1934

Intravenous glucose therapy

Robert Best
University of Nebraska Medical Center

This manuscript is historical in nature and may not reflect current medical research and practice. Search PubMed for current research.

Recommended Citation

INTRAVENOUS GLUCOSE THERAPY
****

A Consideration of the Physiological
Principals, Indications, Concen-
trations, Dosage, and Rate of
Administration...........

******
****
**

UNIVERSITY of NEBRASKA COLLEGE of MEDICINE

SENIOR THESIS (April) 1934

Robert Best

INTRODUCTION

If we wish to discard the more or less mythical and apocryphal references to blood transfusion in ancient literature, the suggestion to introduce blood or medicaments into veins did not formulate itself into mans mind, according to Fantus, until after Harvey , 1613, discovered and demonstrated the circulation of blood.

Macht states that the first actually to inject drugs intravenously into animals belongs to the architect and professor of astronomy, Christopher Wren, who in 1656 injected dogs with drugs by means of a quill attached to a small bladder. After that, intravenous injection was not practiced until about 1900.

In 1907 Fleg made roughly timed intravenous sugar injections. He noted the remarkable diuresis and realized the possible clinical application. Litchfield in 1909 began to use hypotonic glucose solution (15 grams to the liter) intravenously. In 1914 he started using hypertonic solutions in the same manner.

The first clinician to advocate treatment of hepatic diseases with dextrose was A. P. Beddard in 1909. According to Fantus, Erhlick, in 1910, with the introduction of arsphenamine made intravenous injection a matter of every day practice.

The next pioneer in this type of therapy appears to be Kausch, who in 1911 recommended and attempted intravenous nutrition in hysterical vomitting and hyperemesis gravidarum, surgical conditions and acute gatro-intestinal disease.

INTRODUCTION

In 1914 Henriques reorted the use of 30% glucose intravenous for the treatment of heart disease. In 1915 Opie and Alford and independantly Grahm furnished the experimental basis for this therapy by demonstrating that the feeding of carbohydrates lessen the susceptability of rats and dogs to necrosis of the liver caused by chloroform and by phosphorus.

Bernard Fantus states that intravenous injection was discovered and practiced earlier than hypodermic injections.

The reader will observe that the term glucose is very generally used as synonymus with dextrose and sugar. Until dextrose was accepted by the Pharmacopea it was commonly known by the synonym "glucose" and this latter term is occasionally used even at present time to describe dextrose.

PHYSIOLOGICAL PRINCIPALS

There are certain fundamental facts about carbohydrates that are so well established and so well known as not to need discussion. According to La Fetra, sugars, dextrins and starchs are the most economical source of energy. Some being absorbed as ingested and others requiring but little digestive effort. They furnish energy chiefly for heat maintenance and muscular activity. They build up the glycogen reserve and may be converted into stores of fat. They spare proteins thereby lessening the amount of nitrogen excretion otherwise necessary. Moreover, they may be utilized to build up certain useful amino acids. They can replace the fats to a very large extent up to the point of not causing dificiency in the fat soluble A and the anti rachitic vitimins. They serve when properly utilized to prevent acidosis.

Grafe states, that the fate of sugar in the liver varies according to the needs of the entire organism or the momentary demands of the liver. He gives four possibilities: 1. It may be carried off to the peripheral blood stream through the hepatic veins unchanged. 2. It may be synthesized to glycogen. 3. It may be decomposed to CO_2 and H_2O. 4. It may be converted into fat or protein elements. Glycogen is the form of carbohydrate used for storage. He states it is astonishing that the amount and rate of glycogen formation depends on the quanity of glycogen already deposited in the cells. In starving animals the deposition of glycogen is more difficult than under other circumstances. The glycogen content of the liver

is normally 4 - 5% and cannot be made to exceed 14%. The
main duty of sugar is to act as a calory producer. It is
particularly well adapted to this role because of the ease
with which it is oxidized. Lactic acid is the most import-
ant product of decomposition and can be most readily deter-
mined. The quanity is small under Normal conditions, but this is
because the lactic acid which reaches the blood stream is
quickly synthesized by the intact liver into carbohydrate.

It has been shown by Flood, Bodansky and others that
dextrose is most rapidly absorbed into the blood stream and
existed in the blood stream as such.

Holt investigated healthy children from 1 to 18 years
and found that about 51% of the distribution of calories
was derived from carbohydrated of which about 1/2 of this
was given as sugar. Gebhart found that the healthy active
boys of St. Paul's school consumed 600 grams of carbohydrates
daily or nearly 2,500 calories daily. Much of this being
in the form of sweets. Dun, Phillips, Henske, Best, McGoogan
and Wherry state that carbohydrates provide easily utiliz-
able energy and heat. They are stored in small amounts, a
normal starving adult using up his available glycogen stores
in 36 to 72 hours. The bulk of the average diet is in the
form of carbohydrates. Carbohydrates usually furnish 40 to
70% of the total calories of a diet.

Finkelstein has emphasized that though carbohydrate
does not itself enter into the composition of cell cytoplasm
it induces retention of protein salts and water being the
chief influence by which water and water-containing constituents

are stored. When food is given by any route which involves absorption as a prelude to its entering the blood stream the rates which it will enter will depend on the rate at which it is absorbed. By any route of administration but especially by the oral route, the actual rate of entry into the blood stream and hence into the tissues, according to Woodyatt, Sansum and Wilder, must vary with a wide range of physical, physiological and patholigical conditions over which we have no control.

Hendon says when a measured quanity of any substance is introduced into the alimentary tract or the subcutaneous tissues the balance between delivery and distribution is preserved by the physiology of digestion and absorption.

Starches administered by the oral route are changed to maltose a dissaccharid by the diastatic ferment, ptyaline of the saliva. This in turn is acted on by a ferment and becomes glucose or dextrose. These processes are carried on in the mouth and later in the stomach until acted on by the HCL of the gastric secretion when they are stopped. The amylase of the pancreatic secretion and other less important ferments complete the transformation of the starch to glucose in the intestines. The glucose is rapidly taken up by the portal circulation and transported to the liver whence it is synthesized to glycogen, (often spoken of as animal starch). The liver stores the glycogen. The maximum quanity which it may contain varies in different animals, being about 10% by weight in man. The glycogen is given off to the general circulation as glucose. This change occurs at such a rate that normally the percentage of sugar in the

blood remains constant at a level of from .10 to .12

per cent. Some of this glucose in the general circulation

is not made use of immediately by the cells but is re-

synthesized to glycogen to be stored as it was in the liver.

The main subsidary store house is in the muscles. These

can take up glycogen according to Mosenthal, in amount

equivalent to .5% to .9% their weight. This is an amount

approximately equal to that found in the liver.

Claude Bernard, who discovered glycogen, thought it

was a secretion of the liver because he found that it could

be produced by this organ on a diet devoid of starches.

Later glycogen came to be regarded as a storage produce of

carbohydrate material, much in the same manner in which fat

is regarded as a storage produce of lipoid material. Recently,

the work of Barbour, Chaikoff, Macleod and Orr and others

undermined this conception by showing, in the first place,

that it is impossible to rid the liver entirely of glycogen,

which should be the case if it were purely a storage product;

and , in the second place, that during starvation the amount

of glycogen in the liver at first is markedly diminished but

later increases again. These facts were responsible for a

new theory of glycogen, namely, that it is an essential step

in glyconeogenesis, and that the amount of it in the liver

at any given time represents the balance between continuous

processes of production and loss.

According to Garnstein and Swarzmann in normal animals,

administration of suitable amounts of dextrose leads directly

to deposition of glycogen in the liver. In diseases of the

liver, such deposition of glycogen has been denied because the reduction of dextrose tolerance frequently seen in cases of hepatic damage was interpreted as indicating failure on the part of the liver to remove dextrose from the blood for storage. For the correction of this condition, insulin is being commonly advocated, especially abroad.

Macleod states that although the glycogen in the liver may in part at least be regarded as a storage form of surplus carbohydrates much the same as starch is in plants, there is an accumulating evidence to indicate that it has another function. It represents an obligatory stage in the conversion of those portions of the food stuffs that are to be used for combustion purposes in the organism. It has been shown by Best, Hoet and Marks, according to Macleod, that glycogen can be deposited in the muscles out of the sugar carried to them in the blood, provided insulin is present.

