The Conditions

UNDER WHICH

THE STERILISATION OF WOUNDS BY
PHYSIOLOGICAL AGENCY

CAN BE OBTAINED.

BY COLONEL SIR ALMROTH E. WRIGHT, C.B.,

M.D., F.R.S.,

A CONSULTANT PHYSICIAN TO THE ARMY IN FRANCE;

CAPTAIN ALEXANDER FLEMING, M.B., F.R.C.S.,

R.A.M.C.; AND

CAPTAIN LEONARD COLEBROOK, M.B., R.A.M.C.

THE treatment of a bacterial infection is always approached with certain *a priori* assumptions. The surgeon who treats wounds with antiseptics assumes that the organism is unable to deal with the infecting microbes. The proper assumption would be that the organism must—for else there would be bacterial infections from which nobody could recover—be competent to deal with every species of microbe. And clearly it is impossible to know what the body is capable of achieving, or to fix any limit to its bactericidal powers, before we have found out how to bring those powers effectively to bear, and before the conditions essential to success have been realised in wounds.

Let us begin by finding out what destructive effects can be obtained with the blood, and first of all with the blood-fluids. For that we must make graduated bacterial implantations into the different kinds of blood-fluid encountered in the body: (a) into normal serum; (b) into serum whose antitryptic power is abolished, as happens when it stands stagnant upon disintegrated leucocytes; (c) into serum which has been neutralised,

of Welch. That we have here, despite the symbiotic factor, a substantially correct picture of the effects produced by the different blood-fluids is shown by the fact that essentially similar results are obtained with separate implantations of each variety of microbe.

Here there was used for the implantations a mixture of equal volumes of a staphylococcus, streptococcus, colon bacillus, and *Bacillus welchii* culture.

The broad results are set forth in Table I.

In our *unaltered serum* we have in our aerobic and anaerobic tubes and in each case throughout the whole series of after-washes a culture of streptococcus. In the anaerobic tube that culture is in all the later after-washes a pure culture. In the aerobic tube we have superadded irregularly, especially in the earlier after-washes, a culture of staphylococcus, and also a scanty growth of the colon bacillus. The bacillus of Welch nowhere puts in an appearance.

With the *trypsinised serum* cultured anaerobically we have in all the after-washes an extraordinary pullulation of each of the four implanted microbes: the streptococcus, the staphylococcus, the colon bacillus, and the bacillus of Welch. In the anaerobic tube we have again in the whole series of after-washes an extraordinary pullulation of the streptococcus and bacillus of Welch. This last microbe, be it observed, grows in the anaerobic not a whit more freely than in the aerobic tube; indeed, it would seem to grow less freely. The staphylococcus, except in the first after-washes, fails to put in an appearance, and the colon bacillus grows sparingly.

In the *neutralised serum* we have, as in every other blood medium, streptococcus growth in both the aerobic and anaerobic tube in the whole series of after-washes. The staphylococcus also grows in all but the last after-washes. The colon bacillus grows only in the aerobic tube. Lastly, the bacillus of Welch grows in the aerobic tube in all, and in the anaerobic tube in all the earlier after-washes. Here again the anaerobic conditions seem to hinder rather than to favour the growth of this organism.

TABLE I.

(A) *Streptococcus pyogenes*. (B) *Staphylococcus*. (C) *B. coli*. (D) *B. Welchii*.

Serial No. of after-wash.	Unaltered serum from clot.								Serum deprived of its antitryptic power by addition of trypsin.								Serum rendered almost neutral by addition of acid.								Whole blood defibrinated.								
	Aerobic culture.				Anaerobic culture.				Aerobic culture.				Anaerobic culture.				Aerobic culture.				Anaerobic culture.				Aerobic culture.				Anaerobic culture.				
	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	
	+	+	+	0	+	+	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
1	++	++	+	0					+	++	++	++	++	++	+	+	++	++	++	++	++	+	+	+	+	+	+	++	+	+	+	+	+
2	++	+	+	0	++	0	+	0	+	++	++	++	++	++	+	++	++	++	++	+	+	+	++	+	+	+	0	+	+	0	+	0	0
3	++	+	+	0	++	0	+	0	++	++	++	++	++	+	++	++	+	++	+	+	+	+	+	+	+	+	0	+	+	+	+	0	0
4	+	+	+	0	+	0	+	0	++	++	++	++	++	0	++	++	+	+	+	+	+	0	+	+	+	+	+	+	+	+	0	0	0
5	+	0	0	0	+	0	0	0	++	++	++	++	++	0	++	++	+	+	+	+	+	0	+	+	+	+	0	+	+	0	0	0	0
6	+	+	0	0	+	0	0	0	++	++	++	++	++	0	+	++	+	+	+	+	+	0	+	+	0	+	+	0	+	+	0	0	0
7	+	+	0	0	+	0	0	0	++	++	++	++	++	0	+	++	+	+	+	+	+	0	0	+	+	+	0	+	0	0	0	0	0
8	+	0	0	0	+	0	0	0	++	++	++	++	++	0	+	++	+	+	+	0	+	0	0	0	+	0	0	0	+	0	0	0	0
9	+	+	0	0	+	0	0	0	++	++	++	++	++	0	+	++	+	0	+	+	+	0	0	0	+	0	0	0	+	0	0	0	0
10	+	0	0	0	+	0	0	0	++	++	++	0	++	0	0	++	+	0	0	+	+	0	0	0	+	0	0	0	+	0	0	0	0

