se, extravascular injection of the contrast medium, puncture of the external carotid artery, especially likely when the carotid bifurcation is low in the neck, distal internal carotid artery occlusion, and pseudo-occlusion associated with a sudden increase in intracranial pressure. Subintimal injection of part of the contrast medium occurred in some instances even though a good pulsatile backflow of blood was obtained. The authors suggested that this error may be reduced, if one observes the return of blood into the plastic tubing after it has been rapidly cleared with saline. If the returning blood is diluted with saline and therefore pale, one may suspect that the needle point lies in a subintimal position. Serial films will show retention of the contrast agent in a subintimal pocket or a fine negative line within the lumen of the artery representing the stripped intima. A subintimal hematoma can be recognized on the film by a localized negative filling defect in the lumen of the artery at the point of puncture. Distal internal carotid artery occlusions can be differentiated from apparent occlusions in the neck by taking films at 8 to 12 seconds when delayed filling will be observed. Pseudoocclusion associated with a sudden increase in intracranial pressure usually occurs in comatose or moribund patients and is probably due to alterations in cerebral blood flow. Difficulties in demonstrating partial occlusions may be overcome by taking films in multiple projections.

Luchi


Chest x-rays (70 mm.) were taken in the posteroanterior projection and interpreted by a cardiologist and a radiologist as a method of screening patients for cardiovascular disease. Of these films 11.3 per cent were interpreted as suspect for cardiovascular disease. Of those patients referred to their physicians for further evaluation, 67.4 per cent were found to have cardiovascular disease. The cardiologist demonstrated a higher case-finding ability than the radiologist without a statistically significant drop in the percentage of confirmations. Arteriosclerotic heart disease, hypertensive heart disease, and a combination of these two constituted 88.7 per cent of all confirmed patients and 86.6 per cent of the new patients.

Kalmansohn


The author has had 7 years of experience with translumbar aortography and 4 years with percutaneous aortography from the femoral artery.
In general, the latter method is preferable for all arteriographies in the abdominal region unless there are signs of organic circulatory disturbances in the region of the iliac or femoral arteries. In this case low translumbar aortography is preferable, since introduction of the catheter from the femoral artery may lead to traumatic thrombosis or embolism through dislodgment of atherosclerotic plaques. In one patient the tip of the guiding wire became wedged in an atherosclerotic region, broke off, and remained in the arterial wall.

LEPESCHKIN

SURGERY AND CARDIOVASCULAR DISEASE


The results of surgical treatment in 27 patients with pulmonary atresia were described. All of the successful procedures were anastomotic; unfortunately, in some cases, no artery suitable for anastomosis was found. The high operative mortality rate in some patients was thought to be because of the division of collateral vessels. Fifteen per cent obtained extremely good results and 22 per cent good results. Operation is advised only if the heart is not much enlarged and some pulmonary artery is seen on radiography or angiocardiography. The good results have been maintained for the 6 to 7 years that have elapsed. One patient died of cerebral abscess following bacterial endocarditis and one patient died of pulmonary tuberculosis.

KALMANSOHN


Ninety-four cases of aortoiliac atherosclerotic disease were reviewed. All patients were treated with aortoiliac endarterectomy with and without bilateral lumbar sympathectomy. The follow-up period ranged from 1 to 71 months, with a mean of 30 months. The technic used was described in detail and individual results for each patient were presented in graphic form. In sixty cases with no clinically detectable distal involvement, 97 per cent of the patients had normal femoral pulses in the immediate postoperative period. In the remainder, a similar result was obtained in 68 per cent of the group. The immediate mortality, however, was 2 per cent for the first group and 12 per cent for the latter group. In the favorable group, one death followed development of a false aneurysm in a femoral arteriostomy wound. The one poor result occurred 2 months following surgery; thrombosis occurred on one side in the external iliac artery. A good result was "salvaged" by a plastic graft placed across the occluded segment. The three nonoperated deaths were due to myocardial infarction, carcinoma of the pancreas, and 1 from unknown cause 6 years postoperatively. In 16 of these patients, femoropopliteal involvement was subsequently manifested by signs of pulse diminution and recurrence of claudication in the presence of strong femoral pulses. In seven additional patients there was diminution of femoral pulsations, which was usually preceded by a diminution in pedal pulses. The authors interpreted this as evidence of progression in the basic disease process. In these patients there was no symptomatic change or they maintained a pronounced improvement over the preoperative status. In the unfavorable cases, there were four operative deaths. Operations were extensive and time consuming; there were four cases of postoperative amputation. There were an additional two deaths in the late postoperative period. Additionally, there was diminution or loss of femoral pulses in nine patients in the postoperative period. The authors attempted to control the development and progression of the basic disease by advising a diet low in fat and excess carbohydrates, which they invariably found to lower the blood cholesterol. They recommended weight reduction to their lowest "healthy" adult weight.

SHERS


The authors believe that the combination of cardiopulmonary bypass with deep hypothermia has a wide field of application, particularly for lesions associated with extensive bronchial circulation or in circumstances in which elaborate or prolonged surgery is required. The heat exchanger used permits the body temperature to fall to 10 C. in 20 minutes, irrespective of the perfusion rate. The method has been applied to the treatment of large ventricular septal defects with pulmonary hypertension, Fallot's tetralogy, complex forms of pulmonary stenosis, atrioventricular canals, and lesions of the aortic and mitral valves. It should permit surgical intervention in lesions that are still often regarded as inoperable, such as coronary artery disease and transposition of the great vessels, and may facilitate the insertion of plastic valves. Extra-
cardiac indications include certain diseases of the aortic arch, great vessels, and brain; examples of such successful applications are cited.