Litchfield states that glucose is non toxic, it is quickly utilized by the organisms, it is the best sparer of nitrogen, it is a stimulant to the mechanism of cell metabolism, and it is easily obtained and prepared.

According to the United States Dispensatory, dextrose, which is sometimes improperly called glucose in chemical literature, may be obtained from grape sugar which is the re-crystallization product of the complete hydrolysis or conversion of the starch by acids. It usually occurs in the hydrated form $C_6H_{10}O_5$ plus H_2O and is a colorless crystal of a less sweet taste than sucrose. It is very dextrorotary from which fact it takes the name of dextrose. It was introduced into the U. S. P. and the British Pharmacopea in 1914.

INDICATIONS

It is generally and logically accepted that nothing can be more basic or fundamental in the supportive treatment of any serious disease than to supply a patient with food and water in such a form and by such a route that they are immediately available to the starved and thirsty tissues. Glucose is the only food, according to Macleod, existing out side the human body in the same form as that found in the blood stream. Most of the sugar in mamillian blood is glucose. It has been demonstrated by Slemons' simultaneous analys s of maternal and fetal bloods that the nutritive exchange through the placenta is almost entirely in the form of glycogen. In the artificial feeding of infants, according to Potter, the carbohydrates play a most important role. Not only do they supply the necessary calories not furnished by the fat and the protein, but they also are necessary to complete the oxidation of the fats, otherwise ketone acids would be formed and an acid intoxication intervene. In diseases of the liver, insufficient glycogenesis causes 'internal' carbohydrate starvation, which results in a reduction of hepatic glycogen, probably largely through depletion of that part of it which serves as a storage form of carbohydrate. According to Althausen, there are several ways in which dextrose, and the same applies to glycogen, has been proved to have an allaying action in hepatic injury. In the first place, dextrose neutralizes many exogenous and endogenous toxins. This may be accomplished by partial oxidation to less toxic compounds or by complete oxidation to carbon dioxide and water. Another

path lies through conjugation to nontoxic glycuronates.
The latter is known to occur with cresola, phenola, salic-
ylates, camphor, and many substances containing these com-
pounds. And in the second place under carbohydrate ther-
apy, repair of the injured liver proceeds much more rapidly.
In the third place, administration of dextrose reduces pro-
longed coagulation time in jaundice. He also states that it
is unfortunate in hepatic disease when the liver is in ur-
gent need of glycogen, its supply of this substance should
be low. He thinks the reason for a low level of glycogen
in the injured liver is important clinically, and that
experimental data suggest that the lowering of hepatic gly-
cogen may be due, not to an inability on the part of the
liver to store glycogen, but to abnormally slow production
of new glycogen from non-carbohydrate sources--in which
case administration of dextrose would be the indicated
remedy. To test the ability of the injured liver to store
glycogen, experiments were carried out on rabbits. After
poisoning with phosphorus, the damaged livers doubled their
content of glycogen three hours after a single oral admin-
istration of 2.5 grams of dextrose per kilogram of body weight.
The absolute increase of hepatic glycogen in these experi-
ments was much smaller than in normal rabbits, but the low
initial level of glycogen in the liver of the poisoned ani-
mals must be taken into consideration because the same was
also observed in normal rabbits, in which the glycogen of
the liver was markedly reduced by fasting or by medication
with thyroxine. A somewhat different series of observat-

ions was made on a group of patients with marked abdominal
operations. These patients received preoperatively various
amounts of dextrose orally or by intravenous infusion. A
small wedge-shaped piece of the liver was removed in each
instance for microscopic examination. It has been shown
in animals that the liver loses half of its glycogen after
one hour of ether anesthesia---All patients were uniformly
fasted over night and operated on in the morning. For a
control group, several patients were used from whom biopsies
of the liver were obtained prior to 1925, when such cases
were still treated surgically without an intravenous infus-
ion of dextrose as part of the preoperative routine. One
group of patients received 50 to 100 grams of dextrose by
mouth three times a day for from one to two weeks preoper-
atively. In addition, these patients were given intraven-
ous infusion of dextrose twelve hours before the operation.
Another group of patients was given two intravenous infus-
ions of dextrose (from 500 to 1,000 cc. of 10 per cent
solution) a day, for from one to five days, the last inject-
ion being given on the morning of the operation. In these
three groups, biopsy specimens of the liver with approximate-
ly equal degrees of damage were compared microscopically in
in regard to their content of glycogen. The slides were also
compared with sections of rabbit liver containing known amounts
of this substance. Biopsy specimens from fourteen patients
in these three groups were examined in the described manner.
From a comparison of typical sections---it is readily seen
that the livers of patients who received no dextrose before

operation are almost devoid of glycogen and closely
resemble that of the rabbit with a glycogen content of
only 1.5 per cent. The parenchymatous cells of the liver
in these sections are narrow, and their cytoplasm takes
a dark stain. The sinusoids and bile capillaries are wide.
On the other hand, the hepatic cells in sections from pat-
ients who received large amounts of dextrose by mouth are
literally filled with glycogen and have the appearance of
those of the rabbit with 10.8 per cent of glycogen in its
liver. The cells in the thirs group, in which the patients
received dextrose intravenously, contain only moderate
amounts of glycogen---The probable reason for this is that
patients in this group received considerably less dextrose
than those in the second group. The author's observations
prove that even the severely injured liver in the rabbit
and in man does not lose its ability to store glycogen, but
will do so to a marked degree when sufficient exogenous dex-
trose is provided. This also supports the view that the low
level of hepatic glycogen in diseases of the liver is due to
a shortage of carbohydrate in the body, caused by slowing of
the transformation of noncarbohydrate material into dextrose.
When enough sugar is supplied to relieve the persistent
demand on the liver for more carbohydrate this organ at once
begins to store glycogen. The fact that lipemia, ketosis
and relative hypoglycemia are observed in cases of hepatic
disease and also in starvation is another link in this chain
of evidence that in diseases of the liver there is an internal
hunger for carbohydrate.

Administration of dextrose is indicated when it is desired:

INDICATIONS

According to Althausen:

1. To reduce the working load of the liver.

2. To correct metabolic derangements due to hepatic insufficiency.

3. To aid detoxication, especially if the toxins are of unknown origin and cannot be otherwise eliminated.

4. To favor rapid regeneration of hepatic parenchyma.

5. To shorten prolonged coagulation time in jaundice.

One or more of these indications are present in all primary diseases of the liver and also in cases of secondary functional hepatic insufficiency. It is desirable to give to patients with hepatic disease rather large amounts of dextrose because, by supplying enough of it for all energy requirements, one is sparing the liver the effort of producing dextrose from noncarbohydrate sources. The human body at rest, according to Althausen, requires 30 calories or, 8 grams of dextrose per kilogram of weight. An individual weighing 70 kilograms needs, thus, 560 grams of dextrose. Assuming that daily about 300 grams of carbohydrate can be readily obtained from the diet, there remains 260 grams of dextrose which can be supplemented advantageously. This figure will be higher if the patient is permitted physical activity. Sections from the liver of patients who received dextrose in amounts satisfying all energy requirements demonstrate by their high content of glycogen that the desired objective had been reached. The best way of giving carbohydrate diet with additional feedings of from 50 to 100 grams of dextrose in fruit juice three times a day. More dextrose can be given with ease by mouth than in any other way. In rectal administration of

5

dextrose the amount absorbed when it is given in dilute solution is too small or uncertain, whereas concentrated solutions are irritating to the colon.

Recent investigative work by Pressman, Levi, McNealy and Smith, working separately, have shown that little if any dextrose is absorbed by the rectal route.

In further support of the intravenous route in preference to rectal injections McNealy and Williams have shown that dextrose is apparently not absorbed by the colon, though salt solution is taken up more readily. However, Taylor states that glucose can be used as a rectal meal with or without normal saline, and that children derive great benefit from this in addition to ordinary diet. According to Althausen, intravenous instillation of dextrose---is, from the point of view of an increase in hepatic glycogen, equally but not more efficacious than a similar oral dose. On the other hand, deposition of glycogen in the heart and the skeletal muscles is greater with the use of the intravenous route and maybe advantageous in diseases of these organs. However, in diseases of the liver, intravenous administration of dextrose is to be preferred only when emesis or some other cause makes the oral route unavailable.

