DICHLORAMINE-T AND CHLORCOSANE.

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1. The keeping of Dichloramine-T without decomposition.
2. The preparation of a pure stable, crystallized Dichloramine-T.
3. "Gas Machine Gasoline" as a diluent for chlorcosane in the preparation of the solution of Dichloramine-T, and also as a "stabilizer" of this solution.

While the Great War cannot very well be called a "blessing in disguise," it is certain that it stimulated advances in science and industry, from which mankind will reap benefits for years to come. In the medical science these advances are especially noticeable. Not only was the technic greatly improved, but certain chemicals were developed which have proved to be valuable therapeutic aids. In one case in particular, that of the Dakin Antiseptics, the raw material—paratoluenesulphonchloride—is a waste product of the manufacture of saccharin.

Much has been written about the antiseptic value of the original Dakin Solution and the Dakin Antiseptics—Chloramine-T and Dichloramine-T; both have proved excellent in military as well as in civil practice.

While, however, they had an extensive use during the war, the Dakin Antiseptics are falling into disuse in civil practice. The reasons for this are manifold:

1. The ordinary practitioner is not sufficiently acquainted with their use.
2. The water-soluble chloramine-T, while it is a most powerful antiseptic, makes a colorless solution having practically no odor. On the other hand tincture of iodine is colored, mercuric bichloride is dispensed in tablets containing a dye, and phenol has a strong odor. This implies efficacy in the mind of the layman.
3. The oil-soluble Dichloramine-T, as usually manufactured, has been found to be unstable both in the powdered form and in solution.
4. Owing to the high viscosity of chlorcosane, the solvent for Dichloramine-T, much difficulty has been experienced in spraying that liquid and made it unsuitable for dispensing.

It has gone so far that one of the largest manufacturers of these products informed me that the utmost is being done to prevent the use of Dichloramine-T because it has been found to be unstable.

The purpose of this article is to show that:

1. Dichloramine-T is a stable chemical, when prepared in a fairly stable form.
2. The solution of Dichloramine-T in chlorcosane (the standard solvent) while necessarily unstable, is not a hindrance to its use.
3. A diluent is proposed, which enables the solution to be easily sprayed by means of an atomizer used for aqueous liquids.

The investigation of Dichloramine-T and its keeping quality was begun when certain dark green (so-called "black") glass bottles, in which the preparation was packed, could not be obtained. Previous investigators had reported that "Dichloramine-T decomposes at the same rate in dark amber and in black glass bottles;" but the rate of decomposition was much greater when the preparation was kept in colorless (flint) glass bottles. (Private communication.) This would tend to show that not only was the compound itself unstable, but its decomposition was hastened by light.

A preliminary study of the problem showed that, when prepared from impure raw materials, the Dichloramine-T tended to decompose rapidly. Only when prepared from paratoluenesulphonamide which had been previously recrystallized, was it possible to obtain a stable product. It was also demonstrated that the correct assay of Dichloramine-T, when freshly prepared, is not a criterion of its quality; some samples quite often decomposed rapidly giving off both chlorine and hydrochloric acid; however, a low assay was always an indication of an inferior product.

A lot of Dichloramine-T was selected which appeared to be stable after having been kept in a sealed container for some time. This lot had been prepared in the factory from a lot of purified paratoluenesulphonamide. The material dissolved to a clear solution—free from residue in both chloroform and chlorcosane.

EXPERIMENTAL.

The Dichloramine-T was put up in 1-ounce dry glass bottles of various colored glass, and stoppered tightly with corks, containing a slip of glazed paper beneath them. The bottles were then placed in a closet with a glass front, so that only diffused light reached them. The temperature was slightly below room temperature of a hot summer, *i. e.*, 25–30° C. The summer having been a particularly humid one, the samples were exposed (when opened for sampling) to the extreme of such weather.