**MARSHALL**


Observations were made on 92 patients subjected to pulmonary valvotomy or infundibulectomy. The results with the transventricular closed method were considered unsatisfactory. The results of infundibulectomy were not fully satisfactory by transventricular or transarterial routes and such patients were thought to be best operated on by the use of cardiopulmonary bypass. If the lateral selective angiocardiogram showed a full opening of the outflow tract in diastole and early systole and there was no evidence of organic infundibular obstruction to the palpating finger, infundibulectomy was not performed even in the presence of residual ventricular-arterial gradient. Sixty-one patients had transarterial open pulmonary valvotomy at normal temperatures by occlusion of the venae cavae and pulmonary artery for 3-minute periods, not to exceed three occlusion periods; there were three operative deaths. The procedure was thought to be adequate for valvular stenosis and some cases of infundibular stenosis but not for correction of all the defects in patients with tetralogy of Fallot.

**KALMANSOHN**


In 124 cases of unruptured aneurysm of the abdominal aorta treated surgically since 1953 with elective resection and graft replacement the mortality was 9.6 per cent (12 patients). Of 26 patients with frank rupture of an abdominal aortic aneurysm 42 per cent were saved by vigorous emergency surgical therapy. The obviously far lower mortality rate of elective surgery argues strongly for the consideration of elective surgical excision and graft replacement in patients with asymptomatic aneurysm of the abdominal aorta.

**SAGALL**


The 20 patients studied were aged 8 to 21 years, and had had resection and end-to-end anastomosis of an aortic coarctation 2 to 7 (mean 4) years previously. The blood pressure was measured simultaneously in the brachial and femoral arteries at rest and during fairly severe exercise (pulse rate 170 per minute). Angiography was performed under light anesthesia by injecting contrast medium into the pulmonary artery or right ventricle (17 cases), left atrium (one case), or thoracic aorta (two cases). The aortic lumen at the site of the anastomosis was calculated from biplane films, exposed during systole, and related to the lumen of the aortic arch (index I) and to body surface area (index II). Of the cases with a normally developed aortic arch all but one had an abnormally low index I. Index II was abnormally low in 17 cases and equivocal in three. The mean systolic pressure gradient between the brachial and femoral arteries varied from -20 to +43 mm. Hg at rest and averaged +12 mm. Hg. There may be no significant systolic gradient at rest even in cases in whom the lumen at the site of anastomosis is reduced by 75 per cent. During exercise the systolic gradient increased to +8 to +94 (mean +47) mm. Hg. These findings indicate that pressure measurements during exercise provide a more reliable index of residual stenosis than do those during rest.

**MARSHALL**


Some considerations in the conduct of anesthesia for patients having cardiovascular surgery at The New York Hospital were presented. The anesthesiologist became acquainted with the patient at a presurgical conference and at a preoperative visit. Preanesthetic medication consisted of 0.2 mg. of atropine sulfate in cases of acquired disease and additional short-acting barbiturate in those with congenital deformities. Anesthesia was induced with a small amount of thiopental sodium followed by nitrous oxide and then ether and oxygen. The lightest possible plane of anesthesia was used in order to avoid hampering bodily functions. A deeper plane of anesthesia was sought to combat hypertension occurring when the aorta was cross-clamped in some cases of coarctation, and occasionally Arfonad was injected to lower the blood pressure further. During open-heart surgery no anesthetic was ordinarily given and no pulmonary ventilation carried out in the bypass period, and
apnea was induced by d-tubocurarine 0.4 mg. per Kg. Arterial blood pressure, systemic venous pressure, electrocardiogram, electroencephalogram, and rectal temperature were monitored and recorded routinely, and blood pH and oxygenation were checked periodically. Potassium citrate or anoxia-induced cardiac arrest was employed for correction of lesions involving the left heart, and cardiac stimulation or defibrillation was sometimes needed thereafter. Weighing the patient before and after operation helped to determine the adequacy of blood replacement. Postoperatively, an oxygen-rich atmosphere was maintained. Only small doses of codeine or meperidine were used, and occasionally there was a need for mechanical assistance to ventilation for a few hours.

Rogers


Ten patients with rheumatic mitral stenosis and who were pregnant were operated upon by the transventricular route by a mechanical splitter to aid in freeing the mitral stenosis. All 10 patients' conditions had deteriorated progressively during their pregnancy and all had pulmonary congestion. In addition, some had pleural effusions as well. In each instance mitral stenosis was confirmed at surgery. Nine of the patients had an immediate excellent result and one patient died 18 hours after surgery. Of the nine patients, four who had been totally incapacitated prior to surgery, were able to resume moderate activities during the remainder of their pregnancies. The other three patients, who were not seriously incapacitated preoperatively, were able to continue a full regime of activity for the remainder of their pregnancies. The authors think that, if surgery is indicated during pregnancy for correction of mitral stenosis, it should be performed early, prior to the thirtieth week. Surgical relief of mitral stenosis during pregnancy is a safe and valuable procedure for those patients whose condition progressively worsened, especially when it reached grades III and IV.

Krause

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