Polak, Mazzola, Zweibel, Physiologists; tell us that glucose is:

1. A food for the vital organs, especially the liver and heart muscle.

2. That its use temporarily improves the quality of the pulse by improving the ventricular filling of the heart.

3. That it temporarily raises the systolic blood pressure and produces a peripheral circulation by its osmotic effect on tissue fluids.

4. That it promotes diuresis and combats acidosis.

5. That it temporarily lowers body temperature.

6. That it increases the protective power of the blood; and according to Hofbauer it stimulates the production of myelocytes.

7. That it decreases the coagulation time in jaundice patients but increases the clotting time in other patients.

8. That in high concentration it prevents agglutination of the blood and in diabetics, glucose, and insulin effect glycogen storage of the heart.

They state that three conditions which attend all operations in varying degree are shock, dehydration and acidosis. In the prevention of shock, concentrated glucose solutions by intravenous injection play an important part, this also holds true in its treatment. Out of a study of more than 200 cases of primary shock and shock and hemorrhage, all of which have geen given a 50 per cent glucose solution, these authors contend that hypertonic solutions have a therapeutic action on the vital organs of the body by their action on the circulatory system, and by their proper use the patient can be prepared for the strain of an operation and her postoperative safety, comfort, reaction and resistance are increased.

In any well-developed case of tramuatic shock with or without hemorrhage there is a partial suspension of the cir-

culation associated with an actual decrease in the volume
of circulating blood---The diminished blood volume bears
a definite relationship to the severity of the patient's
condition, but not to the actual amount of blood lost by
hemorrhage, for even after considerable bleeding there is a
rapid return to normal of the blood plasma volume and the
cell volume. If this occurs (this sensitization to the loss
of blood), no untoward symtoms develop. When, however, the
blood loss continunes or is excessive and there is severe
trauma besides, a condition of profound shock follows.

Experiments on animals, according to Polak, Mazzola
and Zweibel, that hypertonic solutions of glucose affect
the circulation by acting on the heart muscle, temporarily
raise the systolic and pulse pressure and improve and dim-
inish the rate of the pulse by restoration of the blood
volume. When concentrated glucose is given prior to operat-
ion and there is considerable hemorrhage, there is a sharp
drop in the systolic pressure with only a gradual fall in the
pulse pressure. In contrast similar amounts of blood loss
in the controls have been followed by an abrupt fall not only
in the systolic but in the pulse pressure as well. After in-
jections of hypertonic glucose, the pulse pressure promptly
rises, reaches a maximum in about 30 minutes and after 60 to
90 minutes gradually comes down to the normal. The systolic
pressure has a primary fall and gradually increases and re-
mains slightly at a level above normal. The rapidity and
duration of its effect is proportionate to the quantity of
solution injected, the pulse rate is always diminished.

INDICATIONS

The improvement of blood supply by raising the arterial pressure is one of the most important means of treatment of wound shock. He gives two methods; (1) drugs which constrict arterioles and (2) by increasing the volume of blood in the circulation. It is primarily important to get nutrition to the tissues--hense it is obvious that the pressure means nothing unless this is obtained. Baylis has shown that the hemoglobin may be reduced to as low as 25 per cent of the normal. He states there is general agreement that Ringers solution is useless in raising low blood pressure in wounded men. It has been found that there is a temporary rise foldowed by a rapid fall to the presious level or to lower levels. Experiments on cats confirm this experience--if part of the blood be removed and immediately replaced by Ringers solution, the blood pressure is not completely restored to its original height and within one half to one hour it returns to its low level or lower. Glucose solution have some times been recommended on the idea that there may be a carbohydrate starvation in wound shock. Cannon found that the blood sugar is above normal in shock. This might be supportive to Althausen's belief that due to injury, trauma, etc, the liver for some unexplained reason gives up its glycogen.

Rans and Arlson found that a 5.4 per cent solution of glucose had only a transitory affect in raising blood pressure in rabbits. Baylis concludes from this that there is no object in adding glucose solution for intravenous injections. However, this is unjust from the stand point that he was using a hypotonic solution in cases where the blood volume was

already below normal. de Caus says shock is caused by
sudden hydration of the protein particles and their conse-
quent precipitation in the capillaries and pericapillary
lymph vessels which they obstruct. The lowering of the
body temperature is due to the absorption of heat by the
hydrating particles. In mild forms of shock the blood
collects in the big veins. In mild or prolonged shock
congestion is selective and confined to one or more of a
few of the important viscera. The value of glucose lies
in dehydrating rapidly these protein particles.

In an experimental study of the effects of intraven-
ous injections of hypertonic glucose solution (50%) on the
circulation of the cat, Mazzola and Torrey, state that shock
is due to blood stasis in capillaries, transudation of
plasma into tissue spaces, difficult oxygination of tissues
and diminished blood supply. It follows that treatment
must aim to diminish circulatory stasis. It is agreed that
blood is the best fluid to inject. In the absence of this
they conclude that 50 per cent glucose will produce a final
sustained reduction in pulse rate. Slow injection is pre-
ferred. They contend that a preoperative injection of 50
per cent glucose will diminish a fall of blood pressure in
a foretold hemorrhage. Maxwell states that nothing relieves
post-operative shock, vomitting and acidosis as promptly as
glucose.

Bernard Fantus in his book on "The Technic of Medication"
states that blood pressure is not raised by hypertonic infus-
ions. Sugar solutions produce however, a dilatation of the

capillaries whereby the venous pressure is raised.

Intravenous sugar has been most effective in controling the acute vomiting and intoxication of pregnancy. Its value as a supportive measure in any medical or surgical crisis cannot be disputed. Sprague contends that intravenous use of sugar solution appears rational in diseases in which readily available food is urgently needed by active organs like the heart.

(Hayden) Chloroform can destroy one half of the liver tissue in a fasting animal and that with a high carbohydrate diet this liver tissue can be repaired in seven to nine days. Both chloroform and ether cause hyperglycemia followed by lessened glycogen in the liver. Intravenous injection of dextrose and a high carbohydrate diet are indicated before and after anaesthesia in liver disorders. According to Titus glucose injected intravenously as a therapeutic agent in various medical and surgical conditions, has a wide application. The protective action of diets high in carbohydrates is apparently based on an abundance of glycogen in the liver. On the contrary, a low glycogen content of the liver affects unfavorably certain functions of the liver. Diminished tolerance to dextrose follows the reductions of hepatic glycogen.

Von Noorden and Isaac claim that the reduction in tolerance to dextrose of animals with low hepatic glycogen is due to diminished glycogenogenesis, the rate of which depends on the existing supply of glycogen from which energy for polymerization of dextrose is derived through its transformation into lactic

acid. In accord with this theory is the work of Geiger on
hibernating frog, in which marked depletion of hepatic gly-
cogen interferes with the ability of the liver to synthesize
lactic acid to glycogen. Another function of the liver,
that related metabolism of pigments, also becomes disturbed
with a decrease in hepatic glycogen. According to the work
of Bang with human beings, increased urobilinuria appears
whenever carbohydrates in the diet are decreased below a
certain level. Of the greatest importance in deficiency of
glycogen in the liver is the impairment of the hepatic funct-
ion of detoxication. Experimentally, Sansum and Woodyatt
found that animals treated with phlorhizin are easier to
kill with chloroform than are normal animals; while Davis
and Bollman noticed that such hepatic poisons as chloroform,
carbon tetrachloride and phosphorus are more effective in
animals with a reduced glycogen content of the liver.

Guttmann found that under nutrition markedly increases
the incidence of arsphenamine icterus. Baehr and Klemperer
observed similarly that diabetic patients on a low carbo-
hydrate diet took arsenical therapy poorly and frequently
developed jaundice.

