Notes on phleboclysis

William B. Potter

University of Nebraska Medical Center

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NOTES ON PHLEBOCYLISIS

William B. Potter

SENIOR THESIS, presented to
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Some Notes on Phleboclysis*

Introduction

"If a tankard of wine is poured into a river, the wine, together with the water, flows into the sea; in just the same way, whatever liquid is injected into a vein must necessarily reach the heart, together with the circulating blood."

-- S. Elsholz, 1665 (24).

Phleboclysis has been and is rapidly becoming a much more frequently used surgical procedure, adaptable to medical and obstetrical purposes, and of service in a wide variety of requirements. Its development may be traced back...

*The term phleboclysis is proposed by Cuttling (10), and approved by Faatus (19) for the procedure of introducing fluid material directly into a vein. Such terms as intravenous therapy, while technically correct, are lengthy and not specific. The term venoclysis, as proposed by Hendon (32), is not acceptable because of its hybrid derivation.
to the days when Columbus discovered America, yet despite large amounts of experimentation, both in the laboratory and in the clinic, it had not become a safe and rational therapeutic measure until comparatively recently.

In the last decade, however, it has been used with increasing frequency. Today it is a routine procedure in the average hospital.

The enthusiasm in regard to this type of therapy has failed to note several important facts in relation to the introduction of foreign materials directly into the circulatory system. Inasmuch as there are at least five or six preparations in common use, it should seem that there should be definite indications and contra-indications to the use of each. Observation of clinical use, however, suggests that such restrictions are not generally known.

In addition to the problem of the dissolved material, or the suspended matter, there is the problem of solvent. Water is universally used, but there is the possibility that even dosage of water may be limited to definite minimal and maximal amounts. The metabolism of water is an essential part of the total body metabolism; such fact being true, it is
very probable that indiscriminate administration to the semi-comatose or unconscious patient may be definitely harmful.

Considering the solute, the question of kind and amount under varying conditions, must be decided upon. Chemical studies of the blood have conclusively shown that the character of the plasma is remarkably constant in both type and amount of its dissolved and suspended materials. Additionally, there is a delicately adjusted ionic dispersion of certain elements, and a carefully controlled hydrogen ion concentration. Realizing that such fundamental arrangement exists among these circulating elements, is it apparent, that, unless care is taken, phleboclysis may destroy this organization, possibly, or probably, with marked detrimental effect to the patient, both as concerns physiological processes and morbid pathology.

The intravenous injection of preparations of blood, either whole blood or serum, are not considered in this paper, nor are the detailed surgical problems of intravenous technic considered, other than applies to the choice of preparations, and the method of administration that specifically deals with the prevention of reactions and allied ill effects.
Historical Review

The quotation from *Climatica Nova*, by S. Elsholz, in 1665, (See introduction) is the first reference to intravenous procedure obtained. Obsolete reference to a syringe developed by a Johann Daniel Major, in 1668, was also found. There is however no record of its actual use.

Boyle, in a book published in 1720 (25), quotes the following experiments which were performed in 1656:

"I may here mention some later experiments made to show the effects of liquid poisons conveyed immediately into the blood, and particularly that famous one of Mr. Christopher Tren, who contrived a new way of injecting them. 'I procured a large dog, into the vein of whose hinder leg we conveyed by a syringe, a small dose of warm solution of opium in sack. The effects became manifested as soon as we could loose the dog from the cords wherewith his feet were tied, for he immediately began to nod and reel as he walked, whereupon to preserve his life I ordered him to be kept awake by whipping, which after some time brought him to himself, so that he grew fat upon it'".

It is this same Mr. Christopher Tren, later Sir Christopher Tren, who became the famous architect of Saint Paul's cathedral dome. At the age of sixteen he was prosector of anatomy to Doctor Scarborough at Oxford. (32)
According to the historical summary as presented by Warthin (85), Elsholz, in 1661, injected water, Spanish wine, opium, and other drugs into the cranial veins of dogs. Findings that these infusions gave results similar to those obtained when the drugs were taken by mouth, he injected aqua plantagnis, cardui benedicti, and extract of cochleariae into the veins of three human subjects without ill results. He also reviewed the literature and the previous experiments of Francassatus of Pisa, who had repeated those of Wren, (21) of Lower of Oxford, and of Dionysius of Paris. Elsholz cites the work of Mollerius of Denmark, who gave infusions and transfusions to animals and to human beings. The blood of animals was frequently injected into human subjects, and cases were reported in cases of syphilis, epilepsy, and intractable fever after the injection of blood from calves and sheep. Despite this auspicious beginning and the absence of any mention of unfavorable results, many unrecorded failures and fatalities occurred from reactions and sepsis. So hazardous was the practice that transfusions of any type were forbidden in several European countries and intravenous therapy fell into disrepute.

After a lapse of about one hundred years a revival of interest in intravenous injections appeared at the beginning
of the nineteenth century, and from 1802 to 1827 a journal devoted exclusively to transfusions and infusions was published in Copenhagen. In 1823 Hale of Boston described the injection of a therapeutic dose of castor oil into his own circulation with transient but disagreeable effects. Magendie in the same year reported benefit of temporary duration in four cases of hydrophobia treated by the intravenous injection of 600 cc. of warm water. Hayem, in 1855, injected 0.6% saline solution into the veins of patients with cholera.

Haford (85) in 1869 reports favorable results following the intravenous injection of solution of ammonia into patients suffering from snake bite. Bacelli (21) used quinine infusion in the treatment of malaria in 1890, and Crede' (21) used colloidal silver for injection into the veins of patients suffering from severe infections in 1901.

The modern story of intravenous infusion dates back to Matas (57), in 1891, when seven recoveries in nineteen cases of shock were treated by 250 to 1,500 c.c. of isotonic saline. He stated that in all cases of circulatory failure intravenous infusion of saline solution resulted in temporary restoration of blood volume, and that this
benefit is permanent in syncope of simple and uncomplicated hemorrhage. Mayo Robson (72), in 1893, reported a case of severe shock followed by recovery after the intravenous administration of 2,500 c.c. of isotonic sodium chloride.

Mummery (64), in the Hunterian Lectures for 1905, stated that intravenously injected saline solution directly combats the fall in blood pressure by diminishing the disproportion between the quantity of circulating fluid and the capacity of the circulatory system, and also diminishes the viscosity of blood incident to shock. He recommended that 180 to 200 c.c. of saline be given per hour until the blood pressure remained at a safe level. In 1924, Matas (59) reported a series of cases in which 5% dextrose solution in distilled water was given continuously through a Murphuy drip apparatus and a cannula ties in the vein. He felt that in intestinal obstruction, septic peritonitis, biliary obstruction, and hepatic insufficiency, pyloric obstruction, and surgical lesions of the kidney intravenous preparations found their especial indications.

