PATHOLOGIC PHYSIOLOGY

The effects of mercurial diuretics are susceptible to changes in acid-base balance. To study the mechanisms involved dogs were made acutely alkalotic by the infusion of sodium bicarbonate. A refractoriness to mercurials was noted. However, when alkalosis of a similar degree was produced by potassium depletion the diuresis was normal or increased. It would appear that factors other than the filtered chloride load determine the effectiveness of mercurial diuretics. The authors think it likely that tubular pH plays an important role. An in-crease in the acidity of the tubular cells may facilitate the interaction of a cellular constituent and the mercurial.

WAIFE


Although there are many reports in the literature describing the histopathologic effects of thermal injury, there are few reports describing the circulatory responses. In view of this, the present study was initiated in order to define some of the hemodynamic responses to thermal radiation.

The parameters measured were cardiac output by the dye injection technic, arterial pressure, right atrial pressure, plasma volume by the T-1824 technic, hematocrit, blood volume, heart rate, and plasma proteins. After control determinations, shaved areas of anesthetized dogs were exposed to a burn apparatus for varying periods of time (average 70 sec.) to give a 30 per cent surface area burn. Following the burning, determinations were made at 1/4, 1, 3, 6, and 12 hours. All dogs were autopsied and histologic studies made.

Third degree burns were produced in this way. Thermal radiation decreased mean arterial blood

SCHERF

pressure (24 mm. Hg) at 15 min. After this the pressure rose until the sixth hour and then gradually fell to the 15 min. post-burn level. There was no significant change in right atrial pressure until 3 hours post-burn when a gradual inconsistent decline started and continued. Heart rate decreased at 15 min., but increased above control levels thereafter. Thermal radiation decreased cardiac output to 45 per cent of the control at 15 min., 37 per cent at 1 hour, and 21 per cent at 12 hours. Hematocrit increased 15 per cent above the control at 15 min. and a maximum of 50 per cent at 12 hours. Hemolysis was observed, so that hematocrit was probably not a true measure of hemoconcentration. Plasma volume was lowered 19 per cent at 15 min., 27 per cent at 6 hours, and 37 per cent at 12 hours. There were no consistent changes in plasma proteins. Albuminuria and hematuria were found. Hypothermia, reaching a maximum 12 hours after burning, occurred in most dogs. All animals died from 6 to 21 hours after burning. Death usually occurred precipitously. Control studies without burns were accomplished and failed to produce the changes noted above. Hemodynamic responses of 14 dogs to a severe third degree 30 per cent surface area burn are described. Plasma volume loss is not the initiating factor of burn shock and the possibility of a toxin as this initiating factor is discussed.

WECHSLER


Attempts to activate the Bezold-Jarisch reflex (bradycardia, vasodilatation and apnea) with anything other than foreign chemicals have proved unsuccessful. One must therefore conclude either that the responsible nerve elements are normally activated by unknown chemical agents or that they are not a true chemoreceptor system but are only the manifestation of an accidental stimulation of normal pressoreceptors by certain foreign chemicals. The latter view is not compatible with the fact that veratridine, 1 of the most potent stimulators of the Bezold-Jarisch reflex, did not affect 1 of the most sensitive known baroreceptors, the carotid sinus. The present study was undertaken to explore the possibility that this result occurred because of the peculiarities in the blood supply of the carotid baroreceptors. Another point of some interest was the explanation for the occasional occurrence of vasodilatation after intracarotid injection of veratridine following section of Hering's nerve.

Respiration, femoral blood pressure and heart rate were recorded in anesthetized dogs. The aortic depressor nerves were cut. Carotid pressodenervation (by cutting fibers between carotid sinus and carotid body) and additional chemodenervation (by cutting Hering's nerve) were accomplished. Injections were made into the following (a) cannula in femoral vein, (b) plastic catheter inserted through external jugular into the right atrium, (c) plastic catheter through a parietal burr hole into the extradural space, (d) cannulated vertebral artery supplied continuously with blood from a femoral artery, (e) needle cannula in central end of superior thyroid artery, and (f) needle cannula into lingual artery.

The results obtained in these studies confirm the ability of veratridine to activate the pressoreceptors of the carotid sinus. The inability of veratridine to elicit a response, when administered into the lumens of the carotid sinus, can now be explained on the nature of the blood supply to the pressoreceptors. Two intracranial reactive areas have been demonstrated, a stimulatory area, probably medulla accessible to vertebral and intracranial injections and an inhibitory area, probably meningeal receptor, accessible to occipital artery and extradural injections. Both areas can affect respiration, heart rate, and arterial blood pressure. The fact that veratridine can activate pressoreceptors in the carotid sinus lends support to the belief that the drug reflexes (Bezold-Jarisch reflexes) from the heart and lungs are arising from previously described cardiopulmonary pressoreceptors.

WECHSLER

PHARMACOLOGY


Blood flow in the dog's superior mesenteric artery was measured with an electromagnetic flowmeter. In view of the fact that the resistance to blockade (to Ilidar) of the constrictor responses to splanchnic nerve stimulation corresponded more closely to intra-arterial injections of norepinephrine than to epinephrine, it would appear that the mediator of the neurogenically induced vasconstriction is more likely norepinephrine. Since atropine was without effect on the apparent mesenteric dilator responses to nerve stimulation, the presence of cholinergic dilator fibers in the splanchnic nerves was not demonstrable.

AVIADO


The above anticoagulant produces a decline in blood pressure when given intravenously to cats in doses ranging from 5 to 90 mg./Kg. Concomitant with the decline in blood pressure there is an increase in respiratory rate and depth. The hypotension appears to be the result of rapid vasodilation.
that has been described following dicumarol administration in dogs.

**AVIADO**


Reserpine and alderoxylin are markedly effective in antagonizing emesis in dogs induced by apomorphine, morphine, and ergot, but ineffective against emesis induced by veratrum and copper sulfate. Like chlorpromazine, the rauwolfia alkaloids appear to depress the chemoreceptor trigger zone in the medulla, which is the site of action of central emetics. Another point of similarity is depressant action on the hypothalamus of both drugs which is related to the hypotensive action of the rauwolfia alkaloids. It may be worthwhile to try these alkaloids as antiemetic agents in certain pathologic conditions, especially if they are associated with hypertension, as in toxemia of pregnancy.

**AVIADO**


Ajmaline and serpentine, 2 alkaloids of *Rauwolfia serpentina*, have been found to be more active than quinidine in the following tests: (1) refractory period of isolated rabbit atria, (2) atrial fibrillation evoked in dogs by acetylcholine or acenitone, (3) atrial flutter produced in dogs by the injury-stimulation procedure, and (4) hydrocarbon-epinephrine-induced ventricular arrhythmias in dogs. Although projection of results from animal experiments to man is attended with hazards, it is suggested on the basis of these observations that ajmaline shows sufficient promise to warrant clinical trials in selected cases of cardiac arrhythmias.

**AVIADO**


Sodium salicylate, aspirin, and methyl salicylate uncouple oxidative phosphorylation in liver, kidney, and brain mitochondrial preparations. The uncoupling action is qualitatively similar to that seen with the classical uncoupling agent, 2,4-dinitrophenol. The concentration of salicylates used in these studies is comparable to toxic levels in the intact animals. No attempt is made to relate these in vitro effects with the specific pharmacologic actions of the salicylates such as antipyresis, analgesia, or antirheumatic action. It is suggested that the toxic symptoms associated with salicylate overdosage could be attributed to the ability of this class of compounds to uncouple oxidative phosphorylation.

**AVIADO**


Renal protein-bound sulfhydryl concentrations were studied by a quantitative histochemical method. Mersalyl lowered the concentration of sulfhydryl cells of the terminal portions of proximal tubules, ascending limbs of the loops of Henle, and collecting ducts. BAL effectively counteracted mercurial diuresis and simultaneously restored sulfhydryl concentrations to control levels. These data parallel results previously obtained in rats and thus strengthen the view that the mechanism of mercurial action is somehow related to sulfhydryl systems, which in turn may actively support a renal transport mechanism. Protein-bound sulfhydryl could represent a large group of enzyme systems related to energy production or it may be a necessary component of the carrier substance postulated for the transport of electrolytes across membranes.

**AVIADO**


After its local intra-arterial administration in the hind limb of dogs, dibenzyline can produce a local blockade without any evidence of a systemic blockade 24 hours after administration. Cross-circulation experiments reveal that the sojourn of an effective concentration of the drug in the donor cats circulation is no longer than 7 hours and was always incompletely transferred to the recipient cat. It is concluded that the long duration of action of this adrenergic blocking drug (peripheral vasodilator) is not due to its storage in body fat but is due to a firm chemical combination of the drug with a cellular receptor substance.