The method used for testing the Dichloramine-T for the "available chlorine" content was as follows:

> Weigh out 0.1000 gram of Dichloramine-T in a 150-mil Erlenmeyer flask. Dissolve in 10 mils of chloroform and stopper the flask with a cork. Add a solution of 3 grams KI in water sufficient to make 10 mils. Shake once, and add 5 mils glacial acetic acid (tested against KI). Allow to stand for 30 minutes in diffused light, shaking occasionally, then add 50 mils of water, shake, and titrate at once, with $N/10$ sodium thiosulphate solution until the yellow color disappears. No indicator is necessary.

Samples of Dichloramine-T were taken from the top of the bottle, then a layer about 0.25 inch thick was removed, and another sample taken.

It was observed that a superficial layer about 0.25 inch thick (in a small bottle) was sufficient to protect the remainder of the Dichloramine-T from the decomposing action of the air.

Results and observations are given in Table 1.

During the course of the investigation, the original stock of standardized volumetric solution of sodium thiosulphate became exhausted, and a new lot was prepared. It was found that while the two volumetric solutions—both checked against pure iodine—checked, when titrated, against pure Dichloramine-T, the same relationship did not exist when a sample of commercial Dichloramine-T was assayed. This is shown in Table 1.

An investigation made in this direction, on available samples, showed that a number of sodium thiosulphate volumetric solutions with the same factor, *e. g.*, F = 1.000, would give different titers for a definite "chlorine equivalent." In one case 16.50 mils, in another 16.60 mils and in an extreme case even 16.80 mils would be required. The error in the determination of the "available chlorine" of the Dichloramine-T would thus amount to as much as 0.6 per cent. in the extreme case.

TABLE 1.

Key: A = Very dark brown ("black") glass bottle. B = Dark green glass bottle.
D = Light amber glass bottle. E = Flint glass bottle.

Note: Figures indicate the number of mils of $N/10$ sodium thiosulphate solution required for 0.1000 gram of Dichloramine-T.

	DATA.									
Date.	"A."	Remarks.	"B."	Remarks.	"C."	Remarks.	"D."	Remarks.	"E."	Remarks.
7/15[1]	16.70		16.70		16.70		16.70		16.70	
7/23[2]	16.60		16.50		...		16.50		16.50	
7/30[3]	16.49		16.52		16.56		...		16.60	
8/6[4]	16.40		16.41		...		16.40		16.42	
8/8[5]	...		...		*16.30		...		...	
* 9/8[6]	16.68		16.58		16.61		16.70		16.92	Slight odor of chlorine
* 9/8[7]	16.79	Slight odor of Cl	16.60	Odor of Cl stronger than "A"	16.72	Practically no odor of Cl	16.75	As in "C"	16.80	Odor of Cl less than above
*10/6[8]	16.76	Faint odor of Cl	16.65	Very strong odor of Cl	16.79	Slight odor of Cl	16.78	As in "C"	16.80	Odor of Cl
*10/7[9]	16.80		16.87		16.79		16.80		16.88	

* In the above determinations there was used a different solution of $N/10$ sodium thiosulphate. See report for explanation of results.

[1] On the day samples were prepared, the weather was rainy and very humid.

[2] Weather as above.

[3] All the samples had a faint odor of chlorine, that of "E" being slightly stronger. Weather as above.

[4] All the samples had a faint odor of Cl. On removing the top layer of Dichloramine-T, the odor of Cl becomes hardly noticeable.

[5] Sample taken from a 2-lb. bottle of dark amber glass which was only one-third full of Dichloramine-T.

[6] Sample taken from surface.

[7] Sample taken after a surface layer about 0.25 inch thick had been removed.

[8] Sample taken from surface.

[9] Sample taken after a surface layer about 0.25 inch thick had been removed.

