

It has been repeatedly observed in my private practice that power might begin to return in a very faint degree to a muscle while under muscle training, and that with care this power would steadily increase, but if that muscle were exercised even very gently every day, that power would diminish or disappear, so that we exercise such muscles only once in three days at the outset, increasing the work most carefully.

A young man under my care, severely paralyzed in both legs, six months after the attack showed some return of power in the peroneals. This developed and was exercised in the usual way, but he was so delighted with the new function that one year after the attack he tried it at intervals all of one day on the principle that if a little exercise were good a large amount would be better, and the power promptly disappeared, never to return in full amount after some five months.

A young man with a paralysis of the left arm acquired in Vermont in September, 1914, was brought from New York to see me in December, 1914. He was having massage and exercises daily from an apparently competent masseur, and was urged to use his arm as much as he could to stimulate returning function; but for a month he had not improved, and the parents therefore decided to send him to me for treatment. He could not, however, come to Boston for a month, and asked what treatment he should pursue in the meantime. A sling supporting the shoulder was put on, he was forbidden to use the arm except at meals, and massage was stopped. After a month of this routine he showed at least 25 per cent. of increase of power.

I saw with Dr. F. B. Percy of Brookline, Oct. 19, 1914, a child of 10 with a total paralysis of the anterior tibial muscle and partial paralysis of the gastrocnemius. Ten days after the attack, sensitiveness had gone, but the child could only walk badly and unsteadily. She was kept quiet for a month more, when she was allowed to walk a few steps daily. She made a remarkable gain, and massage and muscle training were begun, Jan. 6, 1915, although the amount of walking was not increased to any extent, the child walking only a very little. In four months the gastrocnemius and tibialis anticus had apparently nearly normal power when their resistance was tested by the hand, but the child still limped a little. Feb. 24, 1915, four months after the attack, the mother was asked to keep this child practically off of her feet for two weeks while the other conditions of treatment were the same. At the end of this time the limp had disappeared.

Oct. 5, 1914, I saw a child of 5 with nearly complete paralysis of one leg below the knee from an attack three months previous. The child walked badly, but was much helped by a brace to hold the foot at right angles to the leg. Muscle training was started, and the child improved satisfactorily, evidences of returning muscle power becoming plain. March 6, 1915, the mother made a statement that attracted my attention, namely, that the child walked better in the morning than at night. She was asked to keep the child off of his feet as much as possible for a month, restricting walking to the greatest possible degree. April 6, 1915, examination showed during the month a very striking increase in power in the muscles controlling the foot, and it was evident that the progress in the last month had been far greater than in any previous month, and the child walked as well at night as in the morning.

These illustrative cases seem to me to show that much smaller degrees of overuse may be deleterious than is generally supposed. Probably any of us would agree that gross and persistent overuse of partly paralyzed muscles would be undesirable; but it seems to me reasonable that in the early stage of returning power, we should be exceedingly careful in the use of muscles in walking and in the use of heavy and prolonged massage, much more careful than we are at

present, if I may judge the practice of others by my own previous methods.

I hesitate to reason from an unproved conclusion in this connection; but may I once more call attention to the fact that the proportion of total to partial paralysis is greatest in the muscles which have the greatest weight to oppose in the standing and walking position and least in those which have the least weight, in a series of cases observed some months after the acute attack. If overuse is the harmful factor that I believe it to be in retarding recovery, its effect would be noted in just those muscles which show the highest proportion of total paralysis.

234 Marlborough Street.

EXPERIMENTAL STUDIES OF VARIOUS ANTISEPTIC SUBSTANCES FOR USE IN TREATMENT OF WOUNDS

BASED ON THE WORK OF SIR W. WATSON CHEYNE*

ROBERT A. KEILTY, M.D.

AND

JESSE E. PACKER, M.D.

PHILADELPHIA

The purpose of this paper is the experimental study of the antiseptic power and diffusibility of various substances commonly used to check bacterial growth. The study is based on and largely follows the report of Sir W. Watson Cheyne.¹

The study by Cheyne grew out of a desire to prevent sepsis in the wounds of soldiers received while on duty in the trenches and at the battle front during the present war. As a result of these wounds, an enormous number of serious infections have occurred, followed by a high mortality. This is due in part to a delay in reaching the base hospital and in part to the large number of wounded needing treatment at one time. It was Cheyne's idea that each man should carry a convenient package of some antiseptic diffused in a proper vehicle which could be introduced into wounds immediately after their occurrence, thus preventing or retarding bacterial growth locally, until a thorough disinfection could be carried out at a more convenient time and place.

