ON THE USE OF CERTAIN ANTISEPTIC SUBSTANCES IN THE TREATMENT OF INFECTED WOUNDS.

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In order to make a judicious choice of the antiseptic most likely to give useful results in the treatment of infected wounds many different factors have to be considered in addition to germicidal activity, including the irritating properties of the substance to the patient, their toxicity, solubility, ability to penetrate tissues and to be absorbed, and their chemical reactions with proteins and other tissue constituents.

The killing of bacteria by ordinary antiseptic substances is essentially a chemical reaction between the antiseptic on the one hand and the proteins and other cell constituents of the micro-organism on the other. The destruction by antiseptics of bacteria suspended in water is relatively easy effected, because no proteins are present in the mixture other than those derived from the micro-organism. The destruction by antiseptics of bacteria mixed with blood serum, pus, and other exudate is much more difficult because the antiseptic acts not only on the micro-organisms but on other protein substances as well. Therefore, in judging of the antiseptic action of a substance suitable for the treatment of wounds, it is essential that its germicidal action be tested against micro-organisms mixed with blood serum or similar substances, and not simply tested against bacteria suspended in water.

The germicidal activity of all known antiseptics is greatly reduced by the presence of blood serum or similar substances, and in some cases this reduction is so great that the compound loses all practical antiseptic value.

The following table contains results which illustrate this enormous reduction in germicidal action by blood serum in the case of several common antiseptics.

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Without Blood Serum</th>
<th>With Blood Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>1:250 – 1:500</td>
<td>1:50</td>
</tr>
<tr>
<td>Salylic acid</td>
<td>2:200 – 1:800</td>
<td>1:400</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>1:500 – 1:800</td>
<td>1:400</td>
</tr>
<tr>
<td>Iodine</td>
<td>1:100 – 1:200</td>
<td>1:200</td>
</tr>
<tr>
<td>Mercurochrome</td>
<td>1:5000 – 1:20000</td>
<td>1:1000</td>
</tr>
<tr>
<td>Silver nitrate</td>
<td>1:1000 – 1:10000</td>
<td>1:500</td>
</tr>
<tr>
<td>Sodium hypochlorite</td>
<td>1:5000 – 1:10000</td>
<td>1:1000</td>
</tr>
<tr>
<td>Para-phenylene sodium sulphonchloramide</td>
<td>1:5000 – 1:10000</td>
<td>1:1000</td>
</tr>
</tbody>
</table>

The figures indicate the concentration of antiseptic necessary to sterilize one drop of a fresh culture of Staphylococcus aureus in a total volume of 3 c.c.m. acting for two hours. \( + \) indicates growth; \( - \) indicates complete sterilization.

But in choosing a suitable antiseptic many other factors than germicidal action need be considered. Mercurochrome, which among the substances referred to in the table shows the highest germicidal action, is probably the least useful and most objectionable as an antiseptic for the treatment of infected wounds. It may be of use to consider some of the limitations of the commonly used substances referred to in the above table.

Phenol is characterized by very low germicidal power, especially when acting in the presence of serum. When used in sufficiently high concentration its germicidal efficiency is decisively destructive of healthy tissue.

Hydrogen peroxide gives encouraging results when tested against bacteria in the test tube, but when used on wounds the substance has little germicidal action, for it is decomposed with the greatest ease by the enzyme catalase present in all tissues and in the blood cells. Hence its action can only be exerted during a trifling interval of time. The mechanical detergent action connected with the rapid disengagement of oxygen gas on infected surfaces is probably of greater value than any antiseptic action exerted by the hydrogen peroxide.

An interesting experiment related to use by Professor E. K. Dunham may be quoted here. A rabbit which had received an intravenous injection of the Welch bacillus (B. aureus capsulatus or B. perfringens) was killed, and the infected liver was removed and carefully sectioned. It was found that cubes of the infected liver only 1 mm. in size could be immersed in and incubated with hydrogen peroxide of moderate concentration without destruction of the micro-organisms.

Hydrogen peroxide, as regards its antiseptic action, must be regarded as of slight value, even against anaerobic organisms. Hydrogen peroxide, as, regards its antiseptic action, must be regarded as of slight value, even against anaerobic organisms.

Silver nitrate is of greater value than mercuric chloride, but when used in sufficiently high concentration is irritating. Many tissue constituents inhibit its action markedly. The photo-sensitiveness of the silver compounds formed is objectionable.

Iodine, which has proved so valuable for the disinfection of skin, has given much less satisfactory results in its use for deep wounds owing to protein coagulation and irritation of the tissues. The penetrating power of iodine is slight, and wounds which have been freely treated with it are apt to cicatrize more slowly than usual.

Sodium hypochlorite has high germicidal action, and has many other desirable properties. But sodium hypochlorite as ordinarily prepared is of extremely variable composition, contains free alkali and sometimes free chlorate, and is consequently irritating when applied to wounds. By a simple process, which will now be described, it has been possible to render the hypochlorites much less irritating while retaining their antiseptic action unchanged.

