ON THE INFLUENCE OF ANTISEPTICS ON THE ACTIVITIES OF LEUCOCYTES AND ON THE HEALING OF WOUNDS.

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PART I.

IN the BRITISH MEDICAL JOURNAL, March 6th, 1915, I recorded some observations which seemed to show that the application of various antiseptics (even in a concentrated form) to the surfaces of aseptic wounds at the time of operation did not prevent primary healing. In the course of that inquiry certain effects on the blood were observed which suggested the desirability of a closer analysis of the problem.

In the first place, if any antiseptic in a concentrated form is applied to the tissues of a wound, efficient drainage of that wound is necessary, and it seemed important to devise some method of drainage which would not only carry off the blood and effused lymph but which would also serve as a trap to catch the emigrating leucocytes. In this way the cells could be recovered for microscopic examination at various intervals after operation, and the influence of various antiseptics could be observed on the behaviour of the leucocytes towards inert pigment particles, and albuminoid and other organic substances introduced into the wound.

A cotton thread of standard thickness and known number of fibres is boiled in water containing powdered indigo in suspension. By this means the thread is uniformly permeated with indigo granules, and can either be dried or kept in the indigo mixture and boiled before use on each occasion. A convenient length of this indigo thread is laid in the wound before suture and one end brought out at one angle of the wound. The usual sterile gauze dressing is applied.

If such an indigo thread drain be removed from an aseptic wound, say twenty hours after operation, and examined in warm normal saline, the fibres of the thread will be found glued together and covered by coagulated lymph containing in its meshes large numbers of living leucocytes, of which a certain percentage will have ingested the indigo granules. The percentage of such indigo-loaded cells will depend on (a) the time the thread has lain in the wound, and (b) the treatment of the wound by antiseptics or other reagents at the time of operation.

If a wound made for the radical cure of hernia or for the removal of varicose veins be so drained under aseptic conditions, and if the indigo thread drain be removed after an interval of twenty-four to forty-eight hours, the portion of the thread which lies in the cavity of the wound will be decolorized. The extent to which this decolorization has been effected affords an indication of the activities of the leucocytes in three directions: (a) Their capacity to leave the vessels and to enter the thread; (b) their capacity to ingest the pigment granules; (c) their capacity to leave the thread and carry the indigo particles with them.

The objection will, no doubt, be made that the decolorization of the thread is not due to phagocytosis, but to the washing out of the pigment granules by the flow of lymph from the wound. The following experiment, however, shows that this is not the case.

Two small beakers were filled, one with normal saline and one with human serum. One end of an indigo thread was placed in each solution, and the other end was allowed to hang over the glass in contact with white gauze; in

each case the fluid was drained out of the beaker into the gauze without washing the indigo out of the thread or depositing it on the gauze (Fig. 1). This shows that the decolorization of the thread drain while lying in the wound is not due to the flow of lymph or blood on to the surface of the wound, and further observations show that it is due to phagocytosis by leucocytes.

We may now ask what becomes of the leucocytes which have ingested the pigment granules. We know that in aseptic wounds the phagocytes do not leave the wound in the form of pus; they must, therefore, after entering the thread and ingesting the pigment, either (1) render the indigo granules unrecognizable by decolorization, or (2) eject the granules after temporary ingestion, or (3) transport the pigment from the thread back to the blood or lymph stream or the tissues. This question of the fate of leucocytes of different kinds, after emigration and phagocytosis, is a point of much interest about which it will be desirable to say more later; meanwhile, having shown that the decolorization of the thread is due to the vital activity of wandering cells, and is not merely a physical question of irrigation by fluids escaping from the wound, we are in a position to use this fact of decolorization and transportation of pigment as a means of testing the influence of various antiseptics on the activities of leucocytes while still living in the wound. The fact that the observations are carried out in the wound itself has considerable advantages. It serves to check observations made *in vitro*, and it is free from some of the fallacies inherent in experiments carried out under more abnormal conditions.

I have made a large number of observations on a considerable number of wounds under strict aseptic conditions in the human subject, and many antiseptics in different degrees of concentration have been tested by this method of the decolorization of the indigo thread.

Further, the behaviour of leucocytes in relation to other substances such as egg albumin, serum albumin, starch albumin, glycogen, lecithin, has also been observed in wounds treated with and without antiseptics, though in this paper I propose to deal only with pigment particles. In some cases the wound itself has been washed out before closure with the antiseptic solution; in others the indigo thread alone

has been saturated before introduction with various antiseptics in a concentrated form. By the first method the tissues from which the leucocytes emigrate are acted on by the reagent, and by the second method the pigment thread into which they pass.