On May 12, 1924, Hendon (32) first employed the use of intravenous therapy, for which he proposed the name venoclysis. He again employed it in June, 1924, as a result of a paper, on "Continuous Intravenous Drip, by Dr. Rudolph Matas. (58)"
Hendon attempted for the first time to supply nourishment exclusive of the oral route. He used a silver cannula, gold-plated, and with blunt point. The vein was exposed, opened, and the needle inserted and tied. The rate of flow and the dosage for an adult was 4,000 to 6,000 c.c. of 10% dextrose in a twenty-four hour period, at a temperature of 100 °F. He presents a list of cases treated and cured by this method exclusively—peptic ulcer, septicemia, pernicious vomiting, tularemia, etc.

Palmedo (68), in 1928, reported 150 cases of intravenous therapy. He regarded this as an excellent treatment of shock and hemorrhage, and of especial use in emergency. He recommended its use in peritonitis, dehydration, ectopic pregnancy, and preceding and following surgery upon the gastro-intestinal tract. He warned against over-burdening the heart with fluids and considered lesions of the kidney, high blood pressure, and pneumonia and bronchitis as contraindications.

Warthen (84) reported a case of intestinal obstruction in 1930, following gastro-enterostomy, and two subsequent operations, in which the release of adhesions and entero-enterostomy was performed. 54,000 c.c. of 5% dextrose in isotonic saline was given over a period of eighteen days. The solution contained
2,700 grams of dextrose or 10,800 calories, and was the only fluid or nutriment taken. Autopsy revealed surgical pathology, but no evidence of circulatory damage or damage that was in any way referable to the intravenous therapy.

Most of the previously mentioned investigators had worked exclusively with saline or glucid preparations in water. A few had used citrated blood (which does not come within the scope of this paper), but none of them had used heavy colloidal preparations.

The first reference in the literature to such use of colloidal preparations is that of Hogan (35) who in 1915 described the clinical use of intravenous injection of colloidal solution for the purpose of raising the blood pressure and increasing the blood volume in conditions of shock and hemorrhage. He used 2.5% gelatin solution in several injury cases and in shock. This had been preceded by the work of Czerny (11), in Germany, who had concluded that considerable amount of protein or acacia could be injected into animals without apparent injury. The injection of colloids intravenously was not clinically practised to any degree until Baylis (3), in 1918, re-introduced its use in wound shock during the World War. Since that time the evidence for the efficiency of acacia solution in the treat-
ment of shock in man has been substantiated by many investigators. (43,49,51,61,74)

Incidentally, its use had been extended experimentally to the treatment of Asiatic cholera by Rogers in 1919 (73), to traumatic shock, by Erlanger in 1919 (17), and to cases of hemorrhage by Masson, in 1927 (56), Farrar, in 1921 (20), and by Coburn, in 1924 (7). Huffman, in 1929 (36), reports the successful use of acacia in over 200 surgical and obstetrical cases.

The following notes on the subject of blood transfusion are of interest in connection with this subject:

In 1492, a Jewish physician bled to death three boys in an effort to administer a transfusion to Pope Innocent VIII. (21) The blood was given as a drink, both because of a lack of instruments by which it might be introduced within the venous system, and because knowledge of the circulation of blood did not appear until 1628, at which time Harvey described the circulation of the blood. (53)

Richard Lauer, of England, experimentally transfused animals in 1665, and Jean Baptiste Denys, of France, performed an authenticated transfusion on man, in 1667, giving blood of a lamb to a boy dying of repeated blood-letting. He
repeated this several times, and reported the passage of black urine, probably due to massive agglutination and hemolysis, with hemoglobinuria. (53)

In 1901, Landsteiner made three blood groupings; in 1907 Jansky and Ross made four divisions. (53)
Water Requirements and Metabolism

According to Panton (19), the average daily water turnover in the adult man is approximately sixteen liters. This figure includes those secretions, such as gastric juice and lacrimation, which are resorbed, as well as lymph which returns the water which it drains from the blood.

The above statement is made to explain the tremendous problem of water economy. The handling and transportation of sixteen liters of fluid calls forth many of the body's abilities.

Additionally the lack of water imposes an even greater strain. Clinical evidence of lack of water and the embarrassment that develops in the body economy for that reason is abundant, but explanation for these clinical symptoms is difficult to obtain. It is suggested (19) that when capillaries are insufficiently supplied with fluid for some time, the increased vascular tone produced by vasomotor nerve excitation gives way to vaso-dilatation. This is possibly due to the action of histamine-like bodies. As a result the capillaries become more diffusible and decrease further the supply of circulating fluid due to lowering of the oncotic pressure. Thus the already lowed blood pressure is further decreased,
and the pulse becomes more rapid.

Water Sources:

The total body weight is approximated to consist of about 70% water. The fluid drunk in the course of the day varies from 800 to 2,000 c.c. a day. This varies with the type of labor, humidity, temperature, and etc. (8)

The water derived from solid food supplies, usually, over one half of the daily requirement for water. A little more than 0.9 grams of water is available during the course of metabolism for each gram of food. Thus, the daily food intake becomes the source of 1,000 to 5,000 c.c. of water. If no food is ingested, the body tissue materials are metabolized. From this source it would be unusual for more than 400 c.c. of water to be obtained, inasmuch as a large share of the food of endogenous source is fat, which is low in metabolic water production. (8)

Water Disposal:

Water is lost from the body as urine, in the feces, by vaporization, or in the formation of exudate or transudate. The most important source of drain is that associated with the dissipation of heat. Twenty-four per cent of the body
heat is normally disposed of by the loss of water alone. At this rate 1,000 to 1,500 c.c. is the daily loss. The remaining seventy-six per cent of the heat is dissipated by radiation, convection, and conduction. In the event of high environmental temperature, one hundred per cent of the excess body heat may be dissipated by the vaporization of water. (8)

It is important to realize that vaporization in response to temperature is not effected by the amount of water available, but, in such a case, the kidney is deprived—that is, water for vaporization has preferential rights over water for kidney use. (8)

It is of interest, at this point, to present some definite figures concerning the daily water loss of an average adult, whether or not in morbid state. The following figures have been compiled by Collar (8):

The weight of patients (surgical, post-operative), carefully checked, showed that 1,000 to 1,500 c.c. of water were lost in the course of a day by vaporization. With fever existant, this amount was markedly increased, as from 2,000 to 2,500 c.c. Inasmuch as water is used for vaporization before it is available for kidney function, then on usual intake, it is interest to know how much water is left for the formation of urine, vapor-
ization having occurred. This figure was determined to be
1,500 c.c. a day for the function of the kidneys in the
adult man.

It is estimated that thirty-five grams of material requires
excretion a day by the urinary route. On that basis,
at the specific gravity listed below, the amount of water
required for the excretion of thirty-five grams of material
was determined.