+ = Growth. ++ = Abundant growth. 0 = No growth.

or nearly neutralised, by acid, as happens whenever there is any collapse or interruption of the circulation¹; and (d) into whole blood. Such graduated implantations are most conveniently made in capillary pipettes by the "method of after-washes." We draw into our pipette first a unit-volume of a bacterial suspension, and then follow on—so long as there is room in the stem—with unit-volumes of serum separated by bubbles of air, or, for anaerobic culture, by bubbles of hydrogen or coal-gas. This procedure gives in the successive after-washes diminishing implantations of microbes. For present purposes we may eliminate from consideration the first after-washes—for these contain a certain proportion of the medium with which we are implanting—and may focus our attention upon the later after-washes where we have undiluted serum. We set out below in the form of a table the general result of a series of aerobic and anaerobic sero- and hæmo-cultures implanted with a mixture of staphylococcus, streptococcus, colon bacillus, and bacillus

Finally, in the *whole blood* the streptococcus and staphylococcus again grow both in the aerobic and anaerobic tubes—the former microbe in each tube in all the after-washes, and the latter more irregularly, especially when we come to the later after-washes. It may also be incidentally noted that in the aerobic tube the colon bacillus and the bacillus of Welch put in in the earlier after-washes an occasional appearance.

For the surgeon these are too many bacteriological details. Let us try to extract from them only what is of practical use. The important generalisations are these:—

(1) *Serum from normal blood and normal lymph* constitute for the vast majority of microbes met with in foul wounds a very unfavourable culture-medium. Of the microbes encountered in wounds only the streptococcus, the staphylococcus, and certain diphtheroid bacilli can grow in unaltered serum; and when we make a minimal implantation the streptococcus alone gives a growth. In other words, the microbes of wounds fall into two categories: *sero-saprophytes*, which grow in corrupted, and *serophytes* in

uncorrupted blood-fluids. Two practical points emerge: (a) when a wound contains sero-saprophytic organisms we may know that we have there corrupted discharges. And (b) if we can then flood the wound with wholesome serum and keep that serum uncorrupted the sero-saprophytes will disappear and the infection will be reduced to a purely serophytic, generally to a streptococcic and staphylococcic, infection. We have then, instead of a foul, a "clean" wound.

(2) *Trypsinised serum*—in other words, the kind of serum we have in the wound cavity and tissues when any exudate stands stagnant upon disintegrated leucocytes—provides an excellent culture medium for practically every species of microbe. In this medium the bacillus of Welch, the streptococcus and countless other microbes all luxuriate. It must therefore be our great aim to prevent, or put an end to, the corruption of the discharges. We shall presently see all that that implies.

(3) *Neutralised or partially neutralised serum*—and we have such a serum in every condition of collapse—is a medium in which not only the ordinary serophytes, but also all the microbes of gas-gangrene class, flourish. These gas-gangrene microbes—and this is important for treatment—are not genuine serophytes, but serophytes only of the acidosed blood-fluids. That means that a gas-gangrene infection in tissues, in the case where the circulation is uninterrupted, can be combated by draining away the acidosed lymph through incisions and replacing it by an alkaline lymph. Where the general blood-fluid is acidosed we must begin by remedying that.

(4) *The whole blood* constitutes a medium of essentially the same quality as the serum. In it, as in the serum, only

a streptococcus escapes from the corpuscles into the serum it will, precisely as if originally inoculated into the serum, be quite out of reach of the phagocytes. Again, if a streptococcus remains lodged in the corpuscular layer or clot it will have to be discovered and killed by the phagocyte. And if not quickly discovered it will grow out into a colony, and then the phagocytes will be kept at bay. Reflection thus shows us that, even on the postulate that leucocytes can kill every species of microbe, it is only natural that streptococci should succeed in growing in whole blood.

With this we have obtained a clue as to what we must do and leave undone if we want to get ocular demonstration of bactericidal effects achieved by leucocytic agency. First, we must get rid of the serum which provides a culture medium; and, secondly, we must take steps to bring to bear upon the infection a maximum force of phagocytes. The simplest way will be to centrifuge defibrinated blood. By that we separate the blood into three layers. Above will be the serum; immediately below this is a layer of leucocytes admixed with a few red corpuscles; and below this again a deposit of red corpuscles with only a very small admixture of leucocytes. We now take an agar plate; implant it fairly heavily with streptococcus or staphylococcus; and then transfer to it a drop of each of the three layers of our centrifuged blood, carefully siphoning off the last drop of serum before taking the sample of the leucocytic layer, and taking our sample of red blood corpuscles from the bottom of the tube. We then cover in each case with a cover-glass. Here in the sample from the leucocytic layer are realised all the conditions required for the destruction of microbes by leucocytic agency. A considerable force of leucocytes has been brought together. A moist chamber is provided to keep them alive. Their locomotion is facilitated by their disposal between two closely apposed surfaces. And the excess of serum which provides a culture medium for the microbes, and conveys them out of reach of the phagocytes, has been removed.

