lecture. Further, it has been shown that disease of the arteries materially affects the course of most nervous affections at this period. Since nervous tissue, once destroyed, cannot be restored, the prevention of vascular disease becomes of paramount importance. How this is to be accomplished I cannot consider at length. Often the tendency to vascular disease is hereditary, and beyond our powers to remedy, but apart from such cases it is certain that the chief measures to prevent degenerative changes in the circulatory system are abstinence in eating and drinking, care to keep efficient the organs of digestion and excretion, and regular physical exercise. The simple life may prevent, and certainly mitigates, the progress of vascular decay.

Again, granular kidney, a disease for which unfortunately our treatment is merely palliative and not preventive, is the cause of a large proportion of cases of cerebral haemorrhage. Whilst on the one hand over-feeding has to be avoided, on the other excessive work with insufficient nutrition is also a danger. Exhaustion, over-fatigue, or overstrain are doubtless causes of such diseases as the muscular atrophies in later life. The need for moderation of former activities, both mental and physical, is a lesson that many learn too late. Defect of nutrition, again, may be local in the nervous system from defective supply of blood, due to localized arterial disease.

Turning from the vascular degenerations to those affections more purely of nervous origin, the period from 50 to 70 compares favourably with that of either childhood and adolescence or the age from 25 to 50. In both the latter periods falls the incidence of the nervous diseases due to infections and intoxications, from which the age after 50 is mostly exempt. The main period of onset of the hereditary and familial diseases, those included under Gowers's designation of "abiotrophy," occurs in childhood or adolescence; whilst from 25 to 50, together with some abiotrophic diseases whose onset is late, the numerous nervous affections due to syphilis and alcohol are rife.

We have seen that, with regard to syphilis after 50, the chances of the occurrence of cerebro-spinal syphilis are comparatively slight.

Lastly, the purely nervous diseases which are especially characteristic of this period of life are paralysis agitans, some of the combined scleroses of the spinal cord, and certain muscular atrophies of central origin. It is possible that some of these affections owe their origin to that process of premature senescence or defective vital endurance of certain neuronic systems known as abiotrophy, and that this pathological process may occur at any age. Paralysis agitans especially, in its narrow age incidence, uniformity of symptoms, steadily progressive character, and occasional familial tendency, suggests this mode of origin.

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THE *Weekly Bulletin* of the U.S. Health Department quotes from the summary of the investigation concerning the physiological aspects of the liquor problem, by Dr. John S. Billings, junr., which was prepared for a special committee, showing that the common idea that a large part of the injury to health from the use of alcoholic drinks is caused by injurious substances in the liquor, such as fusel oil and furfurol which have not been properly removed, is erroneous, as is also the notion that cheap liquors contain larger quantities of such ingredients than others. The injurious effects of the fusel oil are trifling in comparison with those of ethyl alcohol. The general conclusion is that fine old brandies and whiskies are nearly as likely to produce ill effects as the cheaper varieties if taken in the same quantities, and the injurious effect is in proportion to the ethyl alcohol contained.

A Lecture

ON

WOUND INFECTIONS AND THEIR TREATMENT.

DELIVERED (WITH DEMONSTRATIONS) AT THE OPENING OF AN EXHIBITION OF SURGICAL APPLIANCES FOR THE TREATMENT OF THE WOUNDED HELD AT THE ROYAL SOCIETY OF MEDICINE FROM OCTOBER 8TH TO 14TH.

By COLONEL SIR ALMROTH E. WRIGHT, M.D., F.R.S., C.B.,

A CONSULTANT PHYSICIAN TO THE EXPEDITIONARY FORCE IN FRANCE.
(From the Research Laboratory attached to No. 13 General Hospital, Boulogne-sur-Mer.)

PART II.

FROM the introductory studies which have up to this occupied our attention I pass to the subject-matter proper of this lecture,

THE TREATMENT OF MICROBIAL INFECTIONS OF WOUNDS.

I would propose, despite the fact that this will sometimes carry me over ground traversed in my last lecture, to discuss with you, one by one, the various therapeutic procedures which have been employed or suggested for use. And then at the end it will perhaps be possible to draw up something in the nature of a general programme for the treatment of infected wounds in their different stages.

Let me tell you—for you will then see our road ahead—what are the therapeutic procedures we shall be dealing with. These are—and I enumerate them in the order which I shall follow—*treatment by antiseptics; treatment by surgical procedures; treatment by "physiological," or, as I would now for the sake of clearer definition wish to call them, "phylacagogic" methods; and, lastly, treatment by vaccines.*

TREATMENT BY ANTISEPTICS.

That one ought, where the organism is unable to deal effectually with an infection, to resort to the use of antiseptics seems to many minds to be perfectly clear *a priori*. Now when a proposition of this sort is said to be evident *a priori*, what this really means is, not that the proposition has been established by clinical experience, but that it has been demonstrated by laboratory experiments; and that we may confidently take those laboratory experiments as our guide.

But, of course, everything will here hinge upon the question whether the laboratory experiments which we trust accurately reproduce the conditions in the wound. Now the earlier experiments on antiseptics—and it is always upon antiquated experiments that the current doctrine of the day rests—did not even aim at reproducing the conditions in the wound. The antiseptics came into application, not as in the wound upon microbes enveloped in albuminous fluids, but upon microbes simply suspended in water. And again it passed as an axiom that if *in vitro* all the microbes were destroyed, then also all the microbes *in vivo* would be destroyed; and there was no thought that the microbes in the cavity and the recesses of the wound, and, above all, the microbes in the infiltrated or granulating wall, might escape destruction.