The Effect of Antiseptics on the Decolorization of an Indigo Thread.

Without entering into the details of each case it may be stated in general terms that the application of a fairly strong antiseptic like mercury biniodide 1 in 1,000, or carbolic acid 1 in 20, to a wound such as that made for the radical cure of hernia, or for the removal of varicose veins, does delay to some slight extent the decolorization of an indigo thread placed in it as a drain.

In a wound to which no antiseptic solution has been applied an indigo thread of standard thickness will be almost decolorized in forty-eight hours, and will show very definite sign of partial decolorization twenty-four hours after insertion into the wound. If, on the other hand, the wound be treated before closure with any of the strong antiseptics, or if the thread itself be soaked in any of the same solutions, there will be only slight evidence of decolorization after twenty-four hours, and the thread will still show a blue tinge forty-eight hours after insertion.

The effect of salt solution, both in the 5 per cent. concentration and as normal saline, on decolorization, is about the same as in wounds in which no reagent at all has been used. This occurs when the wound is treated with the solution and when the thread is soaked with it before introduction.

FIG. 1.—Drawing from a photograph showing non-decolorization of indigo thread by capillary flow of serum or saline fluid. 1, Serum; 2, saline.

Little difference could be detected (Figs. 2 and 3) in the effect on decolorization between the 5 per cent. salt solution and the 0.9 per cent. solution; and this, indeed, we should expect, because the stronger solution doubtless undergoes rapid dilution by the blood and lymph poured into the wound.

There is some evidence pointing to the fact that different individuals under similar conditions of wound treatment vary in the rapidity with which decolorization is effected; in other words, individual patients vary in the capacity of their leucocytes to (1) emigrate, (2) to ingest foreign particles, and (3) to transport the pigment granules so ingested under the stimulus of injury.

In its clinical aspect this fact is of course familiar to surgeons, and it is no doubt associated with the observed differences in the rapidity with which blood and other effusions are absorbed in persons of different ages and in different states of health. It is a problem of much interest, and will, I hope, be the subject of further inquiry.

The question now arises as to the method by which various antiseptic reagents exercise a retarding or accelerating influence on decolorization.

We have already seen that, in the case of indigo particles at any rate, the removal of the

surface, and the whole covered with protective. The entangled phagocytes were examined in warm saline twenty-four hours later. A large number of cells were found loaded with indigo and others with carmine particles, but only a few cells were seen which contained both kinds of pigment granules.

A composite cotton-thread drain, containing both indigo and carmine particles, was introduced into an aseptic wound and the same result obtained. I am inclined to think that this apparent disinclination on the part of leucocytes to ingest different kinds of pigment granules at the same time in wounds is not due to any injurious effect exercised by the indigo (or the carmine) on the cell, but that it is really the outcome of inertia on the part of the loaded cell, since all inert particles seem to have the same effect in this respect. I say inert particles, because it is necessary to distinguish between such bodies as carbon or other pigment particles around which no digestive vacuole is formed, and assimilable substances like albumin and starch, around which, when ingested, digestive vacuoles are formed.

Indigo-containing leucocytes recovered from an aseptic wound were also incubated in saline fluid containing neutral red in solution as used by Ehrlich, and as recommended by Achard of Paris as a test for living leucocytes. The cytoplasm of the indigo-containing cells takes up the neutral red freely while the nucleus remains unstained. Examined also on Ross's auxetic agar jelly to which atropine sulphate has been added, the indigo-containing cells show active movements.

From these and other observations, both *in vivo* and *in vitro*, we must, I think, conclude that the indigo granules, which are insoluble in the body fluids (except the bile), do not exercise any marked injurious effect on the white blood corpuscles.

Any delay that takes place in the removal of the indigo from the cavity of a wound which has been treated with an antiseptic may be regarded, therefore, as due to the action of that antiseptic solution, and not to any deleterious influence exercised by the indigo on the phagocytes.

We have already seen that in the process of decolorization of the indigo thread three different factors are involved, and the question now arises which of these three factors—*Emigration*, *Ingestion*, or *Transportation*—is responsible for the delay in the removal of the pigment.