In a later communication as a result of this work, the British government is now forwarding two packages to each man in the navy, one a paste made up of 20 per cent. phenol (carbolic acid) in a lanolin base and the other a powder of equal parts of boric and salicylic acids. A paste was chosen as a vehicle because of its ease in handling, because of the danger of liquids being lost and because of the fact that the recesses of lacerated tissues are more easily reached. Cheyne advised a paste composed of lanolin, 6 parts, and white wax, 1 part. This proved best from every point of view according to his experience. In our own work we have used this, and find one made up of castor oil, 70 parts, white wax, 20 parts, and spermaceti, 10 parts, to be equally advantageous, to diffuse a little more readily and to be considerably cheaper.

* From McManes Laboratory of Pathology, University of Pennsylvania.

¹ Read before the Pathological Society of Philadelphia, May 13, 1915.
1. Cheyne, W. W.: *Lancet*, London, Feb. 27, 1915.

The relative inhibitory, germicidal power and diffusibility of various antiseptics used and the most effective strength was determined by incorporating them into the base and growing bacteria on a slab of agar-agar over the paste. It was found that blood clot and agar worked equally well, and our work has been confined to agar.

The general scheme is to place the paste on the bottom of a Petri dish underneath the slab of nutrient agar, and to inoculate the upper surface of the agar with a bouillon suspension of bacteria. The activity of the antiseptic can be easily judged by observing the presence or absence and extent of growth on the surface of the medium.

TECHNIC

In order to obtain comparative results, conditions must be exactly the same for each substance tested. Hence 0.5 gm. of the antiseptic substance is used in each instance. This is spread on a coverslip three-quarters inch in diameter. Where drugs are to be tested in liquid form, two thicknesses of filter paper three-quarters inch in diameter are saturated with the substance, and the experiment carried on as with the paste. The agar slab must be the same thickness in every case. For this Edmund's chamber is used (Fig. 1). This consists of two glass plates, a brass ring one-quarter inch in thickness, a small portion of which has been removed, and three heavy paper clips. One plate is sterilized by passing through a flame and laid on a support, and the brass ring is flamed and laid on the plate, the open portion of the ring at one margin. The second plate is sterilized and placed over the ring. These are bound together with the paper clips. This forms a chamber open at one point into which melted agar is poured and allowed to solidify. When solid, the paper clips are removed, and the upper plate and brass ring

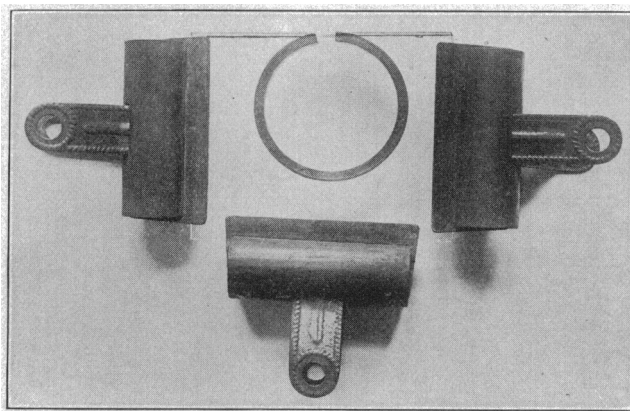


Fig. 1.—Edmund's chamber: a brass ring, two slides and three paper clips.

lifted. This leaves the agar slab on the lower plate. The coverslip with the paste is placed on the center of the exposed agar, care being taken to have the paste next to the agar. The lower part of a Petri dish is inverted over the agar, and the Petri dish, agar and glass plate turned upside down. With a platinum rod the agar is easily transferred to the Petri dish. A tube of melted agar is poured around the slab to hold it in place. Finally the upper surface of the slab is inoculated by gently stroking with two loopfuls of a bouillon suspension of bacteria. The suspension is made by transferring two loopfuls of a twenty-four to forty-eight hour bouillon culture to a tube of sterile bouillon. This technic is that used by Cheyne with but slight modification for convenience. The plates are incubated for twenty-four hours at 37 C. (98.6 F), and the results recorded. The results remain remarkably fixed after the initial growth, even for days and weeks.

The organisms used in our work were the *Staphylococcus aureus*, *Streptococcus pyogenes* and *Bacillus coli*. It was found that substances inhibiting *B. coli* acted on the streptococcus to the same degree and on the staphylococcus to a greater degree, so that in most of this work *B. coli* has been used.

In comparative results the points observed include: 1. Is growth present and to what extent? 2. Is the growth directly over the paste? 3. How close to the

margin of the paste does the growth extend? 4. What are the size and number of the colonies in relation to their distance from the paste?