We have now in the matter of theoretical requirements made satisfactory advance. We now ask of laboratory experiments with antiseptics that they shall conform more closely to the conditions in the wound; and we ask in particular that it shall be kept in view that we have to deal in the wound with microbes enveloped in albuminous fluids; and that antiseptic solutions cannot come into direct contact with all the microbes which we wish to destroy. In other words, we now ask in connexion with every antiseptic for a testimonial of bactericidal efficacy in albuminous fluids, and for a testimonial of penetrating power. And in accordance with this we find in the prospectus of every new-hatched antiseptic this double certificate of character. It would plainly be beyond the scope of this lecture to look into all these certificates; but I think it will, perhaps, be useful to explain in a general way what sort of an attitude one ought to take up when traffic is made with such credentials.

On Certificates of Character which Testify to the Bactericidal Efficacy of Antiseptics in Albuminous Fluids.

It is familiar matter that the ordinary antiseptics (I shall return later to the case of some very special antiseptics) form chemical combinations indifferently with all native albumins, and not specifically with those which compose bacterial protoplasm. It is a corollary to this that whenever we have in an experiment an antiseptic, and albuminous substances, and microbes, it will, if we propose to sterilize our albuminous fluid, be necessary to cut down very severely its content in albuminous substances. And, again, it will follow from this that every promoter of antiseptics will, if he is conducting his experiments with any of the albuminous fluids of the body, find it to his advantage to employ serum rather than whole blood, and whole blood rather than pus. And, again, when he is operating with serum he will find it to his advantage either to operate with very little serum, or—and this amounts to the same—to use a large number of volumes of antiseptic to every volume of serum. This particular device is, one can see, legitimate or illegitimate according as the experiment is designed to elicit what strength of antiseptic is required for flushing out and irrigating a wound; or to create the impression that the circle has been squared, and that an albuminotropic antiseptic can do its office efficiently in the presence of albuminous substances. Let us reflect that if our ordinary antiseptics, instead of combining as they do with the albuminous substances of the blood, combined only with microbial protoplasm, it would be a perfectly proper policy to administer them intravenously in septicaemia.

Let us, however—for the above may be thought to savour of theoretical discussion—come down to the hard fact. It is, we have found, practically impossible, when employing as material pus from foul, suppurating wounds, to sterilize it by addition of any ordinary antiseptic.

Let me, with the aid of these rough coloured diagrams

Fig. 8.

(reproduced with shading instead of colour in Fig. 8), indicate what I mean in our way. In Fig. 8, B, I have a representation of a test-tube full of thick pus, and I have represented the thick albuminous pus by a uniform wash of deep yellow, and the contained microbes by a stippling of orange. In Fig. 8, A, I have represented in a very rough way, by quite irregular hatchings of blue chalk, the effect that would be obtained by an addition of antiseptic. You will appreciate that no matter how long I go on imposing blue strokes upon my yellow ground, there will, because my blue strokes will never fuse and run into each other, still remain over small islands of yellow stippled with specks of orange. Now we have here a rough representation of what occurs when we add an antiseptic to pus and shake it up. What that gives us is a system made up of islands of pus intersected by channels of antiseptic—the sphere of action of the antiseptic being in each case limited

by confining banks of coagulated albumin.

When we dilute pus with very many volumes of an antiseptic solution, as we do in washing out a wound, we, of course, effectively sterilize.

Certificates of Character attributing to the Antiseptic Penetrating Powers such as would render it Efficacious in the Sterilization of the Wound.

It will be well in embarking upon the discussion of this question to place it clearly before ourselves that when we speak of an antiseptic having *penetrating power*, we mean that the active agent will diffuse out into, and come into operation in, any contiguous fluid.

In other words—if I may illustrate exactly what I mean by the aid of this diagram (Fig. 9)—we say that a chemical agent has penetrating power when, applied in a fluid *a*, it

passes out into, and produces its effects in, a contiguous fluid *b*—and let me, for the sake of facilitating exposition, call *a* the *disbursing fluid*, and *b* the *recipient fluid*.

Having recognized that penetration is only diffusion under another name, it will be plain that we shall be able to consider the question of penetration without travelling outside familiar ground. We know in connexion with chemical agents generally that their rate of diffusion, that is, the rate at which they will pass out from a disbursing into a recipient fluid, will—exclusive of the influences exerted by temperature, extent of surface of contact, and such like—be determined by the concentration of the chemical agent in the disbursing fluid, and the receptivity of the recipient fluid—in other words, it will depend upon the respective *plenitude* and the *avidity* of the contiguous fluids.

Now, in the case of the ordinary antiseptics which are employed in wounds we have chemical agents, which, owing to their toxicity and escharotic properties, are of necessity brought into application only in dilute solutions; and, moreover, many of these chemical agents are not very soluble in water. By consequence we are, when dealing with ordinary antiseptics, confronted with conditions which are anything but favourable to diffusion.

They will resemble those roughly indicated in the diagram on the blackboard (reproduced with stippling for colour in Fig. 9, A), where we have a dark blue disbursing fluid superposed upon a colourless recipient fluid, and have below the line of contact of the fluids a comparatively narrow zone of paler blue representing a slight carrying over of colour by diffusion.

But in reality the conditions in the wound, where our recipient fluid is, instead of water, a concentrated albuminous fluid, much more nearly resemble those depicted at C (Fig. 9, C). Here we have, as before, our blue disbursing fluid, but there has been substituted for the colourless watery recipient a deep yellow fluid stippled with orange, representing pus with scattered microbes. And you see what we get. Instead of the narrow blue zone which diffusion gave us in Fig. 9, A, we have now a much narrower zone which is—for yellow quenches blue—nearly colourless. I think you will recognize that under conditions such as are here postulated, the prospect of getting any penetration which would be worth while may be abandoned as hopeless.

But perhaps you will suggest that one ought not to place too much confidence in demonstrations conducted on blackboards with coloured chalks; and you would wish the experiment transposed from the blackboard into the real world in order to see whether it would also apply there. Let me suggest such an experiment.

