It is prohibitive to feed diabetic patients, who have a very low carbohydrate tolerance, even a moderate amount of natural fat, because of the danger of inducing a severe ketosis which may prove fatal. It was thought advisable, therefore, to prepare a synthetic fat to contain fatty acids of odd-carbon number, which, if they are absorbed and if the theory of intermediate fat metabolism described above, holds, should catabolize in the body without the production of the acetoacetic acid, etc.

In collaboration with Dr. H. O. Nolan such synthetic fat was made and fed to typical diabetic and ketotic patients. It was found that the fat was absorbed, that large quantities of it could be fed to these patients without inducing any acidosis, and that the nutrition of such individuals was improved. We are now studying the intermediate metabolism of this fat, and its feeding effect on all types of diabetic and normal individuals.

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## Hydrogen-ion concentration studies of solutions used for intravenous medication and clinical investigation.

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We advance the hypothesis that there is a relationship between the hydrogen-ion concentration of fluids injected intravenously and some of the reactions which follow their use. We base this belief on clinical observations and on extended chemical analyses of fluids commonly used for therapeusis and clinical investigation. We wish to briefly report here some of our more important studies. It should be understood that the hydrogen-ion concentration of normal acid is $P_H$ 2; normal alkali $P_H$ 14; pure water $P_H$ 7; and human blood $P_H$ 7.4, and that this latter figure is fixed and cannot be varied without causing serious disaster or death. If a fluid with a much higher or lower $P_H$ than that of the blood is introduced into the circulation at a rate or in an amount greater than the blood can neutralize or buffer, reactions, as chills, fever and

prostration ensue. This is particularly true in individuals whose blood supply is impaired in either quantity or quality.

Since distilled water is the solvent used in most intravenous medication we have studied it with care under the conditions which it is commonly produced in hospitals and laboratories. Rochester tap water has a $P_H$ of 8.29. Boiling was found to increase this slightly. Various samples of stock distilled water varied from $P_H$ 6.89 to $P_H$ 5.05. Distilled water becomes acid even when the distillation is in progress from the absorption of carbonic acid of the atmosphere when the ordinary type of metal or glass still is used.

Tap water, $P_H$ 8.27; first distillate (first 10 c.c.) $P_H$ 7.30; after 200 c.c. had been distilled $P_H$ 6.90. When stored in container, whether sealed with a cotton plug, cork or glass stopper, distilled water becomes quite acid. Example: freshly distilled water has a $P_H$ 6.8, after 48 hours, $P_H$ 5.23. Proximity to bottles containing fuming HCl or $NH_4OH$ made no appreciable difference.

The stock glucose solutions of the hospital prepared from stock distilled water and so-called chemically pure glucose were found to have a $P_H$ of less than 5. Three well-known brands of glucose were tested. Boiling, autoclaving and storing for 24 hours all cause glucose to rapidly become acid. Fresh unheated, 10 per cent. glucose, $P_H$ 6.20; after boiling 10 minutes, $P_H$ 5.47; after boiling 20 minutes, $P_H$ 5.17; after boiling 30 minutes $P_H$ 5. A fresh unheated solution ranged in $P_H$ from 6.2 to 4.15 after standing 48 hours.

Glucose solutions were buffered with the salts of mono- and di-potassium phosphates so as to give a concentration approximating that of the blood. They have been used repeatedly in the hospital without producing reactions. The method of buffering was devised and materials provided by Dr. E. A. Slagle and S. F. Acree. Buffering must be done after sterilization since the latter precipitates out the buffer substances.

The normal salt solutions of the hospital were found to be very acid ranging from $P_H$ 6.4 to $P_H$ 4.95. This was due in part to the use of stock distilled water. One well-advertised brand of normal salt solution put up in ampoule form had a $P_H$ 4.95. This high concentration in normal salt solution was found to be due in

part to the salt but chiefly to the acid distilled water. A salt solution to be normal physiologically, should contain that amount of salt which will make it isotonic with the blood. It should also have the same hydrogen-ion concentration.

One specimen of sodium citrate solution used in a transfusion where a violent reaction followed, had a $P_H$ of 10.25. We have had no reactions in seven transfusions with the citrate method since we have buffered the citrate solutions. Several specimens of phenolsulphonephthalein, the intravenous and intramuscular use of which was followed by reactions, had a $P_H$ 5.0. We have had no reactions since with phthalein solutions properly buffered. We have observed also in a series of twelve cases tested with a dye having a concentration of $P_H$ 5.0 and later with a dye with a $P_H$ 6.95 that from 10 to 40 per cent. more of the properly buffered dye is eliminated in two hours than is the acid type in the same time. We believe that the hydrogen-ion concentration of chemicals or drugs is an important feature in their absorption and elimination both when injected or applied to mucous membranes of the human body.

Several preparations of salvarsan, when prepared according to the directions of the manufacturers, ranged in $P_H$ from 11.53 to 11.99. Silber-salvarsan, $P_H$ 10.71; Neo-salvarsan, $P_H$ 8.15 to 9.22.

A long list of sera, vaccines, and antitoxins prepared by the New York State Department of Health approximated the $P_H$ of the blood except tetanus antitoxin which had a $P_H$ 8.60 and anti-pneumococcus serum, type I, $P_H$ 8.10. Triple pneumococcus vaccine, U. S. Army Medical School, $P_H$ 8.95. These might be sufficiently alkaline to produce local reactions.

All of the common drugs used for hypodermatic medication, both in tablet and ampoule form, were tested. Liquid digitalis and strophanthus preparations were found to have a high concentration, as were preparations made from the pituitary body and suprarenal bodies. Novocaine becomes acid on standing. We found much of the medication sold in ampoule form much more acid than the body tissues or fluids. We believe this to be the main cause of sore arms after the subcutaneous injections of such drugs.