<table>
<thead>
<tr>
<th>Specific Gravity</th>
<th>Am't Water required for Excretion of 35 g. material</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.032-1.029</td>
<td>-</td>
</tr>
<tr>
<td>1.028-1.025</td>
<td>-</td>
</tr>
<tr>
<td>1.024-1.020</td>
<td>-</td>
</tr>
<tr>
<td>1.019-1.015</td>
<td>-</td>
</tr>
<tr>
<td>1.014-1.010</td>
<td>-</td>
</tr>
</tbody>
</table>

Thus, with normal kidneys, at a specific gravity of
above 1.029, about 500 c.c. of water, as urine, will suffice.
For patients with kidney disease, or, if the specific gravity
is to be lowered below 1.020, as it is during the day in
normal patients, a supply of 1,000 c.c. would be desireable,
or even 1,500 c.c. for the sick patient. (8)
In addition to the above outline of fluid loss, there are other sources:

The mere application of extra bedding, during or after surgery, due to the production of sweating, may be a source of definite fluid loss.

The loss of blood due to hemorrhage must be considered as definite fluid loss to the patient. In Collar's investigation of hemorrhage (8), it was found that surgeons consistently under-estimated, on the low side, the amount of hemorrhage that had occurred. "As high as 1,200 c.c. of blood was lost in surgery without the condition being designated as hemorrhage."

Additional, very appreciable, sources of fluid loss are vomitus, diarrhea, exudation, and spumum.

Dehydration:

There are no quantitative tests to show the degree of dehydration, so we (8) determined the amount of water that must be lost before the clinical signs of dehydration appeared. We then planned to give patients, showing these signs, that amount of water. Two subjects were dehydrated by withholding water until the following signs appeared: hot dry skin, dry tongue, sunken eyes, slight fever, low urinary output, and high urinary specific gravity. In these two cases the signs of serious dehydration appeared when an amount of
water equal to about six per cent of the body weight was lost, or:

<table>
<thead>
<tr>
<th>Weight of Patient</th>
<th>Amount of Water Equal to 6% of Body Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 kg. - 22 lbs.</td>
<td>600 c.c.</td>
</tr>
<tr>
<td>20 kg. - 44 lbs.</td>
<td>1,200 c.c.</td>
</tr>
<tr>
<td>60 kg. - 132 lbs.</td>
<td>3,600 c.c.</td>
</tr>
<tr>
<td>80 kg. - 176 lbs.</td>
<td>4,800 c.c.</td>
</tr>
</tbody>
</table>

Thus, in the case of a dehydrated adult man of 60 kg., the water requirements for the first twenty-four hours would be:

- Water for vaporization: 2,000 c.c.
- Water for urine: 1,500 c.c.
- Abnormal loss, as vomiting, diarrhea, etc.: 3,600 c.c.
- 6% of 60 kg. (dehydration): 7,100 c.c.

Therapy in Dehydration:

Water, of course, is the specific remedy in the treatment of dehydration. In a great many cases the familiar practice of "forcing fluid" may be carried out very successfully, orally. However, in the very sick patient, in the comatose patient, and the patient in shock state, another route must be chosen, for Fantus (19) has shown that when the ingestion of water is impossible, there is no way of supplying an adequate amount for the treatment of dehydration other than by the intravenous route.

In the conscious patient thirst is a good indication of
dehydration. The relief of thirst may be the prevention of collapse. If the patient is in semi-comatose shock state, the drinking of water does no good for it is not absorbed from the stomach. (19) In these cases only small sips should be allowed to prevent gastric dilatation. Another light on this aspect regards that patient who receives an intake of only 600 c.c. per day. This is approximately one-third the required daily intake, and constitutes an indication for intravenous therapy.

Distilled water has been experimentally administered intravenously without demonstrable ill effect. It is a definitely hypotonic solution and is capable in producing marked changes in the oncotic plasma pressure.

Saline has frequently been injudiciously used for the treatment of dehydration. Fantus (19) indicates the futility of saline for the relief of dehydration in the following quotation: "Water, water, everywhere, but not a drop to drink". Not only is isotonic saline a poor thirst quencher, but if sufficient quantities of water are given (2,000 to 3,000 c.c.) the kidney must eliminate 17 to 25.5 grams of sodium chloride. This is no little burden for the normal kidney. Additionally, in infusing such a large amount of fluid with sodium
chloride dissolved there is marked possibility of producing edema, due to the water-holding action of sodium chloride.

The preparation that is properly used is a dextrose solution. In using this solution, the dextrose is quickly metabolized (with the advantage of providing a definite source of energy) and the water content is freed, without imposing a burden upon the kidneys. Isotonic dextrose is a 5.1% solution; in this concentration it will not cause shrinking or laking of corpuscles. [88]

Reference to the previously given tables will indicate quite accurately the amount of isotonic dextrose solution which may be given in dehydration.

Vantus (19), in considering the desirable dosage of water makes the following considerations: Under normal circumstances 700 c.c. is vaporized daily by the lungs and skin, and about 300 c.c. is lost in the feces. Hence about 1,000 c.c. are taken care of extra-renal. This means that any fluid administered in excess of 1,000 c.c. must reappear as urine or be stored in the tissues in the form of edema, the initial stages of which may be harmful although imperceptible. The total bulk of fluid infused daily should not exceed, therefore, 1,000 c.c., plus the quantity of urine, plus the dehydration deficit. The exception to this rule is
seen in the patient who suffers vomiting, diarrhea, or exudation. In these cases the losses should be accurately compensated.

When the system has lost much fluid, this loss must be made good before there is an increase in the quantity of urine. Thus, when, after fluid has been given, the body weight becomes stationary and the urine dilute with lowered specific gravity, it is clear that the tissues have received sufficient water. (63)

Striving to obtain and maintain an adequate urinary output at normal specific gravity is the most reliable guide for the administration of intravenous fluid.

Problem of Edema:

It has frequently been noted that the introduction of large amounts of fluid intravenously has resulted in edema. There is no condition in which the introduction of fluids to this extent is indicated. In general, the use of solutions of sodium chloride have a more marked tendency to produce edema than do any other solutions. This is, of course, due to the water-holding power of tissue sodium chloride. Sodium chloride is, under such conditions, not excreted as rapidly by the tissues as it is introduced. In the case of glucose, the water
holding power is not marked, and the glucose is promptly metabolized.