Direct observation shows that a thread that has lain in a wound which has been treated by a strong antiseptic solution like carbolic acid 1 in 20 contains apparently about as many leucocytes as a thread which has lain in a wound to which no antiseptic has been applied. Of course, if the raw surface has been cauterized by an escharotic, then the coagulation of the tissue cells and the closure of the blood vessels will prevent the emigration of leucocytes into the cavity of the wound. This, however, does not occur when antiseptics are used in ordinary concentrations under surgical conditions in a recent wound. In several cases of septic wounds, complicated with extensive bone injury, which were being treated by daily irrigation and soaks of chloramine, tampons of indigo gauze were laid in the wound for twenty-four hours. These tampons were found on removal to be covered with pus cells and phagocytes, of which large numbers had ingested indigo granules.

In a case of operation for the radical cure of hydrocele in a young adult, after turning back the tunica vaginalis, the surface of the testis was freely rubbed with pure carbolic acid, with a view to the destruction of the secreting endothelial cells, a rubber tube was inserted down to the testis, and through this rubber tube an indigo thread drain was placed in contact with the cauterized tissues. On examining this thread after removal forty-eight hours later large numbers of leucocytes loaded with indigo granules were found amongst its fibres. Owing to the isolated position of the thread in the rubber tube, the phagocytes which had been carried into it by the flow of lymph had remained in the thread and had been unable to return to the tissues. In this case, although little or no decolorization had taken place, the result was not due to lack of emigration. Quinine has been for long supposed to have a special influence in preventing the emigration of white blood cells. An indigo thread soaked in a 1 per cent. solution of quinine hydrochloride placed in an

FIG. 2.—Drawing from a photograph showing indigo thread after forty-eight hours in wounds treated—1, without antiseptic; 2, with carbolic acid 1 in 20; 3, with salt solution 5 per cent.

FIG. 3.—Drawing from a photograph showing the decolorization of indigo threads soaked in different solutions after forty-eight hours' exposure in the same wound. 1, Thread before introduction; 2, thread without any antiseptic; 3, thread with carbolic acid 1 in 20; 4, thread with salt solution 5 per cent.

pigment is the work of the leucocytes, and is independent of the blood stream and body fluids. In delayed decolorization the delay may be the result of

- (1) Deficient emigration of leucocytes; or
- (2) Impaired ingestion of pigment particles; or
- (3) Failure on the part of the leucocytes to return to the tissues with their loads of pigment.

Before attempting to answer this problem we must first ascertain whether the indigo or other pigment has any injurious effect *per se* on the leucocytes. If an indigo thread drain, removed from a wound which has not been treated with any antiseptic, be teased in warm normal saline and the entrapped leucocytes be watched on the warm stage, the cells which contain pigment granules will be seen to throw out pseudopodia freely, though perhaps not quite so freely as unloaded cells.

The vitality and activity of these loaded phagocytes has been tested in various ways under different conditions. Thus indigo-containing cells were incubated in a saline fluid containing 0.005 per cent. calcium chloride to which carbon particles has also been added as recommended by Hamburger.¹ Although a considerable number of empty cells take up the carbon under these conditions, it is not usual to find many cells which already contain indigo taking up the carbon particles in addition. This point was also tested in the actual wound. Two pieces of gauze, one permeated with indigo and one with carmine, were placed one above the other on a healthy granulating

aseptic wound was largely decolorized in thirty-six hours; thus, whatever may be the case outside the body, quinine does not seem to prevent phagocytosis of pigment granules in a wound.

These facts all suggest that antiseptic solutions, surgically applied to aseptic and to infected wounds, do not tend to prevent the emigration of leucocytes from the injured tissues; in fact, as we shall see when dealing with organic substances, many antiseptic solutions in moderate concentration stimulate the flow of wandering cells. Neither does the evidence suggest that leucocytes which escape into wounds so treated are unable to ingest indigo or other pigment granules present in the wound.

What does seem to happen is that leucocytes which have so escaped and which have ingested pigment granules are less active in transporting their pigment loads back to the walls of the wound when antiseptics in a concentrated form have been previously applied to that wound.

The Return Immigration of Leucocytes in Wounds.

Metchnikoff showed that leucocytes which had emigrated into the peritoneal cavity to repel bacterial invasion returned in large numbers to the general circulation. Macallum later established the fact that white cells which had wandered into the lumen of the bowel during digestion returned to the portal and systemic circulation. The facts, however, are not so fully known in regard to cells which have emigrated in response to the stimulus of injury either of a mechanical or chemical kind. The problem of the return emigration of leucocytes from wounds has not yet been fully worked out in different tissues, in different kinds of animals, in different varieties of wounds.

In considering this problem it is necessary to distinguish carefully between infected and non-infected wounds.

