

THE TREATMENT OF WOUNDED BY VACCINES.

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A VERY large number of wounded must have been treated with vaccines since the commencement of the war. Very little has been published on the subject, nor is the reason for this difficult to find. The results have not been impressive. Temperatures do not fall by crisis, nor discharges cease as if by magic. Careful statistics, compiled long after the termination of the war, may show some day that the duration of wounds has been shortened by vaccine treatment. At present we have to rely on clinical impressions to decide whether vaccines do any good at all. Perhaps we may reflect that it is not only vaccines which fail to find distinct confirmatory evidence of success in the severe septic cases brought over to Great Britain. If the principles of Listerism and modern surgery depended for their proof on the lessons of the war, probably the scoffer would remain unconverted. After watching a discharging wound being dressed for many months with sterilised dressings and gloved hands with little obvious improvement, he might be inclined to suggest that a little sepsis should be tried. Indeed, some of the best descriptions of the medical conditions of the present war are those written by Larrey, Napoleon's chief medical officer.

The following article is based on experience of the treatment of wounded at the British Red Cross Hospital, Netley. The principles stated are those which appear to be the best working rules. When diverging from them bad results have often followed. But the statements made are not intended to be too dogmatic. The slighter cases are rarely treated with vaccines, nor do they call for it. Hence the article in general applies to severe or indolent cases. Further, the patients are rarely seen within a week of being wounded, and the interval is usually two or three weeks or longer. I do not doubt that vaccines do good in such circumstances. In few instances will definite evidence be found, and the surgeon can sometimes parallel these with cases in which no injections were given. Certainly the effect of vaccines is not so marked as to render it justifiable to run risks of making the patient worse. Therefore the dose must always be on the side of caution, especially at the commencement. The greatest care must be used in this calculation of doses, but the weapon of vaccines is too powerful to be laid aside lightly.

The Measurement of the Action of a Vaccine.

The conditions to consider in deciding what action a vaccine is having are the temperature, the general condition, the amount of discharge, and the rapidity of healing of the wound. The temperature is the main guide.

Temperature.—The typical vaccine curve would be a slight rise, 0.5° to 1° F. for the negative phase followed by a fall. After a few days the temperature commences to rise again. A second dose may be given before this occurs, and then the cycle is repeated. Such typical curves are very rarely seen. If an injection causes a rise of more than half a degree, the patient is usually made definitely worse. Hence such a rise must be avoided. Even a rise of half a degree should be looked upon as a signal that the dose was too large. The curve to hope for

is one which falls steadily without rises after injections. As this is what occurs when a case does well without vaccines, by aiming at this we are cutting away any evidence of the action of the injection. Yet this gives the best results. Thus the object is to give the largest dose which causes no rise of temperature, and those cases do best which stand the biggest doses. The difficulty of attaining this object is obvious.

In chronic cases with normal or almost normal temperature, the object should be the same—that is, to give the largest doses possible without causing a rise of temperature. The afternoon or evening temperature on the day following injection is the most important. A rise of temperature more than 48 hours after injection may be referred to other causes. After such an interval the surgeon will similarly claim the credit of a fall.

The amount of discharge.—An increase may occur temporarily after an injection, but this has not the importance of a rise in temperature. If the temperature is falling an increased discharge is not an indication to give a smaller dose.

General condition.—Patients frequently describe headache and all manner of symptoms following an injection. Most of these may be neglected, but the general appearance, the pulse, and the appetite should be taken into consideration during a course of vaccines.

Indications for and against Vaccine Treatment.

Vaccine treatment is unnecessary for mild cases. Given by suitable methods, a vaccine is not contra-indicated by any degree of severity or acuteness. Whenever possible, an autogenous vaccine should be given. Obviously it is impossible to prepare a separate vaccine for each case. The more acute the condition is the more important it becomes that an autogenous vaccine should be employed, but while this is being prepared a stock vaccine should be used.

Character of the Bacteria Present in Wounds.