According to Stone, Williams and Ewing working separ-
ately on toxemia pregnancy, the liver is always affected
showing areas of focal necrosis. They agree that the liver
is the glycogen or sugar storing organ and also detoxicating
organ of the body, and it functions less powerfully as such
if depleted of its sugar, as is proved by the fact that an
animal starved of carbohydrates may be killed by a smaller

dose of any poison than is required for a similar animal
that has been well fed. The experiments of Davis and
Whipple also haveshown that starved animals are especially
susceptable to liver injury from chloroform and other
poisons, whereas sugar and diets rich in carbohydrates
exert a marked protective action against such liver injury.

The question of the essential nature of hepatic gly-
cogen is of interest to any one attempting to influence the
content of glycogen passed through the three stages and is
now entering a fourth stage.

Titus has shown that in experimentally injured livers
the addition of insulin to dextrose administration has the
effect of reducing the glycogen content of the liver. It
is desirable to give patients with hepatic disease rather
large amounts of dextrose because, by supplying enough of
if for all energy requirements, one is sparing the liver
the effort of producing dextrose from non-carbohydrate
sources.

The supply of a suitable amount of hypertonic glucose
solution intravenously, according to Litchfield has the
following affect. The general appearance improves at once.
The features are less pinched. The patient looks brighter
and less "toxic". The respiration becomes slower. The
pulse amplitude is markedly and persistently increased.
Erlanger noted much more affect from glucose than from con-
trol injections of salt solution. The tongue becomes moist.
The patient asks for water and food. The kidneys and bowels
become active. If the patient was restless or delirious he

becomes quiet and often goes to sleep while the injection is
being given. Sprague has used the injection of 50 cc. of
50 per cent glucose in the treatment for congestive heart
failure, diphtheratic myocarditis, coronary thrombosis
in which shock was the presenting factor and paroxysmal
dyspnea.

According to Wood and Ross patients suffering from
acute toxemia notably those of infantile dysentery due to
Flexner's bacillus, are definitely benefited by small trans-
fusions, in conjunction with the administration of fluids
by the intravenous and other routes.

The administration of dextrose has also been shown to
be of value in treating the crisis of exophthalmic goiter,
the toxemias of pregnancy, eclampsia, postoperative vomit-
ing, recurrent vomiting of children, asthma, epidemic enceph-
alitis and in the preparation of poor surgical risks for
operation.

According to Titus, a further result of carbohydrate
depletion is the consumption of body protein. This "toxic
destruction" of protein is especially marked during the
course of febrile diseases. Under such conditions the
administration of carbohydrate in assimilable form, such as
destrose, acts to spare the protein of the body from destruct-
ion. Dextrose may be given by mouth and is then more rapidly
utilized than other forms of carbohydrate as it requires no
digestion and is quickly absorbed. When oral administration
is not feasible because of food intolerance, or when more
immediate effects are desired, recourse may be had to intra-

venous, intramuscular, subcutaneous or intraperitoneal
injection. There are certain conditions associated with
carbohydrate depletion and ketosis in which the admin-
istration of dextrose has proved especially effective
as a therapeutic agen. Recurrent or cyclic vomiting
of childhood is associated with derangement of carbo-
hydrate and fat metabolism and often accompanied by
dehydration. The administration of carbohydrate is in-
dicated to prevent the accompanying acidosis, but only
too often no food or fluid can be retained by the stomach.

The parenteral administration of dextrose solutions
provides the necessary carbohydrate in utilizable form and
also relieves the dehydration. Dextrose is given in 10 per
cent solution intravenously in an amount of from 10 to 20 cc.
prt kilogram of body weight. According to Hill and Adelman,
the dextrose injections are much more effective if insulin
is administered at the same time in an amount not exceeding
one unit of insulin to each 3 grams of dextrose.

With subsidence of the vomiting, dextrose may be given
by mouth dissolved in fruit juices, or as dextrose candy.
In diabetic coma, ketone acids accumulate because insuffic-
ient dextrose is being utilized to provide for the perfect
metabolism of fats. Dextrose is present in excess but
cannot be used because of insufficiency of insulin. There
is virtually a starvation in the midst of plenty. Under
such circumstances the administration of insulin permits
the dextrose present to be metabolized, and if the amount
of dextrose is sufficient, the ketone acids present may be

completely transformed. In some cases of diabetic coma,
however, the amount of ketone acids present may be so
large in proportion to dextrose that complete conversion
does not occur, even when sufficient insulin has been
administered to provide for the metabolism of the accum-
ulated dextrose. It is in such cases that the administrat-
ion of extra dextrose has been recommended by Bulger and
John Levi and others.

It would appear at first sight illogical to admin-
ister dextrose to a diabetic, and although there is some
difference of opinion, it is nevertheless possible to
administer larger amounts of insulin and to cause a more
rapid disappearance of the ketosis when dextrose is admin-
istered simultaneously. The intravelous injection of
dextrose combined with insulin has a further advantage in
relieving dehydration and promoting diuresis and also, accord-
ing to Levi in restocking the liver and heart muscle with
glycogen. Levi further recommends the use of dextrose com-
bined with insulin in preparing diabetics for surgical oper-
ations. He advises the administration of 250 cc. of 10 per
cent dextrose together with 20 to 25 units of insulin.

For severely athreptic infants Marriott advises the
administration of a 10 to 20 per cent solution of dextrose
intravenously in amounts up to 25 cc. per kilogram of body
weight, repeated at daily or more frequent intervals. The
dextrose may be given alone or may be combined with insulin
in an amount not exceeding one unit to each 2 grams of dextrose.

In the treatment of post-operative shock with acidosis,

the combination of dextrose and insulin is especially effective. (Fisher, Snell and Wade--Authors) For this purpose a 10 per cent dextrose solution is given slowly intravenously in amounts of from 500 to 1000 cc. and insulin is injected subcutaneously in an amount corresponding to one unit to each 3 grams of dextrose administered.

In the presence of severe desiccation of the body, or anhydremia, a symptomatology closely resembling that of surgical shock is seen. The blood becomes concentrated and diminished in volume. Anhydremia occurs as the result of decreased fluid intake, vomiting, excessive heat or the severe diarrhea of Asiatic Cholera or of cholera infantum or "alimentary intoxication" of infants. When anhydremia occurs, fluid is urgently needed, but often cannot be retained by mouth, so that intravenous, subcutaneous or intraperitoneal administration becomes necessary. Dextrose solutions present certain distinct advantages over normal saline, inasmuch as salt injection may result in a dangerous accumulation of chlorides in the body. (Hartmann and Straus).

Dextrose may be completely utilized, leaving behind only water to restore the normal fluid balance; in addition, it serves to supply necessary nutriment. It has been shown by Tisdale, Drake and Brown that the dextrose tolerance of infants with alimentary intoxication is distinctly increased, and Karelitz working in Shick's clinic, has reported excellent results in the treatment of alimentary intoxication by continuous intravenous infusion of dextrose solution.

INDICATIONS

In pneumonia, dextrose appears to be of particular value. As early as 1914 Henriques and Anderson observed good results following the administration of 25 per cent dextrose solution intravenously to pneumonia patients. The injections were given three or four times daily in amounts of 250 cc. at a time. Litchfield used a similar technic. During the influenza epidemic of 1918-19 dextrose was used extensively, usually intravenously in the form of a 10 per cent solution given at frequent intervals. More concentrated solutions, up to 50 per cent have been used with the idea of relieving pulmonary edema according to Koons, and Meyer.

Bennett and Dodds advocated the administration of fairly large amounts (200 to 500 grams daily) of dextrose by mouth to patients with pneumonia. MacLachlan, Kastlin and Lynch gave up to 500 or 600 grams of dextrose a day by mouth, and in the case of severely toxic patients administered additional dextrose in the form of a 25 per cent solution intravenously four to six times daily. In a carefully controlled series of observations by MacLachlan and his associates, the mortality from pneumonia was distinctly less in a group of patients who received generous amounts of dextrose as compared with a control group.

In other bacterial toxemias and septicemias, dextrose appears to be of definite value, especially in those cases in which the administration of food by mouth is impossible or impractical.