I will suppose that we have as our disbursing fluid a dilute solution of nitrate of silver standing over a recipient fluid consisting, in the one case, of water derived from a fresh-water pond; and, in the other case, of sea-water—both peopled with living organisms. You will discern what would then happen. In the case of the pond water, the nitrate of silver will slowly diffuse into it: killing, as it is carried in, all the living organisms it encounters. In the case of the sea-water, the effect would be quite other. Where the two fluids meet, the nitrate of silver would be thrown down and rendered inert. And below, the marine life would go on absolutely unaffected.

Fig. 9.—In A is represented a test-tube containing: above a watery solution of methylene blue, and below clear water. In B is represented a test-tube with a watery solution of methylene blue above and strong salt solution below. In C we have represented above a deep blue, and below a deep yellow fluid.

But you will wish for actual experiments conducted with an antiseptic, and blood fluids, and leucocytes, and microbes such as we have in the wound. Let me therefore show you here in the form of a rough diagram the results of typical experiments—experiments carried out with blood implanted with streptococci, and then centrifugalized and allowed to clot in emigration tubes, and then covered in

Fig. 10.

with carbolic acid in strengths of from 1 in 50 to 1 in 20 (Fig. 10). You will see that we have here in our white clot, and—I want you to note—quite close up under the covering layer of antiseptic, colonies of streptococci derived from those we have implanted. And below—as you discerned would happen in our sea-water—you have the living elements going about their avocations quite unaffected. The leucocytes have, as you see, emigrated into the white clot; and they have, in point of fact, been hunting down and ingesting the microbes. And I see no reason to doubt that the results would have come out just the same if we had in our experiments used instead of carbolic acid any other of the antiseptics which are employed in wounds.

With this, I think, we have, in connexion with the sterilizing and penetrating power of ordinary antiseptics, got before us all the really vital points in the evidence furnished by laboratory experiments. And let me now—for you will bear in mind that the advocates of antiseptics rest their case almost exclusively on the data of laboratory experiments—try to summarize for you what these

experiments really teach.

And there are here, as I see the matter, two distinct issues. The *first* has reference to the effect exerted upon the microbes of pus which are removed by washing; the *second* to the effect exerted on the microbes which are left behind in the wound.

In connexion with the first of these issues, it has been shown that while it is all but impossible to sterilize undiluted pus by any addition of antiseptics, it is quite practicable, by diluting and mixing the pus thoroughly with many times its volume of an antiseptic fluid, to kill all the microbes.

But, note, to kill these microbes is simply a work of supererogation; for they are in any case destined to go down the drain. And, moreover, pus is not in the same case with typhoid stools, which we might hesitate to put down the drain unsterilized.

Coming, then, to the microbes we have really to combat—those that washing does not remove from the wound—it will be clear that these will be killed off only so far as the antiseptic may possess penetrating power. And we have seen how the case stands with regard to this. We have appreciated that our antiseptics are incapable of penetrating through anything more than the very thinnest film of pus. They will therefore fail to kill the microbes which washing does not dislodge from the blind passages and cul-de-sacs and pockets of the wound. And *a fortiori* the antiseptic will not come into operation upon the microbes in the solid barriers of albuminous substance provided, in the early stages of the wound, by exposed muscle and connective tissue, and, in the later stages, by infiltrated walls or granulating membrane.

And what holds true of the suppurating wound would clearly hold true also of that filled with blood clot. The antiseptic will, if it exerts any influence at all, exert it here only at the particular spot to which it is applied.

I am not at all sure that the kind of evidence I have just tried to summarize—or, indeed, any array of laboratory experiments—could convert from his beliefs the man who knows with *a priori* knowledge that antiseptics must be useful in wounds. And with regard to that type of man I feel that, despite the fact that his faith in antiseptics is really based upon laboratory experiments, he will, now that the old laboratory experiments have been invalidated by the new, desire to appeal from these to the tribunal of clinical experience. And he will, I take it, desire to discover by cross examination whether clinical or bac-

teriological investigation has not furnished data which might tend to show that the course of wound infections has sometimes been favourably modified by treatment with antiseptics.

On the important principle of logic which is here raised—that is, on the issue as to how far therapeutic measures ought to be adjudicated upon by laboratory methods, and how far by an appeal to clinical observation—I would here only say this. What we are, in difficult issues such as that in which we are here involved, concerned to arrive at is a verdict based on unambiguous evidence; and I feel confident that clinical observation cannot safely adjudicate upon a therapeutic measure unless it happen to give either outstandingly good or outstandingly bad results. Where the results are neither brilliantly successful nor the reverse—and antiseptic treatment of wound infections is precisely an instance in point—I submit that we shall be well advised if we guide ourselves, when this is unambiguous, by the verdict of laboratory experiments.

With thus much by way of protest and explanation, I will try to put before you the clinical evidence as I see it; and to resume for you the data of our bacteriological examinations of wounds treated with antiseptics.

I can put what I have to say in a very few words. I have not myself come across—and I have the permission of all my fellow-workers to say that they also have not come across—any satisfactory clinical or bacteriological evidence of the utility of antiseptics as employed in infected wounds. In connexion with this, let me say that working as we have been for the last year in the largest base hospital in Boulogne, we must, I think, have watched and examined bacteriologically very many thousands of wounds—to say nothing of our having conducted the bacteriological examinations in no less than four long series of clinical experiments undertaken to put to the test the confident prognostications of reputable promoters of this or that antiseptic. And let me also say here that the opinion I have just expressed—that is, the opinion that, judged by its clinical results, the antiseptic treatment of infected wounds is of quite doubtful utility—is that which is, I believe, held by the very large majority of those who have had prolonged practical experience in this war.