The results obtained on cultivating the three specimens are shown in Fig. 1. In the serum specimen we have just the same number of colonies as upon the surrounding agar. Under the cover-glass which covers the specimen from the leucocytic layer almost no colonies make their appearance. And in the specimen where we have practically only red corpuscles again a great number of colonies come up.

The concentration of the leucocytes and the elimination of the excess of serum here shown to be requisite for the achievement of conspicuous bactericidal effects can be obtained also in another way—that is to say, by emigration. Just as in the body leucocytes will come out from the capillary blood, so outside the body they will come out from a blood clot. They will attach themselves to glass, and we can then apply this to an agar surface implanted with microbes.² Where we want to operate with denser masses of leucocytes than simple imposition of blood upon glass will furnish, we can—and this will be analogous to emigration from capillaries crowded with leucocytes—concentrate our leucocytes by centrifugalisation before we set them to emigrate. The technique is quite simple. We prick the finger and fill our blood into a tube about 8 mm. in diameter and 3 to 5 cm. in length. We now centrifuge, having first inserted into the blood a glass lath cut from a thin microscope slide—or, better, as shown in Fig. 2, a couple of such laths placed back-to-back. We now incubate for an hour. During this time the leucocytes attach themselves in ever-increasing numbers to the laths (Fig. 3), giving us

FIG. 1.—Effect of imposing samples taken from centrifuged blood upon an agar surface thickly implanted with staphylococcus. A, Sample of serum. B, Sample of leucocytic layer. C, Sample of red blood corpuscle layer.

serophytic microbes—and of the microbes usually found in wounds only the streptococcus and staphylococcus—will grow. And in whole blood, as in serum, the streptococcus in particular will grow from quite minimal implantations.

We must not misinterpret this. It is, as we have seen, difficult to believe that there should be microbes which can be killed neither by the blood-fluids nor by leucocytes. We must therefore scrutinise our experiment to see how the microbes can have escaped destruction. Here we must take note of the fact that the blood *in vitro* always separates itself into a corpuscular and a serum element. In defibrinated blood we have a layer of serum above and corpuscles below; in coagulated blood we have a cylinder of corpuscles surrounded by serum. If now

FIG. 2.—Glass laths in centrifuged blood, showing the red clot below, above this the leucocytic layer, and above this the white clot contracted round the laths.

² Wright: *New Methods for the Study of Emigration*, &c., THE LANCET, Jan. 26th, 1918.

across the middle a band some 3 to 5 mm. in breadth in which the leucocytes lie absolutely edge to edge, and below this band a certain number of scattered leucocytes. We now with forceps gently disengage our laths from the clot, draining off superfluous serum; turn the leucocyte-covered face down and apply it to an agar surface thickly implanted with staphylococcus, streptococcus, or, if we like, any other organism. We then incubate and take note of what happens. Under the upper part of the lath—that part which is quite free from leucocytes—the streptococcal or staphylococcal colonies come up just as thickly as on the surrounding agar—the staphylococcal colonies, however (because of the anaerobic conditions) less luxuriantly. Across the middle of the lath where the leucocytes are densest we have a clear band entirely free from colonies. And on the lower part of the lath we have only scattered colonies. (Fig. 4.) Control experiments with laths dried before they were imposed upon implanted agar show that it is the living leucocytes that are here the sterilising agents. And again control experiments with laths washed off with physiological salt solution or heated serum show that the opsonic properties of the serum are not essential to the achievement of bactericidal effects.

With these and the foregoing experiments the problem of killing serophytic microbes by leucocytic agency has at last found its solution.

An idea of the magnitude of the bactericidal effects achieved can be obtained from Table II. The films of leucocytes here employed were derived in each case from a clot imposed upon a glass surface.

We pass now to consider the application of this to wounds. It will have an application—not to foul wounds with corrupted exudate and a sero-saprophytic infection, for in such wounds phagocytosis is

TABLE II.—Showing the Bactericidal Effect Exerted by Emigrated Leucocytes Operating in their Own Serum upon Streptococcus Pyogenes and Staphylococcus.

From whom obtained.	Nature of microbe with which tested.	No. of colonies which developed upon 1 sq. cm. of implanted agar imposed upon glass surface covered with emigrated leucocytes.	No. of colonies* which developed upon same area of same implanted agar imposed upon clean glass surface.	Proportion of im- planted microbes killed.
A. E. W.	Strepto- coccus.	16	210	Per cent. 92.4
W. D. T.	"	8	210	96.2
N. M. K.	"	15	210	93
A. F.	"	12	100	88
A. F.	"	31 40 } average 35. 42 26 }	4,900	99
L. C.	"	3	5,000	Over 99.9
Bloods from Patients whose Wounds were Infected with Streptococcus				
Pte. C.	Strepto- coccus.	0	50,000	100
Pte. F.	"	0	50,000	100
Sgt. S.	"	0	50,000	100
Pte. H.	"	20	5,000	99.6
Normal Bloods.				
J. F.	Staphylo- coccus.	9	80	88
L. C.	"	20	252	90
A. F.	"	0 2 } duplicate tests.	250	100 } 99 }

* Where these were too numerous for direct numeration their number was arrived at by counting the number of colonies which developed on agar implanted with a 100- or 1000-fold dilution of the original bacterial suspension.

abolished—but to clean wounds, that is, wounds with uncorrupted exudate and purely serophytic infection. If we take from such a clean wound a drop of thick pus, place it upon an agar plate, and put down upon it a cover-glass—let us call this a *bio-pyo-culture*—we shall have there substantially the same conditions as when we imposed our leucocyte-covered laths on an infected agar surface. Fig. 5 A shows that we obtain a precisely similar result. The central area of the specimen where the leuco- cytes form a continuous sheet remains sterile. On the

FIG. 3.—Emigrated leucocytes on a glass lath incubated in centrifuged blood for one hour.