**AVIADO**


Hepatic cholesterol synthesis in rabbits, as measured by the incorporation of C14-labeled acetate, was inhibited by addition of nontoxic amounts of vanadyl sulfate to the diet. This diet reduced excess aortic cholesterol in cholesterol-prefer rabbits when fed during a 6-week period. In both control and vanadium animals, following the cholesterol-prefeeding period, there is an almost complete mobilization of excess cholesterol from the various tissues except the aorta. During this period of time a
homeostatic effect is causing decreased hepatic cholesterol synthesis. When the concentration of hepatic cholesterol has been reduced toward normal in the control animals, there is a resumption of normal hepatic synthesis. Consequently, the degree of negative cholesterol balance is markedly lessened and mobilization of excess aortic cholesterol proceeds very slowly. In the vanadium-fed animals, however, this resumption of normal cholesterol synthesis is inhibited by the vanadium with maintenance of a negative cholesterol balance and resultant mobilization of more aortic cholesterol.

BERNSTEIN


Dubois used nitrogen mustard in patients with lupus and renal impairment. The benefit seemed to be greatest in edematous patients. The 31-year-old female patient described by the author had a long-standing recurrent picture interpretable as lupus: polyarthritis, generalized edema, blood urea nitrogen of 50 mg./100 ml., Krupp's telescopic urinary sediment, LE cells in the peripheral blood. Both cortisone and ACTH produced general clinical deterioration and severe mental disturbance without diuresis. The blood urea rose to 140 mg./100 ml. Within 2 days of nitrogen mustard therapy there was a marked diuresis. The patient became edema-free and the blood urea fell to 25 mg./100 ml. The patient was able to return to doing her own housework but there was still a trace of albuminuria, elevated erythrocyte sedimentation rate, and blood cholesterol of 550 mg./100 ml.

McKUSICK


Seven case reports are given to indicate the therapeutic effectiveness of a carbonic anhydrase inhibitor (acetozolamide) as an aid in the care of patients with chronic renal disease and patients with an increase in the level of serum potassium. The urinary excretion of potassium is increased. With repeated administrations of the drug, precautions must be taken to prevent an increase in metabolic acidosis.

RINZLER


Acetyl-digitoxin by mouth was used in the therapy of 166 patients in congestive heart failure and was demonstrated to be a well-tolerated and effective new digitalis glycoside. Sixty-two of these patients were hospitalized and 104 were followed daily or every third day as ambulatory patients.

The initial digitalizing dose can be given as a single dose or over a period of several days. The amount required must be adjusted for the patient, and usually varied from 1.6 to 2.0 mg., averaging 1.84 mg. In the single-dose method, 1.6 to 1.8 mg. was well tolerated, but occasionally supplementary amounts were necessary for full digitalization. Maintenance was also effective, and most patients could be maintained on 0.1 to 0.2 mg., the average being 0.15 mg./day. The excretion is slow, but appears somewhat more rapid than that of digitoxin. Toxic effects disappeared generally in 1 to 3 days, but the total elimination of drug effect from patients in atrial fibrillation required 13 to 17 days. Toxic effects were generally deliberately attained, and consisted of gastrointestinal symptoms in the majority of patients. There were no serious arrhythmias and no fatalities that could be ascribed to the drug. It appears that acetyl-digitoxin will attain merit as a long-acting glycoside that is well tolerated even in single digitalizing dosage by mouth and that is effective therapeutically. It has the advantage over digitoxin of somewhat more rapid dissipation, and toxic effects are usually gastrointestinal symptoms instead of potentially dangerous arrhythmias.

RINZLER


It has previously been found that hypothermic rats treated with lanatoside C show less disturbances of rhythm during hypothermia. In dogs some beneficial effects of digoxin on right heart failure during hypothermia have been observed.

The authors studied 8 cats to determine the effect of digitalis glycosides during hypothermia. The animals were anesthetized with ether and pentobarbital sodium, 30 mg./Kg. In 4 animals serving as controls without hypothermia 12 ml. of Digilanid were infused. In the second group of 4 animals, cooling of the body with ice and water was employed. The temperature fell from 37-37.5 C. to 20-20.5 C. within 35 min. Digilanid was then given in the same amount as to the controls. The dosage required to produce cardiac arrest was found to be significantly higher during hypothermia.

The authors conclude that the observed changes in the RST segment and flattening of an inverted T wave during digitalis infusion signify a beneficial effect on the heart. An increase of the potassium content of the heart muscle following administration of therapeutic doses of digitalis is considered responsible.

SCHEF

Bellet, S., Wasserman, F., and Brody, J. I.: Further Observations on the Cardiovascular Effects of

The effect of intravenous molar lactate was studied in 5 normal patients and in 27 patients with various conditions including partial A-V heart block, sinus bradycardia, carotid sinus sensitivity, and premature contractions. The effect of the infusion of 100 to 200 ml. of M sodium lactate upon the electrocardiogram, serum sodium, potassium, calcium, chloride, and blood pH was determined. Electrocardiographic changes were observed in patients with slow rates occurring with sinus bradycardia and A-V heart block. An increase in heart rate was observed in these patients with maximum changes being noted at or within a few minutes after completion of the infusion. Narrowing of widened QRS deflections was noted in 8 instances in this series. Carotid sinus sensitivity was unaltered in 4 subjects by lactate infusion. In 3 subjects, ventricular extrasystoles were observed during the course of the infusion; these patients had advanced heart disease and 1 was noted to have digitalis toxicity. In 1 other patient without heart disease extrasystoles disappeared following lactate.

The possible mechanisms involved in the effect of sodium lactate upon the heart are not clear. A mild alkalosis manifested by an increase in pH and CO2 combining power is noted regularly; electrolyte changes include a rise in serum sodium and a fall in potassium and calcium levels. The serum sodium increments are minor in degree and develop slowly. Whether the electrolyte shifts influence heart rate or whether the utilization of lactate itself by the myocardium is responsible for the observed cardiovascular effects cannot be stated at this time.


Three patients were studied following the appearance of hemorrhagic symptoms while receiving salicylate therapy. Hematemesis, melaena, and excessive bleeding from biopsy site were the manifestations observed. A battery of studies of the hemostatic mechanism was performed in each instance. All patients were found to have a positive Rumpel-Leeds test and abnormal bleeding time. No significant change in prothrombin time was noted. Interruption of salicylate therapy corrected the abnormal findings. Retreatment in 2 instances produced a recurrence of abnormal bleeding times and capillary fragility. The author concludes that salicylate represents an important factor to be considered in cases of acquired hemorrhagic diathesis.


Mercaptoprimer sodium (Thimerin) was made available in suppository form in cocoa butter containing equivalent to 165 mg. of mercury in each dose. This preparation was administered to 23 patients under treatment for congestive heart failure receiving digitalis and previously given parenteral mercurial diuretics. In 5 instances, a double blind method was used. The effectiveness of suppository treatment was based on clinical findings and comparison of the number of weekly injections of mercurials before, during, and after its use. The mean parenteral mercurial requirement before suppository treatment was 1.2 injections/week. On an average of 7.3 suppositories/week, the mean number of injections decreased to 0.5/week. When suppositories were stopped, the injections increased to 1.2/week. The clinical response on suppository therapy was not significantly changed from that observed with mercurial injection therapy. The suppository treatment was not associated with local toxic or irritative effects despite prolonged use. It is concluded that mercaptoprimerin suppositories are effective in reducing or eliminating the need for parenteral mercury in the treatment of congestive heart failure.


Electrolyte studies were carried out in 2 normal adults. The observations indicate that recovery from the effects of the ingestion of the oral diuretic, Diamox, proceeds along mechanisms seen in other forms of metabolic acidosis. An exchange of Na+ or K+ for the secreted H+ occurs; in this study 75 per cent of the increased H+ excretion during recovery was associated with fixed cation conservation. It is also possible that chloride ion is withdrawn together with H+, and is replaced by the bicarbonate ion.

The actual time needed for full recovery from the effects of this diuretic depends on the relative magnitudes of the original buffer depletion, and on the rate at which excess H+ can be secreted by the renal tubules. The total buffer decrement caused by Diamox under the conditions of this study ranged from 250 to 400 mEq. There is evidence that 2 to 4 days are needed for electrolyte recovery from an initial single dose of the drug, and 5 to 6 days for full recovery from a series of doses.