I am well aware that also contrary opinions have been expressed. I would, however, submit that these should be very largely discounted. For the more part they are opinions expressed by persons possessing a very limited experience and unfamiliar with the course the wound follows when left to itself. Moreover, the observers here in question were, as I think, deceived by the fallaciously favourable appearance of the wound in the stage that precedes the advent of suppuration. Coming to those favourable opinions which have, as I hear, been expressed by a few experienced and very competent observers, I would submit that it is possible that credit may have been given to the antiseptic, where it ought really to have been given either to the menstruum in which it was applied, or to incidental circumstances attendant upon the treatment. Thus, for instance, continuous irrigation practised with antiseptic solutions would effectively wash out the wound and keep it constantly moist; a hypertonic menstruum used as an excipient for the antiseptic would act as a lymphagogue; peroxide of hydrogen would effectively assist in the evacuation of the pus; carbolic acid or other antiseptic used in the form of hot fomentations would bring heat and moisture to bear; and no doubt many different varieties of antiseptic would induce temporary hyperaemia. I think it will be seen that favourable results occasionally manifesting themselves after antiseptic treatment, might quite well be interpreted in the sense here suggested.

So far we have considered in connexion with the clinical data only the question whether the antiseptic has had any beneficial effect in the wound. Let us now turn the leaf, and see whether there are entries also on the debit side; and let us here consider the effects produced in the wound itself, dealing afterwards with those produced on the healthy skin in its neighbourhood. In connexion with this let me first emphasize the fact that disastrous results—I am thinking more particularly of the development of gaseous gangrene—supervene when antiseptics made up in viscid or semi-solid excipients are introduced into the wound. For

this result the excipient which confines the discharges and imprisons the infection would seem to be primarily responsible.

It is, however, not only antiseptics in unsuitable menstrua which arrest the outflow of lymph and imprison the infection. With perhaps the exception of carbolic acid employed in concentrated form, all antiseptics in their degree, and strong antiseptics in particular, would seem, by coagulating the albuminous substances on the surface of the wound, to exert this prejudicial effect.

Coming now to the application of antiseptics to the skin surface in the neighbourhood of the wound, we have, of course, here a procedure which has exactly the same aims as the preparation of the skin for operation, except only that it is here foreseen that the wound will remain open.

The usual procedure for the sterilization of the skin in field ambulances is to paint strong iodine all round the wound, and then—plant for sterilizing dressings not being available so far to the front—to cover in the wound with cyanide gauze. This in many cases is followed by results like those which used to be obtained when carbolic fomentations were used as a prelude to surgical operations. There is produced—and this applies quite generally in connexion with every application which “irritates the skin”—first, reddening of the epidermis; then effusion and blistering; and then there develops in the blisters a luxuriant growth of serophytic microbes. In other words, by our misdirected energy we cultivate at the very doors of our wound, upon the very area of skin which we intended to keep free from microbes, a copious harvest of streptococci and staphylococci.

This, however, has been of the nature of a digression, and I must now, before saying something about a fundamentally different variety of antiseptics, come back and try to make clear what is the general conclusion which emerges from the clinical study of the effects of antiseptic treatment. It can be put into a sentence. The data of clinical observation, such as they are, not only confirm the verdict of the laboratory as to the inefficacy of antiseptic treatment; but they suggest that such treatment may sometimes be not only useless but prejudicial.

Antiseptics which are, instead of Indiscriminately Albuminotropic, Specifically Bacteriotropic.

I have now to say just one word about a kind of antiseptic which concentrates its chemical energy upon the microbe; instead of, like the ordinary antiseptic, expending it wastefully upon the albuminous substances in which the microbe may be embedded. Those of you who have followed the development of “chemiotherapy” will immediately perceive that I refer to *salvarsan* and ethyl-hydrocuprein hydrochlorate* (now known as *optoquin*), and will appreciate that, if these chemical agents can be shown to exert a powerful bactericidal effect upon pyogenic organisms, and in particular upon serophytes, they might perhaps usefully be applied both directly in the wound and also by the channel of the blood: reaching in these ways all the microbes in the body with the exception only of those embedded in dead spaces and infiltrated tissues.

We have made in connexion with this subject-matter as yet only preliminary researches; and I do not here propose to say anything more than that my fellow-workers, Captain S. R. Douglas and Lieutenant A. C. Inman, working the one with *salvarsan* and neo-*salvarsan*, and the other with *optoquin*, have found that these kill off the streptococcus in serum, and that *optoquin* in particular kills the streptococcus in serum in very high dilutions.

TREATMENT BY SURGICAL PROCEDURES.

A long series of surgical procedures all having reference to the treatment of wound infections might quite properly come up for consideration here if this were a treatise instead of an introductory lecture. Let me, however, just run over the list, indicating in connexion with each the place that it would take in the treatment of the wound infections. We have, *first*, the opening up of the wound, and the incision of the tissues undertaken to get drainage for imprisoned infections; *secondly*, the washing out of the wound and the irrigation of the walls with therapeutic

fluids; *thirdly*, the immobilization of the limb for the avoidance of autoinoculations; *fourthly*, the ablation of the heavily infected and infiltrated walls and floor of the wound; and, *fifthly*, the secondary suturing of the wound for restricting the area of exposed and infected surface, and closing the wound when the infection has been overcome.

The first of these procedures I have already treated of. Its *rationale* and the methods of making it really effective were considered in a Memorandum on Wounds which was officially circulated to the Medical Service of the Army and which was published in the BRITISH MEDICAL JOURNAL of April 24th, 1915, p. 735.

The second and third procedures—those for the irrigation of wounds and the splinting of fractured limbs—form the subject matter of the demonstrations which are to be given in this exhibition.[†]

The principles involved in the so-called “excision” and “secondary suture” of wounds I propose here very briefly to consider.