It is not intended to deal with this question beyond its bearing on vaccine treatment. At the present time streptococci are present in the great majority of septic wounds. Other organisms commonly found are staphylococci, bacillus coli, bacillus proteus, numerous strains of coliform bacilli, and bacillus pyocyaneus. Anaerobic and diphtheroid bacilli need not be considered.

Streptococcus.—The streptococci isolated agree, almost without exception, with the cultural characteristics of streptococcus pyogenes. Morphologically considerable differences occur in the size of the coccus and the length of chain. The smaller the coccus the more virulent it appears to be. When several varieties of bacteria are present it is not always possible to isolate the streptococcus in culture. The size of the coccus can be judged from the film, but it is doubtful whether the length of chain can be decided when only a few are present. When possible the growth in milk should be used for this purpose. Streptococcic vaccines may be labelled according to these differences—viz., size of coccus and length of chain, and when a stock vaccine is used that one is selected which appears to be nearest to the coccus of the case.

Bacillus coli.—Typical strains are frequently isolated. A bacillus which grows on McConkey's neutral-red bile-salt lactose-agar medium with permanent red colonies almost invariably gives the other typical cultural characteristics of bacillus coli. A stock vaccine of this may be employed.

Coliform bacilli.—Numerous strains of coliform bacilli are met with, differing in their cultural characteristics in various degrees and certainly differing in virulence. These strains grow on McConkey's medium with orange or yellow colonies and differ in the production of acid and gas in various carbohydrates, in the formation of acidity and clotting in milk, and in their action on gelatin, neutral-red broth, and other media. For example, a strain may have the following characteristics: Litmus milk, acid but no clotting; dextrose and lactose, acid but no gas; mannite and raffinose, no change; gelatin, no liquefaction; neutral-red broth, fluorescence produced; indol reaction negative. When possible, autogenous vaccines should be prepared. Apart from doing this, a separate vaccine should be prepared from each strain as it is found. The complete cultural characteristics of the bacillus are kept recorded, and when a stock vaccine has to be employed that one is selected of which the cultural characteristics agree with the bacillus of the case in question. This is a more satisfactory plan than the use of a polyvalent vaccine combined from many strains.

A laboratory can soon accumulate vaccines prepared from fifteen or twenty strains and can gain some knowledge of suitable doses to give of each. Different strains vary in virulence, and it appears that the less gas and the less acid formed in carbohydrate media, the greater is the virulence of the organism. It is possible that this may be extended to say the less change the bacillus produces in the culture media in which it grows the greater is its virulence.

Bacillus proteus.—This is found very frequently. It may be considered to fall within the group last described.

Bacillus pyocyaneus.—When this is the predominant organism the condition is nearly always mild or rapidly improving.

The presence of these groups of bacilli may be due to secondary infection of the wound by the patient, or they may be present on the muddy clothes and in the dirt carried into the wound on infliction. In a flesh wound of the leg of an officer a Gram-negative bacillus was present in pure culture with the following characteristics: McConkey's medium, orange colonies; litmus milk, acid, no clot; dextrose, lactose, and mannite, acid but no gas; raffinose and salicin, no change; gelatin, no liquefaction; neutral-red broth, no change. Such characteristics are distinct and not common. Had the infection been secondary and due to the patient this bacillus should have been recoverable from the stools, but no such organism could be found.

Staphylococci albus or *aureus* are present in most wounds. In comparison with the other bacteria they are of slight importance.

Dosage.

The endeavour is to give as large a dose as possible without producing a rise of temperature. The method of dosage described is based entirely on the treatment of wounds at Netley. Probably much larger initial doses and more rapid increases can be given without bad results in numerous cases, but if this is done there will be occasionally an unfortunate result with marked rise of temperature and severe symptoms, and when this happens the results are usually prolonged. The best improvement which can be expected from vaccines in the wounded cannot be held to counter-

balance a few such instances. When this hospital was first opened, larger doses were given and the results were unsatisfactory. Therefore it is only justifiable to commence with very small doses.