The time of onset of the first heart sound is related to the simultaneous electrocardiogram in subjects with mitral stenosis, mitral insufficiency, and heart disease without mitral valve disease. A delay in the first heart sound occurred in patients with only mitral stenosis and proved of diagnostic value. The degree of delay paralleled the severity of the mitral stenosis. The mechanism by which the first sound is delayed in mitral stenosis can be readily explained by the hypothesis that the first heart sound is caused by sudden tensing of the atrioventricular valves and chordae tendineae when the atrioventricular septum is pushed in the direction of the atrium. In mitral stenosis, the left atrial pressure is high, while the end diastolic pressure in the left ventricle is low. The mitral valve does not close until the left ventricular pressure exceeds that of the left atrium. This disparity of pressures in the atrium and ventricle is found consistently in mitral stenosis. Significant shortening of the Q-first sound interval occurs with successful enlargement of the mitral orifice. Ventricular contraction does not contribute to the audible portion of the first sound. Moreover, this sound probably arises chiefly in the mitral rather than in the tricuspid valve. The length of the interval between the second sound and the opening snap of the mitral valve is generally inversely related to the severity of the mitral stenosis. This interval lengthens with successful mitral surgery. The presence of an opening snap is of great diagnostic significance. It is a more frequent finding in severe mitral stenosis than is a diastolic murmur.

Although the electric-mechanical intervals were determined by needle puncture of the ventricle at operation, this same information may be obtained by the simple, nonhazardous method of recording the apex impulse. The onset of the systolic deflection of the apex beat coincides perfectly with the ventricular pressure rise determined directly.

**Harris**


Normal and pathologic conditions resulting in splitting of heart sounds are reviewed. The influence of respiration on splitting of the second sound can assist in identifying the type of bundle-branch block present and in distinguishing true splitting of heart sounds from simulating conditions. Arterial hypertension is not a cause of splitting of heart sounds. Asynchronism of valve closures is the fundamental basis for splitting of heart sounds and may have 2 general bases designated as electric (asynchronism resulting from ventricular activation abnormality as in bundle-branch block, ventricular extrasystoles, and idioventricular rhythm) and mechanical (asynchronism resulting from discrep-

aney in ventricular stroke volumes, as in atrial septal defect, or in rate of ejection, as in mitral and aortic regurgitation). In a patient over 40 years old, without other evidence of heart disease, striking inspiratory splitting of heart sounds suggests respiratory disease that is accompanied by exaggeration of intrapleural negativity of pressure during inspiration. Early and late systolic clicks and the mitral opening snap are the conditions most likely to simulate splitting of heart sounds.

Splitting of heart sounds is of limited diagnostic value in the pathologic states with which it may occur: interatrial septal defect, bundle-branch block, mitral or aortic regurgitation, and respiratory disease resulting in exaggerated cyclical variations in intrapleural pressure. In general, splitting has more significance (1) when it occurs in adults, (2) when splitting is exaggerated with expiration rather than with inspiration (left bundle-branch block), (3) when there is no clinical evidence of respiratory disease and labored respirations, and (4) when it persists throughout all phases of respiration (as is usually the case in interatrial septal defect).

**Harris**


The venous hum, a physiologic extracardiac murmur, heard in a high percentage of children and in some adults, is characteristic of a continuous murmur with accentuation during diastole. The venous hum is louder with the subject in the sitting or erect position and diminishes or usually disappears altogether in recumbency. With the stethoscope on the point of maximum intensity over the jugular vein, light pressure tends to increase the intensity of the murmur and heavy pressure abolishes the sound. On auscultation over the precordium, pressure with the finger on 1 or both jugular veins will cause a murmur due to venous hum to disappear completely. Turning the subject's head away from the site of origin of the venous hum increases the murmur. It is more prominent during inspiration than during expiration. Its importance is that it may simulate pathologic murmurs.

**Kitchell**


The common syndrome of precordial pain occurring in essentially healthy persons of light or medium body build in the younger age group (below 35 years) is described. The pain is severe, sudden in onset, does not radiate, and is regularly located near or above the cardiac apex. The pain occurs at rest or during mild activity and is frequently related to a “slouched” posture. This benign syndrome should
be considered in any differential diagnosis of precordial pain.

**Kitchell**


In 15 patients with atrial fibrillation and congestive heart failure variations of the intensity of the first heart sound were studied before and after intravenous injection of a digitalis preparation. Simultaneous piezoelectric registrations of the carotid pulse served for the determination of the time of isometric contraction and of the ejection time.

Moderate reduction of the ventricular rate by digitalis caused an increase; marked reduction, a decrease of the sound intensity. Under both circumstances the isometric contraction was shortened and ejection time lengthened. When this was related to the duration of the preceding diastole, a positive inotropic effect of digitalis could be demonstrated, regardless of the intensity of the first heart sound. This demonstrates that heart-sound intensity is primarily a function of the heart rate and may vary independently of cardiodynamic alterations.

**Pick**


Phonocardiographic tracings were taken of the presumably nonpathologic murmurs of children; those usually heard in the second intercostal space at the left sternal border. These tracings were compared with clearly identified murmurs of mitral valvular insufficiency and of some precordial vibratory (twanging-string) murmurs. The wave form of the pulmonary-systolic murmur showed some similarity to that of the precordial vibratory murmur, in that a simple wave could be discerned. However, whereas the form of the precordial vibratory murmur is generally quite uniform, resembling a sine wave of constant frequency, that of the pulmonic-systolic murmur almost invariably showed some distortion. Traces of pulmonic-systolic murmurs as obtained from patients with rheumatic fever, did not differ in any observable way as a group from those recorded from presumably normal subjects.

**Rinzler**


It is pointed out that a murmur can be heard in presystole in cases of mitral stenosis with atrial fibrillation when diastole is short. No atrial systolic murmur is heard before the first sound of a ventricular premature beat but the presystolic murmur may also be absent in the beat that follows the ventricular premature beat. It is thought that this may be due to the fact that the left ventricle becomes so filled with blood during the long compensatory pause that atrial systole cannot force enough additional blood through the mitral orifice to produce a murmur. The Valsalva maneuver may convert a presystolic murmur into an atrial sound, producing a presystolic gallop, by decreasing venous return and in turn reducing the flow through the mitral valve orifice. The effects of mitral valve surgery upon the diastolic murmur have been found to vary greatly.

The opening snap of the mitral valve is described and the history of its appreciation is reviewed. It is due to a delay and accentuation of the normal fourth component of the second heart sound; that is, the opening of the atroventricular valves. The opening snap must be differentiated from a third sound or a split second sound and, in conjunction with this latter question, it is mentioned that the opening snap, though usually heard best at the apex, may be heard best at the base. In relation to an apex cardiogram, the split second sound has its second component before the 0 point, an opening snap is synchronous with the 0 point, and a third sound occurs at the summit of the rapid inflow wave. So far as time intervals are concerned, the duration between the 2 components of a split second sound is usually less than 0.07 sec., the interval between the beginning of the second sound and the opening snap is at least 0.08 sec., and that between the beginning of the second sound and the third sound is about 0.12 sec. The opening snap may persist even when the murmurs of mitral stenosis become equivocal or absent as during atrial fibrillation, failure, or both.

The first heart sound at the apex is often loud and snapping in mitral stenosis. It is mentioned that earlier observers have noted that even when not increased in intensity the first sound may be delayed in displaying its main components. The authors point out that the third heart sound may be used as an index to the severity of mitral stenosis, since this sound is attributed to the rapid inflow of blood from the left atrium to the left ventricle early in diastole. This sound diminishes in intensity and finally disappears as the narrowed mitral orifice interferes with this rapid inflow.

The factors that reduce the intensity of the mitral diastolic murmur include a loud apical systolic murmur or loud opening snap or loud second heart sound, producing masking or fatigue effects upon the hearing mechanism of the examiner, tachycardia, congestive heart failure, or unusual features of distortion or deformity of the valve. In order to assist in the detection of the diastolic murmur the authors recommend auscultation under ideally quiet conditions, examination during moderate expiration, concentration on individual events of the cardiac cycle, using the bell of the stethoscope and adjusting the pressure with which it is held.
against the chest very carefully, exercising the patient and turning him on his left side, searching the area of the apex carefully, and appreciating the many factors causing variations in the murmur.

Rosenbaum

PHYSIOLOGY


The chemoreceptors in the carotid body, which are known to be responsible for the circulatory and respiratory adjustments to anoxia, were studied by intracarotid injection of agents related to carbohydrate metabolism. All high-energy phosphates tested (ATP, AMP, and pyrophosphate) excited the electric activity of the sinus nerve in the cat. Azide displayed excitatory action similar to and competitive to cyanide. Glucose and several other products of carbohydrate metabolism depressed chemoreceptor activity. Although the recordings were not derived from single fibers and were not correlated with reflex responses, they are suggestive evidence for new chemoreceptor excitants. The data show that several excitatory mechanisms may operate. Since uncoupling agents (which depress phosphorylation without affecting oxygen consumption) depressed or enhanced chemoreceptor activity, it is unlikely that the depression of oxidative phosphorylation is a factor influencing chemoreceptors.