The development of edema is, of course, a definite sign for the withdrawal of fluid administration, unless it is shown that this edema is of other source than the intravenous administration. (53, 19, 85)
Saline Phleoclysis

In the early stages of undue water loss, regardless of cause, the composition of blood in respect to both water content and electrolyte pattern tends to remain unaltered because of the stabilizing or buffering effects of the intercellular fluid. This portion of the body may be looked upon as a reservoir which may shrink appreciably in order that changes in the blood and also the tissue cells, may be kept at a minimum. When the intercellular fluid becomes exhausted, changes do occur in the blood which are indicative of this exhaustion. The nature of the changes is largely dependent upon the manner in which fluid is lost. Sometimes acidosis may accompany dehydration, at other times alkalosis. Rarely, a tendency toward one such change may be exactly counterbalanced by a tendency in the opposite direction. (29)

Some of the causes of acidosis are acute non-specific diarrhea, acute bacillary dysentery, diabetes, acute hemorrhagic nephritis, chronic renal insufficiency, and severe acute infections.

Causes of alkalosis are pyloric stenosis, intestinal obstruction, non-obstructive vomiting, and other conditions of loss of gastric secretion.
Occasionally certain changes of both acidosis and alkalosis may be seen concurrently, as in sepsis.

By the chemical examination of the blood one can usually obtain proof of loss of water, chlorides, carbonates, and total fixed base. Loss of potassium and calcium are not usually so indicated, as their concentration in plasma tends to remain fixed, the tissue cells and bone acting as reservoirs. These facts should be borne in mind if effort is made to replace lost intercellular water, so that restitution may be chemically adequate. Even in dehydration, the loss of electrolytes may require replacement. It may also be desirable to replace plasma protein in an effort to make more normal the colloidal osmotic pressure in order to re-establish normal circulation.

In order to accomplish such restoration of blood without too much reliance upon the kidney or upon intestinal absorption, the parenteral route may be chosen. Sodium chloride is the most important salt as far as amount is concerned. It is to be expected that the administration of isotonic saline solution should go far toward the relief of dehydration, but very definite care must be exercised that only the required amount of saline be given to restore sodium and chloride values of the blood. The addition of potassium and calcium is theoretically
indicated in those cases to whom saline is given. When such an addition is made, in the same proportion in which these elements exist in the plasma, Ringer's solution results. Still more perfect modifications of Ringer's solution might be made, such as Locke's solution or Tyrrode's solution.

It is characteristic of all of these solutions, that the bicarbonate value is much less than that of the plasma. This is necessary because calcium and carbonate will precipitate as the combined salt, if it were added. Such solutions, for this reason, are not greatly superior to the original Ringer's, when the administration of carbonate (acidosis) is desired. That such restoration occurs after such solutions are injected is admitted, but the reason is not inherent in the solution; it is concerned in secondary effects due to the stimulation of the circulation and renal capacity.

Sodium lactate preparations may be substituted for the use of carbonates, and in this way the two solutions combined into one. (30) The combination of sodium lactate with Ringer's solution makes an ideal duplication of normal plasma values.

Indications for Various Saline Preparations:

1. Sodium chloride is the most frequently used of the
numerous saline preparations. There is no indication for the use of other than isotonic (5%) saline solution. While it has been arbitrarily used in the treatment of dehydration states, this does not constitute an indication for its use; the loss of chlorides, which implies the loss of sodium, is a specific indication for isotonic sodium chloride. The chloride content of the plasma is normally maintained at 0.349 to 0.387%.

In obstinate emesis, profuse diarrhea, extreme sweating, and copious exudation, Haden and Orr (27) have conclusively demonstrated the remedial value of sodium chloride. It may be added at this point, that all of these conditions some degree of ketosis may be seen and nutritional insufficiency is common. On this basis 5% dextrose in isotonic saline is usually the preparation chosen. It would, however, be serious to administer dextrose alone in hypochloridation states, for dextrose tends to lower the chloride concentration in both the blood and the plasma. (62) Additionally, when much salt is lost, the secretory activity of the kidney becomes impaired, and the quantity of the urine is diminished, with rise in non-protein nitrogen values. Thus the maintenance of liberal urinary output is of value too. (19)
2. Ringer's solution is indicated in all conditions in which sodium chloride is indicated. Thereby, it should replace the use of sodium chloride inasmuch as it is a much more accurate duplication of the plasma fluid.

3. Sodium lactate solution is indicated in conditions of severe acidosis, other than those associated with congenital heart disease and persistent cyanosis. If the CO₂ content of the blood is known, the amount of sodium lactate that will be required to raise the CO₂ content to the normal value of 60 vol./% may be calculated. (30) Since the chief use of sodium lactate is in the presence of CO₂ content below 25 vol./%, a routine dose of the equivalent of 10 c.c. of molar solution per kilogram will be generally satisfactory. This amount will tend to increase the CO₂ combining power by 25 - 35 vol./%.

Rapid alkalization of the urine may be obtained by this method. 5 c.c. of a molar solution per kilogram, sufficiently diluted, is usually the correct quantity for this purpose.

The dilution of one part of molar solution of sodium lactate with five parts of water makes a isotonic solution.
4. Lactate-Ringer's solution is an ideal imitation of the blood plasma, and does away with the necessity of administration of two separate preparations. It relieves acidosis or alkalosis of metabolic types, and may be used to advantage in dehydration. Its use in this instance, however, is limited to the restrictions previously mentioned in connection with the treatment of dehydration.

When severe alkalosis of metabolic type is known to exist, the addition of the lactate to Ringer's solution is without benefit aside from its antiketogenic and glycogenic properties. There is, however, no danger connected with the use of sodium lactate under such conditions (29). If, however, the condition is one of acidosis, some much lactate will be required as to make separate administration more practicable. The combined solution finds its ideal in moderate acidosis (29).

5. Sodium bicarbonate has never been widely used for intravenous purposes. It is subject to the same conditions as outlined for sodium lactate, to which it is superior only in cases of impaired lactate (dextrose) metabolism.
such as is seen in congestive heart disease with cyanosis. Many disadvantages have been described. (30) A somewhat hypotonic solution may be used in severe acidosis.

Dosage of various saline preparations:

It is impossible to give definite dosage for the use of saline preparations. In the case of vomiting, irregardless of cause, and in diarrhea, the best method of determining the dosage is the measurement of the loss and the administration of that amount of saline. Blood chloride determinations and CO₂-combining power determinations are of value. In general, Hartmann (29) recommends the use of 80 to 100 c.c. of the above mentioned isotonic preparation per kilogram of body weight. In the case of sodium bicarbonate 0.5 grams per kilogram is recommended. In the case of sodium lactate CO₂-combining power must be known. The equivalent of 10 c.c. of molar solution tends to raise the CO₂-combining power by 25 to 35 vol.-%.