From this comparison a convenient classification of the results may be given under three groups. 1. Those drugs which are markedly active. 2. Those drugs which are slightly active. 3. Those drugs which are inactive.

In order for a drug to fall under the first group, it must have not only antiseptic powers but also a wide range of diffusibility. The phenol group stands out preeminently, so much so that it is almost alone. Thus, too, the activity of the drug should be within a non-toxic dose as compared to common usage in an ointment, or as to its known absorbability in internal administration. Under the second heading drugs may be quite antiseptic locally, and yet according to this method show little or no diffusibility, except immediately over the paste, which means in distance a diffusing power of one-quarter inch through agar. Substances, for example, the dyes, may be quite diffusible and yet have little antiseptic power. If this range of diffusibility applies in vivo and the percentage of the drug used is carefully worked out,

I see no reason why there is not offered a wide variety to be applied in the rational treatment of wounds not only in war but in civil life.

A summary of the substances tested follows:

1. Those drugs which are markedly active; under this we may include the following: tricresol, 10 to 20 per cent.; phenol, 10 to 20 per cent.; thymol, 10 to 20 per cent.; creosote, 25 per cent.; mercuric iodid, 10 to 30 per cent.; tincture of iodine, 5 to 10 per cent.

2. Those drugs which are slightly active: salicylic acid, 20 to 30 per cent.; Japanese powder, salicylic acid and boric acid, 20 to 30 per cent.; zinc chlorid, 20 per cent.; mercuric chlorid, 0.2 to 0.4 per cent. (in solution, 1:750, and 1:625); guaiacol ointment, 10 per cent.; mercuric ointment, 33 per cent.; creosote, 10 per cent.; carbolfuchsin (contains 5 per cent. phenol).

3. Those drugs which are inactive: iodine, 2 to 6 per cent. (crude drug); menthol and camphor, of each, 20 per cent.; boric acid, 30 per cent.; iodoform, 90 per cent.; zinc sulphate, 1 to 5 per cent.; alcohol absolute, alcohol methyl, alcohol, 95 per cent.; calcium chlorid, 20 per cent.; liquor formaldehydi, 0.1 and 0.5 per cent. (in solution 1:1,000, 1:500); lead nitrate, 5 to 10 per cent.; silver nitrate, 5 per cent. (in solution, 20 grains to 1 ounce); turpentine, 1 per cent.; ether, chloroform, Delafield's hematoxylin, sudan III, Loeffler's methylene blue, eosin watery solution; iodine green, glycerin, bismuth betanaphthol, 20 per cent.; salol, 20 per cent.; hexamethylenamin, 20 per cent.; zinc oxid, 25 per cent. scarlet red (2 per cent. scharlach R); bismuth subnitrate, 50 per cent.; balsam Peru, ointment, 25 per cent.; scharlach R saturated solution.

It might be well here to include a little detail concerning some of the more important drugs. Of all the substances used, thymol and tricresol stood out prominently. This was noticed in two ways. They had a wide range of diffusibility, at the same time

inhibiting the active growth of those few colonies which formed. Alone they were both active, while in combination this activity seemed somewhat increased. Tricresol was used in percentages of 5, 10, 15, 20 and 25. It was noticed that with *B. coli*, for instance, in a 5 per cent. paste, a diffuse growth took place over the entire surface but much thinner over the paste; in 10 per cent., no growth over and one-quarter inch beyond the paste; in 15 per cent., very few and small colonies on the outer one-quarter inch of the agar; in 20 per cent., no growth. Thymol had about the same action, and possibly from all standpoints showed a little more activity.

Many combinations were tried, including phenol, creosote, thymol, salicylic acid, mercuric iodid and tricresol in varying percentages. Out of this group tricresol and thymol were selected as the best. Tincture of iodine (Fig. 2) gave the following: in 0.5 and 1 per cent., growth over the entire slab; in 2 and 4 per cent., up to the filter paper; in 5 per cent., one-quarter inch beyond the paper, and in 10 per cent., no growth. Crude iodine in 6 per cent. in paste failed to inhibit the growth over the entire surface,² but this solution contains only a small amount of iodine: about 0.35 per cent. Salicylic and boric acids, in equal parts as a dusting powder known as Japanese powder, because of its use in the Russo-Japanese War, in a 30 per cent. paste seemed to be quite efficient.

Those substances listed under the inactive heading in the percentages given all show diffuse growths over the agar slab. Silver nitrate, while it showed colonies over the entire surface, reduced the size of those colonies quite appreciably. Scarlet R (scharlach R 2 per cent.), a much used antiseptic, showed large colonies. Scharlach R in saturated alcoholic solution showed large colonies. Sudan III, an allied substance, showed quite an extensive growth.