Ablation of the Heavily Infected and Infiltrated Lining of the Wound.

The customary procedure in connexion with wounds is to remove only those portions which are sloughing; and to amputate, where a limb is involved, only that portion which is deprived of its blood supply, or quite hopelessly infected. To Colonel H. M. W. Gray is due the credit of pointing out and enforcing by a long series of cases successfully treated under his supervision in the military hospitals at Rouen, that it is possible in suitable cases to abort wound infections by the excision of the infiltrated wall and floor, the operation being completed by sewing up the wound immediately, or after treatment with hypertonic salt solution. I may explain that the kind of cases which Colonel Gray selects for treatment by excision are scalp wounds and what we may call “gouged out” and “punched in” wounds of soft tissues.

The theoretical considerations which commend the procedure of Colonel Gray are that it removes heavily infected portions of tissue which, though they could be brought back to a healthy condition, are for the moment incapable of contending successfully with infection. And, above all, the method holds out a prospect of immediate victory over the infection; and, of course, practically immediate convalescence.

There, however, suggests itself in connexion with the procedure the plaguy question as to what amount and kind of microbial infection we can allow ourselves to shut up inside a wound. This is the issue which confronts us everywhere in connexion with secondary suture.

Secondary Suture of Wounds.

That a deep wound when once infected must be allowed to granulate up from the bottom, and that a surface wound must be allowed to close by the growing in of skin from the sides, are maxims which would be in their proper place in a system of surgery which aimed at doing all it could to delay healing and keep the patient in hospital for the longest possible time.

On the other hand, it might quite well be imprudent to embark deliberately upon a policy of sewing up microbes in wounds to accelerate healing.

This is the kind of dilemma which sooner or later confronts us in connexion with every wound. To resolve it we must sit down, and take thought, and ask ourselves what precisely are the risks we have to take; and whether there are not precautions to be adopted; and whether we really are, in the matter of the closure of the wound, irretrievably condemned to a policy of inertia and inaction.

Let us place before ourselves first these facts. An infection of subcutaneous tissues is always of more serious import than a mere surface infection. There will always be something unfavourable either in the general condition or in the histological conditions when microbes succeed in maintaining themselves in the tissues. Here at least the leucocytes and the blood fluids ought to be able to hold their own. Exactly the contrary holds true of surface infection. On denuded surfaces, no matter how healthy the condition,

*In connexion with this drug, vide the author's *Treatise on Pharmacotherapy and Preventive Inoculation Applied to Pneumonia in the African Native*, Part I. and Appendix I.

†See the Memorandum by the author on the Employment of Bandages for the Irrigation of Wound-Surfaces with Therapeutic Solutions, and the Draining of Wounds, BRITISH MEDICAL JOURNAL, October 16th, p. 564.

the microbes, though they may sometimes have to struggle, will always find means to maintain themselves. We may, I think, attribute this to the circumstance that on an exposed surface the leucocytes are subjected to every kind of uncongenial condition—to aerobic surroundings, to desiccation, to a tryptic or diminished antitryptic environment, and—who can tell?—perhaps also to conditions of famine.

We now see that where we have an infection of tissues—that is, a form of infection which would, if conditions had been favourable, have been driven out, and been converted into a mere surface infection—we shall be taking a serious risk if we sew up the wound. For that would be to follow leisurely and with deliberation the disastrous practice of those who in the earlier period of the war in the hospitals at the front precipitately sutured infected wounds, or securely sealed up imprisoned infections by resorting to escharotic or gluey antiseptic applications.

On the other hand, we see that, if we are dealing with a purely surface infection, it will be possible, by bringing the opposing surfaces of the wound into intimate contact, to procure for the leucocytes and blood fluids those more favourable conditions which prevail in the interior of tissues; and, by procuring these, to contribute to the destruction of the microbes.

But clearly our decision as to whether we may, or may not, bring the edges of the wound together ought not to be determined solely by whether we are dealing with an imprisoned, or a surface infection. There will in connexion with surface infections be other factors to be taken into account.

There is, for instance, a great deal of sound common sense hidden away in the maxim, that an infected wound which goes down into the depths must be allowed to granulate up from the bottom. The lessons which that precept enforces are, first, that if we allow dead spaces to develop in closed wounds we must expect to find the infection go ahead therein; and, secondly, that, since pus will gravitate downwards, dead spaces will tend to develop at the bottom of the wound, while the upper part unites and converts the dead space into the abscess sac. Of all the mechanical conditions which have to be secured in secondary suturing of wounds, the most important will clearly be the avoidance of such dead spaces.

There is another important consideration to be kept in view—and this time it is not a mechanical consideration. We must expect success or failure in secondary suturing to depend in large measure on the condition of the surfaces, and the number of microbes on those surfaces. Where we have very few microbes and a profusion of active leucocytes we may confidently look forward to success. Where we have a large population of microbes and disintegrated leucocytes it will be only reasonable to expect to fail.

This much by way of general principles. And let us now turn and inquire how these can be applied in practice, and by what methods we ought to proceed in deciding whether a wound is in fit condition to be closed down. We shall have first to certify ourselves that we are dealing only with a surface infection; and then we shall require a method of examination to tell us what is the condition of the leucocytes, and the number of microbes on the surface of the wound.

The first of these points is resolved by a mere clinical examination. As long as the floor and walls of the wound are still indurated we can be sure that we are still dealing with an imprisoned infection. On the other hand, when we have lying naked before us in the wound a system of lymph spaces communicating freely with one another, filled in with clear fluid, and fed from full capillaries, we then know that we have got rid of the imprisoned infection; and that if any infection still lingers it is a purely surface infection.