In the toxemia or severe diphtheria there occurs a

disturbance in carbohydrate metabolism associated with a depletion of the glycogen reserves according to Schwentker. This appears to be a factor in causing the associated cardiac failure. The administration of dextrose alone or of dextrose and insulin has been shown to influence favorably the course of diphtheria, especially in those cases associated with cardiac failure. Edmunds and Cooper showed that the administration of a 10 per cent solution intravenously prevented cardiac death in the case of dogs poisoned with diphtheria toxin. Toomey, used injections of 25 per cent dextrose intravenously in amounts of from 50 to 75 cc. at frequent intervals in cases of severe diphtheria with cardiac failure and noted that this led to a decrease in cyanosis, a rise in systolic and diastolic blood pressures and general improvement of the patients. In the treatment of severe toxemia with early circulatory failure in diphtheria, Schwentker and Noell recommend the administration of 20 cc. of a 50 per cent solution of dextrose intravenously repeated in from 12 to 24 hours. Following this a 10 per cent solution in somewhat larger amounts is injected at frequent intervals. In addition insulin in an amount of one unit to each 2 grams of dextrose is injected subcutaneously. Kostyal reports a reduction of mortality from severe diphtheria to about one-fourth in a series of patients treated by intravenous injections of dextrose and insulin.

Severe burns are accompanied by a toxemia and concentration of the blood. The injection of large volumes of 10 per cent dextrose solution intravenously serves to supply fluid

to dilute the concentrated blood to promote diuresis and
to diminish the symptoms of toxemia.

In nephritis, the administration of dextrose solut-
ion intravenously is often effective in bringing about
diuresis, decreasing edema and relieving uremic symptoms.
When dextrose in hypertonic solution is given it draws
fluid into the blood from the water-logged tissues and
leads to its excretion by way of the kidneys. Not infreq-
uently there occurs simultaneously a lowering of the high
blood pressure accompanying uremic states. Dextrose solut-
ions of a concentration of 10 to 25 per cent may be employed
for intravenous injection and should be given slowly. It is
usually inadvisable to combine the dextrose with saline, as
the salts must be eliminated by the disabled kidneys. The
administration of dextrose alone introduces nutriment with-
out throwing any load on the kidneys and often is followed
by lowering of the non-protein nitrogen and urea of the
blood. The extra supply of available carbohydrate serves
also to restore the glycogen reserves of the overstrained
heart of uremic patients.

Dextrose has an apparent specific affect in protect-
ing the body, especially the liver, against certain poisons
and its administration also favors the elimination of poisons
through the diuresis produced. Dextrose is of particular
value in preventing the toxic affects of chloroform, ether,
alcohol, the heavy metals and hydrocyanic acid, according
to Opie and Alford, Graham, Davis and Shipple. Consequent-
ly the feeding of carbohydrate and the intravenous admin-

istration of dextrose has been recommended preparatory to
the giving of anaesthetics and as a measure for relief of
post-operative toxemia. Kritschewski demonstrated a pro-
tective action of dextrose against the toxicity of arsphen-
amin. Dextrose has also proved of value in the treatment
of poisoning with barbital and its derivatives. Sanderson
administered 800 cc. of 20 per cent dextrose intravenously
to a patient who had taken 200 grains of barbital and noted
rapid recovery from the toxic symptoms. Anton and Jacobi
have shown that alterations occur in the carbohydrate meta-
bolism in morphine addicts and in a small series of cases
they were able to prevent withdrawal symptoms when fairly
large amounts of dextrose were administered by mouth dur-
ing the period of treatment.

Several reports have appeared on the use of dextrose
in the treatment of angina pectoris, according to Meyer.
A 20 to 25 per cent solution of dextrose is used and 10
to 25 cc. injected intravenously at a time. This often
results in a lowering of blood pressure and an amelioration
of the symptoms. The fall in blood pressure is attributed
by Weil to a dilatation of the capillaries and by Wichels
to a change in the collodial condition of the serum.

Increased intracranial pressure resulting from fract-
ures, cerebral hemorrhage, tumors, meningitis, thrombosis,
obstructive hydrocephalus and acute cerebral edema may be
lowered by the administration of hypertonic dextrose solut-
ions intravenously. Hayden recommends such use of hyper-
tonic dextrose in the preparation of patients for intra-

cranial operations and Kennedy and Wartis make use of a
50 per cent solution of dextrose in amounts up to 100 cc.
injected intravenously two or three times in the 24 hours
for the relief of intracranial pressure. Concentrated salt
solution have also been used, but hypertonic dextrose is
preferable because of its more prolonged action, non-toxi-
city and absence of terminal rise in blood pressure. Dex-
trose is of further value in increasing blood volume, con-
troling acidosis and in providing food, especially in those
patients who are vomiting as the result of the intracranial
condition. In epidemic meningitis not infrequently the
accompanying edema of the spinal cord results in a blocking
of the flow of the cerebrospinal fluid. For the relief of
such blocking, Stookey, Elliott, and Teachenor have used
a 50 per cent solution of dextrose intravenously and have
noted a free flow of spinal fluid following the injection.

SUMMARY

Glucose solution is the only food that can be given
by the intravenous route. This method of administration is
to be restored to, only when emesis or some other cause
makes the oral route inadvisable. It is non-toxic and no
harm is done if some spills in to the urine. It is a readily
available source of food and water for starved and thirsty
tissues. It acts to neutralize endogenous and exogenous
toxins. If given in hypertonic concentration it acts as a
diuretic.

CONCENTRATION DOSAGE AND RATE OF INJECTION

There appears to be a considerable range of difference of opinion in regards to what is the proper amount of dextrose to be injected for full therapeutic effect, what is the concentration or percentage of dextrose dilutions to be used and what is the proper rate of injection.

Erlanger and Woodyatt, in their work on shock, and Litchfield in his intravenous use of glucose for pneumonia, according to Titus, were pioneers in developing this therapeutic measure. Woodyatt, Wilder and Sansum have demonstrated by clinical experiments that 0.8 grams of glucose per kilogram of body weight may be given per hour without causing glycosuria. This indicates, therefore that the average dose for a normal person is about 1 gram for each kilogram of body weight. An average woman weighs between 50 and 60 kilograms so that from 50 to 60 grams of glucose is a full dose. More than this may be spilled out through the urine but, because its appearance there is of no particular significance, it was decided to establish the figure of 75 grams as the usual initial dose, subsequent doses to be 50 grams. Those clinicians who give less than a therapeutic dose should remember that this is comparable to administering 1/50 or 1/100 grain of morphine, and expecting the usual effect merely because it is morphine.

Titus and Lightbody in their report of investigations to determine a therapeutic dose of dextrose administered intravenously, state that the most favorable results seem to follow the use of the strongly hypertonic solution. They and their co-workers prefer a 25% solution. They state that the inter-

change of sugar from blood to tissue is more rapid in the
stronger concentrations. The concentrations to be selected
must depend upon a desired effect and the condition of the
patient. Care being taken not to over tax a weakened heart.
They continue, that the proper rate of injection appears to
be a fixed matter--not more than .8 grams per kilogram of
body weight per hour, as was worked out by Woodyatt, Wilder
and Sansum.

According to Titus, the under dose has been the common
fault and this with loss from too rapid administration may
account for the frequent lack of results. Weak solutions
possibly contribute to reactions and certainly overload the
circulatory system in too short a period of time if sufficient
quantity is given to carry a therapeutic dose of the glucose.
It should be dissolved in distilled water instead of salt
solution as has been variously recommended, because injections
of the latter combination seem so often to be followed by
unpleasant or even dangerous reactions.

Althausen accepts the dosage and concentration worked
out by Woodyatt, Sansum and Wilder. He adds that this figure
will be higher if the patient is permitted physical activity.

According to Horsely, Shelton and Horsely the rate at
which the intravenous flow of dextrose and Ringer's solution
should be amintained depends entirely on the conditions. In
hemorrhage or shock, it should be rapid enough to secure al-
most a normal blood pressure, if low it is impossible to over-
load the heart until the blood pressure has approximated what

is normal for that individual. For other conditions than shock or hemorrhage the solution should be given at a rate of from 75 to 200 cc. per hour.