Initial Doses.

The following remarks refer to injections of simple vaccines. Mixed vaccines containing two or more bacteria are considered later.

Streptococci.—Commence with 1 to 2 millions, not exceeding 2 millions. When an autogenous vaccine is not being used, or during preparation, select a vaccine of similar size of coccus and length of chain. In general, the coarser the coccus the less is its virulence. For the administration of such doses a vaccine should be standardised to contain 10 million cocci to the cubic centimetre, and a stronger vaccine should also be prepared for use when larger doses have to be given. This may contain 50 millions or 100 millions to the cubic centimetre.

Bacillus coli.—An initial dose of 30 millions can be used.

Coliform bacilli.—The varying virulence of different strains has been referred to. Of the types which appear most powerful, forming little little acid and gas in carbohydrate media, the initial dose should be 2 to 5 millions. At the other end of the series will be bacilli more closely related to the typical bacillus coli. Of such strains probably larger initial doses may be given, but as a general rule it is inadvisable to inject as a first dose more than 5 millions of any bacillus which grows on McConkey's medium with yellow colonies. With strains which approximate to the bacillus coli the increase in subsequent doses can be made more rapidly in preference to commencing with larger doses. The same rule applies to bacillus pyocyaneus and also to bacillus proteus, which in wounds appear to be of higher virulence than bacillus coli.

Staphylococcus aureus.—It is rare to find staphylococcus aureus in pure culture except in secondary abscesses. An initial dose of 30 millions may be given.

Subsequent Doses.

As a rule five days should be allowed between successive doses. When a case is progressing satisfactorily each successive dose should be 50 per cent. larger than the previous one. But in the treatment of wounded it is rare for the bacteriologist to have a case which progresses satisfactorily from the first injection, and when he does he may temper his pride with the suspicion that it would have done as well without him. Some time during the course the temperature and progress will cause trouble, and the decision of the correct dose is a matter of very great difficulty. No such thing as routine treatment should be admitted. Every injection must be considered carefully and the surgeon consulted in any difficulty. Frequently he can give a simple explanation of a rise of temperature. The changing of a splint, the gathering of a small abscess, the visit of a relative or other common disturbing influences may be the cause.

Certain difficulties frequently met with will be mentioned. 1. If the temperature has obviously risen as the result of the previous injection, give a dose of half the amount. 2. The greatest difficulty in the vaccine treatment of wounds is the marked irregularity of temperature so commonly present. Thus over a period the evening temperature may be

about 102° F., with occasional rises to 103°. After the injection the evening temperature may be 103°. It is impossible to say whether or not this is the result of the vaccine. The following general rules have been adopted. If such a rise occurs after the first injection the same dose should be repeated. If on a third visit it is found that the temperature as a general average has remained the same, then an increase in dose should be made. This should be 25 per cent. Subsequently the temperature, though gradually subsiding, may remain irregular. The dose should be carefully increased by 25 to 50 per cent. each time. If after any injection the temperature has definitely risen the dose should be reduced to the amount of the last but one, or if the rise is marked to half of the last dose. 3. When a previously irregular temperature has fallen to normal it must be regarded with suspicion for some time, especially if the fall has been rapid. Frequently it will rise again. The opportunity to increase the dose unduly must not be taken.

Cases with acute septicæmia.—Such a condition is not a contra-indication to the administration of vaccines. Almost invariably a streptococcus is the causal organism. Time is so important that a stock vaccine should always be given while an autogenous one is being prepared. The injections should be repeated every two or three days. The initial dose should not exceed 2 million streptococci.

Mixed Vaccines.