In infected wounds the throwing off of the dead leucocytes as pus cells is in itself, of course, evidence that large numbers of the white corpuscles which escape from the blood vessels under such conditions do not return to the lymphatic or general circulation. But even in heavily infected suppurating wounds a considerable number of phagocytes do return to the deeper layers of the granulation tissues which line the cavity of the wound.

Thus, if the granulating surface of an infected wound which is showing some attempt at repair, and in which, therefore, the contest between the defensive cells and the pathogenic organisms is not an entirely one-sided one, be dusted with powdered indigo or dressed with a layer of indigo gauze, and if after an interval of some twenty-four hours a small piece of the granulation tissue so treated be removed, sections cut at right angles to the surface will show a number of indigo-containing cells around the new capillaries in the deeper layers of the tissue. If the edge of the granulating area over which the new epithelium is spreading be carefully examined the indigo-containing cells may be sufficiently numerous in the underlying granulation tissue to give a blue appearance to the edge of the wound. Thus, while large numbers of the emigrating cells perish as pus cells, a considerable number survive and return to the tissues and the circulation. Moreover, there is a quantitative relationship between this "return immigration" of cells and the process of repair in the wound. This is seen clinically in the diminishing flow of pus which accompanies successful resistance to bacterial infection and the commencement of healing in a wound. The reduction of discharge is not wholly accounted for by diminished emigration.

The application of antiseptic solutions to granulating wounds, provided they do not cause death of the cells which compose the granulation tissue, does not seem to lessen the number of cells which contain pigment granules, though it does seem to exercise some influence on the number of cells which return to the tissues. A small wick of indigo gauze was laid in a heavily infected wound treated with compresses of eusol; large numbers of leucocytes loaded with indigo were found among the gauze fibres twenty-four hours later.

While this is the condition of things in the septic open wound, the picture presented by aseptic wounds in which suppuration is absent is quite different.

Here there is no throwing off of dead cells. All the cells which have reached the wound area must therefore either return to the circulation and the tissues or perish, and in their turn undergo removal by other phagocytes.

The Route followed by the Leucocytes in Return Immigration.

I have tried to detect the route by which the phagocytes regain the circulation by laying in the floor of an aseptic wound before suture a compound drain composed of a small indigo-bearing thread encased in or applied to one side of a larger thread of wool, as shown in Fig. 4.

On examining such a drain twenty-four or forty-eight hours later the indigo will have disappeared more or less completely from the indigo thread, and the leucocytes which have ingested it now occupy larger or smaller areas of the wool skein.

The degree of decolorization and the lines of retreat of the pigment-bearing cells seem to depend on certain accidental conditions, such as intimacy of contact between the indigo thread and the living tissues in the floor and sides of the wound. If the indigo thread lies, so to speak, free in the cavity of the wound imbedded in coagulated lymph, then the movements of the phagocytes are restricted, and they may only reach that portion of the wool skein which lies in direct contact with the indigo thread. Where the indigo thread is in direct touch with the living tissues the pigment-bearing phagocytes seem to return directly to the tissues in preference to entering the meshes of the wool fibres, though these are, of course, crowded with freshly emigrating cells which have not yet reached the indigo granules.

Further, the nature and vascularity of the tissues with which the pigment thread lies in contact also exercise an influence on the return flow. For instance, fatty tissues do not offer a favourable site for return immigration. The fibrous aponeurosis of the external oblique (in hernia wounds), if roughly handled and deprived of its feeble blood supply by gauze stripping, does not afford as favourable a clearing ground for rapid decolorization as the more vascular subcutaneous tissue.

This composite thread drain can also be used to test the effect of antiseptic solutions on this current of return immigration.

Fig. 5 shows cross sections of two such drains. In No. 1, from an untreated wound, the phagocytes have removed the indigo from the indigo thread and deposited it in the wool skein. In No. 2, from a wound washed out with mercury biniodide 1 in 1,000, the cotton fibre has undergone little or no decolorization and the wool skein is still white and contains only a few indigo-laden cells. In this case the delayed decolorization of the thread in the wound treated with the antiseptics is not due to failure in either emigration or ingestion because the indigo thread is crowded with loaded leucocytes (Fig. 6).

I also tried to test this problem of the route followed by the phagocytes in return immigration and the influence of different tissues upon it by laying an indigo thread in one angle of the wound and a white cotton thread of like size but free from pigment in the other angle. When examined twenty-four hours later, very few pigment-laden leucocytes were found in the white cotton thread. The phagocytes seem to take the shortest route to the tissues as far as the coagulated lymph and blood which occupies the cavity of the wound will allow, and the cells do not seem to make their way to other foreign substances in other parts of the same wound. This is in harmony with the previous observations that leucocytes which have

FIG. 4.—Diagram showing arrangement of compound thread. I, Indigo thread; W, white wool skein.