Maxwell gives the average dose for an adult as one gram per kilogram of body weight, and the appearance of sugar in the urine after 50 to 70 grams of dextrose, simply represents the kidney spill and is not of great importance. A 25 per cent solution is a very satisfactory concentration, as its use is followed by more rapid and pronounced effects. The hypertonicity favors a more prompt interchange between the blood stream and tissues and therefore quicker utilization by the body. If larger amounts of water are required, a 10 per cent solution may be used with safety; lower dilutions, however, are inadvisable for many unfavorable results have occurred from the overloading of the vascular system with large amounts of a weak glucose solution.

Lynch and Webster in their intravenous glucose treatment of pneumonia, as soon as the diagnosis was established, gave their patients an intravenous injection of 250 cc. of warm 20 per cent glucose-saline solution. The concentrated solution was chosen with a view to putting the least possible strain on the circulatory system of a patient already cyanosed and congested. This injection was given daily in the mild cases and twice daily in the severe ones. It was continued until 24 hours after the crisis. A gravity system was used entirely, and took at least 15 minutes to administer the 250 cc. of solution.

The clincial experiences of Hendon indicate that the rate of administration has as much to do with the subsequent

results in intravenous therapy as does the substance that is used. He states for the average adult individual this rate is approximately 200 cc. of fluid an hour, or a range of between 4,000 and 5,000 cc. of fluid in the twenty-four hours. The estimate of physiologic tolerance has been based, first, on the fact that patients receiving that amount of fluid at the rate here indicated are free from chills and sudden elevation of temperature, which regularly occur when solutions are suddenly or rapidly introduced directly into the circulation. de Caux states glucose solution, to exert its full effect, must be used within twenty-four hours of its preparation. He always uses and recommends a 10 per cent solution at a temperature of 100 degrees F. Before an operation it must be given slowly, or it will rapidly be excreted by the kidneys. When it is administered slowly any excess is absorbed by the liver as glycogen and let loose into the blood stream in the form of glucose as required. If the patient's protein particles are already hydrated, the glucose can be given faster than when it is merely desired to increase the glycogen reserves.

Polak, Mazzola, and Zweibel states in traumatic shock where the blood pressure falls to a very low reading, the introduction of a 50 to 100 cc. of a 50 per cent solution of glucose will raise the pressure from 15 to 50 millimeters of mercury within a period of four to five minutes. This rise is maintained from 20 minutes to one-half hour, when there is a slight secondary drop followed by a gradual rise in both the systolic and pulse pressure. These observations

have been confirmed in the animal as well as by more than 200 studies in the human being.

Weir and Walters in treating pyloric obstruction to relieve dehydration and furnish food do not hesitate to give 10 per cent glucose in 1 per cent saline or water, two or three times per day. In cases of hepatic insufficiency a high intake of carbohydrates and fluids is the chief recommendation. This may be accomplished by taking carbohydrates by mouth in addition to solution of dextrose intravenously in doses of one liter once or twice daily. At times this may be increased to 20 per cent strength, 500 cc. being given at one dose. In renal insufficiency--dextrose in solution 10 percent to 20 percent with or without saline one per cent as a diuretic.

Hendon in giving glucose by the continuous drip method generally uses a 10 per cent solution. He governs the daily aggregate amount to be given by the appearance of sugar in urine. He finds that patients suffering with severe toxemia and high temperature will consume at least twice as much dextrose in twenty-four hours as those with low temperature and not affected with toxemia. For example, in peptic ulcer cases he found that an average of one-half pound of dextrose a day seemed to meet their physiologic needs, while in emesis gravidarm and septic infections, one pound a day was the average requirement. Patients with cancer of the colon could consume as much as 11 pounds in six days without showing sugar in the urine. A patient weighing 150 pounds can easily assimilate two pounds of dextrose a day. His experience

demonstrated that no patient need ever die of dehydration

or starvation alone and that not only life but a fair degree

of physical prosperity can be sustained over a period of

at least sixteen days without alimentary feeding; that veno-

clysis renders the physician and patient absolutely independent

of the gastro-intestinal canal during a given period.

Althausen states that continuous intravenous infusion of

dextrose solutions over a period of several days is a pro-

cedure that should not be undertaken lightly, owing to the

necessity of dissecting a cubital vein for the cannula and

the risk of air emboli. On the other hand, when the condition

of the patient warrants it, this method of giving the dextrose

has important advantages. One of these is the continuous

inflow of dextrose without undue strain on the organs of

assimilation. Another advantage is the large amount of carbo-

hydrate that can be administered in this fashion...This

method of administration of dextrose, which answers the ideal

requirements of therapy for cases of severe acute hepatic

damage, such as acute yellow atrophy of the liver, has not

been given an adequate clinical trial. However, Hendon

mentions two patients with multiple abscesses of the liver

who recovered following its use.

Pendleton, in working out methods for preventing the

agglutination of blood by glucose solution used portions of

fresh prepared glucose solution in distilled water and his

own blood. Glucose solutions and blood were measured in the

stem of a hemocytometer white cell pipette and emptied into

the concave portion of a hollow ground slide. The mixture

was made to the same volume in each test (about 0.016 cc.)
Air was blown through the pipette into the drop long enough
to mix the materials (2 to 3 seconds). A cover-slip was
placed over the drop.

The agglutinating power of the following glucose sol-
utions was tested: 5, 7.5, 10, 15, 20, 30, 40, 50, 80 and
100 per cent. One part of blood was used with four parts
of glucose solution. Tests showed that this volumetric
ratio (of blood to glucose solution) gives roughly the max-
imum agglutination with solutions of varied concentrations.
Solutions containing 5 to 10 per cent of glucose produced
decidedly the most marked gross and microscopic agglutination.
Agglutination was progressively decreased with each solution
of higher concentration. There was no clumping apparent to
the naked eye with the 30 per cent solution, but microscopic
agglutination was very definite. The 30 per cent solution
showed absolutely no gross clumping. The 40, 50, 80 and 100
per cent solutions caused a very loose microscopic agglutination.
Thus approximately isotonic solutions (glucose content of 5
to 10 per cent) produced the most marked agglutination.

The next question is what occurs when a glucose solution
is mixed with larger quantities of blood as would take place
in the passage of the solution into the general circulation?
Successive tests were made with 7.5 per cent glucose solutions
using a larger proportion of blood each time. With a ratio
of blood to glucose solution of 1 to 9 the corpuscles were
too much separated by volume of fluid to form large agglut-
inated masses. Using a ratio of 1 to 4 clumps slightly less

than 0.2 mm. in diameter formed. They appeared very compact under the microscope. Stirring with a teasing needle dissociated practically all clumps, but agglutination was still present microscopically. On standing, clumps about 0.1 mm. in diameter reformed. With a mixture of equal parts of blood and glucose solution the corpuscles showed absolutely no tendency to adhere to one another, but during the first minute crenation was maximum for the series at this point. With a blood to glucose solution ratio of 9 to 1, there was simply a rouleau formation of seemingly normal erythrocytes. Thus on increasing the blood content of a glucose solution in successive steps a cycle occurs in which there is (1) agglutination, (2) absence of agglutination and the appearance of marked crenation, (3) rouleau formation of apparently normal corpuscles. The 40 per cent glucose solution produced a similar cycle but in less distinct steps.

In further tests it was found that a 5 per cent solution of glucose containing 0.2 per cent sodium chloride or sodium hydroxide to N/250 strength (0.016 per cent by weight) would cause no agglutination of blood regardless of the relative amounts of the blood and glucose solutions mixed together. One-half this amount of sodium chloride or of sodium hydroxide was not sufficient to prevent agglutination. So less than one-tenth as much of the sodium hydroxide (by weight) as of the sodium chloride was required to prevent agglutination. Agglutination by a 40 per cent solution was much inhibited but not prevented by 0.2 per cent sodium chloride and N/250

strength of sodium hydroxide respectively.

Acids increased the agglutination. In each test blood was used with 7.5 per cent glucose solutions in the ratio of 1 to 4. Hydrochloric acid in N/1000 concentration seemed to cause about three times the agglutination which occurred in an unacidified glucose control. The presence of citric acid in N/50 concentration in a glucose solution converted the blood into quite firm clumps about 0.8 mm. in diameter. This was the most marked agglutination obtained in the work on glucose.

