The analysis shows that our compound was contaminated with a small amount of $MgSO_4$, but this was held not to interfere with the tests for rectal anesthesia.

The compound, when heated for a long time at 100° C. decomposes with the liberation of HBr, and the formation of water and alcohol-insoluble substance.

The biological tests on compounds reported herein were made in the biological Research Laboratories of E R. Squibb and Sons and we gratefully acknowledge their assistance.

RESEARCH DEPARTMENT OF THE CHEMICAL
AND PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB AND SONS, BROOKLYN, N. Y.

A METHOD FOR THE PREPARATION OF PARENTERAL DEXTROSE SOLUTIONS.

BY HARVEY A. K. WHITNEY.*

As a first premise it may be stated that a solution of dextrose suitable for parenteral administration may be made from a simple solution of chemically pure dextrose in chemically pure water. This statement is made with due consideration for the arguments for and against such factors as distilling apparatus, water, dextrose, hydrogen-ion concentration, buffers, preservatives and glassware. These modifying factors must be given consideration and together with the following elements, introduced at the time of administration, such as infusion apparatus, temperature of solution, velocity of injection and individual idiosyncrasy serve to complicate the apparently simple procedure issued as the original premise.

Distilling apparatus should be of a design that incorporates the following desirable and necessary features. Preferably the entrance of the raw water to the boiling chamber should be through condensers, permitting a preheating of the raw water, and venting the consequent discharge of many volatile substances. The insertion of a spray-trap or baffle-plates is also requisite to prevent the mechanical carry-over of boiling water or wet steam into the distillate. And lastly, the final delivery of the pure dry steam into vented condensers that will permit, if necessary, the delivery of the distillate into a closed system. It is pertinent to add that the whole interior of the distilling system should be lined with block tin.

Water obtained from the apparatus described, and under the circumstances necessary for the proper operation of the still, will provide a suitable solvent that may be used for the preparation of Aqua Destillata Sterilisata, U. S. P. Water distilled within the working hours of the morning or afternoon should be collected and disposed in a sterilized container of insoluble glass. The containers should be stoppered and sterilized under steam pressure giving a temperature of 115° C. for thirty minutes. If an autoclave is not available, close the mouth of flask containing freshly distilled water with a plug of purified absorbent cotton wrapped in gauze, and boil contents actively for one hour. Until ready for use, protect the mouth of flask, and plug from infection through dust, by wrapping top of flask tightly with paper. Sterilized distilled water so prepared should be used within

* Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

twenty-four hours after its distillation. That such water must be protected against microörganic contamination was definitely shown by Seibert (*Am. J. Physiol.*, 67 (1923), 90). The product described by her as "pyrogen" is held to be greatly responsible for post-infusion "bad" reactions. The observations of precautions enumerated by the United States Pharmacopœia are quite sufficient to prevent bacterial infection of water properly distilled.

Dextrose of no less a quality than that defined by the Pharmacopœia should be used. This provides definite limits for water content, ash, dextrin, lactose, soluble starch, sulphites, sulphates, chlorides, heavy metals and optical rotation. Under no circumstances should impure glucose (corn syrup) be employed in this work.

Hydrogen-ion concentration measurement of the simple dextrose solution reveals a figure that is probably never more acidic than p_H 5.0, after sterilization, unless excessive decomposition (caramelization) obtains. In general this measure of hydrogen-ion concentration is indicative of the degree of decomposition after sterilization. It should be further appreciated that this figure also discloses another significant fact in that *practically all available acidity is measured.* Such knowledge should tend to minimize the anticipated physiologic effect of using such dextrose solutions that are more acid than the blood. It may still be admitted, however, that in some extraordinary instances of excessive depletion of the alkali reserve, the extemporaneous addition of an alkali (buffer salts) at the time of administration may be discreet. For the reasons just mentioned it may be concluded that the routine use of buffer salts is to be depreciated.

Preservatives, generally, are not in use at the present time. The use of such materials was quite generally discussed and disposed of by the Council on Pharmacy and Chemistry of the A. M. A. Certainly the introduction of a preservative in this solution is to be regarded as an admission of lack of professional skill.