From our experience, the following paste or ointment is recommended. Thymol and tricresol, of each, 10 per cent. in a base composed of castor oil, 70 parts, white wax, 20 parts and spermaceti 10 parts. Thymol and tricresol are more efficient in 15 and 20 per cent. pastes. They are recommended for use in 10 per cent. when infection has not taken place, or is superficial and not virulent, and in the higher percentages when the infection already exists or is severe. In the

use of this paste, 1 dram of a 10 per cent. ointment represents 0.3 gm. or about 5 grains each of the antiseptic. Thymol internally in twenty-four hours has been recommended in dosage of 7 gm. in three hours (Wood). It is true that this is removed afterward by purgation. Pure cresol may be given internally in 2 to 3 minim doses (Wood). Cresol has the advantages of phenol with greater power, less irritation and lower toxicity. This statement may be open to criticism. However, we feel safe in recommending this ointment in dram doses of 10 or even 20 per cent. In the higher percentages, caution should be taken especially as to frequency of application. Since its object is a germicidal one, in these percentages one application should be sufficient with future asepsis

maintained by less toxic substances. One of us has applied 1 dram of the 10 per cent. ointment, rubbing it well into the unbroken skin surface. There have certainly been no general effects and only the mildest local tingling. Examination of the urine before and two hours after the application showed no appreciable change in the sulphates.

CONCLUSIONS

1. The method as outlined by Cheyne offers an excellent means for the study, experimentally, of the diffusibility and antiseptic power of drugs.

2. The results obtained are confirmatory in some cases and startling in others as to the value of well-known remedies.

3. The phenol group and thymol give the best results as far as our work goes.

4. We are able to recommend an ointment composed of a base, castor oil, 70 parts, white wax, 20 parts, spermaceti, 10 parts, with tricresol and thymol, 10 per cent. each. Lanolin and wax may be

used, but the vegetable base has some advantages.

5. These results are experimental, and must be borne out by clinical application. This we hope to do and report on in the near future.

6. The only drawback is the possibility of toxic effects, and this may be overcome by cautious usage in the amount applied and the interval between dressings.

7. This paste has a wide range in civil life as well as in war, and should prove more effective than those of common usage because of the increased percentages of the drug.

8. At the same time, the principle of the large dose is to establish at once or to maintain an asepsis in a wound, until ideal conditions for surgical treatment are available.

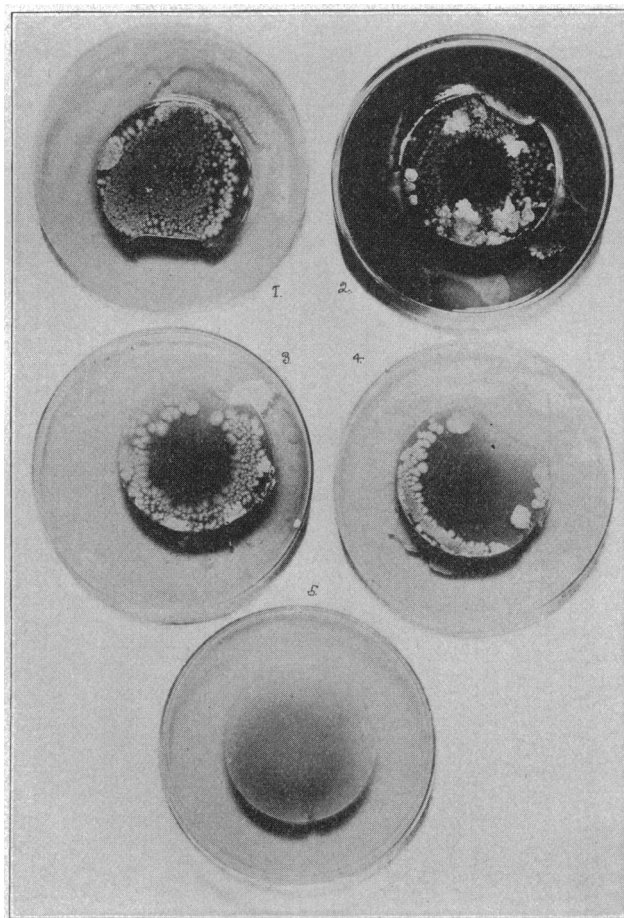


Fig. 2.—Tincture of iodine series: 1, 1 per cent.; 2, 2 per cent.; 3, 4 per cent.; 4, 5 per cent.; 5, 10 per cent.

2. In 10 per cent., mercuric iodid had a fair degree of diffusibility. Lugol's solution showed a growth over the entire surface.