A 7.5 per cent glucose solution with N/50 citric acid content was tested with varied proportions of blood. This gave a cycle almost identical to that obtained with unacidified solutions except for the greatly increased agglutination by the acidified solution at its maximum point. It is especially noteworthy that, regardless of acid content no agglutination persisted when equal parts of blood and glucose solution were well mixed. Buffer substances in the blood would naturally here greatly diminish the activity of the acid. Tests showed potassium acid phosphate and potassium dibasic phosphate to be anti-agglutinating agents as would be expected because of their potassium content. The Ph of N/15 solutions of these salts is 4.49 and 9.18 respectively. No agglutinating properties remained in 7.5 per cent glucose solutions after adding 1.0 to 1.1 per cent of potassium acid phosphate or 0.1 to 0.2 per cent of potassium dibasic phosphate. Here the dibasic salt was at least five times as effective as the mono-basic salt. An N/50 concentration of citric acid necess-

itated the use of 1.1 to 1.2 per cent of sodium cholride
or only 0.4 per cent of dibasic potassium phosphate. The
buffer agent was much more efficient than sodium chloride
in preventing agglutination in an acid medium but in the
absence of acids its effect was about the same.

A 5 per cent glucose solution containing 0.1 per cent
of oxalic acid (a sufficient amount to prevent clotting)
caused a slightly greater agglutination than did the unacid-
ified control. With 0.33 per cent of potassium oxalate in
a 5 per cent glucose solution there was no agglutination.

Sucrose and glycerin solutions caused an agglutination
of blood similar to that of glucose. Sodium chloride and
sodium hydroxide inhibited the agglutination. Citric acid
and hydrochloric acid increased agglutination. Magnesium
sulphate and ammonium sulphate each prevented agglutination
by sucrose solution.

As to a possible relationship between agglutination
and 'glucose reactions' is might be pointed out that the
solution used by Williams and Swett, which they found to
give reactions, were approximately isotonic, a concentration
producing marked agglutination by our tests. The rise in
acidity through autoclaving increases the tendency to
agglutination. The means used by these authors in prevent-
ing the reaction (faintly alkaline phosphate buffers) will
certainly inhibit agglutination in vitro. Of course, if
solution be made from water infected with organisms which
Seibert has shown to give distilled water reactions there
would be an additional point of controversy in explaining

solution reactions.

SUMMARY

The body utilizes glucose at the rate of .8 gram per kilo body weight per hour.

The concentration should not be less than 10 per cent and may range up to 50 per cent, depending on the desired effect.

The rate of administration should not exceed 500 cc. per hour.

BIBLIOGRAPHY

Alderman, Maurice--"Acidosis in Children", Rhode Island
    M. J. , 7:141, 1924.

Althausen, T. L.--"Dextrose Therapy in Disease of the Liver",
    The Journal of A. M. A., 100:1163 (April 15,)1933.

Anton, G. and Jacobi, J.--"The Treatment of Morphinism With
    Insulin and Dextrose", Klin. Wochenschrift, 9:1547, 1930.
    (Consulting Bureau Service--W. F. Prior Co., Inc.)

Baer, G. and Klemperer, P.--"Degenerative and Diffuse Inflam-
    atory Disease of Liver", International Clin., 2:107,
    (June) 1929.

Bang, Q.--"Klinische Urobilinstudien in der leber", Biochem.
    Ztschr., 223:190, (July) 1930.
    (Consulting Bureau Service--W. F. Prior Co., Inc.)

Barbour, A. D. and Chaikoff, I. L.; Macleod, I. J. R. and
    Orr, M. D.--"Influence of Insulin on Liver and Muscle
    Glycogen in the Rat Under Varying Nutritional Conditions",
    Am. J. Phys., 80:243, (April) 1927.

Bayliss, W. M.--"Intravenous Injection in Wound Shock",
    British Med. Jour., (May 18) 1918.

Beddard, A. P.--"Suggestion for the Treatment of Relayed
    Chloroform Poisoning", Lancet, 1:782, (March) 1908.

Bennett, T. I. and Dodds, E. C.--"Oral Administration of
    Large Quanities of Glucose", Lancet, 1:421, 1925.

Bodansky, Meyer--"Introduction to Physiological Chemistry",
    Edition 2, New York, John Wiley & Sons, Inc.

Bollman, J. L.--"Experimental Observations on Glucose as a
    Therapeutic Agent", S. Clinic N. A., 5:871 (June) 1925.

Bugler, Harold A. and Peters, John P.--"The Concentration of
    the Blood and Urine in Diabetic Toxemia", Arch. Int.
    Med., 36:857, 1925.

Davis, N. C.--"The Influence of Diet Upon the Liver Injury
    Produced by Carbontetra Chloride", I. N. Research,
    44:601, (September) 1924.

BIBLIOGRAPHY

Davis, N. C. and Whipple, G. H.--
    (1) "Influence of Fasting and Various Diets on the
        Liver Injury Affected by Chloroform Anesthesia".
    (2) "Influence of Drugs and Chemical Agents".
    (3) "The Rapid Reconstruction of Liver Cell Protein
        on a Strict Carbohydrate Diet Contrasted with
        Fasting".
    (4) "Liver Regeneration Following Chloroform Injury
        as Influence by Various Diets". Arch, Int. Med.,
        23:612, 636, 639, 711.--1919.

de Caux, F. P.--"Glucose--When and How to Use it", Brit.
    Med. Jour., 2:1003, 1929.

Drake, T. H. G. and Snelling, C. E.--"Sugar Tolerance
    Curves in Acute Intoxications in Infants", Canadian
    M. Assoc. Jour., 24:511, 1931.

Dun, F. L., Phillips, A., Henske, J. A., Best, R. R.,
    McGoogan, L. S., and Wherry, W. P.--"Diet Manual",
    U. of N. College of Medicine, Omaha, Nebr.
    613.2 N27, 1933.

Edmunds, C. W. and Cooper, R. G.--"Action of Cardiac
    Stimulants in Circulatory Failure Due to Diphtheria",
    J. A. M. A.,85:1798, 1925.

Enriquez--"J. A. M. A.", 62:1054, 1914.

Erlanger, J. and Woodyatt, R. T.--"Intravenous Glucose
    Injections in Shock", J. A. M. A., 69:1410, 1917.

Ewing, James--"The Pathogenesis of the Toxemia of Pregnancy",
    Am. Jour. of Med. Sc., 139:828, (June) 1910.

Fantus, Bernard--"The Technique of Medication", J. A. M. A.
    1926.

Finkelstein, H.--"Archives of Pediatrics", (April) 1924.
    Page 219.

Flood, R. C.--"Selections of Sugars in Infant Feedings",
    Arch. of Ped. , 42:50, 1925.

Graham, E. A.--"The Resistance of Pups to Late Chloroform
    Poisoning in its Relation to Liver Glycogen", J. Exp.
    Med., 21:188 (February) 1915.

Grafe, Erich--"Metabolic Diseases and Their Treatment",
    Lea amd Febeger, Philadelphia 1933.

2

BIBLIOGRAPHY

"Toxic Effect of the Common Anesthetic Substances",
J. A. M. A., 69:166, 1917.

Guttman, c.--"Erfahrungen uber Icterus bie Syphilitikern",
Dermat. Ztschr, 37:39 1922.

Hartmann, A. F.--"Chemical Changes Occuring in the Body
as the Result of Certain Diseases", Amer. Jour. Dis
Child., 25:557, 1928.

Hayden, R. L.--"Therapeutic Application of the Alteration
of Brain Volume", J. A. M. A., 73:983, 1919.

Hendon, Geo. A.--"Venoclysis", J. A. M. A., 95:1175, 1930.

Henriques, H. and Anderson, A. C.--"Ztschr f. Physiol. Chem.",
92:194, 1914.

Holt--"Food, Health and Growth", MacMillan, 1922, page 142.

Hill, L. W.--"Glucose and Insulin in the Treatment of Recur-
rent Vomitting", M. Clinic N. A., 10:1329, 1927.

Horsely, J. Shelton; and Horsely, Guy W.--"Continuous Intra-
venous Injection of Dextrose in Ringers Solution",
Arch. of Surg. 22:86-93, (July) 1930.