There remains the question as to what number of microbes have to be dealt with on the surface of the wound, and what force of active leucocytes we have there at disposal. It will probably in the case where the walls and the floor of a wound have been freshly resected—provided always that this has been done in a workmanlike way—be unnecessary to insist upon such inquiry. But where we are dealing with a granulating wound whose edges have not been refreshed it will assuredly be required.

The method of obtaining the information is quite simple. We first prepare a number of cover-glasses by coating them on one side with a layer of agar or serum (serum is preferable) and then letting them dry. We then bring the coated side down upon the surface of the wound. And we make in this way (using, of course, a number of cover-glasses) a series of impression preparations. We now fix and stain either by the method of Gram or with carbol thionin. Microscopic examination then tells us whether we have few or many leucocytes; and whether the leucocytes are degenerated or well preserved.

And a concluding word may now be said on the technique of closing in the wound and on the procedure to be followed.

Except possibly in cases where we pass directly from the excision of the wound to secondary suture it will be well always to preface the operation by phylacagogic treatment conducted upon the lines laid down in the next section of my lecture, and controlled, of course, by the making of impression preparations.

Where we are dealing with a deep and extensive wound it will be well to undertake the work in stages and to content oneself at first with bridging and subdividing the wound by bringing the walls into application by sutures passed in from the skin from each side deep into the tissues. And I may add in connexion with such sutures that they ought, in order to prevent extension of the microbes along their track, to be withdrawn at the earliest possible moment. Where bridging operations have been undertaken, the interspaces between the connecting bridges ought still to be irrigated and drained. Where it is a question of the closure of large gaping "gouged-out" wounds, it will be well to choose for the patient such a position as will minimize the gaping of the wound and the strain upon the sutures. Where large surfaces of skin have been carried away grafting ought to be resorted to; or the skin ought to be undercut, and the liberated flaps drawn over the wound by strips of adhesive plaster. Where a limb has been amputated by the flapless operation, the sleeve of skin ought to be slowly drawn down over the stump by an extension apparatus.

TREATMENT BY PHYLACAGOGIC METHODS.

When I was discussing with you the clinical results obtained by the antiseptic treatment of wounds, I drew your attention to the fact that with this a variety of physiological stimuli were brought into application, and that the good results which were upon occasion witnessed might quite well be credited to these.

Now, of course, physiological stimuli are in connexion with wounds applied, not only incidentally to antiseptic treatment, but also of set purpose as therapeutic agents. Dry or moist heat is brought into application; ether is introduced into the cavity of the wound; stimulating ointments and lotions are applied; or, as the case may be, the wounds are uncovered to air; they are exposed to sunlight, or electricity and radium are exploited: each of these measures being resorted to with a more or less vague idea that the particular form of stimulus in question will directly or indirectly assist in combating the wound infection.

So far as I can discern, all these are forms of treatment—and the same holds true also of the surgical procedures we have considered above, of the methods of Bier, and, of course, of saline solutions and vaccines—which are capable of bringing the protective elements of the body—that is, the blood fluids and leucocytes—into application in the wound. And I would submit that they can be useful only so far as they serve as—let me suggest the word—*phylacagogic* agents.

We ought therefore to give up employing these agents as fetishes, and ought to prelude their use by a careful study of their physiological action.

This field of study being so endlessly wide I propose here to confine myself to the study of strong and weak salt solutions. We shall see that we have in these *phylacagogic* agents—in hypertonic saline solution a *lymphagogic*; and in physiological saline solution a *leucocytagogic* agent.

Physical and Physiological Action of Hypertonic Salt Solutions.

Hypertonic salt solutions exert three kinds of effects: a physical effect; a physiological effect; and an effect on

the condition of the wound and the bacterial infection. Let me deal first with the physical action, for it was this which I had chiefly in view when I suggested the employment of hypertonic solutions in the treatment of infiltrated tissues which were the seat of bacterial invasions.

Physical Action of Strong Saline Solutions.—I can perhaps most conveniently introduce what I have to say with reference to the physical action of strong salt solutions if I take up again the discussion of the phenomena of diffusion at the point where I left off when I was discussing with you the penetrative powers of antiseptics.

What we were there considering was the conveyance of the chemical agent outwards by diffusion from the discharging into the recipient fluid; and we did not then need to concern ourselves with the return movement from the recipient into the discharging fluid. But in connexion with every diffusion there is always a process of barter and exchange; so that when we have, as in Fig. 9, A, as our discharging fluid water containing a colouring material, and as our recipient fluid clear water, there is, in point of fact, not only a passing out of colour into the recipient fluid, but also a return flow of water; and, as a result, a certain dilution of the discharging fluid.

It will subserve the purposes of exposition, and perhaps help to call up in the mind clearer pictures, if, speaking as we do of the conveyance of the chemical agent into the recipient fluid as *diffusion*, we may call the conveyance of the water (or other excitant) into the discharging fluid, *infusion*.

Let us now look—for this will carry us a step further—from Fig. 9 A to Fig. 9 B. Here, while the coloured fluid in the upper part of the test-tube remains as before, strong salt solution has at the bottom of the tube been substituted for clear water; and we have now a double process of diffusion—a diffusion of colouring matter downwards into the salt solution, and a diffusion of salt upwards into the coloured water; and along with this we have also infusion into each fluid. This will give, on either side of the surface of contact, a broader zone of mixture; and you have in Fig. 9, B, below the junction of the coloured and colourless fluids a broader band of stippling representing colour.

We can by the aid of a very simple experiment satisfy ourselves that there is a much greater indrawing with a strong salt solution than with a weak solution or simply water. We take a capillary pipette, seal it at the end, fit on a rubber teat, and then squeezing this with the fingers so as to get up a positive pressure in the interior, introduce a small portion of the wall, about half-way down the stem, into the flame of a by-pass. The glass will, as soon as it softens, blow out here and give us a lateral opening. We now resect our capillary stem at some little distance above, and again some little distance below, this opening. Having provided ourselves with such tubes we fill in one with strong salt solution and another with water, and then pour a little watery solution of methylene blue into a Petri dish or other shallow, flat-bottomed vessel. This done, we take up first one, and then the other, of our capillary tubes. We seize it in the middle with a pair of forceps; hold the central orifice uppermost and the two limbs horizontally; and in this position immerse for a matter of a second or two into the coloured fluid. We then wash the outsides and compare the two tubes.

