Similar experiments with many of the same animals under chloroform and ether demonstrated that in dogs cyclopropane had a more marked stimulating or sensitizing effect on the ventricular automatic tissue than either of the other agents.

Although these experiments showed beyond question that adrenalin was contraindicated in cyclopropane anesthesia, they should not be taken to mean that cyclopropane is a particularly dangerous anesthetic. The irregularities with the exception of fibrillation are easily reversible and cyclopropane has the advantage over most anesthetics in that the tissues may be quickly desaturated. Danger may thus usually be quickly averted.

Since adrenalin injected during cyclopropane anesthesia resulted in serious cardiac irregularities, the action of other blood pressure raising amines was investigated. It was found that the following amines acted on the ventricular automatic tissue similarly to adrenalin: arterenol, epinine, kephrine and cobefrine. Ephedrine, propedrine, benzedrine, paredrine, synephrin, and neosynephrin did not exert any such cardiac effects. With the exception of neosynephrin they did, however, markedly accelerate the sino-auricular rate. In the dog under cyclopropane, neosynephrin is the sympathomimetic amine most favorable to the heart.

It has recently been shown that the integrity of some center above the pons is necessary for a cyclopropane-adrenalin response. Cyclopropane sensitization of the heart appears to take place because the anesthetic stimulated a mid-brain center which then sent impulses to the heart by sympathetic pathways. The direct action of adrenalin on the heart thus sensitized produced the ventricular tachycardia. The mechanism of action of cyclopropane has thus been shown to be similar to that described for chloroform.

R. D. D.

MAES, URBAN, AND DAVIS, H. A.: *Fluid Replacement in Surgical States with Particular Reference to Transfusion of Ascitic Fluid: A Clinical and Experimental Study.* Arch. Surg. **42**: 453–479 (March) 1941.

"It is our purpose to present in this paper: (1) a study of the abnormal physiologic picture which results from loss of water, electrolytes and blood; (2) the technic of fluid replacement; (3) a critical evaluation of blood replacement fluids, and (4) the present status of transfusion of ascitic fluid. The indications for fluid replacement fall into four main groups: loss of body water, loss of electrolytes, loss of whole blood [and] loss of plasma. While it is convenient for purposes of discussion to separate each type of depletion state, in actual practice the distinction is not clearcut, and one will find frequently the merging of one state into another. . . . Loss of water from the body in excess of the intake of water results in dehydration. Similarly, desiccation of the blood is known as anhydremia. From the surgical point of view the causes of dehydration may be divided into two groups: (1) exogenous and (2) endogenous. Among the more important exogenous causes are voluntary or enforced deprivation of water, excessive sweating due to sunstroke, heat prostration, traumatic shock and surgical operations. Endogenous causes are prolonged diarrhea due to surgical lesions of the intestinal tract, vomiting due to obstructing lesions of the gastrointestinal tract, and inability to swallow liquids due to obstructing lesions of the esophagus. The physiologic effects of dehydration may be considered at this point. Almost 68 per cent of the total loss of water comes from the muscles, and the major portion of the remainder from the blood and skin. The composition of the blood is altered in the presence of dehydration. . . .

"The blood volume diminishes by as much as 40 to 50 per cent of the initial level, the decrease being mainly in the amount of plasma. As the blood volume diminishes, a compensatory vasoconstriction occurs, leading to a diminished volume flow of blood, particularly in the extremities. The heart gives evidence of a diminished flow of blood through the coronary arteries, as indicated by the electrocardiogram. The blood pressure, however, is usually not greatly lowered, provided that dehydration and anhydremia are gradual in onset. When anhydremia is produced rapidly in the experimental animal, a state resembling secondary shock with lowered blood pressure supervenes. The tissue lesions of acute anhydremia are of interest and consist of widespread capillary distention with numerous petechial hemorrhages into the pulmonary alveoli, the subendocardium, the spleen, the leptomeninx and elsewhere. The adrenal glands may show petechial hemorrhages in the cortices and dense infiltration with polymorphonuclear leukocytes. The question now raises itself: How much loss of water will the body tolerate before death occurs? It is evident that rapidity of loss of water is the most important factor in determining the outcome. In dogs, death will result when an amount of water equivalent to 4 per cent of the body weight is lost rapidly. . . .