FIG. 5.—Drawing from photograph of cross sections of composite indigo and wool drain after removal from wound (+ 5 diam.). 1, From untreated wound, shows decolorization of indigo thread and deposit in wool skein. 2, From wound treated with mercury biniodide 1 in 1,000, no decolorization of indigo thread, no deposit of pigment in wool skein.

already ingested one kind of pigment do not seem very active in ingesting a second variety. In view of the clinical phenomena associated with the spread of infection and the inflammatory reaction which accompanies infection, I also attempted to ascertain whether any extensive migration of pigment-laden cells occurs in the tissues which surround the wound, or, more accurately, whether, having emigrated and ingested foreign substances at the seat of injury, and having returned to the tissues, these pigment-laden phagocytes re-emigrate at the site of a neighbouring wound. To test this point an indigo-thread

FIG. 6.—Drawing from a photomicrograph showing phagocytes containing indigo granules lying on and around a cotton fibre from the wound in Fig. 5, 2 ($\times 500$). It illustrates the fact that absence of decolorization is not due to failure in emigration or ingestion on the part of the leucocytes.

drain was placed in one incision in a case of operation for varicose veins, and a white cotton unpigmented thread was placed in a neighbouring incision a little above the first. When removed, twenty-four hours later, no indigo-bearing cells were recovered from this white thread in a neighbouring wound.

Mention has already been made of the fact that no extensive ingestion of both kinds of pigment by the same cells occurs in two superimposed pieces of indigo and carmine gauze placed on a granulating wound. The same is true of aseptic wounds. Thus, a compound pigment thread containing both carmine and indigo particles removed from such a wound contained both indigo and carmine-loaded cells, but few cells carrying both blue and red granules.

Further observations are needed, but it seems probable that the "return immigration" of phagocytes is not entirely a question of chance, but is subject to a chemiotactic influence just like outward emigration. This does not, of course, mean that the element of chance does not play a large part in the movements of wandering cells in both the outward and the return journey.

Jennings and others have shown that the response of the amoeba and other protozoal organisms to attracting and repelling substances, and to physical stimuli, largely consists in movements of trial and error. The organism assumes various experimental positions along a line of least resistance, and this is probably true of the white blood corpuscles in man.

The Influence of Antiseptic Solutions on Return Immigration.

I have already spoken of the effect of a previously applied antiseptic on the process of decolorization of the indigo thread, and on the movements of the pigment-laden leucocytes in the composite cotton and wool thread. I have shown that the application of a strong reagent like pure carbolic acid to the surfaces of a wound made for the radical cure of hydrocele does not apparently reduce the numbers of wandering cells which crowd into the cavity of the wound, or the ingestion of the pigment by these cells. Evidently the effect of antiseptics used surgically does not check the emigration of leucocytes or their phagocytic activities as far as pigment is concerned—in fact, as we shall see later when dealing with organic substances, emigration is in some cases accelerated. It is, however, quite possible that emigration and phagocytosis may be going on freely, and yet the healing of such a wound may be prejudiced by the accumulation of the phagocytes in the cavity of the wound.

The delayed decolorization of the indigo thread which occurs in wounds which have been treated with certain reagents is probably partly due, therefore, to delayed return immigration.

Return Immigration in Suppurating Wounds.

The extent to which phagocytes which have flowed on to the surface of a suppurating wound can re-enter the tissues or the circulation depends upon, and is an indication of, the degree of injury which these wandering cells have sustained in their struggle with the pathogenic organisms established in the wound.

A certain amount of return immigration probably takes place on all granulating surfaces, as in all injured areas, with the exception perhaps of those wounds in which the infecting organisms have obtained complete mastery—a condition shown clinically by the cessation of discharge, together with signs of general toxæmia. Even in heavily infected granulating wounds, if a portion of the granulation tissue be excised after the surface has been dressed for two or three days with indigo, sections cut at right angles to the surface will reveal the presence of indigo-laden cells around the capillary loops in the newly-formed tissue. This occurs independently of the kind of antiseptic used provided that it is not strong enough to kill the cells.