The bulk stock of Dichloramine-T was usually kept in earthenware crocks with covers which did not fit very tightly. Several times a 2-lb. sample was taken from a crock and put into an amber glass bottle and stoppered with a cork. While the material in the crock would, after a week and in some cases within three days, begin to give off chlorine and hydrochloric acid gas in fairly large quantities and, when dissolved, would give a turbid solution, the Dichloramine-T in the bottle would be as good as when first packed. The latter observations, together with the experiments given in Table 1, indicate that:

1. The opaqueness of the glass of the container is *not* a factor in the keeping quality of a good Dichloramine-T; although dark amber bottles are the best for keeping this material; in case of necessity even flint glass bottles could be used.

2. Dichloramine-T is not affected by diffused light.

3. Air, and especially the moisture of the air, is a very important factor in the decomposition of Dichloramine-T.

4. Dichloramine-T should always be kept in dry, well-stoppered containers which should be filled to the top.

5. A ground-glass stoppered bottle has no advantage over an ordinary cork-stoppered bottle for keeping Dichloramine-T.

RECRYSTALLIZED DICHLORAMINE-T.

A quantity of Dichloramine-T, from the same lot used in the above experiments, was recrystallized from pure carbon tetrachloride. Dichloramine-T is very soluble in carbon tetrachloride, but the latter is an excellent medium for the purpose because it is fully saturated with respect to chlorine, readily volatile, and not readily absorbed by the crystals.

The crystals obtained were small, transparent, and of a pale greenish yellow color. A sample was assayed, and found to have the theoretical value for the chlorine content (29.29 per cent.). The material was put into 2-ounce glass-stoppered, dark amber glass bottles and was left untouched for three months. On opening a bottle, a faintly aromatic odor was noticeable, but there was no trace of HCl or chlorine. The same sample was examined recently, *after it had been kept for four years* in the laboratory. The odor was still aromatic, without any trace of pungency or chlorine. On assaying, the "available chlorine" content was found to be 28.55 per cent., indicating that there was only slight decomposition.

DILUENT FOR CHLORCOSANE.

Before anything is said about the *diluent* for chlorcosane, certain fallacies with regard to chlorcosane and its use as a solvent for Dichloramine-T must be removed.

As is well known, chlorcosane is prepared by running chlorine into molten paraffin until a drop just sinks in water, that is, until a specific gravity of about 1.03 is reached. The brownish yellow oil is washed with water containing sodium carbonate and is then dehydrated. The resultant product is far from being saturated with regard to chlorine and, therefore, when Dichloramine-T is dissolved in it the former, which has a smaller affinity for chlorine than the chlorcosane, readily gives up its chlorine to the latter, and itself breaks down to paratoluenesulphonamide. This has caused the condemnation of Dichloramine-T for medicinal use. However, the important point to be noted is that it is just for this reason—that is, its content of readily available chlorine—that the oil-soluble Dakin Antiseptic is used.

To overcome the disadvantage of the instability of the solution, Dichloramine-T should be dissolved in chlorcosane only when required, which can be done very quickly.

An investigation of the stability of Dichloramine-T in chlorcosane was carried out.

A 2 per cent. solution of uncrystallized Dichloramine-T (called A) and another solution of crystallized Dichloramine-T (called B) were prepared and each put into a 2-oz. cork-stoppered flint glass bottle, which were put in a closet exposed to diffused light. Table 2 shows the results.

TABLE 2.

Time examined.	A.	B.
When prepared	Clear	Clear and bright
After 4 days	Faint odor of HCl. Clear	No odor. Clear and bright
After 13 days	Strong odor of HCl. Clear	Very faint odor. Clear
After 21 days	Strong odor of Cl and HCl. Small crystals present	Very faint odor. Small crystals present
After 23 days	In a cool place for two days. Decomposed	Practically all the solute had crystallized out as the sulphamide. Liquid is mushy. Decomposed

The conclusions to be drawn are, that:

1. Dichloramine-T *does not* form a permanently stable solution when dissolved in ordinary chlorcosane.

2. The purer the Dichloramine-T, the greater the life and stability of the solution.

3. The solution of a pure, *recrystallized* Dichloramine-T in chlorcosane should not be used after it is three days old and, when ordinary Dichloramine-T is used, its solution in chlorocosane should be used on the day it is prepared; that is, a "freshly prepared solution" only should be used.