"The methods of determining the degree of dehydration may now be discussed briefly. The clinical manifestations are obvious. The skin becomes wrinkled and dry, and the mucous membranes are lusterless. The eyeballs become soft. As a result of the deficient flow of blood, the extremities are cold. The respirations may be deep and of the 'air hunger' type due to acidosis. Various other tests of hydration may be used: 1. Those applicable to the skin: standard wheal formation; intradermal salt absorption; intradermal serum absorption. 2. Those applicable to the blood: erythrocyte concentration; hemoglobin concentration; hematocrit reading; specific gravity of the blood plasma. 3. Response to administration of water in terms of: excretion of urine; time curve of blood dilution; rate of oxygen consumption. In practice one will find that the tests of group 3 provide the most comprehensive picture of the state of the dehydrated patient. . . .

"Our discussion at this point will refer only to that form of dehydration which is uncomplicated by gross losses of electrolytes or of blood. Minor grades of dehydration may be treated by water administered by the oral or the rectal route. However, many dehydrated patients require treatment with fluids given intravenously. The response of the dehydrated organism to intravenous fluids must be given consideration. The administration of isotonic dextrose solutions leads to a marked increase in the metabolic rate and in oxygen utilization. Coincidentally there occurs an increased breakdown of protein, as evidenced by the augmented output of nitrogenous products in the urine. Intravenous administration of isotonic sodium chloride solution is followed by only a moderate increase in the metabolic rate. . . . The total water content of the body is directly proportional to the number of osmotically active particles present in the tissues. The major portion of these particles is electrolytes. It has been demonstrated by many workers that sodium is the most important electrolyte in the maintenance of normal osmotic relations between the extracellular and the intracellular fluids. . . . In clinical states, loss of water usually accompanies loss of electrolytes. It is not this loss of water which is significant but rather the fact that as the total amount of electrolytes diminishes the ability of the organism

to retain water decreases proportionately. . . .

"It is necessary to distinguish the effects of loss of electrolytes per se from those of secondary dehydration. . . . In man the rapid loss of electrolytes results in muscular cramps and fatigue. The effects of the gradual loss of electrolytes in man have been investigated by McCance and others. Anorexia, nausea and a tendency toward muscular fatigue and cramps were prominent symptoms. Mental fatigue, inability to concentrate and slowness of mental reactions were noted. There was a fall in the level of plasma and corpuscular chlorides and in that of serum sodium, with an increase in the level of serum potassium. The blood pressure was unchanged in spite of a presumptive reduction of the blood volume as evidenced by hemoconcentration. While these changes comprised the effects of loss of salt, others, equally definite, could be attributed to the resultant dehydration. Among the latter were severe loss of weight, hemoconcentration with respect to erythrocytes and hemoglobin, increase in plasma proteins and blood urea and a negative nitrogen balance. It is apparent, therefore, that the sequence of events initiated by loss of electrolytes, particularly sodium, ends in dehydration with anhydremia, progressive reduction of the blood volume and, finally, generalized anoxemia, shock and death. . . .

"While as much as 2 Gm. of salt may be lost each hour in the perspiration when sweating is excessive, this is not a common source of depletion in surgical patients. More common, however, is a loss of electrolytes via the gastrointestinal secretions. Vomiting due to obstruction of various portions of the alimentary canal results in loss of gastric juice, succus entericus, pancreatic juice or bile. . . . The degree of loss of electrolytes may be determined either directly or indirectly. Estimation of the level of plasma sodium chloride, which varies normally from 560 to 630 mg. per hundred cubic centimeters of blood, gives a direct clue to the extent of electrolyte loss. A study of the secondary effects of electrolyte loss provides an indirect method of evaluating its extent. This may be done in two ways: 1. Estimation of the carbon dioxide-combining power of the plasma. 2. Estimation of the degree of secondary dehydration by means of blood studies, erythrocyte count, hemoglobin determination, etc. . . .

"Whole blood may be lost externally, into body cavities and into tissues. The causes of such loss are too well known to require enumeration here. The physiologic effects are dependent on the ensuing reduction of the blood volume. The removal of 500 cc. of blood has little effect on the blood pressure, and the blood volume is restored within one hour. The loss of 1,000 cc. of blood or more is usually followed by a fall of blood pressure. Recovery is possible after losses up to 30 per cent of the blood volume. Beyond 30 per cent the ability of the organism to restore the lost volume of blood is insufficient, and death results. . . .

"The extent of loss of blood may be gaged approximately by noting the clinical manifestations and by making determinations of the values for erythrocytes, hemoglobin and blood pressure. . . . Various fluids have been advocated for replacement of blood. It is obvious that fresh whole blood is the most efficacious fluid. However, this is expensive, is not always available and is incapable of storage beyond three weeks. As a result, a search for an efficient substitute for whole blood has developed. An ideal substitute for blood should possess the following properties: it should be readily available; it should be effective; it should be capable of prolonged storage without deteriorating; it should be nontoxic

even when administered in large quantities; it should contain one or more of the elements of blood; it should possess one or more of the biologic properties of blood; for example, ability to transport oxygen or ability to maintain the colloidal osmotic pressure. . . . It is apparent that crystalloid solutions cannot be regarded as adequate substitutes for blood, since they do not contain either proteins or hemoglobin. However, in circumstances in which the loss of blood has not been excessive they may exert a favorable influence. . . .

