PAPERS READ BEFORE THE BRANCHES OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

CARREL-DAKIN SOLUTION.*

BY JOHN K. THUM.[1]

It was while working on native black oxide of manganese, which chemical investigators before Scheele had studied more or less unsuccessfully, that he discovered in short order four new substances—chlorine, oxygen, manganese and baryta—and of these four, the first two have undoubtedly been of the utmost importance for the proper understanding of chemical processes. This happened in 1774. Scheele termed the first substance "oxymuriatic acid;" thirty-seven years later, Sir Humphry Davy classified the first of these substances as an element and gave it the name "chlorine." Although Gay-Lussac and Thénard were the first to suggest that from its behavior it might be regarded as an element, Davy proved it.

The practical value of this discovery and the important rôle that chlorine has played in the development of chemistry cannot be overestimated, and now that its value as a germicide has been proved and its practical application made possible by the researches of Carrel, the danger of death from infection has been wonderfully reduced. Knowledge of the disinfecting and germicidal action of chlorine is not by any means recent. Chlorine water has been recommended for years locally as a stimulant and disinfectant for wounds and ulcers. However, its irritating nature and the severe pain produced when applied to wounds has militated against its general use in surgical procedure. Some years ago it was discovered that very attenuated solutions of this gas were efficient for the sterilization of swimming pools, but its use for this purpose has been discarded for the copper sulphate treatment of the water. Like in everything else the personal equation plays a very important part in the handling of chlorine gas for the disinfection of a swimming pool; while one man would exercise great precaution and care in carrying out the technic for the treatment of the water, others would be rather lax in varying degrees, with the result that while the water would probably be thoroughly sterilized, it would also be exceedingly irritating and painful to the eyes. In the copper sulphate treatment of the water this condition is not so prone to occur.

It may be of interest to know that as early as 1846 the disinfecting properties of chlorine were proven by the successful employment of it in eradicating an epidemic of puerperal fever in Vienna. In this case bleaching powder was used.

Undoubtedly the ideal germicide for combating infection that occurs in most

Editor's Note.—The successful use of the Carrel-Dakin solution depends on the chlorine of course, but in combination, and in a nearly neutral solution.

The Eddystone horror afforded the opportunity in this country for applying the Carrel-Dakin treatment, and also that of the paraffin dressing for the burns in a large number of cases, and with gratifying success and relief to the unfortunates.

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wounds, is one that has the power of destroying not only bacteria but spores as well, and is only local in its action and, therefore, without danger to the host. It seems that the hypochlorites have this power. As a matter of fact they have been recognized by public health workers as the most potent germicides that we have, and yet their use in general surgery has been limited for reasons that are obvious. The various hypochlorite solutions are all more or less unstable as to chlorine content and, while they can be made more stable by making them more alkaline, this militates against their use on the tissues.

The first practical application of chlorine in surgical procedure for the eradication and control of infection was undertaken by British surgeons shortly after the beginning of the great war. They immediately recognized their helplessness when the large number of wounded began to arrive from the front with wounds of every description and all terribly infected. They worked with hypochlorous acid in one-half percent aqueous solution, made by adding 12.5 grammes of chlorinated lime and the same quantity of boric acid to a liter of distilled water and allowing the mixture to stand over night. This was then filtered and used as a surgical dressing. In the *British Medical Journal*, July 24, 1915, p. 129, they give their results; while these are good, other workers seem to have been unable to duplicate them.

In their experiments they failed to take into account the extreme variability of chlorinated lime and this may be the main reason why results have been unsatisfactory in different workers' hands.

Dakin's Solution then made its appearance. This is now referred to as Dakin's Original Solution. This solution is very easily made: 140 grammes of dried sodium carbonate are dissolved in 10 liters of water, and 200 grammes of chlorinated lime are added; the mixture is well shaken at intervals during one hour; the supernatant liquid is then siphoned off and filtered, preferably through paper. This solution is somewhat alkaline, but this alkalinity is modified by the addition of 40 grammes of boric acid. This preparation, however, did not prove altogether satisfactory. Sometimes it worked admirably and at other times not. There were times that patients complained that the solution was very irritating and painful, although the original technic followed in its manufacture was always scrupulously duplicated. Of course, the fault laid with the chlorinated lime. While the formula was always rigidly adhered to, the chlorinated lime seldom had the 25 percent chlorine content that was required to make a 0.5 percent solution. When one remembers that the different brands of chlorinated lime available in the open market vary considerably, and that even different packages of the same brand will run all the way from 25 to 35 percent in available chlorine content (at least that was the range found by us of packages put up in this country, and in Europe it must be greater, as the range of chlorine content of packages bought on the open market there run all the way from 20 to 37 percent) it is perfectly obvious as to why results should be so variable in different surgeons' hands.

