SUMMARY.

The composition of phenylmercury nitrate has been studied and evidence which confirms the basic formula $C_6H_5.HgOH.C_6H_5HgNO_3$ obtained. Some other phenylmercury salts have also been described.

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SOME OBSERVATIONS ON THE PREPARATION OF INTRAVENOUS SOLUTIONS IN THE HOSPITAL PHARMACY.*

BY H. C. MCALLISTER[1] AND HENRY M. BURLAGE.[2]

Since the inception of intravenous medication, it has been the practice of many hospitals, at one time or another, to prepare some of the products used for this purpose. Their experience in a large number of cases has been unsatisfactory due to untoward reactions ranging in intensity from mild febrile manifestations and chills to severe reactions with high fever and even death. Many theories have been advanced as to the causes of these undesirable results, with little elimination of them. Some of the causes have been listed by the various investigators as follows:

1. Faulty technique in preparation and administration.
   (*a*) Improperly cleaned apparatus.
   (*b*) Rate of injection.
   (*c*) Temperature of the solution.
2. Personal factors.
   (*a*) Idiosyncrasies.
   (*b*) Individual resistances.
3. Hæmolytic factor.
4. H-ion concentration.
5. Use of impure chemicals.
6. Bacterial proteins.

In reviewing the possible cause or causes of these unfavorable results, it was found that Factors 1, 2 and 3 could be eliminated since unusual conditions were not encountered when commercially prepared solutions were used. (4) The H-ion of "reaction producing" solutions was found to coincide within the limits of those solutions not producing such reactions. These values were obtained by the colorimetric method. (5) The theory of the use of impure chemicals was discarded in the belief that if these were the source of contamination, all solutions made from the same lot of chemicals should give unsatisfactory results. This was not the case

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and no system of relationship could be established between the chemicals and the results.

(6) The bacterial nature of the agent causing the disturbances seemed to be the most logical explanation of the undesirable reactions previously mentioned. Seibert (1) conducted exhaustive studies in this field and concluded that these fever-producing substances, called *pyrogens*, are (*a*) of probable bacterial origin, (*b*) heat-labile, (*c*) non-volatile, (*d*) produced by specific bacteria which grow in distilled water, and (*e*) they pass through a Berkefeld filter. This investigator also concluded that water properly distilled and preserved under ordinary conditions of preservation, would remain free of pyrogens for twenty-four hours. These facts coincide with the results obtained by the authors in the preparation of 6047 units of sterile solutions for parenteral use during a period of one year.

In consideration of these facts, it was deemed practical to prepare solutions for intravenous use in the hospital pharmacy at a considerable saving to the institution. At this point it will not be amiss to enumerate the commercial values of a method for preparing sterile solutions for parenteral use. It may be seen from the following tables that the difference in cost of 6047 units of solutions prepared commercially and in the pharmacy is $2754.09.

TABLE I.—COST OF COMMERCIAL PRODUCTS.

Solution.	Units Used.	Cost per Unit.
1000 cc.—5% Dextrose in Normal Salt Sol.	2263	$0.79
1000 cc.—10% Dextrose in Normal Salt Sol.	308	1.05
500 cc.—Normal Salt Sol.	1632	0.32
100 cc.—Distilled Water	1489	0.26
100 cc.—Procaine HCl Sol. 1%	355	1.40
Total	6047	$3517.55

TABLE II.—COST OF SOLUTIONS PREPARED IN THE HOSPITAL PHARMACY.

Solution.	Amount, Cc.	Dextrose.	Sod. Chlor.	Water.*	Capping.	Sterilization.[1]	Total Cost per Unit.
5% Dextrose in Normal Salt Sol.	1000	$0.0364	$0.0063	$0.0661	$0.0125	$0.061	$0.1823
10% Dextrose in Normal Salt Sol.	1000	0.0728	0.0063	0.0661	0.0125	0.061	0.2187
Normal Salt Sol.	500	....	0.0032	0.0330	0.0096	0.051	0.0963
Distilled Water	100	....	....	0.0066	0.0060	0.048	0.0606
		Procaine HCl					
1% Procaine HCl Sol.	100	0.039	....	0.0066	0.0060	0.048	0.0996

* Includes cost of water, distillation and depreciation of apparatus (Still, etc.).

[1] Includes depreciation of sterilizers, breakage of flasks, etc.