**PRINCIPLES INVOLVED IN THE PREPARATION OF THE HYPOCHLORITE SOLUTION.**

Solutions of sodium hypochlorite always contain free alkali even when prepared with the greatest care. A so-called "neutral" solution of sodium hypochlorite has an alkaline reaction. This is due not only to free alkali which may remain from the process of preparation, but also to the fact that the hypochlorite in solution undergoes hydrolytic dissociation giving free sodium hydroxide and hypochlorous acid.

\[ NaClO + H_2O = NaOH + HClO \]

The extent of this dissociation has been measured by Dewar, and quantitatively it is very considerable. The irritating action of ordinary hypochlorites is largely due to this formation of free alkali. The extent of this hydrolytic dissociation increases with dilution, so that practically hypochlorites cannot be effectively rendered non-irritating by simply reducing the concentration, for a point is soon reached at which germicidal action is impaired while the irritating properties of the solution persist. In addition to the above sources of free alkali, it must not be forgotten that alkali may be liberated by the action of sodium hypochlorite on proteins, a reaction in which the chloride of the hypochlorite is attached to nitrogen in the proteins, as will be shown later.

Now it is well known that certain fluids, such as blood and some other body fluids, also contain artificial salt solutions containing mixtures of salts of polyvalent acids—for example, phosphoric acid—are able to retain their essential neutrality even after the addition of limited quantities of acid or alkali. This is due to the fact that the addition of acid or alkali simply changes the relative...
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proportion of two or more salts of the polybasic acid present in the solution.

Starting with this idea, and employing the feeble polybasic character of the acid, it has been possible to prepare a simple boric acid mixture which contains approximately neutral under all conditions, is practically non-irritating, and, when properly applied, has given most pleasing results in the antiseptic treatment of wounds. It must be understood that the insignificant antiseptic action of boric acid has nothing to do with the excretion of this acid; nor is this acid employed for the purpose of liberating hypochlorous acid, as in Lumière’s or Lorrain Smith’s preparations.

The principle of the preparation is as follows: Chloride of lime (powdered in water) is decomposed with a solution of sodium carbonate and the filtered solution containing sodium borohydrate together with a slight excess of alkalai is mixed with boric acid in such quantity that the solution is acid to phenolphthalein suspended in water but still alkaline to litmus. The resultant solution contains a balanced mixture of boric acid and polyborates of sodium with small amounts of free hypochlorous and boric acids. The irritating action of free caustic alkali is avoided, for even if momentarily formed it would be at once neutralized by the boric acid or acid borates present in the solution.

Preparation of Solutions:

The preparation of a solution for direct application, containing 0.5 to 0.6 per cent. of sodium hypochlorite, may be carried out very simply as follows:

One hundred and forty grams of dry sodium carbonate (Na₂CO₃), or 400 grams of the crystalized salt (washing soda), is dissolved in 10 litres of tap water, and 200 grams of concentrated lime (diluted, at normal time), of good quality, is added. The mixture is well shaken, and, after half an hour, the clear liquid is siphoned off from the precipitate of calcium carbonate and filtered through a plug of cotton. 40 grams of boric acid are added to the clear filtrate, and the resulting solution is ready for use. A slight additional precipitate of calcium salts may slowly occur, but it is of no significance. The solution should not be kept longer than one week. The boric acid must not be added to the mixture before filtering, but afterwards.

A stronger solution may be prepared by decomposing chloride of lime with sodium carbonate in the proportion of 120 grams of the former to 103 grams of the latter dissolved in a litre of water. The mixture is filtered and a measured portion of it (20 c.c.m.) is rapidly titrated with a boric acid solution of known strength (51 grams per litre), using phenolphthalein suspended in water as indicator, in order to determine the amount of solid boric acid to be added to the rest of the filtrate. An excess of boric acid would cause the solution to be too acid; it is therefore necessary to add slightly less than the calculated amount. An ordinary alkaline solution of phenolphthalein cannot be used as indicator, as the alcohol is at once attacked.

The concentrated solution thus prepared contains about 4 per cent. of sodium hypochlorite, and should be mixed with six parts of water before use. It can be kept for a month without serious decomposition. Such a solution is now prepared by Ponelle Pérez, 122 Boulevard St. Germain, Paris, but it can easily be made at a negligible cost by any competent chemist, and I hope that it may be so made generally.

APPLICATION AND RESULTS.

To obtain the best results it is essential to commence the antiseptic treatment of the wound at the earliest possible moment, and to bring fresh quantities of the antiseptic solution in contact with all parts of the wound as frequently as possible for a considerable period of time. This is naturally a difficult problem, requiring different methods for various types of wound. The methods of application are much less good than has been found useful at Compiègne will be described by Dr. Carrel. But to give some idea of the quantities of solution employed it may be mentioned that 5 to 10 c.c.m. may be introduced every two hours by the use of rubber tubes into small wounds, using a pipette or syringe, while for the irrigation of such wounds as fractured femurs, accompanied by much destruction of tissue, as much as 1, or even 2, litres a day may be employed. The disadvantages, prepared as described, may be used in large quantities for the continued irrigation or installation of wounds for more than a week without producing visible irritation. It is extremely rare for slight irritation to occur, and this is due to the action of hypochlorous acid against the application of baseline to the skin adjacent to the wound. As a wet dressing the solution may be used most indifferently. A few comparative tests on similar surface wounds do not indicate that decolorization is delayed, even by its continued use.

