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ON

VACCINE THERAPY IN REGARD TO
GENERAL PRACTICE.*

BY

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I HAVE been practising vaccine therapy since it was in its infancy, and as time goes on I find myself more and more convinced of its efficacy, not only for the more severe cases which are to be seen at a hospital, but also and more especially for the lesser ailments which seldom appear at a hospital, but with which the practitioner has much to do.

An enormous amount of work has been done in the elucidation of the changes which take place in the animal body following the injection of a vaccine and much still remains obscure, but I confine myself to putting before you the clinical aspects of vaccine therapy in general, and to dealing with the treatment by vaccines of certain conditions, more especially those in which there have been advances made in the last few years.

DEFINITION OF A VACCINE.

A vaccine is a substance which, when injected into the animal body, induces the formation of specific antibodies.

This definition makes the term "vaccine" synonymous with the word "antigen." Originally vaccines were differentiated as being preparations of bacteria, but now various protein extracts—for example, pollen extract—are used in the same way in the treatment of disease, and there seems no reason why the term vaccine, if retained at all, should not be used in the wider sense to include all antigens. In the narrower sense, a vaccine may be defined as a standardized suspension of micro-organisms in an inert fluid.

AUTOGENOUS AND STOCK VACCINES.

An autogenous vaccine is a vaccine prepared from cultures obtained directly from the patient. A "stock vaccine" is made, not from cultures obtained from the particular patient who is being treated, but from cultures of the same type of microbe as that which is affecting him. In the preparation of a stock vaccine a considerable number of strains should be employed in order to eliminate as far as possible any small differences there may be in the individual strains.

*Should a Stock Vaccine be Used or an Autogenous One
be Prepared?*

This is not always an easy question to answer. In practice it is frequently dealt with from the point of view of expediency. In many cases where the infecting organism is easy to cultivate and the vaccine is easy to prepare, it is less trouble to prepare an autogenous vaccine than it is to identify the organism exactly. On the other hand, the isolation of the microbe and the preparation of the vaccine is frequently a very tedious and laborious proceeding, and in such cases, if the nature of the infecting agent is obvious, then a stock vaccine is often employed and an autogenous vaccine made only if the stock vaccine fails. In connexion with this question four different classes of cases have to be considered.

Class 1.—Where the vaccine is to be used for prophylaxis.

It is clear that here we have no choice. Only stock vaccines can be used. The fact that stock vaccines have been used with such signal success in the prophylaxis of typhoid, paratyphoid, cholera, plague, and the catarrhal infections of the respiratory tract, is of the utmost importance in that it shows that it is not necessary to insist on a vaccine being made of a microbe of exactly the same parentage as the infecting microbe so long as it belongs to the same species.

Class 2.—Where the nature of the bacterial infection is known but a culture of the microbe cannot readily be obtained from the patient.

Such conditions occur in connexion with tuberculous infections or where the infection is deep-seated—for instance, in the joints or glands. In such cases, again, there is almost no choice and we have to use stock vaccines, and the results which have been obtained with these in such cases show that good immunizing responses can be induced.

Class 3.—Where, owing to the profusion of contaminating microbes, it is difficult to identify and differentiate with sufficient sharpness one microbe from another of the same morphological species.

This applies especially to chronic catarrhal conditions of the respiratory and alimentary tracts, to putrid infections of wounds, and to the erosions often associated with malignant tumours. Here only a very experienced bacteriologist will be able to make satisfactory autogenous vaccines. In some cases it is quite impossible from the examination of a single specimen to say which of the many microbes present is the infecting agent, and in almost all it is extremely difficult to say which of the many varieties of streptococci is really causing the infection and which are merely leading a saprophytic existence. It will be advisable in many such cases, therefore, for treatment, and still more for prophylaxis, to employ the polyvalent stock vaccines made from a large number of strains of the microbes in question, especially as the stock vaccine can be prepared from cases in which there is no doubt as to the nature of the infection.

Class 4.—Where the infecting microbe can easily be obtained from the patient in pure culture.

These cases are very common, and when we have to choose between an autogenous and a stock vaccine in such conditions we have to balance the possible advantage of an autogenous vaccine against the labour and expense involved in procuring it.

A stock vaccine is indicated when the infecting organism belongs to a group the members of which differ very little among themselves. Thus, in staphylococcus infections, a stock vaccine will in almost all cases give as good results as an autogenous, and in some few cases the stock vaccine will prove the more beneficial. Occasionally a strain is encountered which proves to be a bad antigen, and if such a strain is isolated from a patient and an autogenous vaccine made little benefit will be derived from its use, whereas in the same case the stock vaccine, containing, as it does, a number of strains which have proved to be good antigens, would give a good result.