It was found that satisfactory results could be obtained by altering the method of distilling or making simple modifications in the distilling process to give a pyrogen-free water. The method employed in making the above solutions is as follows:

A. Distillation of Water.—By far the most important procedure in the preparation of solutions for parenteral use, and especially intravenous medication, is the distillation of the water. It has been found best to distil the water twice and control the conditions of distillation very carefully. The stills can be arranged for con-

tinuous operation and require little time or attention. The first distillation may be carried out in a block tin still operated so that about 10% of the distillate escapes as vapor, thus eliminating most of the volatile impurities. For the second distillation, an all-Pyrex glass apparatus should be used. The receptacle for the first distillate may be used as a reservoir for the second still and emptied into the second distilling flask by a continuous siphon arrangement. The distillate from the second distillation should be collected in a sterile resistance glass container under as nearly aseptic conditions as possible. If the water thus prepared is not to be used within 24 hours, it should be autoclaved for fifteen minutes under eighteen pounds of pressure, immediately after it is collected. The entire apparatus used for the second distillation should be cleaned and sterilized before each day's operation. If these simple precautions have been observed, one may be assured that this water is of the best quality for the preparation of intravenous solutions.

B. Materials Used and the Preparation of the Solutions.—The solutions are prepared in the usual manner, observing the ordinary precautions to avoid contamination and using the best materials. Chemicals should be of C. P. or reagent quality, purchased from reliable manufacturers. It is not best to purchase these reagents in too large quantities unless the conditions of preservation can be rigidly controlled. Deterioration of chemicals often cause disappointing results. Frequently the solutions thus prepared contain linters or minute shreds of insoluble material which have been introduced in one way or another and these may be removed by the use of hard filter (Whatman No. 50) and subsequent straining through silk cloth (200 mesh). The cloth may be kept in alcohol (95%) when not in use. All utensils should be rinsed with double-distilled water before use.

C. Containers.—The selection of containers for the prepared solutions is of vital importance. Flasks of pyrex glass or other makes of resistant glass are quite satisfactory. It is best to allow dichromate cleaning solution to stand in *new* flasks for 24 hours before using. A very good method of cleaning the flasks for routine work is to wash them thoroughly with cocoanut oil soap inside and out. The outside of the container may be scrubbed with cleaning powder to prevent the collection of carbon during sterilization if this is done by the use of gas flame. The flask should be rinsed well (8–10) times with tap water and twice with double-distilled water and should not be allowed to stand for any length of time after it has been cleaned before it is filled. Flasks used for intravenous solutions should not be employed for any other purposes.

D. Closing the Containers.—Several methods have been used for closing the flasks:

(1) Plugs of non-absorbent cotton, covered with gauze, and the entire mouth of the flask covered with a paper cap.

(2) A layer of gauze, a layer of non-absorbent cotton and a second layer of gauze tied over the top.

(3) Skirted rubber stoppers.

(4) Corrugated hoods of closely woven paper.

For practical purposes, when the solutions are not to be kept more than four days, the last-mentioned method is the most satisfactory. The hoods may be fastened on with two strong rubber bands at a distance of about one inch apart. These caps serve as labels.

E. Sterilization of the Solutions.—The last important step in the preparation of intravenous medication is sterilization. Sufficient heat is necessary to kill organisms, yet excessive heat is undesirable since it causes decomposition of some organic compounds. Distilled water, solutions of inorganic compounds, and a few organic compounds may be sterilized in the autoclave; others should be boiled for ten minutes. For best results the solutions should not be kept for more than four days unless they are hermetically sealed.

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A READY METHOD FOR THE EXTEMPORANEOUS PREPARATION OF ISOTONIC COLLYRIA.*

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WHY ARE ISOTONIC COLLYRIA PREFERRED?

The purpose of adjusting the osmotic pressure of solutions to be instilled into the eye is to obviate the discomfort, or even pain, which, depending upon the sensibility of the patient, results when the collyrium has a different osmotic pressure than that of the surrounding tissues: which discomfort continues until the equilibrium is restored.

This difference in pressure is due to the difference in the degree of concentration and the difference in the physical and chemical properties of the different substances comprising the solute. It is due to this difference in osmotic pressure that distilled water, for example, when instilled into the eye causes discomfort, while we are unconscious of the tear secretion because with it this difference in osmotic pressure does not exist.

Hence the discomfort attending the use of collyria is avoided by adjusting the osmotic pressures and rendering them isotonic with the lachrymal secretion previous to instillation.

Much research has been conducted for the purpose of developing a method for preparing isotonic solutions scientifically accurate. For the most part they involve technical procedure which would generally be considered inexpedient at the prescription desk.

The work of Dr. F. Nicola as given in Scoville's "Art of Compounding" (1927) in the chapter on Adjusted Solutions presents a method sufficiently accurate for the purpose intended and applicable at the dispensing counter.

According to Dr. Nicola, the elements which determine the osmotic pressure in any solution, collyria in particular, are, mainly, the degree of concentration, the degree of dissociation, and the molecular weights of the prescribed substances in solution.

The degree of concentration is expressed by the per cent, weight to volume, of the solute.
The molecular weight by that of the substance dissolved.
The degree of dissociation by the approximate dissociation constants determined as follows:

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