Aviado


Calcium ions and local anesthetics are said to “stabilize” excitable membranes because in their presence, stronger currents are needed to stimulate the tissues, spontaneous rhythms are slowed, and conduction of impulses may be blocked. Single Purkinje fiber of calf’s or sheep’s heart soaked in calcium-rich solutions required more depolarization for excitation. Cocaine, procaine amide, quinidine, and diphenhydramine stopped spontaneous activity and blocked conduction of the fiber. The hypothesis is put forward that both calcium and local anesthetics act on the system that is responsible for carrying sodium ions through the surface membrane.

Aviado


Alteration in posture from the supine to the erect position normally involves a reduction in venous return (due to direct effect of gravity on the circulating blood) and reflex vasoconstriction to maintain blood pressure. The immediate response of the circulation in the hand to such a change in body posture is a vasoconstriction of short duration that is absent in the recently sympathectomized limb. This immediate vasoconstriction (seen in vertical position) is followed by a rise in blood flow to a mean level only slightly less than that recorded in the horizontal position. The sympathectomized hand in the late phase behaves similarly. It would appear that this response is not of nervous origin but may be a mechanical effect. One might therefore conclude that, in the long run, the vessels of the hand do not participate in the vasoconstriction that maintains blood pressure in the vertical position.

Aviado


Simple plethysmographic techniques are described for measuring the resistance to venous drainage from limbs of human subjects. Maximum drainage of the blood vessels by gravity occurs in approximately 30 to 35 sec. in the case of the legs, 15 sec. from the forearm and hand, and 5 sec. from the hand. An approximate assessment of the rate of venous drainage in the first 5 sec. gave the following results: Legs 26.0 ml., forearm and hand 53.3 ml., and hand 53.7 ml. The drainage rate is slower in the legs than in the arms, partly because the muscular action involved in raising the arm may have assisted in the venous drainage. It is apparent from these experiments that the normal limb is provided with a large reserve of drainage capacity to cope with increases of arterial inflow. The presence of edema when there is venous obstruction must be due to a fairly large increase of the obstruction to venous return.

Aviado


Direct needle puncture of the cardiac chambers in 14 patients at operation revealed the following temporal relationships: interval from onset of P wave to onset of left atrial contraction averaged 0.068 sec.; interval from onset of Q wave in lead II to onset of left ventricular contraction averaged 0.041 sec.; isometric contraction period of left
ventricle averaged 0.050 sec. The reported latent periods for the left heart were shorter than those reported by others for the right heart when employing the catheter technic.

**AVIADO**


These anesthetic agents produced approximately equal depressant effects on myocardial contractility. However, the effects of thiopental appeared to be somewhat less than that of the other anesthetics. A decrease in blood pH of 0.5 unit also depressed myocardial contractility. If such effects apply to the human myocardium as well as to the dog heart-lung preparation, the cardiac effects of anesthetic agents per se may be augmented considerably during anesthesia as the result of respiratory acidosis.

**AVIADO**


Hearts of rabbits previously made hypothermic have been perfused with Ringer-Locke solution at 23°C. Coronary blood flow, mechanogram, and electrocardiogram have been compared with those of hearts isolated from normal animals, perfused initially with solution at 38°C, and gradually cooled to 23°C. In the first group of hearts the coronary flow was low, the mechanogram was normal, the electrocardiogram showed prolongation of Q-T, and essentially constant rhythm and contour. In the hearts cooled after isolation, the coronary flow gradually decreases, the rate becomes gradually slower, the mechanogram frequently shows an irregular sequence of systoles of varying amplitude, and arrhythmias, conduction defects, and variations in Q-T duration are also noted. Electrocardiographic changes occurring when the perfusion fluid is gradually rewarmed to 38°C are also described.

**CALABRESI**


Since repeated experimental evidence has associated high cholesterol levels with atherosclerosis, various attempts have been made to lower blood and organ cholesterol content. The effects of several substances on cholesterol absorption have been studied using various experimental animals. Soybean sterols, consisting mainly of β-sitosterol, have been shown to decrease the accumulation of dietary cholesterol. Studies on dihydrocholesterol-treated animals have shown that this substance is also effective in reducing cholesterol absorption. Moreover, it has been found that, in the cockeral, precipitation of bile acids by ferric chloride results in a reduction of blood cholesterol. On the other hand, in the case of the mouse and rat, evidence has been produced that soybean sterols fail to lower organ and blood cholesterol.

The object of this investigation was to study first, the effectiveness of β-sitosterol in prevention of liver cholesterol accumulation and, second, the effectiveness of ferric chloride in a mammalian species. Increasing the cholic acid content of a diet rich in cholesterol significantly increased total liver cholesterol. The addition of β-sitosterol to diets containing cholic acid and cholesterol decreased total liver cholesterol. Addition of ferric chloride, in varying amounts, to diets rich in cholesterol and cholic acid resulted in practically no change in total cholesterol content of mouse liver.

**MAXWELL**


There is some evidence that the altered tryptophane metabolism in normal pregnancy is the result of a deficiency in vitamin B₆, despite the fact that no evidence of B₆ deficiency has been demonstrated by blood, urine, or tissue levels of this vitamin. Pyridoxine derivatives, pyridoxal phosphate, and pyridoxamine phosphate probably serve as coenzymes of transamination reactions. Some tissues of pyridoxine-deficient animals have a reduced transaminase activity. Therefore, the authors investigated the effect of pyridoxine supplements on transaminase activity of certain fetal and maternal tissues as evidence of vitamin B₆ deficiency to justify large supplements of pyridoxine to diets of pregnant women.

The glutamic-aspartic transaminase activity of whole blood from normal pregnant subjects is essentially the same as in nonpregnant subjects. Activity is significantly increased by supplementing the diet with 10 mg. of pyridoxine daily. Transaminase activity of fetal blood is twice as great as in maternal blood in mothers not receiving additional vitamin B₆. The transaminase activity of placental tissue is not altered by prior administration of pyridoxine for several weeks. The results suggest that fetal tissues contain optimal quantities of B₆, whereas adults, both pregnant and nonpregnant, contain suboptimal concentrations for peak enzymatic activity. The method employed is not sufficiently sensitive to demonstrate a reduced “reserve” of B₆ in normal gestation, but the data are compatible with the view that pyridoxine supplementation is desirable in human pregnancy.

**MAXWELL**

The observation that during experimental and clinical myocardial infarction glutamic oxaloacetic transaminase is released from cardiac muscle resulting in increased enzyme activity in the serum suggested that other cardiac tissue enzymes behave similarly during myocardial infarction. Although present in other tissues in greater activity, lactic dehydrogenase, the enzyme concerned primarily with the reduction of pyruvic acid to lactic acid, is present in appreciable activity in cardiac musculature. In order to ascertain whether lactic dehydrogenase (LD) activity is increased in the serum during myocardial infarction, it was necessary to first demonstrate its presence in human and animal blood, and to delineate variations in LD activity in the blood of normal and diseased man.

LD activity is present in the venous serum of normal human adults. Normal activity ranges from 260 to 850 units/ml with a mean value of 470 ± 130 units/ml. Venous whole blood hemolysates of normal adults have LD activity varying between 16,000 to 67,000 units/ml with a mean value of 34,000 ± 12,000 units/ml. Alterations in serum LD have been studied in a selected group of disease states. Experimental and clinical myocardial infarction are associated with a rise in serum LD activity. LD, like serum glutamic oxaloacetic transaminase, rises in a characteristic fashion following myocardial infarction.

MAXWELL


Distributions of inulin and thiosulfate were simultaneously determined. Inulin distribution was 16–20 per cent and thiosulfate 20–25 per cent of body weight. The results were reproducible. Within 1 hour 53 per cent of thiosulfate was excreted in the urine. In 5 hours this quantity was 57 per cent as a maximum. Inulin was given by long constant infusion and the thiosulfate by a single intravenous injection that required 10 min. Since the metabolism of these 2 substances is different and the methods of administration varied, it is not surprising that they measured different volumes.

OPPENHEIMER


With glass spheres of known size the arteriovenous anastomoses of the isolated rabbit’s ear were found to be 47–59 μ. There were only a limited number of vessels between this size and that of capillaries. A group of experiments were carried out with spheres of 30 μ in diameter. These would pass through anastomoses but not capillaries. By this method the mean shunt flow was 36.0 per cent of the total flow. There was a spontaneous variability in this flow of almost ±10 per cent. This shunt flow was largely independent of perfusion pressure in the range 45–105 mm. Hg.