The solution has the valuable property of assisting in the removal of necrotic tissue, and this is largely due to the ability of hypochlorites to attack the (Ni) groups present in proteins with formation of soluble products. It has a certain haemostatic action as well, being actively leucolytic, and should not be injected intravenously.

It is difficult in a printed communication to produce simple convincing evidence of the usefulness of an antiseptic. Records of a few individual cases treated with brilliant results are, of course, of no great value, for many infected wounds do well with a minimum amount of treatment, but the clinical results obtained during six months’ experience of the use of the solution by officers of the army and hospitals warrant the belief that the solution is of genuine value. By far the most striking results are seen in ambulances, where treatment can be commenced a few hours after the wound has been received. The following is the proportion of cases which, at no time show a significant rise in temperature and in which healing without suppuration is not obtained:

An idea of the antiseptic properties of the solution may be gathered from the following figures: Staphylococci suspended in water are killed in two hours at a concentration of hypochlorite between 1: 500,000 and 1: 1,000,000, while in the presence of serum the necessary concentration is between 1: 1,500 and 1: 2,000. Streptococci are more readily killed, while a concentration of 1: 500,000 is sufficient to kill in two hours at a concentration of 1: 1,000,000, while in serum between 1: 2,500 and 1: 5,000 is necessary. Hypochlorites are extremely active substances chemically, and they should not be used in conjunction with other antiseptics nor with alcohol or ether. Wounds which have been previously treated with much iodine may take on a brown colour, due to the re- liberation of iodine, but this is of no importance.

Many other preparations have been employed at various times by different workers. The more commonly recommended preparations are the ordinary alkaline solutions of the hypochlorites of sodium, potassium (van de Javelle), or calcium; while mixtures of powdered chloride of lime with boric acid have been employed by Vincent, Lumière, and others. It is believed that the solution previously described, when properly applied to all parts of the wound, gives better results than can possibly be obtained from powdered preparations of partially soluble materials. The local production of hypochlorites, hypochlorous acid, or chlorine in high concentration, such as results from the application of the powdered material, is much more dangerous for healthy tissue than is the continued application of a weak neutral solution of sodium hypochlorite. Generally speaking, our experiments with powdered substances have given results which are far better than those obtained with solutions. It is true, however, that aqueous solutions need more care for their successful application, for it is essential that they reach each part of the involved area, and that the antiseptic should be renewed from time to time.

MODE OF ACTION OF HYPOCHLORITES.

When a solution of a hypochlorite or of free hypochlorous acid acts upon organic substances containing the
THE USE OF A SLEEVE OF VEIN IN NERVE SUTURE

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DURING the present war many cases of nerve injury have
been recorded. The injuries are produced for the most
part by rifle bullets, fragments of shell, and shrapnel.
Primary suture is frequently out of the question, and
the wounds are allowed to heal without any attempt being
made to suture the divided nerves. Later, secondary
suture is required, and often the divided ends have to be
sought for in a large amount of scar tissue. It is essential
in cases of this sort to protect the junction so as to avoid
ingrowing of scar tissue between the nerve ends, and
consequent failure of the operation. To prevent this
various substances have been used, including decalcified
bone tubes, gelatine tubes, animal’s artery, paraffin wax,
Cargile membrane, and human vein. Sherren (Injuries of
Nerves) prefers chronicized Cargile membrane.

For some years I have been using portions of vein in the
manner here illustrated. The most suitable vein for
nerves of the upper extremity—as, for instance, the
musculo-spiral, the median, and the ulnar—is the basilic
vein at a spot between its commencement and the point at
which it pierces the deep fascia of the upper arm. A
segment of the vein about 1½ in. or 2 in. in length is
excised and threaded on a sinus forceps. Fig. 1. One
end of the nerve is then caught by the forceps, and the
sleeve pulled over as in Fig. 2. The ends of the nerve are
then freshened with a sharp scalpel and sutured with fine
catgut. When the suture is complete the sleeve is pulled
over the junction, as in Fig. 3, and fastened to the nerve
sheath by a few points of suture. The vein thus applied
is intended to form an aseptic sheath for the nerve, to keep
the ends in secure apposition, to direct the growth of the
new axis cylinders, and to prevent the ingrowth of scar
tissue from the outside. Any vein of suitable size will, of
course, do, and in the lower extremity a portion of the
internal or external saphenous will probably be the most
convenient.

The sleeve must be pulled over the first nerve end before
trimming so as to avoid damage to the freshly cut end.
Possibly this method has been in use by others, but I have
not seen it used or described up to the present.

* Periuroenum of the ox.