FIG. 4.—Glass laths, such as are shown in Fig. 3, imposed on agar surfaces implanted (A) with staphylococcus, (B) with a hæmolytic streptococcus pyogenes.

margin of the pus a certain number of colonies—here they are colonies of streptococcus—come up. With this result we may contrast that obtained when we mix a drop of serum with the pus (Fig. 5 B). Here the streptococci, where they have been carried out of reach of the phagocytes, grow unrestrained. We may note also the result (Fig. 5 C) of drying the pus (it was merely spread out thin and left uncovered); and of heating it to 48° C., the thermal death-point of the leucocytes (Fig. 5 D); and of freezing and thawing it (Fig. 5 E). By each of these three methods of *necro-pyo-culture* we obtain preparations in which the pus is thickly studded with microbic colonies.

Of interest in this connexion are also the results displayed in Fig. 6, A and B. In A we have with the unheated pus a perfectly sterile bio-pyo-culture. In the necro-pyo-culture made with the pus heated to 46° C. we have (Fig. 6 B) colonies of the bacillus of Welch with gas formation. The reader will appreciate that these cover-glass preparations give us anaerobic conditions.

The next figures bring before the eye a point of quite cardinal importance—that of the quality of the leucocytes in pus. We have in Fig. 7 a bio-pyo-culture from a boil. The leucocytes here are quite ineffective. In Fig. 8 A we have a bio-pyo-culture from a clean wound which has been left to itself for 24 hours. The pus here is very far from ineffective, but it fails to sterilise itself, and so falls short of standard. In Fig. 8 B we have a bio-pyo-culture from the same kind of wound which had four hours before been carefully washed out with physiological salt solution. We have here a pus that sterilises itself.

FIG. 5.—A, Pus from a clean wound spread out on a sterile agar surface under a cover-glass and incubated. Streptococcus colonies develop only in the narrow ring of serum beyond the edge of the pus. B, The same pus stirred up with serum but in other respects treated in exactly the same way. Streptococcus colonies develop in the serum everywhere round the pus. C, The same pus dried on to the cover-glass before it was imposed upon the agar. D, The same pus heated to 46° C. There are here less numerous colonies than in C and E. E, The same pus frozen and thawed.

FIG. 6.—A, Bio-pyo-culture of a pus containing the gas-gangrene bacillus. B, Necro-pyo-culture of the same pus heated to 46° C. showing growth of the gas-gangrene bacillus with gas formation.

A pus such as this has in point of fact a bactericidal power incomparably greater than manifests itself when we impose it upon a sterile agar surface. How large a surplus of bactericidal power it possesses is made manifest when we impose it upon an agar surface thickly sown with staphylococcus or streptococcus, or, probably, any other microbe. Fig. 9 will convey to the eye a conception of the magnitude of the bactericidal effect then exerted.

We thus see that the results obtained with leucocytes from a clean wound surface are precisely the same as those with leucocytes which emigrate from our blood-clots. In each case what is essential to the achievement of bactericidal effects is the employment of freshly emigrated leucocytes, the keeping of these alive and active, and the removal of the excess of serum which would carry the microbes out of reach.

It will be obvious that the problem of sterilising the actual wound surface must be soluble along these lines. That is part and parcel of the general problem of the treatment of the infected wound, and we shall deal with it in its place. First, however, let us see whether it is possible to sterilise a wound surface by an antiseptic applied directly, and by an antiseptic applied after washing with saline solution.

Effect of direct applications of an antiseptic to flat wound surfaces, and of applications preceded by thorough washing with physiological salt solution.—The results of these applications are brought before the eye in Fig. 10.

In A we have a bio-pyo-culture from a clean wound left to itself overnight. There are here only a few streptococcal colonies—in other words, only a few streptococci have here escaped destruction. In B and C we have cover-glass specimens taken and cultured in exactly the same way after the one half of the surface (B) had been washed with eusol and the other half (C) with physiological salt solution. What calls for notice is, first, that while we have in A only a few bacterial colonies, and a background of pus, we have in B and C very numerous colonies and a quite bare background. That teaches that the mechanical effect of washing is much more important than the chemical effect of the washing fluid. We wash away the leucocytes and leave behind the microbes; and these, now escaping destruction by the leucocytes, grow out into colonies. That the microbes on the wound-surface are after eusol just as numerous as after physiological salt solution is, no doubt, due to the antiseptic expending all its strength upon the overlying pus. The microbes which remain are presumably those which were hidden away under leucocytes. In D and E we have again cultures made by the same method from the wound surface after further treatment with eusol. In D—i.e., in the preparation made from the half of the wound which has been twice treated with eusol—sterilisation is, as we see, incomplete. On the other hand, in E, the preparation made from the half of the wound which was washed first with physiological salt solution and afterwards with eusol, we have complete sterilisation. In D the microbes were no doubt buried under coagulated albumin; in E the washing off of the albuminous discharges must have left the microbes without protection.

