

Secondly, the danger connected with its use: We are all familiar with this liquid and know how highly inflammable it is and while the danger may not be great in treating 100 or 1000 grammes of the drug with this liquid, it often becomes necessary to manufacture 10, 50 or 100 gallons, or more, in which case large quantities of the drug impregnated with this highly inflammable substance must be spread out to dry. While this operation is taking place one cannot rest easily when he realizes that it only requires a spark to start a serious conflagration.

Thirdly, its use is not economical: Owing to its properties previously described, no one would care to take the chance of recovering it by distilling it over a naked flame and while it may be distilled in a steam jacketed pan, the disagreeable odor remains in the pan for a considerable length of time and may contaminate other batches and consequently, if thrown away, it represents a clear loss.

The above shortcomings of petroleum benzene led us to endeavor to find a liquid that would not be open to these objections and which would remove the oily ingredients from the drugs. After considering the list of available substances, we finally decided to try carbon tetrachloride. This liquid readily exhausts completely the fats from such drugs as strophanthus and colchicum seed, while the active therapeutic ingredients are not disturbed, as is shown by subsequent physiological and chemical tests. Upon exposing the drug to the air and sunlight, the carbon tetrachloride may be readily and completely dispelled and there is no odor of this liquid in the finished product. It is absolutely impossible to ignite it, in fact, it is the principal ingredient of several patented fire extinguishers. No danger is connected with distilling it, as we have oftentimes distilled small amounts over a naked flame in our laboratory, as well as treating large quantities in our steam stills without contaminating other batches.

In fact, carbon tetrachloride possesses all the properties of petroleum benzene as far as its use as a solvent is concerned, and it is free from the objections and dangers of the latter.

ANALYTICAL LABORATORIES,  
NORWICH PHARMACAL COMPANY.

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## PHARMACEUTICAL WAR BABIES.\*

BY CURT P. WIMMER.

The term "War Baby" has been jocularly applied to the various creations, both abstract and concrete, of the world war. Popularly created nomenclature is invariably significant if not correct, and I use the term here to mean the newer pharmaceutical preparations created by the war. Truly, they are war babies, for only time can tell whether they will live and become useful members of our formularies or whether they will disappear.

It is the object of this paper to present a brief review of a number of the more important pharmaceutical preparations which have come into use during the last few years. All of these preparations, evolved through the exigencies of war, are used to combat sepsis, and to heal wounds or burns.

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\* Read before Section on Practical Pharmacy and Dispensing, A. Ph. A., Chicago meeting, 1918.

Inasmuch as infected wounds constitute by far the largest number of cases requiring treatment, it is but natural that physicians from the very beginning of the war sought the ideal antiseptic. The first one to become widely used was iodine. This was supplied to the troops put up in ampuls and millions of them have been used.

English physicians tried out a variety of substances. Sir Rickman Godlee treated wounds with pure carbolic acid, following the treatment with applications of a cyanide dressing. G. Lenthal Chetle used a combination of mercuric chloride and carbolic acid; another physician recommended the use of mercuric chloride and serum. Others advocated the use of such substances as garlic juice, urea, turpentine, liquid paraffin, salicylic acid, etc.

To Sir Almroth Wright must be given credit for suggesting the irrigation of wounds and the insertion of antiseptic tablets into wounds. Then came "Eupad," a mixture of equal parts of bleaching powder and boric acid, and "Eusol," consisting of 12.50 Gm. each of bleaching powder and boric acid mixed with 1 liter of water. From this Dakin proposed his original formula, as follows:

Sodium carbonate, dry, 140.00 Gm. Dissolve this in 10 liters of tap water and add 200 Gm. of chlorinated lime of good quality. This is shaken and set aside; then the liquid is syphoned off and filtered through cotton. Now add 40.0 Gm. boric acid and allow to dissolve. The solution is now ready for use. This solution was to contain about 0.50 percent of hypochlorous acid. Carrell, who used this solution in the irrigation of wounds, soon found that it was of importance to have this solution neither too alkaline nor of a too high hypochlorous acid content and placed it by proper modifications upon an exact basis by requiring titration to determine its strength. The details of the preparation and analysis of the Carrel-Dakin solution have been treated in such exhaustive manner in publications of late that I will not touch upon them here. Suffice it to say that of all the pharmaceutical war babies, this is the one most likely to survive.