Saline in the treatment of burns:

In the case of burns a combined problem of both fluid loss and of chloride loss arises. A burn of one sixth of the body surface may cause a loss of 70% of the blood volume in twenty-four hours. Thus this problem must be handled as outlined under dehydration. The water intake must be maintained at such a level as
to allow continued urine formation at normal specific gravity. This requires isotonic dextrose solution. For the loss of chlorides, normal saline or, better, lactate-Ringer's, is of use, inasmuch as there is marked chloride loss and a tendency to acidosis. (53)
Acacia Phleboclysis

In conditions of shock or hemorrhage one of the most characteristic occurrences is that of decreased blood volume. When such a reduction occurs the injection of electrolytes or non-electrolyte colloids of the dextrose type have little effect on the decreased blood volume, since they are free to pass through capillary walls and rapidly diffuse into tissue spaces. The plasma proteins and acacia are normally impermeable, remain in the circulation, and, through their effect in raising the colloidal osmotic or oncotic pressure, tend to maintain the blood volume. Thus, when diffusible substances are injected, with water, as soon as the substance (saline or dextrose) has passed into the extra-capillary spaces, blood volume is no longer maintained.

Such a condition is strikingly illustrated in the case of nephrotic edema, in which, due to the large loss of plasma protein, water is no longer retained within vascular beds, and edema appears.

Acacia has been widely used recently in the restoration of blood volume in conditions of shock and hemorrhage. It has also found use in the relief of nephrotic edema.
Indications for the use of acacia:

McIndoe (50) advocated the routine use of acacia in all surgical operations in which the loss of large volumes of blood might be anticipated. Dieckmann (13) believed acacia to be of value in decreasing the concentration of blood and increasing the low osmotic pressure of the plasma in eclamptics. Mason (53) has recently stated that acacia is absolutely indicated in all conditions of shock and hemorrhage. A 6% concentration of acacia is isotonic and is the strength solution to be preferred. As an emergency procedure 300 to 600 c.c. of 6% solution of acacia is used. (48,64)

A large number of articles have recently appeared in the literature concerning the use of acacia in the treatment of nephrotic edema. In such conditions the glomerular membrane is less permeable to acacia than it is to plasma protein. Thus, through the use of acacia the oncotic pressure of the plasma may be restored to a level sufficiently high to result in the loss of edema. Hartmann (28) has recently reported six nephrotic cases which were treated by acacia in 6% concentration. In five of these cases prompt diuresis followed, but only when enough acacia had been given to bring the oncotic
pressure of the plasma to 13 to 21 c.m. of water. In these patients the edema disappeared entirely. This is in agreement with the work of Epstein (16), who stressed the relation between the reduction in concentration of plasma protein and non-cardiac edema and the value of high protein diet in the treatment of such edema. Since the effect of the injected acacia on edema depends largely upon the concentration of the acacia maintained in the blood plasma, which, in turn, is dependent on the amount given in relation to the original blood volume, the rate of urinary excretion, and the rate of acceptance by other tissues, the dosage of acacia cannot be fixed. (28) In general 1 to 2 grams/kilogram of the ideal body weight was given intravenously over a one hour period. This may be repeated daily until as much as 10 grams/kilogram has been given. (29) Disposal of injected acacia:

Andersch (2) has recently shown, as a result of extensive studies, that only very small amounts of acacia are ever found in the urine after injection. A very large per cent of the total dose was demonstrated to have been stored
in the liver. Once deposited in the liver removal was very slow. In one rabbit thirty per cent of the injected acacia was recovered from the liver after three months. Histological examination of all livers of rabbit, rat, and dog showed characteristic vacuolization of liver cells, which, coupled with certain changes in the composition of the bile, suggested marked liver damage. The Kupfer cells appeared normal. These findings raise the question whether acacia should be used routinely in repeated doses, as, for instance, in the treatment of nephrosis. (2,28)
Dextrose Phleboclysis

The use of solutions of dextrose for intravenous therapy is a very rational and very practical one. There are a large number of conditions that may be treated by such injections, as acidosis, acute infection, and dehydration. There are additionally many specific indications for its use: malnutrition, diabetic acidosis and ketosis, hyperinsulinism, in the production of diuresis and the relief of intracranial pressure.

The ease with which water may be administered and, at the same time, appreciable amounts of energy material, is suggested by Watkins (86) and Hyman (39). They recommend its use in all conditions of surgery as a routine procedure, and especially in state of hemorrhage or shock. Watkins presents 26 cases in which dextrose phleboclysis was used. These cases represent all types of surgical problems.

Use of isotonic dextrose:

Many studies have been made on the toxicity of isotonic intravenous glucose. Wassermann (54) made extensive studies upon 85 normal patients. His consistent finding was that fifty grams of glucose in concentrations of less than 20% produced no untoward clinical findings other than diuresis.
Hendon (33) presents the following record of blood sugar in patients receiving 10% solution intravenously:

<table>
<thead>
<tr>
<th>Time</th>
<th>Blood Sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 hr. pre-phleboclysis</td>
<td>120 mg/dl</td>
</tr>
<tr>
<td>1/2 hr. post-</td>
<td>200 mg/dl</td>
</tr>
<tr>
<td>1 hr. post-</td>
<td>175 mg/dl</td>
</tr>
<tr>
<td>1 1/2 hr. post-</td>
<td>150 mg/dl</td>
</tr>
<tr>
<td>2 hr. post-</td>
<td>135 mg/dl</td>
</tr>
<tr>
<td>2 1/2 hr. post-</td>
<td>120 mg/dl</td>
</tr>
<tr>
<td>3 hr. post-</td>
<td>120 mg/dl</td>
</tr>
<tr>
<td>3 1/2 hr. post-</td>
<td>120 mg/dl</td>
</tr>
<tr>
<td>4 hr. post-</td>
<td>120 mg/dl</td>
</tr>
</tbody>
</table>

From the above results, the conclusion was drawn that 10% glucose is not productive of hyperglycemia.

There is no record in the literature of danger being associated with the injection of glucose in concentrations less than ten per cent.

The primary use of isotonic dextrose is in the treatment of dehydration, in which case the primary requisite is fluid. This type of therapy has been previously considered.

Use of hypertonic dextrose:

In the treatment of many specific conditions the
requirement for dextrose is so high that administration in solutions of greater concentration than 5% is frequently desirable. In this connection, it has been frequently pointed out that the injection of these hypertonic preparations is frequently attended with some danger. Massermann (54) in a large series of patients demonstrated that the intravenous injection of 100 grams of dextrose or more, in 35 to 50% solution caused headache and other adverse signs in a large proportion of patients. More than half of his patients who had received more than 185 grams suffered transient pyrexia. Jacobs (40) has shown that 50% dextrose in amounts of 0.7 to 4.5 grams/kilogram is invariably fatal to animals if continued over a lengthy period. He injected the dextrose continuously, but at all times within the limits of tolerance and without the production of glycosuria. His post-mortem findings were those of a non-ketogenic acidosis, associated with profound congestion and hemorrhage of the pancreas and anterior hypophysis.