John, Henry, J.--"Diabetic Coma", J. A. M. A., 93:425,
(Aug. 10) 1929.
"The Use of Intravenous Glucose in Diabetic Patients",
Sur. Gynec. and Obst., 50:769, (April) 1930.

Karelitz, S--"Treatment of a Toxicosis With the Aid of a
Continuous Drip of Dextrose Solution", Amer. Jour. Dis.
Child., 42:781, 1931.

Kennedy, F. and Wartis, S. B.--"Modern Treatment of Increased
Intracranial Pressure by Intravenous Administration of
Glucose and Hypertonic Ringers Solution", J. A. M. A.,
84-1994, 1925.

Koons, H. H.--"Vaccine and Glucose in Influenza and Broncho
Penumonia", Mil. Surgeon, 46:403, 1920.

Kostyal--"J. A. M. A.", Budapest Correspondent, 96:1329, 1931.

BIBLIOGRAPHY

Kritschewski.--"Dextrose in Salvarsan Poisoning", Chem.
    Zentralbl, 163; 1926.
    (Consulting Bureau Service--W. F. Prior Co., Inc.)

La Fetra, L. E.--"The Role of Carbohydrates in Infant
    Feedings". Reat at the annual meeting of the Medical
    Society of the State of New York at New York City,
    March 31, 1926.

Levy, A. A.--"Diabetic Acidosis and Coma", Amer. Med.
    689 (October) 1929.

Litchfield, Lawrence--"Glucose Intravenously as a Thera-
    peutic Measure", J. A. M. A., 71:503-505, (Aug. 17) 1918.

Loomy, J. A.--"Clincial Observation With Injection of Dextrose
    In Diphtheria", Amer. Jour. Dis. Child., 35:722, 1928.

Lynch, Ralph and Webster, Bruce--"Intravenous Glucose in
    the Treatment of Pneumonia", The Canadian Medical
    Association Journal, 18:52-53, (January) 1928.

McNealy, R. W. and Williams, J. D.--"Absorption of Dextrose
    From Colon Study of Effects of Chemical Excitants and
    of Stimulants of Dextrose Enema", Arch. of Surg.,
    22:649, (April) 1931.

Macht.--"The History of Intravenous and Subcutaneous Admin-
    istration of Drugs", J. A. M. A., 66:856, (March 18) 1916.

Maclachlan, W. W. G.; Kastlin, G. J. and Lynch, R.--"The Use
    of Dextrose in Pneumonia", Amer. Jour. Med. Sci., 179:93,
    1930.

Macleod, J. J. R.--"The Control of the Carbohydrate Metabolism",
    Lancet, 1:1079, (May 21) 1933.

Marriott, W. McKim--"The Food Requirements of Malnourished
    Infants, With a Note on the Use of Insulin", J. A. M. A.,
    83:600, (August) 1924.

Maxwell, Alice F.--"Glucose Reactions and Their Prevention",
    Calif. and Western Medicine, 28:810-811, (June) 1928.

Meyer, E.--"Therapeutic Use of Intravenous Injections of
    Glucose Solution", Abst. J. A. M. A., 86:5219, 1926.

BIBLIOGRAPHY

Mosenthal, H. O.--"Diabetis Mellitis--Maintenance by Diet
    In Treatment", Med. Clin. N. Am., IV, 603-614, 1922.

Opie, R. L.--and Alford, L. B.--"The Influence of Diet
    on Hepatic Neurosis & Toxicity of Chloroform",
    J. A. M. A., 62:895, 1915.

Pendleton, Walter A.--"Methods for the Preventing of the
    Agglutination of Blood by Glucose Solutions", The Jour.
    of Lab. and Clinical Med., 12:359-372, (Jan.) 1927.

Polak, Osborn, Mazzola, Vincent P. and Zweibel, Leonard.--
    "The Value of Glucose Therapy in Pre-Operative and Post-
    Operative Non-Diabetic Acidosis", J. A. M. A., 93:1173,
    (October 19) 1929.

Potter, Phillip S.--"The Metabolism of Carbohydrates in
    Infancy", Arch. of Ped., (July) 1928.

Ravdin, I. S.--"Some Aspects of Carbohydrate Metabolism
    in Hepatic Diseases", The Jour. of A. M. A., 93:1173,
    (October 19) 1929.

Sanderson, G. H.--"Treatment of Barbital Poisoning With
    Glucose", Calif. and Western Medicine, 33:837,
    (December) 1930.

Sansum, W. D.; and Woodyatt, R. T.--"Studies in the Theories
    of Diabetes: V. A. Study of Narcotic Drugs in Phlorizyen
    Diabetes", Jour. Biol. Chem. 21:1, 1915.

Schwentker, F. F. and Noell, W. N.--"The Circulatory Failure
    of Diphtheria: The Clinical Manifestations of Early and
    Late Failure", Bulletin of John Hopkins Hospital,
    45:276, 1929.

Seibert, F. B.--"The Causes of Many Febrile Reactions Follow-
    in Intravenous Injections", Amer. Jour. Physiol., 71:621,
    (February) 1925.

Slemons, J. M.--"The Nutrition of the Foetus", Amer. Jour.
    Obst., 80:194, (August) 1919.

Smith, T. Cook--"Intravenous Injections of Hypertonic Salt
    Solution in Acute Poliomylitis", Amer. Jour. Dis. Child.
    31:360, 1926.

BIBLIOGRAPHY

Sprague, Howard and Camp, Paul D.--"Intravenous Hyper-
    tonic Glucose in the Treatment of Cardiac Disease",
    Preliminary Report, 206:288-290, (February 11) 1932.

Stoddard, I L.--"Avoidance of Intravenous Glucose Reaction",
    Boston M. and S. Journ., 191:1121, (December 11) 1924.

Stone, W. S.--"Toxemia of Pregnancy", Am. Gyn., 3:508,
    (December) 1903.

Straus, H.--"Zuckerinfusionen bei Cholera", Therap. d. Gengenw,
    56:370, (October) 1915.

Stooky, P. F.; Elliott, B. L. and Teachenor, F. R.--"Mechanism
    of Spinal Block in Epidemic Meningitis", J. A. M. A.,
    95:106, 1930.

Taylor, F. O.--"A Note on the Uses of Glucose in General
    Practice", The Practioner, 130:508, (April) 1933.

Thalhimer, W.--"Insulin Treatment of Post-Operative (Non-
    Diabetic) Acidosis", J. A. M. A., 81:383, 1923 and
    87:391, 1926.

Tisdall, F. F.; Drake, C. H. and Brown, A.--"Carbohydrate
    Metabolism of Normal Infants", Amer. Journ. Dis. Child.,
    30:675, (November) 1925.

Titus, P.--"Hyperemesis Gravidarum: Treatment by Intravenous
    Injections of Glucose and Carbohydrate Feedings", J. A.
    M. A., 85:488, 1925.

Titus, P. and Lightbody, H. D.--"Report of Investigations to
    Determine the Therapeutic Dose of Dextrose Administered
    Intravenously", Amer. Journ. Obst. and Gyn., 18:208-
    214, (August) 1929.

Von Noorden, C. And Isaac, S.--"Die Zucherstoffwechsel Des
    Menschen, Ztschr. f.", Lin. Med. 93:89, (January) 1922.

Wade, P. A.--"Destrose-Insulin Treatment of Shock", J. A. M. A.,
    90:1859, 1928.

Weir, James F. and Walters, Waltmer--"J. A. M. A." (January 13)
    1934.

Williams, J. W.--"Pernicious Vomitting of Pregnancy", Bullet.
    of John Hopkins Hospital, 17:71, (March) 1906.

BIBLIOGRAPHY

Williams, J. R. and Swett, Madeline--"Hydrogen Ion Concent-
    ration Studies", J. A. M. A., 78:1624, (April 18) 1922.

Wood, Ivan Jeffreys, and Ross, Wallace--"The Intravenous
    Administration of Blood, Saline Solution and Glucose",
    The Med. Journ. of Australia, 1:815-826, (June 11) 1932.

Woodyatt, R. T.; Sansum. W. D. and Wilder--"Prolonged and
    Accurately Timed Intravenous Injections of Sugar",
    J. A. M. A., 65:2067, (December 11) 1915.