A preparation which is now largely used and which is distinctly a creation of the war is the so-called "Bipp Paste," a bismuth subnitrate, iodoform-paraffin combination. Its formula is as follows:

Iodoform.....	8 ounces
Bismuth Subnitrate...	8 ounces
Liquid Paraffin.....	q. s. to make a paste.

After cleansing the wound it is completely filled with this paste and dressed with sterile gauze. It is not necessary to change the dressing unless pain is experienced by the patient. It is of course very important that this paste be absolutely free from gritty material.

It has been found that the crystallized iodoform, reduced to a very fine powder, is less apt to produce iodoformism than the granular form. If iodoformism sets in, potassium bicarbonate is given in 15-grain doses to combat it. A metallic spatula must not be used in the preparation of this paste.

Chloramine T (sodium para-toluene sulphochloramide) and Dichloramine T (toluene parasulphodichloramine) next engage our attention. Of these two antiseptics the latter is more extensively used because of its solubility in eucalyptol, which solution can then be diluted with paraffin oil. The antiseptic action of this substance depends upon the fact that chlorine is slowly given off, which exerts

the specific effect. In making solutions of Dichloramine T it is preferable to use chlorinated oils to prevent or retard the decomposition of the medicinal ingredient. A nasal spray, for example, may be prepared by dissolving Dichloramine T 0.20 Gm. in 2 Cc. of chlorinated eucalyptol and adding 8 Cc. of liquid paraffin. A 10 percent stock solution of Dichloramine T in chlorinated eucalyptol will keep for about one month. Quite recently Dakin and Dunham (B. M. J.) announced that they had discovered a new solvent for dichloramine by chlorinating hard paraffin. This process is, in short, the following: Paraffin melting at 50° C., or higher, is selected and placed into two flasks connected in series. It is heated to 120° C. and a rapid current of Cl gas is passed through until the paraffin is saturated or until the contents of the flasks have increased 45-55 percent in weight. The oily liquid formed is shaken with 5 percent of its weight of sodium carbonate and filtered through a dry fluted paper. This chlorinated paraffin is a clear, viscid liquid of a yellow color and slightly heavier than water. The authors propose to call this liquid Chlorcosane. It is capable of dissolving 8½ to 10 percent of Dichloramine T. For wound treatment a 7½ percent solution is sufficiently strong. For spraying it may be diluted with 10 percent carbon tetrachloride.

Dichloramine T and its preparations have been fully described in our literature. At the recent meeting of The New Jersey Pharmaceutical Association, Prof. E. Fullerton Cook read an excellent paper on the subject to which I refer those desiring more detailed information.

In the early part of the war there was announced a French proprietary remedy for the treatment of burns. It was called "Ambrine." This remedy proved so successful that it commanded general attention. It was wax-like and when melted and applied to wounds or burns formed an air-tight covering under which the wound healed rapidly. Experiments were made to determine to what particular property or ingredient the remarkable healing qualities of the preparation were due. It was finally found that when hard paraffin was heated to 130° C. by the aid of superheated steam the resulting product has a somewhat lower melting point than the paraffin originally used and that it had properties similar to those of ambrine. It is now universally accepted that ambrine owes its efficacy to the hard paraffin and not to any resin or oil of amber which are claimed to be present. Further investigations showed that it was essential to use a paraffin of suitable melting point and ductility. In the *Journal of the American Medical Association*, 1917, 69, 1525, are outlined the requirements for paraffin for film treatment. The paraffin must be more pliable and ductile than the U. S. P. kind. It must be liquid at 50° C., pliable at or below 28° C. and ductile at or below 31° C. It should readily adhere to the skin but permit of ready detachment from it. From these considerations has resulted the so-called paraffin treatment of wounds, which is, briefly, the following: The burn is first washed with clean water and dried, a layer of melted paraffin is painted on and covered with a layer of cotton; a second coat of paraffin is now applied and the whole covered with wool and a bandage. The dressing must be changed every day.