In the tube of water there will be three narrow, and in the tube of salt, for there is here more indrawing, there will be three very broad bands of blue: one occupying the middle and the others the ends of the tubes.

And let me show you also another experiment which brings clearly before the eye the drawing power of salt. I have here two test-tubes filled in each case to a depth of 3 or 4 centimetres with a watery solution of methylene blue; and standing in these test-tubes I have two pieces of glass tubing, open at both ends and packed with moist cotton-wool*; and, lastly, in the one tube I have at the top of the cotton-wool a layer of salt. These pieces of tubing have been standing, as they are standing now, since last night. I now lift them out, and you see that here again the methylene blue has been drawn far up into the tube where we have the salt; while it has in the companion tube been carried in only a very short way.

With this we have come some little distance on the way

to an understanding of the physical action of hypertonic salt solutions applied in wounds. This further series of test-tube experiments (reproduced in Fig. 11) will, I think, show you exactly what happens.

I have here a tube of water agar (Fig. 11, A). That is to say, I have dissolved in the distilled water, which is here going to serve as a recipient fluid, a sufficiency of agar to set it into a firm jelly. And I have added also a little trace of nitrate of silver. Into the next tube (Fig. 11, B)—a precisely similar tube—I introduced some twelve hours ago a cube of sodium chloride, imposing it upon the surface of the just moist jelly. And you here see the result. The sodium chloride has diffused into the water agar to a considerable depth, discolouring the silver salt. But the important thing to note is the counter movement. Water has been drawn out from the jelly, and we have now, round what remains of the pellet of salt, as you see, a layer of fluid a centimetre or a centimetre and a half in depth.

This is the particular effect which I set out to get when I suggested the employment of hypertonic solutions as a dressing for infected surfaces. I expected to get that combination of diffusion and infusion which we have under our eyes here—in other words, a process of barter in which salt and water should be exchanged, not in volumetrical equivalents, but, as you see here, in the ratio of very many volumes of fluid for one of the solid.

Let me try to make plain another point. The whole question of diffusion and infusion is to the ordinary medical man and biological student complicated by ideas connected with osmosis: his mind being taken up in particular with the idea that crystalloid substances can, and albuminous substances cannot, traverse a so-called vegetable or animal membrane. In fact, some have come to believe that it is the interposition of a membrane between the recipient and discharging fluid which calls into existence the attractive forces of salt for water and all the phenomena of infusion; or, to put it in other words, that it is the interposition of the sieve which confers upon the salt the power of drawing water to itself. It is this confusion of thought which has inspired the criticism: that while hypertonic solutions may be competent to draw fluid out from the walls of a wound, the fluid thus extracted will by theoretical necessity be a fluid deprived of all its albuminous substances, and with these of all its antibacterial powers.

The test-tube I now show you demonstrates to the eye that the theoretical deduction here in question is quite unfounded. You see here (Fig. 11, c) a tube of water agar into which I have incorporated a considerable amount of blood. I have dealt with it in precisely the same way as with the tube of silver nitrate agar; that is to say, I imposed upon it yesterday a cube of sodium chloride. You will see for yourselves that the salt has here drawn out from the agar a very considerable amount of a turbid blood-stained fluid; and when I take a sample of this and boil, you will see that we obtain a very heavy precipitate of albuminous substances (Fig. 11, d).

Fig. 11.—A, A test-tube filled with water agar serving as a control to B and C. B, A test-tube filled with silver nitrate water agar upon which has been imposed a cubical block of sodium chloride, showing the precipitation of the silver salt in the interior of the agar, and on the surface of the agar the fluid which has been drawn out. C, A test-tube containing water agar in which blood has been incorporated on the surface of the agar; a cube of salt and the turbid blood-stained albuminous fluid which has been extracted by the action of the salt is seen. D, A small test-tube showing the albuminous precipitate thrown down on boiling a sample of the fluid obtained from c.

* The actual procedure employed was to fill in the cotton-wool, to immerse in water, and then to remove the superfluous fluid by centrifugalization.

I think we may feel reasonably confident that this is exactly what occurs in the wound. And at any rate we may be sure that neither in the earliest stage of the wound, where the tissues lie exposed; nor yet in the later stage, when the walls are infiltrated; have we in the wound, any more than we have here in this test-tube, anything in the nature of a membrane which could filter out albuminous substances.

Arising directly out of the physical properties of concentrated salt solutions is another point which has a very important bearing on the therapeutical action of these agents. We have seen in connexion with antiseptics that inasmuch as they have as good as no penetrative power, they will exert their effect only at the immediate point where they are applied; and, in the case where the antiseptic marches with an albuminous fluid, only on the face where the two fluids come in contact. In other words, the antiseptic will not diffuse into, and come into application in pus held up in the upper reaches or recesses of the wound, nor even in islands of pus encompassed by antiseptic fluid.

Now the exact contrary of this holds true of strong saline solutions introduced into the wound. No sooner are they introduced than the sodium chloride—for it is, of course, highly diffusible and is not quenched by antiseptics—will radiate out by diffusion through all the fluids of the wound. (In an experiment in which a tube full of water agar was inverted in a shallow receptacle of 4 per cent. salt solution we found that diffusion carried the salt up $4\frac{1}{2}$ centimetres in a night.) We may therefore picture in our mind's eye, in connexion with strong saline solution applied to the mouth of a wound, that the salt will very soon, in the lower reaches of the wound, attain a high concentration and act as a lymphagogue; and that afterwards it will come into operation in the upper reaches in a dilute, but perhaps still therapeutically valuable, form.