Glassware, unquestionably, should be uninfluential to the hydrogen-ion concentration and chemical balance of the solution it contains. To provide for this unchanging condition, the use of insoluble or alkali-free glass is advised. Our own experience with "hard" and "soft" glass has developed some interesting observations. It can well be imagined there are intermediate qualities of glass that make available qualities "harder" than "soft." At present we are using, with considerable satisfaction, such an electric-tempered "harder-than-soft" quality in the shape of a wide-mouth french-square bottle of forty-ounce capacity finished with a shallow continuous screw thread (G. C. A. 400) that permits the use of a special 48-mm. molded screw cap fitted with a packet liner. These bottles will contain one liter of solution with sufficient residual void. In use such bottles routinely receive a preliminary cleansing and subsequent processing generally in accord with the following routine. They are filled with a solution of boric acid, autoclaved, and the solution dispensed for surgical purposes. Upon return of the empty bottles to the pharmacy they are thoroughly washed, rinsed well with freshly distilled water, capped and dried and sterilized in a Lautenschlager-type sterilizer. They are then regarded as conditioned for use with dextrose solutions. Glassware in which the silicates (free-alkali) have been so fixed has proven itself suited for this particular use.

Rubber tubing, unless carefully selected introduces a factor active in the pro-

duction of untoward reactions. Only specially selected pure gum rubber tubing should be used for setting up the infusion apparatus. This tubing should be prepared for use, when new, by thoroughly washing in running tap water. Then soak, or better autoclave, in a 5% solution of sodium carbonate. Finally a rinse in running distilled water for another thirty minutes will provide a suitable tubing. After this preparation it may be wrapped in a towel and sterilized by autoclaving in the approved manner. It is further suggested that after the apparatus has been set up for an infusion it is always best to discard the first fraction of solution being administered that will completely fill the length of tubing used.

Solutions of dextrose in the distilled water should be brought about with all the pharmaceutical skill at one's command. We prefer to pass this solution through a Berkefeld filter, under pressure, more with the thought of clarifying the solution than of obtaining a sterile product. This solution is transferred into the containers described, capped and hooded with a parchment paper cap that protects the lip and neck of the bottle. This hermetically sealed package is placed in the autoclave and processed as described for Aqua Destillata Sterilisata, that is, sterilization is to be preferably accomplished under steam pressure giving a temperature of 115° C. and maintained for thirty minutes. It should be reiterated that a common fault of "soft" glassware, if not properly prepared, is that at this temperature discoloration as by caramelization may develop. Sample bottles are selected from each lot and tested chemically and bacteriologically. The finished solution for parenteral use is a clear, colorless, sterile, physiologically compatible solution. A printed label describing the solution as to composition and character, together with a control number identifying the batch, is then attached. Such solutions remain stable for a considerable time.

THE EXTEMPORANEOUS PREPARATION OF SALINE AND GLUCOSE SOLUTIONS FOR INTRAVENOUS USE.*

BY ROBERT S. FUQUA.[1]

The use of intravenous therapy by physicians and surgeons has been constantly increasing in late years, especially in hospital practice. While manufacturing pharmacists have done much to make intravenous medication safer and more convenient for the physician, it appears that most pharmacists outside the manufacturing field have been slow to accept responsibility for the extemporaneous preparation of suitable solutions for this form of medication. Since the need for much of the intravenous medication is largely of an emergency nature, the writer can think of no valid reason why the trained pharmacist, in either the hospital or retail field, should consider this work to be the sole responsibility of the large manufacturing laboratories.

As indicated in the title, this paper will discuss the preparation of only the two most frequently used solutions of this type—that of Physiological Saline Solution, or "Normal Salt," and the intravenous solutions of Dextrose. Such information regarding these as the writer has been able to obtain, has been gained

* Section on Practical Pharmacy and Dispensing, A. PH. A., Washington meeting, 1934.

[1] Chief Pharmacist, Johns Hopkins Hospital, Baltimore, Md.