A number of modifications have been proposed. One is to use liquid paraffin for the first coat on the wound. This tends to make the application practically painless, for it was found that hard melted paraffin applied to a burn occasioned considerable pain. Another modification consists in the addition of

certain substances to the paraffin to enhance its action. Sollman recommends the addition of  $\frac{1}{2}$  percent of asphalt, or of 10 percent of cacao butter or yellow vaseline, together with antiseptics such as resorcin and eucalyptol. Hull, in the *British Medical Journal*, Dec. 15, '17, claims that it is best to use an antiseptic before applying the paraffin film. He recommends the use of Acriflavine, as a 1:1000 solution. The use of aniline dyes as antiseptics has increased of late, and their value as such is under investigation. We owe the suggestion that aniline dyes may be valuable antiseptics to Ehrlich, the inventor of Salvarsan. Flavine, or diamino-methyl-acridinium chloride, was originally prepared by Benda, a co-worker of Ehrlich. Browning and Gilmore called the attention of the profession to the powerful antiseptic action of this substance. The following dyes are in use as antiseptics: Brilliant green, Flavine, Acriflavine, Proflavine, Scarlet-Red. The question as to the real effectiveness of these dyes is still an open one. Extensive biological experiments are now in progress at the Middlesex Hospital, London, to determine their true value. From results announced it appears that Brilliant Green is about 3-4 times stronger than mercuric chloride, and that it is capable of killing organisms in as high a dilution as 1:30,000. Some of the formulas suggested by Lieutenant Colonel Hull are as follows:

No. 10 Red.		No. 12.	
Scarlet-Red.....	0.20%	Brilliant Green.....	0.05%
Oil of Eucalyptus.....	2.00%	Oil of Eucalyptus.....	2.00%
Olive Oil.....	5.00%	Olive Oil.....	5.00%
Hydrous Woolfat.....	4.00%	Hydrous Woolfat.....	4.00%
Paraffin, soft.....	21.00%	Paraffin, soft.....	21.00%
Paraffin, hard.....	67.80%	Paraffin, hard.....	67.95%
No. 13 Flavine Wax.		No. 14.	
Flavine.....	0.20%	Dichloramine T.....	0.20%
Oil of Eucalyptus.....	2.00%	Oil of Eucalyptus.....	2.00%
Olive Oil.....	5.00%	Olive Oil.....	5.00%
Hydrous Woolfat.....	4.00%	Paraffin, soft.....	25.00%
Paraffin, soft.....	21.00%	Paraffin, hard.....	67.80%
Paraffin, hard.....	67.80%		

The dye is rubbed with the hydrous woolfat until thoroughly mixed, using about  $\frac{1}{2}$  ounce of water to assist the solution of the dye. Melt the hard paraffin, add the liquid paraffin and the olive oil. When the temperature of the mixture is at 50° C., add the lanolin-dye paste, stirring until thoroughly mixed. Lastly add the oil of eucalyptus and stir until cold.

We have reviewed, briefly, Dakin Solution, Bipp Paste, Dichloramine, Ambrine-like preparations, aniline dyes as antiseptics. All have come into extensive use during the war. Let us hope that at least some of them will prove to be of inestimable value to man. Let us also call attention to the fact that much research work remains still to be done on these preparations, especially along pharmaceutical lines. Physicians and chemists have taken the lead in creating and applying these new substances. Will the pharmacist rise to the occasion and endeavor to present them to the medical profession in the form of new and elegant and compatible pharmaceuticals? It is my hope and expectation that he will do so!