OPPENHEIMER


A statistical evaluation is presented of data on normal heart volume assembled in 763 healthy subjects between 9 and 66 years of age. The heart volume was determined roentgenologically by a method developed by the author and his associates, and correlated with height, body weight, body surface, the basal metabolism, and O2 consumption after work. Means and standard deviations of the factors studied are tabulated, and correlation coefficients, regression lines, and standard deviations around the latter are indicated in diagrams.

The correlations, heart volume/body weight and heart volume/body surface, are almost equal (0.41 and 0.44 for men, 0.58 and 0.53, respectively, for women) and agree with the results of previous reports. The possible errors, differing in the 2 sexes are discussed. They attain 2 to 13 per cent when cardiac volume is correlated with square meters of body surface, 20 to 33 per cent when correlated with body weight in kilograms, and sometimes reach 100 per cent in correlations with age. Hence, in spite of the equality of correlations with body surface and body weight, the former is to be preferred when relative heart volumes are calculated.

The results of this study are applicable only for comparison of normal values with normal standards. Other correlations and errors can be expected in pathologic cases.

PICK


The authors applied statistical methods to define criteria for a left-to-right shunt in terms of O2 differences found photometrically in blood samples obtained by cardiac catheterization.

An atrial septal defect or anomalous return of pulmonary veins can be assumed to be present when the O2 concentration of the right atrial blood exceeds by 2.5 vol. per cent that of 1 of the venae cavae, preferably the one with the higher O2 content. An O2 difference of 1.7 vol. per cent between the right ventricle and atrium, or between right ventricular and pulmonary artery is sufficient to diagnose a ventricular septal defect or a patent ductus respectively. These requirements of O2 differences can be
reduced by 1/4 when average values of 3 to 5 samples obtained in different adjacent portions in a heart chamber or in the pulmonary artery are obtainable. Multiple samples from the same position but with varying O₂ contents can be used for a shunt diagnosis when the difference between 2 such samples is more than 1.3 vol. per cent in the right atrium, 1.2 vol. per cent in the right ventricle and 0.9 vol. per cent in the pulmonary artery. The O₂ content in the 2 venae cavae can show considerable differences and can imitate a left-to-right shunt in the atria. In order to avoid diagnostic errors, samples of blood from both these vessels should be obtained and included in the gasometric analysis.

**Pick**


Several procedures for the fractionation of the proteins of a single rat heart are described and a reproducible method for the quantitative determination of the extractable proteins is presented. A sucrose-verseine solution was used for primary extraction. Following centrifugation and further extraction with a phosphate-pyrophosphate buffer, low ionic-strength-extractives, a mitochondrial fraction, and high-ionic-strength extractives were obtained. Electrophoretic analysis of these extracts demonstrated the presence of 5 proteins in the low-ionic-strength extracts and 3 subfractions in the high-ionic-strength extracts.

**SAGALL**


A total of 30 cardiac output determinations were performed in 23 young healthy patients in late pregnancy, during labor, or in the early puerperium. The cardiac output as estimated by means of the pulse pressure method was compared to that determined by the Evans-blue-dye method. In 21 tests the cardiac output was determined by both methods simultaneously. Of the 30 determinations, 27 (90 per cent) of the cardiac output determinations as measured by the blood pressure method agreed with the dye-measured outputs within 25 per cent.

**SAGALL**


In lactescent serums the insoluble lipids may displace serum water sufficiently to produce errors in determinations of water-soluble substances. Misleadingly low concentrations of electrolytes may be found. However, when the insoluble lipids are removed by ultracentrifugation, the electrolytes in the clean fluid may be entirely normal.

The authors describe a method for the rapid determination of serum water based on freezing point depression after the addition of salt. This method checks rather well with the gravimetric technic. By studying water displacement by serum proteins the authors found that a rough estimate of the water (in Gm./100 ml. serum) displaced by serum lipids is about 0.04 times the total fatty acids in mEq./L.

**WAIFE**


This paper describes a method for measuring instantaneous blood flow in the pulmonary capillary system in man. Using an airtight body plethysmograph, a continuous recording of pressure is made before and after nitrous oxide inhalation. As the gas is absorbed by blood entering the pulmonary capillaries, the pressure within the body plethysmograph falls. The rate of gas uptake is proportional to capillary flow. The flow in normal subjects was found to be pulsatile with a rapid acceleration of flow to a rate about twice the mean cardiac output followed by a gradual decline. This cycle is repeated with each ventricular contraction.

It may be difficult to assume a single value for pulmonary capillary blood volume on the basis of a constant flow as had sometimes been assumed. The pulsatile flow may produce certain hemodynamic and gas exchange effects not fully appreciated. Thus the ratio of mean pressure to mean flow commonly known as “pulmonary arteriolar resistance” will include components of elasticity and inertia. The authors suggest the temporary use of the term “pulmonary impedance.”

**WAIFE**


The contractions of a strip of isolated rat heart muscle in Kreb's solution are markedly affected by the sodium content of its environment, being depressed by increased sodium content and augmented by reduction. Since the depression caused by anoxia can be relieved by reducing the sodium in the bath, it is suggested that anoxia brings about an increase in the sodium uptake by the muscle. Thus cardiac muscle is brought into line with the well-known fact that in conditions of salt loss (i.e., intense diarrhea and sweating) stripped muscle is liable to go into states of excessive contraction.

**AVIADO**
ABSTRACTS


The administration of reserpine to rabbits in doses as low as 0.1 mg/Kg, releases serotonin in the brain. The normal occurrence in brain of both serotonin and the potent enzyme, amine oxidase, makes it appear probable that serotonin exists mainly in a bound form. The significance of these results in terms of therapy of hypertension remains obscure.

Aviado


It is common experience that vasodilatation is more difficult to obtain in organs perfused with salt solution than in the intact animal. Perfusion of the ear vessels with heparinized horse blood or washed red corpuscles in a dextran solution kept the vessels sensitive to antidromic vasodilatation. That antidromic vasodilatation could be obtained repeatedly, even in the absence of plasma, suggests that such effects may not be due to the local production of vasodilator substance from plasma proteins. It is possible, however, that proteins derived from interstitial fluid or from slight progressive hemolysis occurring during the experiment may have participated in the vasodilator responses.

Aviado


The role of transmural pressure (absolute level of intraluminal over extraluminal pressure) in determining vascular resistance in the forelimb of a dog was investigated by measuring pressures in the brachial vessels in the small (1-mm. diameter) vessels. Elevation of pressure in the veins, small vessels and arteries by venous obstruction with flow rate constant was associated with no change in total resistance but elevated small vessel resistance. When all the nerves were blocked high in the leg with procaine, total resistance decreased and the small vessels failed to constrict. A “venous-arteriolar reflex” is postulated on the basis that elevation of arterial pressure alone did not elicit small vessel constriction. It is not absolutely certain if the sympathetic or somatic nerves are involved at all, since the local anesthetic may be carried distally to affect the local reactivity of the vessels. Surgical denervation will help establish this reflex, which may in turn explain the increased vascular resistance of congestive heart failure.

Aviado


Interpolated extra beats augment the next beat but this augmentation decreases regularly in those that follow. Augmentation of the first beat after the interpolated extra beat is increased when this extrasystole occurs closer to the last regular beat. Rest after the extra beat allows the augmentation to reach a peak in 10 sec. and persist for 5 min. It is pointed out that the augmentation cannot depend on decreased time interval for diffusion of substances into or out of the cell because of this previously mentioned finding. During diastolic pauses, the heart muscle is probably not at rest, but is building up energy for the next contraction.

Oppenheimer


The authors reviewed clinical, hemodynamic and electrocardiographic data collected in 27 cases with proved interatrial communication and arrived at the following conclusions. As a rule this congenital malformation produces, through an arteriovenous shunt, a marked increase in pulmonary flow, without significant elevation of pulmonary arterial pressure. These findings account for the clinical and radiologic aspects of the disease including the hypertrophy of the right ventricle, the enlargement of the pulmonary artery and its branches, and the marked pulsation of these vessels. With increasing age, usually after 40 years, the pulmonary arterial pressure begins to rise and this may lead to the development of right heart failure. Such a slow course of evolution of the disease justifies surgery in younger persons. In exceptional instances, an atrial septal defect may be associated with pulmonary hypertension in infancy and then the interatrial shunt is partially or completely reversed. Under such circumstances the walls of the pulmonary vessels may show significant anatomic alterations and even calcification. Such a condition is badly tolerated and not amenable to surgery. The outstanding electrocardiographic feature is a right-sided ventricular conduction defect, the degree of which depends on the extent of the hemodynamic alterations.