"Various investigators have shown that acacia solutions (6 per cent in 0.9 per cent sodium chloride or 5 per cent dextrose solutions) are capable of raising the blood pressure and maintaining the blood volume after hemorrhage. Unsatisfactory results have been reported, however, with acacia solutions after loss of blood. . . . Acacia solutions . . . are not devoid of toxicity. Deaths have followed their use. Anaphylactic reactions to acacia occur in man and in guinea pigs. Acacia solutions in vitro produce agglutination of the red blood cells. They may also lower the oxygen content of the blood by coating the red blood cells. The last-mentioned fact may render their use dangerous when the red cell count has been reduced to very low levels by hemorrhage. Acacia is engulfed by the cells of the reticuloendothelial system and may remain in the body for months or even for years. Regeneration of plasma proteins by the liver is interfered with, and repeated injections of acacia solutions may lead to hypoproteinemia. Finally, it has been demonstrated that acacia solutions leave the blood stream fairly readily and cannot maintain the osmotic pressure of the blood for more than forty-eight hours. . . .

"The transfusion of preserved blood was first performed by Hédon in 1902. During the World War preserved blood was used in human beings by Robertson. Little was done with this substitute for fresh blood until it was reintroduced by Jeanneny and his coworkers and by Palazzo and Teneoni in 1934. Despite the use of various blood-preservative solutions, such as sodium citrate solution, Rous-Turner solution and I. H. T. solution, the safe maximal period of preservation of whole blood does not exceed three weeks. The incidence of post-transfusion reactions increases with the period of preservation. In most respects, however, preserved blood retains the biologic properties of fresh blood. There are many difficulties associated with the maintenance of an adequate supply of preserved blood from living donors. For that reason, the use of placental blood has been advocated. However, only 50 to 70 cc. of blood can be obtained from the average placenta, and a high incidence of staphylococcic contamination has been reported. Applying to man the experimental work of Shamov on animals, Judine has utilized the blood obtained from cadavers for transfusion. As much as 1,500 cc. of blood may be obtained from a single cadaver. The incidence of post-transfusion reactions is high—21 per cent—and several fatalities have occurred. In spite of the fact that fresh defibrinated blood is known to be very toxic, Behr has used it for transfusion, reporting a 17 per cent incidence of reactions. . . .

"The functional value of hemoglobin in solution has been investigated with a view to its possible use for blood replacement. . . . It is evident that hemoglobin in solution does not represent, at its present stage of development, a practical blood replacement fluid. . . . Although both blood plasma and blood serum contain vasopressor and vasodepressor substances, this fact has not prevented their use as blood replacement fluids. Despite the lack of hemoglobin, the physiologic availa-

bility of plasma and serum as substitutes for blood after hemorrhage has been demonstrated in animals. Plasma apparently is more efficacious than serum. . . . Blood plasma and serum constitute an acceptable form of blood substitute in conditions resulting from loss of whole blood, provided that sufficient hemoglobin remains in the blood stream to carry on oxygen transportation. . . . Human ascitic fluid as a blood substitute has been investigated both with animals and with man. The fluid is obtained from patients suffering from ascites due to cardiac failure or to portal cirrhosis of the liver, from whom it is frequently necessary to remove 12 to 15 liters of fluid every two to three weeks. The fluid is sterile and, if removed with aseptic precautions, can be stored in sterile flasks at temperatures of 0 to 5 C. for periods up to five months or longer. In our earlier work with this fluid no preservatives or anticoagulants were used. However, of late we have been adding sodium citrate (50 cc. of a sterile 5 per cent solution) to each 1,000 cc. of ascitic fluid. This prevents the formation of fibrin clots in the fluid and may obviate the possible occurrence of so-called 'serum reactions.' . . .