The experimental data just set out make it clear—and, indeed, it never could have been doubted—that it is possible to sterilise out of hand the superficies of a wound by the agency of antiseptics, provided that that surface has been washed perfectly clean from albuminous substances.

Practical application of the physiological and biological lessons we have learned to the treatment of wound infections.—It will be obvious to all who have not the blinkers of

tradition over their eyes that our treatment of wounds will be successful or unsuccessful according as it falls in with or disregards physiological and biological facts such as those we have been dealing with. And it is clear that whenever new facts of this kind are brought to light we are bound to review the whole of our treatment, and see whether any of our treatment runs counter to the facts we have learned, and whether each of these is turned to full account. Let us carry this out, asking ourselves in connexion with each successive phase of the wound what would be the proper treatment to follow. We may—though loth to waste time in discussing treatment which is obviously right and widely accepted—say first a word on the subject of early primary suture.

Early primary suture.—This procedure, recently taken by us over from the Belgians and French, stands on precisely the same footing as primary suture of wounds as carried out after ordinary surgical operations. In wounds which have received early surgical treatment—that is to say, in wounds

FIG. 7.—Bio-pyo-culture. Pus from a furuncle spread out on agar under a cover-glass and incubated. Innumerable staphylococcus colonies have developed in the pus and in the surrounding liquor puris.

which have been fully opened up and mechanically cleansed and resected—the conditions encountered are, one may say, identical with those in most civil operations. In both cases we are closing upon healthy tissues on which there is at most a minimal microbic implantation. And in both cases—except when we leave dead spaces and allow these to fill up with lymph, and have in these a streptococcus implantation—the body can very safely be trusted to deal with the few scattered microbes. The limitation here enunciated is one which every intelligent man, who had read the first column of the first experiment in this paper, would have anticipated.

From early primary suture we turn to the infected wound. There are two categories of infected wounds. The first is that of *foul wounds*. These will be (a) wounds which have never been opened up and cleansed and resected. With these may be grouped (b) wounds that have been sutured,

FIG. 8.—Bio-pyo-cultures: A, from a clean wound in which pus had collected over-night (a certain number of colonies are seen in and around the pus); B, from a clean wound which had been carefully washed out four hours before. The pus sterilises itself.

but have, by reason of imperfect cleansing and resection, afterwards broken down; and (c) wounds originally clean which have been long untended. The second category is that of *clean wounds*. These may be (a) unsutured wounds which have at the outset been properly cleansed and resected and have afterwards received due attention; and (b) wounds originally foul which have been cleansed. In the class of clean wounds we may perhaps also place properly resected

FIG. 9.—Pus spread out under a cover-glass upon an agar surface heavily implanted with staphylococcus. Here the agar surface which is covered by pus is sterile, while the portions of the surface which are not covered by pus have grown innumerable colonies.

sutured wounds with a streptococcus infection which have at the first sign of trouble been reopened.

All wounds which fall into the category of *foul wounds*—i.e., all those with unwholesome slough-covered walls, tryptic discharges, and a sero-saprophytic infection—ought to be treated in one way; all *clean wounds*—i.e., all those with wholesome walls, uncorrupted (i.e., antitryptic) discharges, and a purely serophytic infection, in another.

Treatment of foul wounds.—The first step here must be to clean off all the sloughs which, by continuously corrupting the exudation, favour the pullulation of every species of microbe in the wound. Then, having rendered our wound surface wholesome, we must get rid of all the sero-saprophytic bacteria. The first object can be achieved by tryptic digestion. When it has done its work the second can be achieved by an inpouring of wholesome lymph into the wound. If the wound is simply left to itself, Nature herself slowly takes in hand the digestive cleansing of the wound, making use of the trypsin set free from leucocytes which are broken down by microbic agency. But infinitely faster digestive cleansing can be obtained if we ourselves rapidly break down the leucocytes in the sloughs and in the pus. We can do so by soaking the slough-covered walls with 5 per cent.

FIG. 10.—Bio-pyo-culture from clean wound and cultures made from it after washing with eusol and physiological salt solution. Description in text.

salt, afterwards permitting this to dilute itself by diffusing out into the exudation which the hypertonic salt draws into the wound cavity. Cleansing digestion completed, the hypertonic salt continues to act as a lymphagogue, and the

inpouring of antitryptic serum makes an end to the sero-saprophytic infection. The serophytic infection also is held in check so long as the concentration of salt in the discharges is maintained at a high level.³

Immediately related with the treatment of foul wounds is that of gas-gangrene infection of the tissues. Here we have, as in the foul wound: (a) necrotic tissues which must be removed—in this case by the knife; (b) altered lymph to be got rid of and be replaced by wholesome lymph; and (c) a saprophytic microbe (the bacillus of Welch) which can subsist only in degenerated—i.e., acidosed or trypsinised—blood fluids. The point of treatment which is every day overlooked, and therefore requires to be emphasised, relates to the necessity of replacing, when extirpation has to be left incomplete, the degenerated by wholesome lymph. The proper agency for doing this is a local lymphagogue such as is available in hypertonic salt solution. Neither in foul slough-covered wounds nor in gas-gangrene infection are antiseptics of any service whatever. For these cannot penetrate sloughs, or pockets of pus, or infected tissues; nor do they influence that corruption of the discharges which favours the pullulation of every species of microbe. Nor again can closure of the wound—a procedure

sulci, or islands of inspissated pus, we shall inevitably, by reason of the incomplete washing, have unsterilised patches. From such foci, from the septic lacunæ in pus already spoken of, from bacterial niduses below the surface, and from the skin margin and the exterior, the sterilised tracts of the wound will continually be subject to reinvasion. From this we see that that method of sterilisation will be the method of choice which, leaving the fewest septic foci, most efficiently protects the sterilised tracts against reinfection.