Pick


A specially designed manifold of glass and rubber tubes was perfused with water to simulate certain mechanical aspects of the pulmonary circulation. A pressure head (pulmonary artery) caused flow through 4 tubes in parallel (pulmonary arterioli) spaced 10 cm. apart. Vertical positioning of such a pulmonary manifold caused preferential flow through the dependent channels, while little perfused the
elevated portions. This effect was exaggerated at low pressure heads. As the pulmonary arterial pressure head was raised, the elevated or apical segments received an improved supply. Slight to moderate "intrapulmonary" air pressure, uniformly applied to all 4 "capillaries," shunted flow away from the elevated vessels and increased that through the dependent tubes. High levels of such air pressure reduced flow as a whole and resulted in a requirement of a high pulmonary arterial pressure if "normal" flow was to be perfused through the "lung." Elevation of the level of the outlet (pulmonary venous pressure) increased flow through the elevated segments until it equalled that through the base. When the (intrapulmonary) air pressure was then raised, the apical flow was markedly reduced and almost the entire flow shunted through the dependent channels. Enhancement of precapillary resistance equalized flow through the elevated and dependent portions of the manifold, but reduced the total flow for a given pressure head, thereby requiring a higher arterial pressure to maintain perfusion of the system at "normal" flow rates. Elevation of intrapulmonary air pressure in these circumstances had only a limited effect in redistributing flow to the base. Alterations in blood flow have clinical implications in such conditions as pulmonary hypertension subsequent to arteriosclerosis of the lesser circulation, emphysematoid states, congestive heart failure, orthopnea, the tendency to pulmonary edema in the dependent portions of the lung, and the predisposition to apical involvement of reinfection tuberculosis.

**Rinzler**

**ABSTRACTS**

**Bronner, F., Harris, R. S., Maletskos, J., and Benda, C. E.: Studies in Calcium Metabolism: The Fate of Intravenously Injected Radiocalcium in Human Beings. J. Clin. Invest. 35: 78 (Jan.), 1956.**

Calcium metabolism is incompletely understood in man. In this study radiocalcium (Ca\(^{40}\)) was administered intravenously to 9 adolescent boys and 1 young man, all of whom were normal except for mental inadequacy.

The urine contained from 1½ to 2 times the quantity of radiocalcium excreted in the feces. Calculations reveal that about 15 per cent of the average daily fecal output of calcium in the adult was endogenous in origin. Only a minor fraction of the calcium absorbed on any 1 day is re-excreted promptly; the major portion is retained for some time. The peak output of Ca\(^{40}\) in the feces occurred on the second or third day. Excretion was low, for in no case did the combined output of isotope exceed 7 per cent of the injected radiocalcium during any 1 day. Nearly all the calcium that enters the body at a given moment is at first retained, presumably chiefly by the skeleton, and equilibrium is maintained by excreting calcium that had been previously absorbed.

**Waife**

**RHEUMATIC FEVER**


A case is reported of a 30-year-old white man who claimed good health and denied rheumatic fever, heart disease, or any symptoms thereof prior to the onset of profuse hemoptysis. He developed pulmonary edema and had a massive pulmonary hemorrhage due to what proved to be rheumatic mitral stenosis. The occurrence of hemoptysis in mitral stenosis is briefly discussed in the light of other authors' findings and of experience at a general hospital.

**Bernstein**


A chelating agent, ethylenediamine tetracetic acid (EDTA), was used in the treatment of a patient with typical scleroderma, sclerodactyly, calcinosis, and arthritis (rheumatoid?). Treatment was fol-
lowed by improvement as indicated by x-ray evidence of marked diminution in the articular and cutaneous metastatic calcific deposits, histologic evidence of regression of the sclerodermatous changes in the skin, and return of mobility of the affected joints. The chelating agent was probably responsible for the remission. During treatment there was a definite increase in the output of urinary calcium, but no marked change in the level of serum calcium.

HARRIS


In view of the interest shown in salicylamide for its analgesic and antirheumatic effect, it was thought advisable to study both of these under conditions that would lead to statistical evaluation with placebo and other salicylate therapy. It was found that salicylamide is not an effective analgesic or antirheumatic medicament in man. The double-blind technic showed no differentiation between placebo or effective medicaments when applied to an evaluation of analgesic and antirheumatic drugs in ambulatory patients. Each investigatory group should determine the responsiveness to placebo medication for its particular type of patients and use these data as a control for evaluation of unknown analgesic or antirheumatic drugs.

KITCHELL


The authors observed aortic stenosis in a predominantly male group of 50 patients, especially in the "undetermined" group without evidence of congenital or rheumatic basis. In fact, in the latter 2 groups females predominated. There were 6 cases classified congenital and, in addition, the drawing is shown of the specimen in a 6-year-old boy with aortic stenosis "due to fibro-elastosis." In 20 cases rheumatism was considered the certain basis of the valve deformity. In the remaining 2 cases the cause was "undetermined."

In general, the clinical findings of the authors are in agreement with those presented by other students of this subject. In 30 of the 50 patients, the second aortic sound was normal. The aortic systolic murmur tended to diminish during cardiac failure. Prominence of the first part of the aorta to the right and anteriorly was observed in 30 of the 50 patients.

The critical value area in isolated aortic stenosis seemed to be 0.5 cm.² but was larger if there was co-existing regurgitation.

The familiar natural history of aortic stenosis—rapid deterioration after symptoms once have their onset, sudden death at any time including the asymptomatic period—is reviewed.

One case, presumably congenital, had calcification of the aortic valve.

McKUSICK


Sixty patients submitted to mitral commissurotomy were studied. Fourteen of them were treated with cortisone before as well as after surgery in order to evaluate the incidence of asymptomatic but active cardiac rheumatic lesions, the effects of cortisone on these lesions as well as upon the inflammatory reactions secondary to the surgical trauma, and whether or not the postoperative follow-up in the treated patients is more favorable than in the untreated group. A large group (60 per cent) of patients submitted to commissurotomy shows active but asymptomatic rheumatic cardiac lesions. The use of cortisone diminishes the presence of such lesions from 67.4 per cent to 35.7 per cent. It increases the frequency of lesions moving toward cicatrization or already healed from 10.9 per cent to 28.6 per cent and from 21.7 per cent to 35.7 per cent, respectively. Cortisone can decrease the inflammatory surgical reactions of the pericardium and endomyocardium. Through clinical, phonocardiographic, electrocardiographic, and histopathologic studies the frequency of pericarditis has been shown to decrease from 86.3 per cent to 38.4 per cent, from 72.7 per cent to 36.3 per cent, and from 50 per cent to 21.4 per cent, respectively. It was not possible to establish clearly a better evolution in the postoperative period in those patients treated with cortisone as compared with the untreated. However, relapses and postcommisurotomy syndrome were less frequently observed in the first group.

RINZLER


Sixty-five patients, manifesting various features of rheumatic disease (bursitis, fibrositis, arthritis), were treated with injections of aqueous histamine diphasphate. In the last 10 patients (chronologically) repository histamine (Histapon) was employed to supplement the action of the aqueous preparation. The repository preparation kept these patients symptom-free for longer periods of time, obviated the necessity for frequent injections of aqueous histamine, and permitted lengthening of the interval between injections. Most of the patients had experi-
enced painful rheumatic disorders for long periods of time and had received the usual treatment (x-ray, gold, salicylates, phenylbutazone, cortisone, and ACTH). These previous treatments had been failures. Such patients required longer treatment with histamine. Other patients in this series with rheumatic disorders of more recent origin made more dramatic recoveries and required treatment for shorter periods of time. The marked improvement bears a striking resemblance, in terms of symptom-response, to that which may be achieved with cortisone or ACTH, with this important difference: side effects which are common during administration of these hormones do not occur with the histamine preparations. Similarly, eosinopenia resulting from histamine treatment resembles that achieved with cortisone or ACTH. This profound decrease in circulating eosinophils occurs much more rapidly and more definitely with histamine. The improvement in the course of the disease and the satisfactory response to histamine are closely paralleled by the fall in eosinophil levels. There were 4 therapeutic failures in this series of 65 patients, all of them in patients with atrophic arthritis. In all 4 there was no effect on the eosinophil count.

**Rinzler**


A case of a 55-year-old woman with rheumatic heart disease and congestive heart failure is presented in detail. A diagnosis of progressive acute rheumatic carditis was made because of a protracted febrile course, changing auscultatory phenomena, increasing cardiac enlargement, recurrent arthralgias, persistent prolongation of the P-R interval, and compatible changes in the laboratory tests. The patient received 7210 mg. of cortisone in 39 days, 2525 mg. of prednisone over 47 days, and 265 mg. of prednisolone over 6 days. No clinical amelioration of the rheumatic carditis resulted. An intercurrent pulmonary infection occurred while the patient was receiving prednisolone, with precipitation of acute left ventricular failure and death. Although there were calcific changes in both the mitral and aortic valves, the myocardium showed abnormalities suggesting rheumatic myocarditis. An acute gastric ulcer was also found to be present. While receiving prednisone and a diet containing 5 Gm. of sodium, substantial retention of sodium occurred. Histologic examination of the adrenal glands also disclosed atrophy of the inner 2 layers although it was less in degree than that reported in patients receiving the usual doses of cortisone.