I have attempted to investigate this question of the effect of antiseptic reagents on return-immigration in suppurating wounds experimentally in animals. Two small skin flaps were raised one on either side of the spine in the lumbar region in a guinea pig. A piece of white gauze was laid in each wound so formed, and the flaps resutured over the gauze. Three days later (under an anaesthetic) the flaps were again raised, and indigo-saturated gauze was substituted for the plain gauze; on the right side no antiseptic was used, but on the left side the granulating surface was washed with carbolic acid 1 in 20, and the indigo gauze was soaked in the same solution before insertion in the wound, which was dressed later with the same lotion. The animal was killed two days later, and both wounds with the surrounding tissues excised and hardened in formalin. Sections embracing the entire thickness of the wounds show that indigo-laden phagocytes have wandered freely into the granulation tissue on both sides. In the wound to which the antiseptic had been applied the flow of pigment was less regular round the margins of the wound. It had not penetrated so far into the tissues except at one part, along the aponeurosis between the subcutaneous and muscular tissues at the deep end of the wound, where possibly the antiseptic had not penetrated so freely.

Pus—Not Only Composed of Dead Cells.

Various samples of pus from heavily infected wounds have been tested from the point of view of the capacity of the pus cells to ingest foreign particles *in vitro*. Starting with the preconceived idea, which I think is still shared

FIG. 7.—Drawing from a photomicrograph showing "pus" from a case of peritonitis incubated with indigo for eight hours. It contains a single field (one-twelfth water immersion and A ocular). Several "pus" cells are loaded with indigo granules and masses. P, Pus cell containing indigo; c, indigo escaped from ruptured cell.

by some surgeons, that pus is always composed of "dead" cells, I have been impressed with the fact that very few samples when incubated with pigment granules in normal saline have failed to give evidence of some capacity of ingestion on the part of a certain number of the cells of which the liquid is composed (Fig. 7).

If we regard capacity to flow round and ingest foreign particles as evidence of vitality then we must conclude that while most of the cells in pus from infected wounds are dead cells, yet a certain proportion are still living and capable under favourable conditions of active phagocytosis. This observation on the behaviour of pus cells *in vitro* is in harmony with the previously recorded activities of pus cells in the actual granulating wound. The proportion of living to dead cells bears some relation to the number and virulence of the infecting organisms and the digestive changes in the liquor puris.

In samples of pus taken from wounds infected with pyogenic organisms which show some attempt at successful reaction, the amount of carbolic acid in normal saline necessary to inhibit the ingestion of carmine particles by the pus cells when incubated for twenty-four hours is somewhere between 1 in 640 and 1 in 1,000.

This applies to pus removed from a wound and incubated with pigment *in vitro*. When, however, the pus cells are brought in contact with the indigo particles *in situ*, and are allowed to collect upon a layer of indigo-saturated gauze laid on a granulating surface and covered with protective, the incubation is carried out in the wound and a much larger number of indigo-containing cells can be recovered from the gauze. The proportion between living and dead cells, as judged by the test of ingestion, depends upon the healthiness of the wound. The strength of the acid carbolic solution necessary to inhibit the ingestion of pigment particles by the cells under these conditions must be judged by another standard. If indigo gauze soaked in normal saline be used as the control, then it will be found that ingestion of pigment goes on freely in gauze which has been soaked in acid carbolic solution, 1 in 60, before application to the wound. This method of testing the ingestive capacity of pus cells by incubating them with pigment granules in the wound itself affords a striking proof of the fact that many samples of pus contain considerable numbers of living leucocytes. It also affords a means of ascertaining the healthiness or unhealthiness of any wound, and of testing the effect of different antiseptic solutions on the life and activities of the leucocytes in the wound itself. Of the many factors which affect the vitality of leucocytes in a wound one of the most important (apart from the number and virulence of the infecting organisms) is the length of time which elapses after the cells have emigrated from the circulation and during which they have been exposed to the unnatural environment of an open wound. It is the recently emigrated cells which seem to retain the capacity to ingest foreign particles, and this fact bears on the very important problem of the efficient drainage of wounds. The object of drainage should be not only to provide for the escape of dead cells, but to further the emigration of living phagocytes.

We know that laudable pus (in other words, pus containing living phagocytes) indicates healthy activity in a granulating wound. It is possible that (in the absence of aseptic human leucocytes), if some means could be found to kill the ingested organisms without injuring the phagocytes, and to wash the cells so treated free from contaminating liquor puris, such revitalized pus would form a useful dressing for suppurating wounds.

The Difference between Suppurating and Non-suppurating Wounds.