With *Streptococcus pyogenes* also, which is the cause of erysipelas, cellulitis, lymphangitis and many other septic conditions, it has been shown that if an animal is immunized to one strain its serum will agglutinate to the same extent all the strains. This experimental observation is in accordance with the fact observed clinically that *Streptococcus pyogenes* vaccine is one of the most effective of the stock vaccines.

Some species of bacteria, such as pneumococci, which were formerly thought to be very homogeneous groups, have recently been split up by immunological methods into three or four subgroups, and it is essential that a stock vaccine of these organisms should contain representatives of all the groups. When this is done stock vaccines of these organisms are very effective.

In connexion with some bacteria, such as *B. proteus*, it has been found that some of the strains when injected into animals give a good immunizing response against all the different strains of the microbe, while others give immunity only to one or two strains. When dealing with such microbes it is essential that the stock vaccine should be made from strains of general antigenic power and not from strains which are merely partial antigens. If the stock vaccine is not made in this way it is better to use an autogenous vaccine.

Other organisms, such as Pfeiffer's bacillus of influenza, differ even more one from another in their antigenic powers, so that if an animal is immunized with only one strain its serum will agglutinate that strain and not more than a very small proportion of the other strains. In such a case the stock vaccine must be made from a very large

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number of strains to ensure a wide polyvalency. A stock vaccine of Pfeiffer's bacillus made in this way has proved extremely efficacious, but in view of the immunological differences between the different strains an autogenous vaccine should be preferable.

A stock vaccine is indicated also in acute cases where it is desired to proceed with vaccine therapy at once without waiting for the preparation of an autogenous vaccine. In such cases it may be given in small doses while the autogenous vaccine is being prepared. If this is done it will often be found that by the time the autogenous vaccine is prepared the condition will have improved to such an extent that there will be little need to use it.

It is desirable to use an autogenous vaccine (a) when the infecting agent belongs to an ill-defined group of microbes. This is well exemplified in the so-called "*B. coli* infections," for the name is loosely applied to a large group of organisms which, as regards their antigenic properties, are very different. It is therefore more satisfactory in such infections to employ an autogenous vaccine. (b) When the infection is severe and it is felt to be too great a risk to wait to see whether the stock vaccine is effective; but it is wise in such cases to give a small dose of the stock vaccine while the autogenous one is being prepared. (c) When treatment with a stock vaccine has failed.

CLINICAL EFFECTS.

The clinical effects of the injection of a bacterial vaccine may be divided into two classes: (a) toxic and (b) immunizatory.

Toxic Effects.

These follow soon after the injection and the term "reaction" is applied to them. They fall under three headings:

1. *Local Reaction*.—This is the effect produced at the site of the inoculation. It varies enormously in the same individual with different vaccines and in different individuals with the same vaccine, and the intensity of the reaction has no known bearing on the general changes occurring in the individual in response to the inoculation. It varies from nothing at all to a brawny swelling extending for some distance from the site of the inoculation. Usually it consists merely of a slight local swelling and tenderness, and causes little discomfort. Apart from this discomfort it is of no importance. The local reaction is always more severe when the injection is made in a region which is subject to pressure of the clothing, or which does not contain much subcutaneous fat, and is situated over muscles which are constantly in use (for example, the forearm). The best sites for inoculation seem to be in women about two inches below the centre of the clavicle or behind the shoulder, and in men the flank also is very suitable.

2. *Focal Reaction*.—This is the term applied to the effect of an inoculation of vaccine on the focus of infection. With a small dose there is no apparent focal reaction. With a larger dose there is some increase of the inflammatory signs in the infected focus. With a very large dose there may be a very great exacerbation of the symptoms which may result in the necrosis of the infected tissues. With the average dose there is, however, little or no focal reaction.

3. *General Reaction*.—Small doses of vaccine are not followed by any general toxic manifestations, but very large doses are apt to be followed after a few hours by signs of a general intoxication. A mild general reaction consists merely of a little malaise, but if the reaction is severe then there may be rigors, sweating, high fever, and even diarrhoea, sickness, or collapse. Doses of vaccine causing severe reactions should never be used. This general reaction is caused in part by the toxic substances which are introduced in the vaccine, but it is also probably caused largely by the absorption of toxic material from the infected focus which has at the same time been much disturbed by the focal reaction.

Immunizatory Phenomena.

1. *Focal*.—These focal changes vary so much in their character, and the time it takes for any appreciable benefit to ensue varies so much with the nature of the infection, that it is not possible to generalize further than to say that after twelve hours or longer there is a diminution in the inflammatory symptoms.