**Rosenbaum**


Ten to 20 mg. of 1-hydrazinophthalazine introduced into the pulmonary artery of 10 individuals with mitral valve disease produced in 9 a rise in pulmonary artery pressure, tachycardia, and a slight increase in cardiac output. The higher the mitral pulmonary artery pressure, the higher was the rise. The rise tended to outlast the tachycardia.

The use of 1-hydrazinophthalazine appears contraindicated in individuals with hypertension associated with mitral valve disease.

**Solloff**


The capillaries of the conjunctiva and the nailbed have been studied by both slit-lamp and capillary microscopy in 100 patients with acute rheumatic fever or rheumatic heart disease. A characteristic capillary pattern was found in the conjunctiva of 79 patients and in the nailbed in 31 of these 100 patients—a considerably higher proportion than was found among control patients. In the conjunctiva, the special feature is the repeated subdivision of vessels (arborization) and the abrupt thinning of many of the terminal vessels, which often appeared to terminate as end-vessels, having no apparent connection with adjacent vessels. This was in marked contrast with the usual picture of an interlacing latticework of the small conjunctival vessels. In the nailbed, the capillaries often branched from a common stem, giving the appearance of multibranched candlesticks. The possibility that the pattern may be present before the onset of rheumatism and may be a sign of a rheumatic diathesis is discussed. The presence of these capillary signs may help diagnosis in borderline cases.

**Bernstein**


Rabbits subjected to pharyngeal infections with group A streptococci developed cardiac lesions characterized by myofibril necrosis and a nongranulocytic cellular reaction. The histopathologic changes were demonstrable within 24 hours of inoculation, were maximal 72 hours after induction of infection and, thereafter, healed in the course of the following 2 weeks. The extent of involvement was variable, and with healing the necrotic areas were replaced by fibrous tissue.

When intradermal infections with the same organisms were produced in rabbits, cardiac lesions, indistinguishable from those observed in the pharyngeally infected group, appeared in a much smaller number of animals. The hearts of 5 of 6 rabbits sacrificed a month or
more following the last of a series of streptococcal pharyngeal infections, exhibited lesions characterized chiefly by fibrosis, although mononuclear cellular infiltrations were also noted. In these repetitively infected animals, the presence of occasional multinucleated giant cells and a few small foci of calcification were features not encountered in the single infection group. In none of the lesions were bacteria demonstrable, either in histologic sections or in cultures of myocardial tissue. The implications of these findings, in terms of the non-suppurative sequela of streptococcal infections in man, are discussed.

Bernstein


Using certain criteria for the detection of an active rheumatic process in tissues, the authors examined 400 auricular appendages obtained from patients undergoing cardiac surgery for the treatment of valvular disease. The findings of Aschoff body of juvenile character, alteration in collagen fibers and ground substance, exudative inflammatory reaction in the section, and degeneration of myofibers were regarded as indicating the presence of an active rheumatic carditis. Eight of the tissues submitted presented an appearance of active carditis. In 67 additional cases, Aschoff bodies of the senescent type were described together with myocardial and endocardial fibrosis, findings consistent with a diagnosis of healed rheumatic carditis. In the remaining 324 appendages no Aschoff bodies were found. In this series 22 patients died shortly after mitral commissurotomy; the findings in other areas of heart muscle were similar to those seen in the auricular appendage. Extensive preoperative studies revealed no sign of rheumatic activity except for the sedimentation rate which, in the majority, correlated with pathologic findings. The postoperative course was similar in all groups of cases, with no signs of recrudescence of rheumatic activity.

Shuman


The clinical diagnosis of rheumatic fever pneumonitis is warranted when there is (1) disproportionate respiratory distress with severe cough, chest pain, cyanosis, and hemoptysis, not relieved by oxygen and the customary supportive measures, (2) evidence of carditis, but not of sufficient severity to explain the pulmonary findings, in the presence of prolonged high fever and negative blood cultures that do not respond to salicylates, (3) chest x-ray finding of increased perivascular markings arising at the hilus and progressing to nodulation, confluence, and massive consolidation with relatively clear apices and bases. The gross pathologic changes are rubbery consistency, various dark hues of focal hemorrhages, fine granularity, and spotty vesicular emphysema. The histologic changes are alveolar hemorrhages, necrotizing alveolitis, hyaline membranes, alveolar lining-cell proliferation, organization of exudate, fibrinoid necrosis of the bronchiolar lamina propria, and arteritis.

Wendkos

ROENTGENOLOGY


The diagnosis of congenital cardiac abnormalities in infants by usual clinical, fluoroscopic, and radiologic technics is difficult because as the authors point out, physical signs are unreliable, characteristic radiographic patterns are not present, since not enough time has elapsed for their development, and usually an enlarged thymus shadow obscures cardiac boundaries. The authors have made use of an additional technic: retrograde aortography by the introduction of a radiopaque medium into the brachial artery and thence into the aorta. They present the clinical history and x-ray findings using this technic of 5 cases whose doubtful diagnosis was established. These cases were ones of patent ductus, coarctation of the aorta, truncus arteriosus, ventricular septal defect, and aortic stenosis.

Harvey


The author describes preliminary results where subepicardial fat layers were demonstrated that had a lesser density than the overlying pericardial fluid or thickening. Rapid laminography (\(\frac{3}{50}\) sec.) is preferable to show this difference, but on several occasions the perivascular fat deposits were demonstrable with the aid of the usual current types of laminographic technics.

Schwedel


The authors present the progressive changes occurring in the hilar shadows of patients followed for 4 to 15 years. Along with progressive widening of the pulmonary arteries they stress the narrowing of the tertiary and smaller branches and correlate such findings with the deterioration in the clinical state from group I (New York Heart Association criteria) to groups III and IV.
Evidence is cited in favor of a relationship between such narrowing (with resulting oligemia of the lung) and increased pulmonary arterial pressure and resistance.

**Schwedel**


After incision of a femoral or brachial artery a catheter is passed into the aorta and advanced to a predetermined site, or into a main branch by means of an electromagnet attracting a chain of small steel links at the catheter tip. In 7 attempts at renal artery visualization 6 were satisfactory.

The author suggests that occasional arterial spasm and the complicated electromagnetic equipment are drawbacks, but insists that the method is safe and reliable.

**Schwedel**

**SURGERY AND CARDIOVASCULAR DISEASE**


The authors describe a case of persistent common atrioventricular canal defect that was successfully treated by surgery. This type of atrial septal abnormality is one in which the lower part of the atrial septum is absent and the interatrial communication lies immediately above the ventricular septum. It is attributable to lack of fusion of the components of the atrial septum to the atriocentrical endocardial cushions.

The patient operated upon was a 27-year-old white woman who complained of progressive dyspnea, fatigue, and mild chest pain on exertion. Fluoroscopic and x-ray examination revealed enlargement of the pulmonary trunk, pulmonary arteries, and right ventricle, with increased pulsation of the pulmonary arteries. Catheterization demonstrated arterIALIZATION in the right atrium, while dye-dilution curves indicated a large left-to-right shunt.

By means of the atrial well of Gross, the right atrium was entered and a piece of polyvinyl was sutured into the defect. The postoperative course was uneventful. Study by cardiac catheterization 4 months after surgery showed that the defects in both the atrial and ventricular septa were completely closed and the heart was hemodynamically normal.

**Abramson**


The authors discuss the use of a multiple-layered arterial prosthesis, made from inert synthetic fabrics and consisting of an inner tube and an external "wrap around." They believe that the immediate results obtained with inert synthetics are satisfactory and greatly simplify arterial replacement. However, they realize that it is difficult to assess the ultimate value of such an approach.

The authors conclude that clinical use of the inert synthetic fabrics for arterial prostheses is as equally justified as that of arterial homografts.

**Abramson**


The authors discussed the various surgical approaches to the treatment of segmental thrombosis of the main arterial channels in the lower extremities and described the method of by-pass of the diseased area with a graft. The latter operation was attempted in 40 extremities, and in 37 the blood flow was successfully re-established. This was determined by arteriography and the return of palpable pulses distal to the block.

Following operation, intermittent claudication and rest pain were relieved, and ulcers became painless and healed rapidly. All the grafts remained patient for periods up to 18 months.