Now Dr. Carrel's method for combating infection is simply a more or less continuous irrigation of the wounds with a modification of Dakin's solution, or, to be more exact, a modification of the well-known Labarrque's solution, officially known as *Liquor Sodae Chlorinatae*. This official solution of sodium hypochlorite contains 2.5 percent of available chlorine and is markedly alkaline. This makes

its use as a dressing for infected wounds prohibitive, it being exceedingly irritating and painful. Dilution of this solution with water to reduce it to 0.5 percent of available chlorine (the strength of the Carrel-Dakin solution) is impracticable, as it is still too alkaline. Such a diluted solution, first neutralized by the addition of boric acid, has been used but with very unsatisfactory results, it rapidly losing its chlorine, and proving otherwise objectionable.

Of course, making the preparation in this manner simplifies matters very much and also saves time, a factor of some importance where large quantities must always be available. It was Daufresne who pointed out the disadvantages of neutralization with boric acid, to which he attributed much of the irritation and painfulness, and the extreme variability of the chlorinated lime was also noted by the same observer.

Naturally, this illuminating fact put an entirely new aspect on the matter and brought forcibly to mind that estimation of the chlorine content of each new lot of chlorinated lime was absolutely essential before concordant results could follow.

Accordingly Daufresne evolved the following technic for making this preparation, and this only, and no other, should be used when Dakin's or Carrel-Dakin Solution is called for:

Chlorinated Lime (25 percent chlorine)	184 Gm.
Sodium Carbonate, dried	92 Gm.
Sodium Bicarbonate	76 Gm.

Into a 12-liter bottle put the chlorinated lime and five liters of water and shake frequently during a period of six hours; dissolve the two sodium salts in five liters of water and after six hours add this solution to the mixture of chlorinated lime and water and shake well for several minutes. Allow to stand for at least half an hour until reaction is complete and then siphon off the supernatant liquor and filter through paper. The solution, undiluted, is then ready for use.

When the chlorine content of the chlorinated lime is above or below 25 percent, the proportions of the three ingredients entering into this solution must be increased or reduced accordingly. To avoid the necessary calculation that this entails, Daufresne has prepared the following table:

QUANTITIES OF INGREDIENTS FOR TEN LITERS OF DAKIN'S SOLUTION.

Titer of Chlorinated Lime.	Chlorinated Lime. Gm.	Anhydrous Sodium Carbonate, Gm.	Sodium Bicarbonate. Gm.
20	230	115	96
21	220	110	92
22	210	105	88
23	200	100	84
24	192	96	80
25	184	92	76
26	177	89	72
27	170	85	70
28	164	82	68
29	159	80	66
30	154	77	64
31	148	74	62
32	144	72	60
33	140	70	59
34	135	68	57
35	132	66	55
36	128	64	53
37	124	62	52

It would be well to take the titer of this solution occasionally. The same substances used for determining the activity of the chlorine in the lime are used for this purpose.

To ten mils of the finished solution add 20 mils of 10 percent solution of potassium iodide and 2 mils of acetic or hydrochloric acid. Measure into this mixture, drop by drop, from a burette, a decinormal solution of sodium thiosulphate until decoloration is complete. The number of mils used multiplied by 0.03725 will give the weight of the sodium hypochlorite in 100 mils of the preparation.

In order to determine the alkalinity of the Carrel-Dakin solution or note its freedom from caustic sodium, add to 20 mils of the solution 0.2 of phenolphthalein; if correctly prepared no red coloration should appear.

Estimation of the amount of chlorine in the chlorinated lime is of the utmost importance and the method for doing this is simplicity itself. One may use the method given in the U. S. Pharmacopoeia, or the following, which is the one mentioned by Carrel in his note to the *Journal A. M. A.*, December 9, 1916, p. 1777, and which note is reprinted in the *American Journal of Pharmacy*, February, 1917, p. 84:

"Weigh out 20 grammes of the average sample, mix it as completely as possible with 1 liter of ordinary water and leave it in contact for a few hours, agitating it from time to time. Filter.

"Measure exactly with the gaged pipette 10 mils of the clear fluid; add to it 20 mils of a 1 : 10 solution of potassium iodide and 2 mils of acetic or hydrochloric acid. Drop a drop at a time into this mixture a decinormal solution of sodium thiosulphate until decoloration is complete.

"The number of mils of the thiosulphate solution required for complete decoloration, multiplied by 1.775, gives the weight of the active chlorine contained in 100 grammes of the chlorinated lime."

SOME EXPONENTS OF AMERICAN PHARMACY.*

BY JOHN F. PATTON.

The history of pharmacy, like that of any other branch of science, is a story of evolution. Embracing not only the compounding of medicine but a host of collateral branches allied to it, the history of each would make a tome of large proportion.

The development or progress of any branch of human endeavor must take into account the individual exponent, so that its history is but an amplified biography. It is always interesting as well as instructive to know something of the character of a person who has developed an industry, exploited some branch of the sciences, or invented a useful implement; hence, biography forms an important part of our libraries.

It is a well-known fact that those engaged in scientific pursuits develop a subtle condition of mind free from the weakness of selfishness, which is so inherent in human nature. Those of us who were acquainted with the subjects of the following sketches will bear testimony to the truth of the above statement.

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