THE DILUENT.

The chlorcosane having a high viscosity, a special apparatus is necessary in order to spray the heavy oil; this has always been a hindrance to its use. A diluent, which would facilitate the spraying of the solvent, must of necessity have the following properties:

1. A very low viscosity.
2. Must be miscible in all proportions with chlorcosane.
3. Must not be irritating to the mucous membrane.
4. Must not have a disagreeable odor, nor develop one.
5. The diluent must not react with, or affect the stability of, the solution of Dichloramine-T in chlorcosane.
6. The diluent should preferably be readily volatile.
7. Its cost must be low.

Previous investigators had been unable to find a suitable solvent. Having the points enumerated above in view, the author investigated a long list of possible solvents and came to the conclusion that petroleum ether is the ideal liquid for the purpose. Seeking a material which would have all the properties of petroleum ether and be of a lower cost, it was found that "Gas Machine Gasoline" is as good a diluent for chlorcosane as petroleum ether.

An investigation was made of the effect of this diluent on the solution of Dichloramine-T in chlorcosane.

EXPERIMENTAL.

A 2 per cent. solution of Dichloramine-T in chlorcosane was made up and put into a 4-oz. cork-stoppered flint glass bottle, and put into a dark closet at room temperature. This was called "Sample A."

Another 2 per cent. solution of Dichloramine-T was made up, using as a solvent a mixture of four volumes of chlorcosane and one volume of "Gas Machine Gaso-

line." This solution was also put into a 4-oz. cork-stoppered flint glass bottle, and was called "Sample B." It was kept under the same conditions as Sample A.

At various periods about 5 mils of the liquid were withdrawn and assayed for "available chlorine" by the same method as was employed for the Dichloramine-T (*vide supra*). The results are shown in Table 3.

TABLE 3.

	Loss in per cent. of the amount of "available chlorine" present.	
	Sample "A."	Sample "B."
Original solution	..	...
On 9th day	7.1	12.4
On 22nd day	22.0	25.0
On 35th day	32.0	34.0

We can thus see that both solutions lose "available chlorine," but that the loss tends to the same limit in both cases, when the solutions are about one month old.

While the solution which contained the diluent had practically no odor even at the end of one month, the other (chlorcosane only) had acquired an odor of chlorine at the end of one week, and this odor became more pronounced in time.

We can thus see that the diluent has not only the effect of lowering the viscosity of the chlorcosane, but has also the beneficial effect of absorbing the chlorine evolved in the decomposition of the Dichloramine-T.

SUMMARY.

The conclusions to be drawn from the investigation outlined above may be summarized as follows:

1. Dichloramine-T dissolved in chlorcosane is an excellent antiseptic. It is a powerful, non-irritating germicide; possessing the additional advantage of giving off the active ingredient (chlorine) slowly in the amount required.

2. When commercially pure intermediates are used, and a reasonable amount of care is employed in its manufacture, a stable Dichloramine-T is the result. Further purification can be obtained by crystallizing the product from carbon tetrachloride.

3. While chlorcosane is the best solvent for Dichoramine-T, it does not produce a solution which is stable for any great length of time. When this fact is taken into consideration, the preparation leaves little to be desired from the viewpoint of an antiseptic.

4. "Gas Machine Gasoline," when used as a diluent for chlorcosane in dissolving the Dichloramine-T, greatly enhances the value of the preparation for nose and throat work. Its value in private practice is greatly increased, because this solution can easily be sprayed from a suitable atomizer.

5. Only the precautions ordinarily employed in keeping volatile or hydroscopic substances are required for keeping Dichloramine-T. It is the absence of this precaution which has caused this important medicinal product to lose its popularity.

It is to be hoped that the spread of the information hereby presented will cause Dichloramine-T to come back to its own.

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