In relation to this it is evident that a tract which has been washed quite clear of leucocytes, and then sterilised by antiseptics, is a tract left quite without protection against bacterial invasion. As soon as ever a drop of fluid from a septic focus reaches it, infection will be re-started, and the sterile area will remain in such unprotected condition until, sooner or later—that will depend upon the antiseptic—the leucocytic guard returns. Quite different are the conditions upon a clean wound surface which is being sterilised by leucocytic agency. Pus from such a surface possesses—we saw this in our experiments—a quite astonishing phylactic power. With that the superiority of sterilisation by leucocytes over sterilisation by antiseptics is, as it seems to us, quite settled. But it is of interest and importance to inquire

how long the protection afforded by leucocytes will last. The data of a typical experiment are brought before the eye in Fig. 11.

We have here a series of bio-pyo-cultures from a clean wound. A is a specimen taken from the wound after it had been left to itself for a night. A few colonies of streptococcus are in evidence. They suffice to show that this pus can no longer give effective protection. In B we have an impression-preparation of the wound taken immediately after washing with physiological salt solution and implanted on agar. It will be seen that the cultural result is exactly the same as in a similar washing experiment already figured (Fig. 10). In C, D, and E, we have bio-pyo-cultures taken respectively 2, 4, and 8 hours after washing. The first of these is almost and the other two are quite sterile. And finally we have in F a bio-pyo-culture taken the next morning. Here the original conditions have returned—that is to say, we have again a pus which can no longer give effective protection.

FIG. 11.—The description will be found in the text.

which is, as we shall realise, applicable to clean wounds with serophytic infection—be resorted to where we have corrupted discharges and a sero-saprophytic infection.

Treatment of clean wounds.—We have seen that treatment in the case of foul wounds resolves itself into a cleansing digestion of the wound cavity, followed by an elimination of the sero-saprophytes by local auto-sero-therapy. In the case of clean wounds we have to complete the sterilisation by the destruction of the serophytic bacteria. We can, as we have seen, have recourse to the patient's leucocytes or to chemical antiseptics—i.e., to auto-leucocyto-therapy or chemotherapy.

By both methods sterilising effects can be obtained. But the difficulty is to obtain a sterilisation which shall be topographically complete. In our bio-pyo-cultures we had colonies of streptococcus coming up around the margin of the preparation whenever there was in the pus any trace of superfluous fluid. Exactly the same must happen on the face of the wound. There will often be lacunæ in the leucocytic covering, and in these there will be septic fluid. In the case where we go to work with an antiseptic we must, as we have seen, as a preliminary, wash off every albuminous element which might quench that antiseptic or prevent it penetrating. This—it is not necessary to insist—will often be difficult of attainment. If we have upon the face of our wound pits or

Question as to whether and in what respects the closure of the wound furnishes more favourable conditions for sterilisation.—We have learned in our experiments conducted with blood the conditions which are requisite for sterilisation by leucocytic agency. We have seen that we must employ freshly emigrated leucocytes, employ them if possible in serried masses, that we must keep them in good condition, provide them with ready access to the microbes, and must, when combating serophytic microbes, drain off every drop of superfluous serum so as to prevent proliferation out of reach of the phagocytes. And in our experiments conducted with pus there has been brought out that while our bio-pyo-cultures are not unfrequently, our necro-pyo-cultures are only very rarely sterile. That teaches that the leucocytes from a clean wound surface are competent to do much more effective sterilising work than they are actually doing in the open wound. It follows as a corollary that if conditions more like those which our experiments have shown to be requisite can be obtained by suturing, we shall by suture assist sterilisation.

Let us therefore ask ourselves in what way suturing would change the conditions in the wound. It will, of course, keep off external infection. This is not worth spending any words on.

Let us see what we do for the leucocytes. By bringing together the two faces of our wound we double the leucocytic forces available at any point, filling in the lacunæ

³ To this point we shall recur when we come to deal with the question of a phylactic dressing for use where the wound cannot be at the time surgically cleansed and resected.

arising from irregular distribution of the leucocytes, and dispersing the serum which has collected in those lacunæ. Further, we protect the leucocytes from desiccation, and by the fact that we dispose them between two apposed surfaces we enable them to move about more freely and to congregate to infected points. In illustration of this we subjoin Fig. 12. Here a bio-pyo-culture was made by disposing

FIG. 12.—Leucocytes of pus aggregating themselves in dense rings round colonies of staphylococcus.

pus in a thin layer between an agar surface and a cover-glass. The prominent objects in the illustration are colonies of staphylococcus encircled by leucocytes. These, of course, are leucocytes which have rallied to the focus of infection.