Apart from the all-important factor of the presence or absence of infecting organisms, the differences between a suppurating and a non-suppurating wound are chiefly differences of degree and not of kind. We know that the tissues and the spaces between the tissues in the primarily healing aseptic wound are crowded with living phagocytes capable of ingesting both foreign particles and dead cells. We have also seen that a considerable number of the cells which compose the purulent discharge from a suppurating wound are also living cells capable of ingesting foreign material and acting as phagocytes. Emigration and capacity for ingestion are therefore factors common to both kinds of wound. The main difference between them lies in the fact that, while the proportion of phagocytes which find their way back to the tissues or the circulation is large in the primarily healing wound, it is relatively small in the suppurating wound. The degree of return immigration constitutes, in fact, the main distinction between the aseptic and the suppurating wound.

SUMMARY AND CONCLUSIONS.

I am fully conscious of the incomplete character of these observations. No attempt has been made to differentiate between the different varieties of phagocytes. Although this point has not been entirely lost sight of, the overwhelming numerical superiority and the greater importance of the polynuclear leucocytes in wound reactions has led me to limit my remarks at present to this group.

Further, the different ways in which different tissues and different organs respond both to different kinds of infecting organisms and to different kinds of antiseptic solutions is a wide and important subject. The work required to elucidate the method of such a comparatively simple reaction as the deportation of foreign pigment in the brain, liver, and other organs is very considerable, and must form the subject of further inquiry.

It will no doubt appear to many that the all-important factor of the infecting organism has not received adequate attention. The problem of wound reaction and wound treatment is, however, so enormous that some subdivision of the subject is absolutely necessary, and in this paper I have tried to deal only with the effect of various antiseptic reagents on emigration, phagocytosis (or ingestion), and return immigration of leucocytes when carrying pigment granules.

The outcome of the inquiry seems to be that antiseptic solutions in moderate degrees of concentration exercise less influence over emigration and phagocytosis than many surgeons have supposed. There are, however, reasons for concluding that antiseptics do exert a considerable inhibitive effect on the return immigration of living phagocytes. This aspect of the subject should, I think, be borne in mind in descriptions of the effect of different antiseptics in killing off pathogenic organisms in pus and other liquids *in vitro* and on the sterilization of wounds.

Provided efficient drainage is ensured, the surgical application of most antiseptic solutions does not apparently materially prejudice the defensive activity of the tissues in either infected or non-infected wounds. If it can be shown that the use of antiseptic reagents does at any stage diminish the numbers or inhibit the activities of pathogenic organisms, not merely *in vitro* but in the actual wound, then, although these reagents do undoubtedly cause the death of a certain number of body cells and prevent others from again reaching the tissues, this is a small matter if the invading organisms are at the same time materially diminished in numbers or in offensive capacity. It is the continuous and increasing effect of infection which is so inimical to healing. The occasional death of even large numbers of phagocytes is well borne if time be given to make up the loss. It is the strain of continued cell multiplication and the providing for the removal of organisms and cells that have perished in the struggle that tells.

The experimental introduction of pigment particles into a wound also throws a valuable sidelight on wound infection. In a general way the transportation of the pigment follows the same routes and the same lines of least resistance as those traversed by infecting organisms. The same peculiarities are apparent in the permeation of tissues and organs by the pigment granules. The liver, the spleen, the kidney, and the brain each presents its own special problem in emigration, phagocytosis, and return immigration.

Bearing in mind the fact that pigment particles are incapable of intrinsic movement, or multiplication, or growth, any transportation of pigment, in so far as it is not due to currents in the lymph or other fluids bathing the wound, must be due to the action of living cells.

It is interesting to find that the route taken by the pigment in the tissues generally coincides with the route taken by the infecting organisms; thus infection and return immigration roughly coincide. Several side-issues of considerable interest arise out of this problem of the return immigration of phagocytes. Unless the ingested cocci and bacteria which are carried into the tissues by the phagocytes on their return journey are killed, or sufficiently attenuated to render them incapable of further growth, they may start into renewed activity on the death and disintegration of the cells which contain them. It is possible that some cases of recrudescence of local sepsis may owe their origin to this cause.

The extent to which intrinsic motility and capacity for continuous growth enable pathogenic organisms to establish themselves in the walls rather than in the cavity or on the surfaces of a wound, no doubt varies with different organisms and in different tissues. The fact, however, that phagocytes are constantly transporting organisms from the cavity or the surface to the tissues which form the walls of a wound means that any adverse influence acting on these loaded cells on their return journey calculated to interfere with their power of retaining and digesting these ingested organisms is a source of danger. It is possibly in this way that antiseptic solutions act prejudicially when used too continuously or in a too concentrated form.

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REFERENCE.