1. Dextrose in the treatment of acidosis and ketosis

A certain concentration of carbonate in the blood plasma is essential. Acidosis is an extremely common pathological state, more common
than fever, and due, frequently to a decrease in the carbonate concentration. The simplest way of recognizing and preventing it is the administration of enough sodium bicarbonate to make the urine amphoteric or slightly alkaline. When this is accomplished, it is known that acidosis cannot exist, and that the patient has not been harmed by the production of alkaloisis.

However, it will be found that in all conditions in which dextrose is inadequately catabolized, whether this is in starvation or in diabetes, excessively large quantities of alkali would be required to secure this result, and even then the effect would be temporary.

One must, in such case, proceed more fundamentally, and relieve the cause of the acidosis by supplying the dextrose in the case of starvation acidosis and ketosis, or insulin in the diabetic case. The intravenous administration of dextrose may thus prevent the appearance of ketosis in a patient unable to ingest food. In case of diabetic ketosis, dextrose is not required; insulin, in such cases, is usually administered by the subcutaneous route.
There are certain types of patients who, because of marked increase in metabolic rate, there is a definite tendency to acidosis. Thus children, and patients with thyrotoxicosis or hyperpyrexia, there is this marked tendency to acidosis as a result of accelerated metabolism. Dextrose in these cases is a specific remedy. [81] By phleboclysis a 10% solution can be introduced at the rate of 500 c.c. per hour before the sugar tolerance of the average individual is overcome by glycosuria. At this rate, 6,000 calories may be introduced in a 24 hour period, which is twice the caloric requirement of a resting patient, hence intravenous nutrition is very possible, as has been clinically shown by Marriott (52) and Porter et al. (69). Jensen (41) has suggested covering 20% of the dextrose with insulin at a ratio of one unit per gram of dextrose. Stokes (79) has shown the advantage of dextrose in malnutrition of children. In this connection it is noted that the injection of large amounts of intravenous fluid may further dilute already lowered plasma colloids with the production of edema (53).

2. Dextrose osmotherapy

The injection of 25 to 50% dextrose should not be undertaken without definite demand for osmotherapy - the osmotic changes produced thereby
in the system. Venous obliteration has been described as resulting from the use of 50% solutions (19).

a. The colloidoclastic crisis, due to the destruction of a certain percentage of the corpuscles and possibly of other tissue elements may be of advantage as a non-specific form of proteo-therapy - to stimulate latent powers of antibacterial resistance. It shortens the bleeding time and has been advocated by Opitz (65) in the treatment of internal hemorrhage. It is considered to be of especial value in cases of bleeding from the bowel (19).

b. The first capillary territory affected by hypertonic solution is that of lung. This is the reason for Stejskal's (78) report of a favorable influence in pulmonary edema, whether of inflammatory or transudative nature. This has been confirmed by others, as Litchfield (46), John (42), and Wells (87) reports favorable results from the use of large volumes (250 to 500 c.c.) of hypertonic (25%) dextrose in pneumonia.

c. Hypertonic dextrose in amounts of 100 to 200 grams of 20 to 35% solution, according to Massermann (54)
causes an initial rise in the cerebrospinal fluid. This is followed by a secondary fall, and, after three hours, a tertiary rise to normal. Hypertonic salt solution has been used for the purpose of reducing cerebrospinal fluid pressure, but Haden (26) advocates the use of dextrose. He infuses 250 c.c. of 25% dextrose solution over a one hour period, every twelve hours, from the onset of any disease associated with brain edema, until there are no longer any evidences of brain pressure. In meningitis these injections are given in addition to intrathecal injections of antiserum, and are combined with spinal fluid drainage. Bennett (4) has shown that the prompt use of hypertonic dextrose may prevent cerebellar herniation through the foramen magnum. In head injuries, or after brain operations when slow pulse and low blood pressure and stertorius breathing increased intracranial pressure hypertonic dextrose may be indicated, providing the emergency of the situation precludes the possibility of giving 30 c.c. of a saturated solution of Magnesium sulphate by mouth or, twice that quantity by rectum. It may be employed in addition to these measures. The use of dextrose solution is in no way a substitute for surgery; additionally, it should not be used in conditions of brain hemorrhage. (89)
d. Hypertonic dextrose seems to have a special value in the treatment of heart weakness, with or without edema. In the presence of edema absorption of intracellular fluid would no doubt account for a part of this action. Its alleged value in myocardial weakness without edema in which it is considered a useful aid to digitalis may possibly be explained by its demonstrated vaso-dilator action, lessening the work of the heart. Nourishment is a probable factor. (60) Ginsberg (23) has shown that intravenous hypertonic (50%) glucose produces a marked and sustained increase in the coronary circulation. Hypertonic

e. In the administration of dextrose approximately 0.4 grams/lb/hr is metabolized. If more than this amount is given glycosuria appears with marked diuresis. (53) Thus if 50 - 100 c.c. of 50% dextrose is given at interval of 3 hours diuresis will result. This may be used in any condition in which diuresis is desireable. Obviously, if diuresis is not desired, the appearance of glycosuria is an indication for decreasing the rate of administration.
Dextrose in the Treatment of Poisoning:

Cutter (9) has stated that the treatment of poisoning should consist of the routine use of 5% dextrose solution intravenously. Pantus (19) explains the theory of intravenous therapy in poisoning cases as follows: It is important to distinguish between poisoning of diffusible and non-diffusible bodies when "washing the blood" by means of phleboclysis. Some poison conditions respond; many do not, and are harmed by such attempts. Thus, tetanus, diphtheria, pneumonia, etc., are harmed because the toxins are colloidal and non-diffusible. In diffusible toxins phleboclysis is essential. In mercuric chloride dextrose is of value. The use of sodium chloride depends upon the amount of vomiting in such a case. It is omitted in nephritis. In phosphorus, cinchophen, and chloroform poisoning, there may be a tendency to acidosis and fatty degeneration of the liver. Dextrose is given as a part of a liberal carbohydrate administrative plan. (66,14,1)

Whether to use isotonic or hypertonic dextrose depends upon the following: If there is a probability that unabsorbed poison still exists at the point of its application, hypertonic infusion would be contraindicated, as it increases absorption. Isotonic dextrose should be used. When this danger does not exist, and one wishes to draw absorbed toxin back into the circulation, the use of 25% dextrose is of value, especially in cases of heart weakness and pulmonary edema.
Sucrose Phleboclysis

The use of sucrose by phleboclysis is a relatively new therapeutic method. Rather extensive investigation of its possibilities has been made, however, and numerous writers have interested themselves in the possibility of its being toxic. Masserman has shown (55) that very mild reactions follow its introduction into the subcutaneous tissues at the time of phleboclysis. In the general circulation he has been unable to demonstrate any toxic reaction as being specifically due to sucrose. Helmholz (31) also has found it to be non-toxic.