But when we suture the wound we affect also elements other than the leucocytes. In particular we influence the lymph exudation. If our operative procedure is really successful we give effective support to the walls, and, by the pressure thus brought to bear, restrict the exudation. If, on the other hand, we leave behind in the wound hollow spaces, then suture simply confines the fluid. And then if streptococci find access to that fluid all the good we have done is undone. For the streptococcus is provided with the means of multiplying out of reach of the phagocytes.

Question of policy as between suturing the wound and leaving it open, and method of pursuing the sterilising procedures when the wound is left open.—The question of policy is here that of balancing the advantages of closing the wound, bound up as these are with the risk of occasional failure, against the disadvantage of leaving the wound open. We have seen that if hollow spaces are left and these fill up and become infected the wound will have to be reopened. There will be two ways of reducing this risk. Precautions can be taken against leaving dead spaces. This is a question of surgical technique and also a question of choosing for the operation a time when some of the hollows have filled up, and the tissues are not yet too much indurated by scar formation. And again the microbe infection can be restricted. This is a question of making our sterilising operations as effective as is possible in an open wound. The important point to emphasise here is that to promote exudation—as, for instance, by the application of hypertonic saline solution—is to promote the serophytic infection; to leave the discharges to take care of themselves under impermeable protective is generally to leave the infection unaltered; and that to remove all superfluous fluid, while keeping the wound surface moist, is the way to diminish the infection.

We bring before the reader's eyes in Fig. 13 the result of a comparative experiment undertaken upon a clean wound. In A is depicted a bio-pyo-culture made from the wound merely covered in with impervious protective. We note that a certain number of colonies of streptococcus have come up. That was to be expected from a procedure which confines the serum and so provides a culture medium for the streptococcus. In B we have a bio-pyo-culture made from the same wound after it had been left for 24 hours under a dressing of dry gauze. Our culture is here almost sterile. In C we have another bio-pyo-culture from the same wound after return to simple protective covering. Here, again, we have a growth of streptococcus.

We thus see that by merely absorbing the excess of serum we can carry the sterilisation of the wound up to the point where we get a sterile bio-pyo-culture.

Question as to whether it is possible to obtain a pansement d'attente—i.e., a phylactic dressing for use where the wound cannot at the time be surgically cleansed and resected.—Among the problems of treatment there is one which up to this has been omitted from consideration. This is the question as to whether anything can be done to restrain the bacterial infection in the case of patients brought in off the field who have large open wounds and cannot for the time being receive full operative attention. A word may be devoted to this. We believe that hypertonic salt solution fulfils all the requirements of a phylactic dressing and pansement d'attente. In the first place, by inhibiting leucocytic emigration, it prevents that corruption of the discharges which prepares the

FIG. 13.—The description will be found in the text.

way for sero-saprophytic infections, and above all for gas-gangrene infection. Again hypertonic saline solution, by virtue of its lymphagocic properties, prevents that drying up of the wound and shutting down of the surface capillary circulation which must, more than any other factor, produce sloughing of the wound surface. And, lastly, by direct action of the salt the hypertonic saline solution will, so long as it remains sufficiently concentrated, inhibit the growth of serophytic microbes in the exudation. All that would be necessary would be to cover over the whole wound surface with several layers of gauze soaked in 5 per cent. salt (i.e., saturated salt solution seven times diluted); to back this with a plugging of gauze steeped in saturated salt solution, and then to cover with a layer of impervious protective.

What we have to unlearn.—It is a very penetrating observation—made by Professor William James—that we never fully

grasp the import of any true statement until the opposite untrue statement is clearly set over against it in our minds. To this end, we may now, in concluding, set over against what has been ascertained to be true what is erroneous.

1. It has been erroneously inculcated that every wound should be sterilised before closure; and that, therefore, *primary suture* should be avoided and *secondary suture* undertaken only after a course of antiseptics. There is now no question, with respect to primary suture, that the wound taken after early surgical cleansing and resection is as good as sterile; and, with regard to *secondary suture*, undertaken with a wound in good condition and a purely serophytic infection, that such operative procedure, provided it leaves behind no infected dead spaces, directly contributes to sterilisation.

2. It has been taught that we should judge of the fitness of the wound for closure by necro-pyo-cultures and direct microscopic examination of the pus. We have learned that it would be infinitely more reasonable to base our judgments upon the results of bio-pyo-culture.

3. It has been taught that suture cannot be successful in a wound containing a hæmolytic *Streptococcus pyogenes*. We have seen that leucocytes can, given proper conditions, successfully combat this, and of course all other streptococci; and that these conditions can be realised in connexion with the suture of wounds.

4. It has been taught that for the removal of sloughs from foul wounds chemical solvents are required. We have learned that sloughs can be removed by tryptic ferment set free from disintegrated leucocytes, and that the liberation of this ferment can be greatly accelerated by breaking down the leucocytes in the discharges with hypertonic saline solution.

5. Lastly, it has been taught in connexion with antiseptics that sterilisation is obtainable only by continuous or very frequently repeated application. We have learned that there is nothing to prevent any part of a wound surface which has been washed quite clear of albuminous matter being sterilised by a single application of antiseptics.

In concluding we wish to express to Sergeant A. K. Maxwell, our illustrator, our thanks for his care and skill.