The authors concluded that the by-pass procedure, owing to its simplicity in concept and application, is the most effective in achieving the desired objectives and is associated with the fewest disadvantages.

**Abramson**


The authors analyzed a group of 114 patients with complete transposition of the pulmonary artery and aorta and found that only 4 per cent were alive at 7 years of age; 78 per cent expired during the first year of life. If any attempt at surgical intervention is to be carried out, it must be done at an early age and at the first signs of deterioration of the general condition of the patient.

The authors presented the results of attempts at surgical palliation in 32 patients with complete transposition. In each case associated congenital defects were present. Among the types of surgical procedures attempted was establishment of a venous shunt to the right atrium by means of transplanting the right pulmonary artery and
systemic arterialization of the pulmonary vascular bed. Of the 52 patients operated upon, 7 survived.

**Abramson**


Repair of an experimentally produced ventricular septal defect was performed upon dogs cooled to a body temperature of 30 C. by immersion in a bath of ice and water. Considerable difficulty was encountered because of adhesions between the heart and pericardium resulting from the previous procedure. Eight of the dogs survived successful repair of the defect, while the remainder died during or immediately after the operation.

In another group the defect was made and then repaired during the course of 1 operation. However, the closure of the defect was more difficult than in the first group. The authors expressed doubt as to whether the approach described was applicable for clinical repair of ventricular septal defects.

**Abramson**


During 16 operations for mitral stenosis, repeated measurements were taken in the left atrium by means of an indwelling cardiac catheter. Plotting of the obtained values in a pressure-time system demonstrated that the left atrial pressure in the pre- and post-valvotomy period varied considerably, and rendered a single pressure measurement before and after valvotomy valueless for an assessment of the effect of the operation on left atrial pressure. In 1 of 5 successful valvotomies a slight overlapping of pre- and post-valvotomy pressures was present. In 2 less successful valvotomies an unmistakable decrease of pressure was recorded. It must be concluded that serial measurements of the left atrial pressure add little or nothing to the surgeon's assessment of the result. The factors that may influence the atrial pressure during operative conditions were discussed. The left atrial pressure had a direct relation to the heart rate in a few cases in the prevalvotomy period; no relation was demonstrable in any case in the post-valvotomy period. No other known factor bore any clear relation to the left atrial pressure, and the unpredictable course of the pressure curves cannot be explained at the present.

**Bernstein**


The anatomic variations of the left atrial appendage observed in 700 operations for mitral commissurotomies are reported. Nonpathologic variations in shape and volume are described, and especially the stricture at the union with the atrium proper and the very small appendage. A large atrium is usually associated with mitral regurgitation. The atrial wall may be unusually thin or calcified. Other pathologic changes described are pericardial adhesions, the frequent endocarditic thrombosis, and posterior displacement of the appendage. In re-operation for recurrence of stenosis, entry in the atrial cavity through the auricular appendage may be impossible.

**Calabresi**


Use of homologous aortic grafts in the treatment of adult coarctation of the aorta is a well-established procedure. Infantile coarctation, on the other hand, often cannot be corrected by present surgical procedures. It consists of a relatively long segment of partial obliteration involving the distal aortic arch, may involve 1 or both of the carotid vessels, and frequently involves the left subclavian artery, causing the characteristic manifestation of hypertension limited to the right upper extremity. Occasionally, a large patent ductus arteriosus supplies blood to the descending aorta. Local excision of these long segments of infantile coarctation is usually impossible. In most cases, the condition is not compatible with long life.

By using arterial homografts, segmental arterial lesions can be treated effectively by a direct surgical approach with restoration of arterial continuity and normal function. This form of surgical therapy was employed in 67 arteriosclerotic obstructions, of which involved the iliac and 39, the femoral artery. Short occlusions were excised completely and replaced by the graft. In the majority of cases the occlusion was simply bypassed by anastomosing the graft to the host artery above and below the lesion. All iliac occlusions and 87 per cent of the femoral occlusions were treated successfully, and the results obtained were superior to all other forms of therapy. Ten peripheral aneurysms in 9 extremities were excised and the defect bridged with homografts. Two of these failed because of technical errors. In the treatment of 20 arteriovenous fistulas, homografts were required in 4, while the others were treated by simple excision and suture repair. The circulatory changes were corrected in all, and the grafts have remained patent. Arterial homografts were used to bridge 10 traumatic defects of major peripheral arteries with successful restoration of circulation in all.
In a review of all operative and autopsied cases entering the Children's Memorial Hospital of Chicago since 1940, 105 cases of coarctation of the aorta were collected. Fifty-nine cases were amenable to excision and end-to-end anastomosis. Twenty-six cases had long infantile coarctation of the aortic arch, and aortic grafts to shunt the aortic stream around the coarctation into the descending thoracic aorta could have been used. In 43 mongrel dogs the technical aspects of the proposed operation were developed. The ascending limb of the aortic arch was anastomosed to the descending limb with a homologous aortic graft, and then the arch was ligated between the sites of anastomosis. The last 12 dogs were operated upon without any immediate or delayed operative mortality. A 6-month postoperative follow-up was completed. Twelve dogs with obligatory shunts through homologous grafts were available. Two grafts were examined after 1 month, 5 after 3 months, and 5 after 6 months. All were widely patent and successfully carried the entire aortic stream around the obstruction in the distal aortic arch. All had been well revascularized by adhesions from the adjacent pericardium, pulmonary artery, and left lung. Calcium had been laid down in the walls of some of the older grafts, and their intima showed evidence of furrowing. There was, however, no evidence of intimal destruction or aneurysmal dilatation.

MAXWELL


The fibrous ring supporting the mitral valve can be effectively narrowed by passing a double floss-silk circular suture around it. In the initial 18 experiments, where the suture lay below the left coronary artery, although 11 animals recovered from operation, 3 died from acute coronary occlusion. In 9 subsequent experiments, where the suture lay above the left coronary artery, all animals recovered. The resulting narrowing and thickening of the A-V ring did not interfere with the action of the mitral valve cusps and chordae tendineae.

It is concluded that this method may well prove to have a real place in the surgical correction of mitral insufficiency, especially in patients with a widely dilated mitral valve ring. Cardiotomy would be the first step to assess the pathologic type of mitral insufficiency. Thereafter, the circular suture would be inserted, and the degree of tightening judged by intracardiac palpation.

MAXWELL


A means of arterializing the blood during a total bypass is presented. The basic principle is the passing of O2 and CO2 through a metallic plate with holes of 10 μ in diameter. This produces tiny bubbles that come in contact with the venous blood by a swirling action. Instead of using 100 per cent O2, which removes excess CO2, the authors used 98 per cent O2 and 2 per cent CO2. The addition of 2 per cent CO2 to the O2 keeps the CO2 at essentially a normal level and, therefore, the pH is not excessively altered.

Studies on dogs utilizing the apparatus described with total bypass for periods of up to 30 min. revealed normal arterial O2 saturation, CO2 content, pH of arterialized blood, blood counts, platelet counts, and fragility tests. The recovery rate with a total bypass in the dog with the right ventricle open for 30 min. was 75 per cent.

MAXWELL


The fate of branched arterial homografts following replacement of the terminal aorta and its 3 major branches was determined in 35 dogs. The abdominal aorta, just distal to the renal arteries and approximately 6 to 8 cm. of each iliac artery as well as 1 cm. of the middle branch (the abdominal aorta in dogs divides into 3 branches), was resected from donor dogs within 4 hours of death. Three methods of preserving the homografts were employed. 1. The technique described by Gross with a modified Tyrode's solution, penicillin, streptomycin, and homologous dog serum was used in the first group of dogs. These grafts were stored at 4 C. for varying periods of time, but not over 21 days. 2. Homografts were frozen quickly in a bath of dry ice and alcohol and stored at −70 C. from 7 to 99 days. 3. Homografts were prepared by freeze-drying and then Carrel suture of no. 5-0 silk was used. Plastic shunts to maintain circulation or anticoagulants were not used. All dogs were examined post mortem. The dogs were followed from 1 to 536 days.

Satisfactory grafts were obtained in 7 of 11 "Tyrode" grafts, 4 out of 13 frozen grafts, and 3 out of 10 lyophilized grafts. The straight segments of the grafts were patent in 10 of 11 "Tyrode" grafts, in 8 of 13 frozen grafts, and in 6 of 10 lyophilized grafts. Calcification occurred in 3 of the frozen grafts. Atrophy to a marked degree occurred in 3 of the frozen grafts and in 1 of the lyophilized grafts. On the basis of this study, preservation of homografts in modified Tyrode's solution was superior to preservation in the frozen state or after lyophilization.

MAXWELL