Mixed infections occur in the majority of wounds. Numerous bacteria may be present—streptococci, staphylococci, bacillus coli, coliform bacilli, and bacillus pyocyaneus. The question arises whether a vaccine containing a mixture of bacteria should be given or whether we should confine ourselves to giving one species at a time. In the treatment of wounds this is a practical problem of great difficulty. Obviously it is far simpler to watch the effect of a simple vaccine. Undoubtedly the most important infecting bacterium is the streptococcus. Yet in the more slowly progressing cases the frequency and number of the coli group of bacilli impress one. In such circumstances a small dose of coliform bacilli may produce a marked reaction and tolerance to increases may be very small. It appears possible that the older and more indolent a wound is the greater is the importance of this group of bacilli. In deciding whether to give a mixed vaccine special attention should be directed to this point. Thus in a recent case a streptococcus should be treated as the predominant organism almost or completely to the exclusion of everything else, but the more chronic and resistant a case has been the greater should be the importance ascribed to the coli group of bacilli in the administration of the vaccine. Hence in the latter case a mixed vaccine of streptococci and bacilli should be given.

Next we have to consider, with a view to dosage, whether we can arrive at any conclusions as to the relative number of the different bacteria which were present actually in the wound. If we can do so it will influence the proportions to be given in a mixed vaccine. Undoubtedly this is very uncertain. A film of the pus will give some idea of the comparative number of cocci and bacilli, but it must be noted:—

1. With regard to cocci. When both are present it is usually impossible to estimate the relative number of streptococci and staphylococci from a

film, while in cultures a streptococcus is often hopelessly overgrown by staphylococci or diphtheroid or coliform bacilli.

2. With regard to bacilli. In a film the coli and coliform organisms cannot be distinguished. The incubation and plating of mixtures of known strength—for example, equal numbers of bacillus coli and bacillus typhosus—show how unreliable this would be as a measure of the relative numbers present in a wound.

Thus in practice a film of pus rarely tells more than the approximate relation of cocci and bacilli, and subsequent cultures cannot be relied upon. A further difficulty is the variation in virulence of different bacteria from the standpoint of numbers. Hence occasionally the film of pus may prove the predominance of a streptococcus. On the other hand, it is improbable that any excess of bacilli over streptococci would justify the assumption from this evidence that the bacilli were more important than the cocci. Therefore, practically, in deciding the doses of streptococci and bacilli to be given in a mixed vaccine the relative numbers found in a film or in cultures afford little assistance.

Dosage of Mixed Vaccines.

The initial dose of each bacterium need not be smaller than the amounts given above under the different headings. In subsequent doses the bacteria considered to be most important should be increased more rapidly than the other or others. If more than one is increased simultaneously to the same extent the cause of a rise of temperature after an injection cannot be ascribed to one species, and the dose of each has to be diminished. The most important bacteria should be increased according to the description given above—that is, by increases of 50 per cent.—while the others are increased by 33 per cent. In order to be able to vary the proportions in this way the vaccine of each type must be kept separate and the required dose measured from each bottle at the time of injection. However, some of the commoner combinations may be kept mixed. Thus frequently streptococci, bacillus coli, and bacillus proteus are present together, and a stock mixture of bacillus coli and bacillus proteus may be used in the proportion of three bacillus coli to two bacillus proteus, while the streptococcus is kept separate. It can rarely be advisable to give more than three types at the same time.

Operations on Septic Wounds.

A vaccine should not be given within 36 hours previous to any operation on a patient with a septic wound. Even a small counter-incision through healthy tissues is followed frequently by an immediate and marked rise of temperature and much discharge. During a course of vaccines such an operation should be considered to take the place of an injection, the next dose being given five days later. This does not apply to the commencement of injections in acute streptococcal cases of a septicæmic type.

NEW SANATORIUM FOR CONSUMPTIVES AT HAM GREEN, BRISTOL.—The erection of the new sanatorium for consumptives at Ham Green was commenced last September. The sanatorium will contain two pavilions for the treatment of convalescent patients, with 20 beds in each; one pavilion with 20 beds will be occupied by acute cases; and in addition there will be an administration block of three floors. The estimated cost is £12,000.