But let us note that this will apply only if the concentration of the saline solution is maintained throughout. Where the salt solution is applied in the form of a damp pad, and is then very rapidly diluted by the exudation, we shall get, but only very temporarily, a hypertonic solution in the lower reaches of the wound, and after that we should obtain only the same effects as with an isotonic salt solution.

Finally—and this is a point which may upon occasion have a practical interest—let us remember that 4 per cent. salt solutions have a specific gravity equivalent to that of the serum; and more concentrated solutions of course a higher specific gravity. It will therefore be theoretically possible, by availing ourselves of gravity, to get strong saline solutions directly to the bottom, not perhaps of a wound filled with pus, but certainly of a wound in which we have only blood clot and serum.

(To be continued.)

THE OPERATIVE TREATMENT OF GUNSHOT INJURIES OF NERVES.*

BY

SIR FREDERIC EVE, F.R.C.S.,

TEMPORARY LIEUTENANT-COLONEL R.A.M.C.,
CONSULTING SURGEON, EASTERN COMMAND; VICE-PRESIDENT, ROYAL
COLLEGE OF SURGEONS; CONSULTING SURGEON AND EMERITUS
LECTURER ON SURGERY, LONDON HOSPITAL;

AND

R. S. WOODS, M.D. LOND.,

PHYSICIAN TO THE ELECTRO-THERAPEUTIC DEPARTMENT, LONDON
HOSPITAL.

THE majority of the patients were in the section of the War Hospital at Croydon which the Surgeon-General of the Eastern Command has set aside for the treatment of injuries of the peripheral nerves and for stiff joints arising from wounds, and which he requested Dr. Woods and myself to organize. Other patients were in military or V.A.D. hospitals in other portions of the Eastern Command, and three in H.R.H. Princess Henry of Battenberg's Hospital for Officers.

The cases operated on by one of us (F. E.) numbered

28, of which 21 were due to bullets, and 6 to shrapnel or shell wounds. As regards the distribution of the lesions: 5 were injuries of the brachial plexus, 8 of the musculo-spiral nerve, 1 of the posterior interosseous nerve, 5 of the ulnar, 2 of the median and ulnar nerves together, and 7 of the sciatic or external and internal popliteal nerves. In 6 cases the injured nerve or nerves were completely divided. The sciatic nerve, as might be anticipated on account of its size, was divided three times; the other nerves divided were the median and ulnar together in one case, musculo-spiral and posterior interosseous once each. In one instance the sciatic nerve was perforated with incomplete division of the external popliteal portion. Many of the cases having been in V.A.D. hospitals before being transferred to Croydon, the period elapsing between the receipt of the wound and the operation was often considerable. This period in all but 4 cases was three months or over; in the remainder the shortest period was seven weeks. In the absence of evidence of improvement, and if the electrical reactions indicate a severe injury of the nerve, we are of opinion that an operation should be performed as soon as the condition of the wound permits of its being carried out aseptically. Excluding the 5 injuries of the brachial plexus, it was thought necessary in 8 cases out of the remaining 23 to resect the damaged portion of the nerve, or to refresh the ends if they were separated. In other cases the nerve was separated from adhesions and surrounded with Cargile's membrane. The various reasons determining the procedure adopted are given below in considering the electrical reactions. The smallest nerve operated on was the posterior interosseous. This was found to have been completely severed (the ends being separated) by a bullet which had comminuted the head of the radius. The nerve was exposed by an incision on the outer side of the forearm, just below the external condyle and on a plane corresponding with the palmar surface of the head of the radius. After dividing the muscles attached to the external condyle, the proximal end of the nerve was at once found. The ends were refreshed and the junction surrounded by a portion of the basilic vein. As regards the 8 cases of injuries of the musculo-spiral nerve, half of them were associated with fracture of the humerus.

In those cases in which resection was performed the fibrotic tissue, or bulbous end, was removed on the proximal side until the section showed well-defined nerve bundles; and the distal end was refreshed. The ends were pierced with a round shafted needle, and united with one or, in the case of large trunks, two sutures of twenty day chromic catgut (0 or 1 size). It was always found possible to get the ends together by freeing the nerve above and below, and flexing the nearest joint or adducting the upper arm. Where a portion of the nerve was thickened and appeared to be "hidebound," chiefly from thickening of the perineurium, an incision was made into the thickened tissue.

The five cases of injuries to the brachial plexus furnished many points of interest. One was due to a bullet smashing the centre of the clavicle. The clavicle was divided, and fragments of bone were found pressing upon the anterior divisions of the fifth, sixth, and seventh nerves, which were enveloped by dense scar tissue. This was removed, the nerves were surrounded with Cargile's membrane, and the clavicle wired. In another case the injury was by a bullet at the root of the neck. At an operation, two months after the injury, the trunks of the fifth, sixth, and seventh cervical nerves were found thickened and more or less adherent. The condenser reaction of the paralysed muscles read from 1 to 4 micro-farads charged at 70 volts. The thickened nerves were separated from adhesions and surrounded with Cargile's membrane. Five months after the operation there was a good return of movement in the paralysed muscles. In the other cases the injuries were below the clavicle, and in two instances were of a most extensive character. The difficulty in dealing with these cases is increased by the fact that the axillary artery and vein are usually involved in the scar tissue and require careful separation. In one case it was found necessary to ligature the artery and vein above and below the lesion. No trouble occurred as regards the circulation of the limb, probably because the anastomotic circulation had been enlarged owing to partial occlusion of the axillary artery. A dense mass of

* A paper read before the Medical Society of London on November 1st, 1915.