Sucrose in the treatment of increased intracranial tension:

It has been shown by Masserman (55) that hypertonic dextrose in effective amounts and concentration will reduce the pressure of the cerebrospinal fluid, but that this lowering is usually followed by a secondary rise in pressure and the development of unfavorable clinical signs.

The injection of 100 c.c. or more of 50% solution of sucrose caused an initial rise in the pressure of the cerebrospinal fluid for 20 to 80 minutes. Then 300 c.c. were administered the pressure dropped to 21 to 76 m.m. of water below the base line. The average drop was 40 m.m. The pressure slowly rose for the period of the next two to five hours. The administration
of 500 c.c. of water produced a fall in pressure that ranged from 75 to 140 m.m. of water and persisted for 2 to 5 hours. After the secondary rise was completed, mild hypertension of the cerebrospinal fluid was noted in thirty per cent of the cases. In another thirty per cent the pressure was below normal at the end of five hours.

When 300 to 500 c.c. of sucrose in 50% concentration is administered intravenously the initial rise in cerebrospinal pressure (probably coincident with the increase in blood volume and increased venous pressure) is not as marked in degree or in duration as it is in the case of dextrose or solutions of electrolytes. Subsequently, desired diminution in intracranial pressure, due to diuresis and tissue dehydration, is greater and more prolonged.

Corresponding to the relative impermeability of the blood-cerebrospinal fluid barrier to sucrose, there is only a slight and transient hypertension as a final hydrodynamic effect. Dextrose and most salts pass readily from the blood into the central nervous system, and thereby induce, as a terminal osmotic effect, a marked and prolonged increase in spinal fluid pressure. (25,55)

The use of sucrose in 50% concentration intravenously for the reduction of spinal fluid pressure is shown to be
an effective method; the dosage used is 100 to 500 c.c., repeated if necessary when the secondary rise is well marked. Its use is suggested in pre-operative conditions of increased intracranial tension, and also in conditions in which the brain is to be exposed and handled. It is also suggested in inflammatory conditions of the brain of the meningitic type. (55)

Diuretic action of Sucrose:

Both Helmholz (31) and Keith (45) noted that the intravenous introduction of sucrose was followed by an increase in the urinary output. Strohm (80) has recently shown its effect. In several cases of anuria, dextrose, caffeine, sodium benzoate, and alkali were used without effect. It was not considered advisable to use a mercurial. 50% sucrose in repeated intravenous doses of 20 to 50 c.c., however, produced startling results. Diuresis was uniformly produced. Experiments were subsequently performed upon ten laboratory animals, and the observation in each case was roughly doubled urinary output. (80)
Solutions: Preparation and Administration

Preparation of solutions: [29, 82]

1. Ringer's solution:
   Dissolve the following salts in water, freshly distilled, and make up to five liters:

   \[
   \begin{align*}
   \text{NaCl} & \quad 750 \text{ g.} \\
   \text{KCl} & \quad 50 \text{ g.} \\
   \text{CaCl}_2 & \quad 25 \text{ g.} \\
   \text{MgCl}_2 & \quad 25 \text{ g.}
   \end{align*}
   \]

   To use, dilute 25 times, sterilize at 20 lbs. for 30 minutes.

2. Sodium lactate:
   Neutralize 100 c.c. of lactic acid (USP) with concentrated carbonate-free sodium hydroxide, (40%). Phenol red is used as the indicator. Make solution up to 800 c.c. with distilled water and heat to boiling for thirty minutes, adding small amounts of alkali as needed. Make up to 1,000 c.c. and autoclave. This is a molar solution, which must be diluted with five parts of water (M/6) to make an isotonic preparation suitable for intravenous use.

3. Lactate-Ringer's solution:
   100 c.c. of molar sodium lactate is added to 400 to 450 c.c. of diluted Ringer's solution.

4. Dextrose
   1,000 grams of dextrose (CP) is dissolved in 1,950 c.c. of hot water. This is made up to 2,000 c.c.

   Isotonic dextrose is made by diluting 55 c.c. above to 500 c.c. This is 5.5% solution.

   Ongoing acids may develop, but these are of negligible importance from the standpoint of producing reactions unless alkali has been added to the solution, in which case the production of acid is accelerated.

5. Acacia solution:
   Made up in 30% concentration in 4.5% sodium chloride. Dilute five times with water or 20% dextrose, so final concentration is 6% acacia in 0.9% sodium chloride or 5% dextrose.
6. Sucrose: Sucrose solution is made up in 50% concentration, in sterile distilled water.
Administration of solutions:

1. Prevention of reactions

Selbert (76) in 1925, stated that the cause of many of the febrile reactions following the intravenous use of water preparations was the presence of pyrogens. These were defined as being substances of bacterial origin, which were found in all waters, and, which, when introduced into the vein gave rise to definite evidence of toxic reaction. At that time she recommended more careful distillation of water as the method for removal of these bodies. Elser (15) has recently shown that the number of times a water is distilled has little to do with the presence or absence of pyrogens. He has shown that the use of the water trap and one thorough distillation is sufficient to remove all pyrogenic substances from water. A simple and reliable test for the presence of pyrogens in water has been modified by Carter from that recommended by the U.S. Pharmacopeia. [6]

2. "Speed Shock"

The rapid injection into the vein of any molecule may result in wide disturbances or death. This syndrome has been termed speed shock (34). Irrespective of the sub-
stance used, the symptoms develop in 40 to 60 seconds after rapid injection and comprise of salivation, vomiting, diarrhea, dyspnea, atony, and spasm. They are irregular in character. The blood pressure falls, and dyspnea becomes marked. Pulmonary thrombi and atelectasis are frequently seen at autopsy. In our experience [34] 1 - 5 c.c. of any substance could be made to produce speed shock. In general the hypertonic solutions and the larger molecule preparations gave quicker shock. Species idiosyncrasy was excluded, by the use of dogs, cats, and monkeys. The type and degree of anesthesia made no difference.

At the suggestion of R. Loeb, functional hepatic damage was suspected. Hepatic exclusion was done by the removal of the liver; in these cases speed shock could not be produced. [34] The work of Dale [12] suggests that this mechanism may be due to histamine, but the blood of animals dying in such shock could not be made to produce symptoms in a second animal. The damage seems to be a physical one of the liver, with the liberation of toxic substance. [70]

3. Reactions due to Apparatus

It is difficult to determine what reactions are
due in improperly prepared apparatus. However, extreme care is absolutely requisite in their preparation.

All glassware is carefully sterilized according to the usual routine. At the time of use the mouths of containers are flamed. In cutting glass, care is taken that chips do not fall into the containers or the tubing system (18).