NOTE ON

A METHOD OF DEALING WITH THE DIVIDED URETERS

WHEN IMPLANTATION INTO THE BLADDER IS IMPOSSIBLE, OR WHEN THAT VISCUS IS ABSENT.

By W. BLAIR BELL, B.S., M.D. LOND.,

GYNÆCOLOGICAL SURGEON, ROYAL INFIRMARY, LIVERPOOL; LECTURER IN CLINICAL GYNÆCOLOGY IN THE UNIVERSITY OF LIVERPOOL.

ALTHOUGH probably the gynæcologist is most often concerned in dealing with intentionally, and sometimes unintentionally, divided ureters, the general surgeon, too, is often confronted with problems concerning these ducts which in the past have either been impossible of solution or have been imperfectly solved.

Objects of Method.

In a very large proportion of all cases in which the ureter is accidentally divided, or in which a small distal portion is deliberately excised during a radical operation for cancer of the cervix uteri, implantation into the bladder is easily and successfully accomplished if a suitable technique be employed; and such procedures have no relation to the method I am about to describe. This method takes into account a very much more serious problem: it concerns the fate of the ureters which cannot be implanted into the bladder, either because they have been divided too far away or because there is no bladder in which to implant them—that is to say, there is a condition of ectopia vesicæ, or removal of the bladder is indicated in the treatment of neoplasms.

Hitherto, of course, in these difficult circumstances the ureters have been implanted into the intestinal canal; but I think it will be generally conceded by all clinicians and pathologists that to lead the ureters into the bowel which is swarming with bacteria is the very essence of unscientific surgery. If a patient here and there should escape fatal

renal sepsis, no one knows how this miracle happens. The life of most patients in these circumstances is short and stormy.

I have therefore attempted to devise a safer procedure than those hitherto employed, primarily with the object of extending the ratio of operability in cases of carcinoma cervicis uteri.

It is well known that cancer of the cervix is a very local disease—that is to say, metastases are rare—and the lethal effects are for the most part produced locally and chiefly from involvement of the ureters. It is, too, a disappointing fact that a large proportion of all cases are in an advanced stage before they present themselves for treatment. I have seen only two early cases of cancer of the cervix in the last 12 months and both refused treatment because they had so few symptoms. This disheartening state of affairs, and the fact that during the last few years I have obtained good results in what would usually be considered inoperable cases of cancer of the cervix by wide removal of the pelvic organs and tissues and the insertion of radium in the cavity so created, have led me to contemplate the possibility of deliberately dividing the ureters—which may be dilated from invasion by the malignant growth, or simply from constriction—at the pelvic brim, in order more easily and extensively to clear the pelvis and excise the base of the bladder where it is in relation with the supravaginal cervix, and is therefore often involved in the cancerous lesion.

Technique.

I shall now describe the technique of the various procedures that go to make up the method of treatment in advanced—that is, hitherto inoperable—cases of cancer of the cervix. The details of the method should, of course, be varied to suit the peculiarities of other lesions such as ectopia vesicæ. Naturally in such a complicated method one only attains perfection after repeated attempts; and it is probable that in many details further improvements will be effected. There are two, or possibly three, stages in the method.

At the first operation laparotomy is performed through a central subumbilical incision. The anterior branch of the internal iliac artery is tied on either side to diminish the blood supply to the pelvic organs, and so to facilitate the subsequent procedures. Next, a loop of the lower ileum, about 18 inches in length, with its mesentery, is isolated, and an anastomosis is made to carry on the function of the intestinal tract from which the loop has been excised. The apex of the isolated piece of bowel is now superficially attached to the fundus of the bladder, and the two ends of the loop are brought out through stab-wounds in the iliac region on either side and fixed in position.

I need not go into all the obvious details which should be taken to avoid contamination.

The central incision in the parietes is then closed. The dressings over the open ends of bowel should be changed frequently, as there is a good deal of discharge, especially from the distal end, for a few days. When the attachments at these orifices are quite firm swabs are taken from the interior of the bowel with precautions against superficial contamination. Subsequently the loop of bowel is washed out twice daily with a 1-30 solution of Milton fluid. Within ten days the bowel is sterile or practically so.

The figures from a case investigated by Professor E. E. Glynn are interesting. Two swabs were taken from each end of bowel at intervals of a few days and examined bacteriologically with the following results:—

June 21st: Before sterilisation of the bowel was commenced.

No. of colonies grown upon nasgar after 24 hours' incubation at 37° C.

1. Right side, first swab...	25,692
2. Right side, second swab ...	19,248
3. Left side, first swab ...	15,960
4. Left side, second swab ...	10,080

The organisms grown were *B. Coli*, *Gram-positive staphylococci*, and *Gram-positive diplococci*.

June 25th: After irrigation of the loop of bowel for four days.

No. of colonies grown upon nasgar after 48 hours' incubation at 37° C.

1. Right side, first swab (<i>B. coli</i> and <i>Staphylococcus albus</i>)	396
2. Right side, second swab (<i>Staphylococcus albus</i> only) ...	12
3. Left side, first swab (<i>B. coli</i> and <i>Gram-positive bacillus</i> , resembling <i>megaterium</i>)...	2,592
4. Left side, second swab (<i>B. coli</i> and <i>Gram-positive bacillus</i> , resembling <i>megaterium</i>)...	720