¹ BRITISH MEDICAL JOURNAL, January 16th, 1915.

Notes on Military Orthopaedics.

III. THE SOLDIER'S FOOT AND THE TREATMENT OF COMMON DEFORMITIES OF THE FOOT.

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(Continued from page 753.)

PART III.

HAMMER-TOE.

HAMMER-TOE is a deformity which usually affects the second toe, though it is common to find slighter degrees of the condition in other toes. It consists of flexion of the proximal interphalangeal joint and dorsiflexion of the metatarso-phalangeal joint (Fig. 1). The prominent knuckle of the proximal interphalangeal joint chafes on the upper of the boot, while the tip of the toe is pressed on the sole. Painful corns naturally develop at these points of pressure, making the man unfit to march.

FIG. 1.—Hammer-toe.

The causes are numerous: sometimes the deformity runs in families, but the commonest cause is the crowding of the toes in ill-fitting, badly designed boots. Hence it is common to find hammer-toe associated with hallux valgus.

Treatment.

In the adult operative procedure is indicated if we are to produce a quick and lasting recovery. Neither amputation of the toe nor an attempt at pseudo-arthritis of the proximal interphalangeal should ever be undertaken. Amputation should not be done, because the absence of the second toe increases the tendency to the production of hallux valgus, and often leads to a second disability more serious than the original hammer-toe (Fig. 2).

FIG. 2.—The disability produced by amputation of second toe.

Some surgeons, when operating to correct the deformity, leave the articular cartilage on one side of the joint in order to obtain a new joint. My experience is that this is followed by recurrence so frequently that the operation should be condemned as uncertain.

Operation.

The operation found most uniformly satisfactory is a wedge-shaped excision removing the articular cartilage on

both sides of the joint, so as definitely to ankylose the joint in extension. An oval piece of skin, including the corn, is excised over the prominent knuckle. A wedge, base upwards, including the joint, is then excised, of sufficient size to allow the toe to be straightened (Fig. 3). The flexor tendon is divided by tenotomy. The skin incision is then

FIG. 3.—Wedge excision of joint for hammer-toe.

stitched so as to leave a transverse linear scar. The toe is fixed down to the toe-splint shown in Fig. 4, and the patient walks about, still wearing the splint inside his boots, for some weeks, to make sure that solid ankylosis occurs without any return of the deformity.

FIG. 4.—Splint for hammer-toe.

DISPLACEMENT OF THE LITTLE TOE.

A displacement of the little toe, similar in nature to hallux valgus, frequently occurs, usually as the result of wearing boots which are too tight and too pointed. Occasionally the condition is congenital. The toe is displaced inwards either over the dorsal or under the palmar aspect of the fourth toe. In either position it is subjected to undue pressure in any ordinary boot, and therefore becomes painful.

Treatment.

This condition is very troublesome, and when it occurs in a soldier an operation is essential. The treatment which may be applied successfully in children has no place here, as the structures have become so contracted, especially the skin, that tenotomies, excisions, or simple splintings are wholly inefficient. Amputation of the toe is simple and effective in most cases, especially if no callosities have formed under the metatarsal head. In amputating it is advisable to make an ample flap to obviate the result of subsequent contractures and to secure a lax fleshy covering for the bone. If a callosity has formed, no pressure should be allowed upon that area until by rest and treatment it has become soft and normal. If the head of the bone is arthritic and the condition is complicated by exostoses or irregularities, these should be pared away. Only in very exceptional circumstances should the head of the metatarsal be removed, for, as pointed out in a previous article, this forms one of the points of support in the foot on which a soldier's marching powers depend.

METATARSALGIA.

Metatarsalgia is a peculiarly painful disability of the foot associated with flattening of the transverse arch. The characteristic pain is usually felt in the fourth metatarso-phalangeal joint, frequently in the third, and less often in the second. The pain is variously described as a sharp stab, a burning pain, or as if the patient was "stepping on a red-hot pea." The pain may come on suddenly as the patient is walking in the street, and cripple him, so that he has to hobble into a shop and get his boot off. The device adopted by most patients to obtain relief is to grasp the metatarsals in the hands and squeeze them so as to restore the transverse arch. In more chronic cases the affected toe becomes glazed and shows signs of trophic disturbance, while in some cases there is complaint of severe pain shooting up the leg.

Morton in his original description attributed the pain to pinching of the digital nerves between the metatarsal heads. The fact that relief is obtained by squeezing the metatarsal heads casts doubt on the truth of this. I described the condition fully in 1897, and stated that,