"States associated with loss of plasma or plasma-like fluid from the blood stream present peculiar therapeutic problems and, therefore, merit separate consideration. In order to clarify this discussion, one may regard plasma as a mixture of proteins and water. Loss of either the protein or the aqueous fraction, or of both, may occur, and this loss may be acute or chronic. . . . Reduction of the plasma volume due to dehydration will not be reconsidered in the following discussion. In cases of acute loss of plasma with hemoconcentration and its sequelae, the crux of the therapeutic problem is the institution of fluid replacement before the capillary walls have been irreversibly damaged by oxygen lack. Crystalloid solutions should be used with caution, are often ineffective and may actually reduce the plasma proteins still further by washing them out of the blood stream into the interstitial tissue spaces, the peritoneal cavity and the site of trauma. Acacia solutions likewise are contraindicated. . . . The presence of hemoconcentration and increased viscosity of the blood would suggest that solutions of normal human proteins without red blood cells might prove more effective than whole blood. Such solutions are plasma, serum and human ascitic fluid. . . .

"Trusler and his co-workers stated the belief that water intoxication may follow the excessive administration of fluids to patients suffering from shock due to burns. The reduction of the total plasma volume will not be revealed by simple determination of the level of serum protein. If an effort is made to replace the plasma which has been lost by administering solutions containing proteins, preferably of human origin, the subsequent use of crystalloid solutions is less likely to be attended with untoward results. . . . The therapeutic problem in cases of chronic loss of the protein fraction of the plasma is not prevention of secondary shock but correction of the disturbance of distribution of the body fluids resulting from lowering of the osmotic pressure of the blood. It is apparent that only protein-containing fluids, such as whole blood, plasma, serum and ascitic fluid, are indicated. It should be pointed out that in treating hypoproteinemia with ascitic fluid transfusions it is not necessary to limit the amount of fluid transfused to 500 cc. As much as 2,500 cc. of ascitic fluid may be transfused during a period of twenty-four hours. Lyophile plasma has been utilized in such hypoproteinemic states, but post-transfusion reactions have been severe. Acacia solutions are contraindicated because of their proved deleterious action on

protein regeneration. Elmann and Weiner have recommended the use of intravenous fluids containing amine acid mixtures. Finally, the danger of intravenous hypertonic and even isotonic solutions of sodium chloride should be kept in mind when hypoproteinemia is present. Edema of the body tissues may be precipitated, due to fixation of the sodium chloride and water in the tissues. Such 'salt' edemas are apt to resist treatment. The use of desoxycorticosterone acetate is contraindicated. . . .

"Since this paper was submitted for publication, we have transfused into human beings ascitic fluid which preliminary cross-matching tests had revealed to be incompatible with the blood of the prospective recipient. No reactions occurred." 122 references.

J. C. M. C.

ALEXANDER, JOHN: *Preoperative and Postoperative Care of Patients with Surgical Diseases of the Chest.* Arch. Surg. **40**: 1133–1150 (June) 1940.

"Countless patients have failed to recover their health or have died after technically perfect thoracic operations solely because the surgeons failed to apply with intelligent understanding those preoperative and postoperative measures that are based on a thorough familiarity with thoracic physiology and pathology and with the behavior of diseases of the chest.

"*Diagnostic and Observation Period.*—. . . the decision as to which patients should be treated surgically, the choice of operation and the surgical management of the patient require of the internist or surgeon a deep knowledge of both the medical and surgical aspects of thoracic disease and the reaction of one on the other. Cardiocirculatory disease, including compensated valvular lesions, does not necessarily contraindicate extensive thoracic operations, which, however, should be performed in stages when possible.

"The slightest objective evidence of dyspnea and cyanosis at rest in bed or after slight exertion is an ominous sign if the contemplated operation is one that would reduce the respiratory functional reserve. . . .

"Roentgen Examination. . . . detailed roentgen examination is the most important means of diagnosis.

"*Pneumothorax.*—Preoperative induction of pneumothorax may give useful roentgen information as to whether neoplasms and other lesions are in the lung, thoracic wall or mediastinum. . . . Exceptionally, inspection with the thoracoscope and removal of a specimen for microscopic examination may give valuable diagnostic aid.

"*Bronchograms.*—The value of intrabronchial instillation of iodized oil followed by taking of roentgenograms is well known, but the danger that the oil may cause an acute and dangerous increase in tuberculous or nontuberculous pneumonitis is less generally recognized. The recommendation is therefore made that major operations should not be carried out within two months of the instillation of iodized oil if more than traces of the oil have been retained.

"*Bronchoscopy.*— . . . universally recognized as an indispensable diagnostic and therapeutic measure. Ideally, the bronchoscopist for patients on whom thoracic operations are to be done should be the thoracic surgeon.

"*Preparation for Operation.—Postponement of Operation.*—The results of surgical treatment will be better in certain chronic diseases if patients who are "run down" are given a preoperative period of rest in bed and adequate diet. . . .

"*Interval between stages.*—Sufficient time should be allowed between the stages of staged operations for the patient to recover fully from any debility