**Tubing** is prepared as follows: New tubing is rinsed in 10% sodium hydroxide for one-half hour, and then washed in running water for two hours. It is sterilized by boiling for one-half hour in distilled water. Old tubing is merely rinsed and boiled. (71)

The needle used is 20-gauge. (47)

4. **Rate of injection**

Titus (83) states that a rate of 2 to 5 c.c./minute is a slow rate. The Council on Pharmacology of the American Medical Association (37) recognizes 10 to 20 c.c./minute as slow. Keith (44) has referred to 30 to 40 c.c./minute as slow. Osborn (57) suggests 30 c.c./minute. Hise (15) suggests a rate of "less than 5 c.c./minute". This less suggestion seems to be the most acceptable for routine use, and especially in conditions where large amounts are to be injected.
Hirschfield and Hyman (59) suggest the following rules in regard to rate:

a. Slow rate for hypertonic preparations.

b. Slow rate for solutions suspending large molecules.

c. A very slow rate is used for solutions other than dextrose and saline and acacia. If such are used an intermittent rate is suggested.

d. A rate of 1 c.c./minute is suggested for amounts under 100 c.c., and a rate of 3 c.c./minute for amounts over 100 c.c.

5. Temperature of Solution

The temperature of the solution should be approximately blood temperature. There should be no sudden change in temperature during administration. In the treatment of a fevered patient a solution ten to fifteen degrees below blood temperature may be used. In surgical shock, a solution as warm as 120 d. F. may be used. (19)

6. Mixing of solutions

As previously outlined, solutions may frequently be mixed and administered with greater simplicity as a single solution. The incompatibility and sodium bicarbonate with dextrose is due to acceleration of
decomposition in alkali; in Ringer's solution sodium bicarbonate causes the precipitation of calcium bicarbonate. The presence of calcium in acacia, will for the same reason, cause a precipitation of calcium bicarbonate if sodium bicarbonate is added. Acacia cannot be added to citrated whole blood solutions, because the acacia (calcium) will neutralize the citrate and permit clotting. (29)

7. Apparatus Set-up

This phase of the subject of injection is not to be considered here. However, it is suggested (22) that a small vein be used, that there be no cessation in the flow of the fluid with regurgitation of blood and clotting, and that the fluid be allowed to run rapidly for the first few minutes, to insure a free channel. If the cannula becomes plugged, the entire set-up should be remade.

8. Dangers of Phleboclysis

Many dangers have already been noted under the subjects of various preparations in use. Orr (66) points out that nature never intended that the human being be fed and watered by vein, and that the insult of such procedure should be respected. He suggests that the main dangers
are reactions with chills and fever, over-burdening of the circulatory system by sudden increase in blood volume, and the production of general and lung edema, and possibly hematuria. Rumold (75) emphasizes the dangers of thrombosis and embolism.
Summary

Fantus (19) has stated that phleboclysis is, in certain conditions, a life-saving measure. It would be a shocking revelation, he points out, if statistics could be collected as to the number of people who annually die of dehydration when their lives might have been saved by the parenteral administration of 5% dextrose, the number of patients lost by hypochloridation, when their lives might have been saved by dextrose-saline phleboclysis, and the number of ketosis deaths that might not have occurred had dextrose been given. This does not include the occasional life that might be saved by osmo-therapy. Occasionally, dextrose therapy has been administered with later fatality simply because the patient was not given enough of the proper intravenous remedy.

Fantus suggests, as an added advantage of phleboclysis, the giving of small continuous doses of specific therapeutic agents in the intravenous fluid. He refers to Hyman (38) who administered various antisera without the production of anaphylactic shock, and with clinical improvement of the patient. Fantus points out that injection of drugs directly into the tubing is often very practicable. He recommends that epinephrine, sodium iodide (in thyroid crisis), and morphine (pain), paraaldehyde (mania), and caffeine (stimulant) be given this way. (77). In
administration in this manner one-half of the oral dose is used, repeated as necessary. Insulin is believed to have superior action when injected subcutaneously, however in diabetic coma or in the appearance of undesired glycosuria, it may be added to the dextrose solution in quantity of one unit of insulin per gram of dextrose, covering from twenty to eighty per cent of the dextrose administered.

From the material organized within the body of this paper, we believe the following conclusions may be drawn:

1. The daily water requirements are subject to very strict limits, and must be recognized in the treatment of any patient, with emphasis on these requirements in the case of the comatose or shock-state patient. In the treatment of dehydration a dextrose solution, usually isotonic, is preferable. Saline solution is used only if vomiting, diarrhea, or massive exudation has occurred, in which case, the loss is replaced with an equal amount of saline solution. Dehydration has not been adequately treated until thirst disappears, urinary volume rises, and the urinary specific gravity falls to normal limits.

2. Edema may be easily produced by the over-administration of water, especially of the salines. This is a definite indication for the withdrawal of forced fluids.

3. Sodium chloride is used only in case of hypochloridation, in which case it is administered in amount approximating the
fluid volume lost as in vomiting, diarrhe, or exudation. There is no indication for its use in other than isotonic solution.

4. Sodium lactate solution is indicated in cases of severe acidosis. It may be used to alkalinize the urine. M/6 solution is isotonic.

5. Lactate-saline or Lactate-Ringer's solutions are similar to the blood plasma in composition. These solutions are of especial value in mild acidosis.

6. Isotonic dextrose is of value in the treatment of dehydration. It is the preparation of choice.

7. Hypertonic dextrose is of definite value in the treatment of acidosis and ketosis, especially of starvation or metabolic origin.

Hypertonic dextrose is used in the production of colloidoclastic crisis, for dehydration of the lung in condition of inflammation or transudation, and for the production or decreased cerebrospinal fluid pressure as a result of dehydration of the brain.

Hypertonic dextrose is of value in coronary disease, probably through a combination of dehydration and nutritive effects. It has been demonstrated that hypertonic dextrose may be used in providing both caloric and fluid intake for a period of several weeks.

The injection of hypertonic dextrose will produce diuresis,
which may or may not be desired.

Dextrose solution, in isotonic or hypertonic concentration may be of occasional value in the treatment of poisoning.

8. Sucrose phleboclysis with 50% solution has been shown to stimulate marked diuresis and decrease in cerebrospinal fluid pressure.

9. Acacia has been shown to be of value in increasing plasma colloids with secondary increase in osmotic tension. This is of value in the treatment of edema of the nephrotic type which is due to lowered plasma oncotic pressure. It is also of value in the emergency treatment of hemorrhage and shock.

10. Phleboclysis has been shown to be a very valuable surgical procedure. It is necessary that the correct solution in proper amount be used. Definite indications and contraindication of the used of each has been noted.

There is rarely occasion for the use of phleboclysis in the ambulatory or conscious patient, with the exception of those with alimentary pathology.

Definite dangers of phleboclysis have been noted, and suggestions made for their elimination.
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