2. *General*.—Usually the first beneficial effect following the administration of a vaccine is a feeling of well-being in the patient. When small doses are used this may follow within an hour or two, and it is frequently very striking. When the patient is running a slight temperature, a small dose of vaccine administered in the morning will bring the temperature down the same evening. This fall in the temperature coincides with a rise in the antibacterial content of the blood.

It has frequently been urged that in acute cases it is of little use to give vaccines, as it takes a week or more before any result of the vaccine can be seen. As I have stated above, the beneficial result of a suitable dose of vaccine may be manifest in a few hours, and a reference to the accompanying

chart will show the effect of the correct dose of vaccine on the temperature chart. It will be observed that the effect of the vaccine administered about midday

was to prevent the evening rise of temperature the same day and to keep the temperature down for some days. The same effect on the temperature is seen after the second inoculation.

The patient to whom this chart refers was suffering from a septic compound fracture of the femur, and for about three weeks had had a septic type of temperature similar to that for the three days indicated in the chart previous to the inoculation.

DOSAGE OF VACCINES.

Speaking generally, the aim of the vaccine therapist is to give the maximum dose which will not give rise to a general reaction in the patient. In the consideration of the dose which is to be administered to any particular patient there are several factors which have to be taken into account. In the first place, it is a general rule that the more severe the infection the smaller should be the dose of vaccine administered. This, on the face of it, does not seem to be unreasonable, as the patient who is suffering from an acute infection is absorbing much toxic bacterial substance from the focus of infection, and if a large dose of vaccine is administered on the top of this, then it may easily constitute an overdose, and it is in just such a case that an overdose is to be avoided. Secondly, the toxicity of the particular vaccine which is going to be administered has to be considered. Some vaccines can be given in large doses, even in acute cases, without the slightest reaction, whereas with others great care must be taken in feeling one's way, otherwise an alarming reaction may occur. Thus, with *Streptococcus pyogenes* in an acute case it is well to begin with not more than two million cocci, whereas with Bordet's bacillus of whooping-cough or with Pfeiffer's bacillus of influenza very large doses can be given even in acute cases with impunity. In connexion with the dosage of vaccine, therefore, we have to consider several different classes of cases:

1. Where the infection is a chronic one, and where even if there is a small flare-up it will not seriously inconvenience the patient—for example, sycosis or furunculosis. Here the dose should be rapidly increased—and by a rapid increase I mean successive increments of 50 to 100 per cent.—until there is a very marked improvement or until there is evidence that a slight overdose has been given as evidenced by an exacerbation of the local condition or by some fever or malaise after the inoculation—that is, until there is a focal or a general reaction. When there is evidence of this overdose, then the next dose should be reduced to the last one which failed to produce any "reaction," and the subsequent increases should only be gradual. If there is marked improvement before any "reaction" is evident (as is very often the case), then the same dose which has induced the improvement should be repeated several times, as evidently something approaching the optimum dose for the particular patient has been found.

2. Where the infection is a chronic one, but where it is not safe to risk any considerable exacerbation of the condition

—for example, chronic bronchitis. Here the best procedure is to give a safe dose and to increase the dose only gradually. By this means improvement will be seen without any danger of upsetting the patient. A little time may be lost in finding the most suitable dose, but in such a case this is infinitely preferable to the risk of setting up an acute infection.

3. In acute infections where it is essential that no "reaction" should be induced—for example, bronchopneumonia, erysipelas, etc. The same procedure should be adopted as in the preceding case, but the initial dose should be smaller (roughly one-quarter). In cases of this description it is wise to give very small doses and to repeat them often (every twenty-four or forty-eight hours if necessary). In all cases where with a certain dose there is definite improvement manifested, it is wise to repeat the same dose next time and possibly for several times. If, instead of doing this, the practitioner increases the dose according to a definite prearranged scale, then it is quite likely that he will rapidly increase the dose beyond the optimum and undo all the good which he has done with his first doses.

Here I should like to put in a word of caution to the practitioner against slavishly following the scale of doses which commonly accompany a vaccine from the laboratory. In many cases an autogenous vaccine is sent out from a laboratory in a series of ampoules, each ampoule containing a larger dose of the vaccine than its predecessor, and in many cases these doses are injected into the patient at intervals of a week or thereabouts without regard to the action of any one of them on the patient's condition. The scale of doses is given in all good faith by the bacteriologist, but it must be remembered that at the best this scale only represents the average dose and any individual may differ far from the average. It must be remembered, also, that in a great many laboratories, and especially in the commercial laboratories not attached to hospitals, the bacteriologist may have very little experience of the actual treatment of patients with vaccines, however skilful he may be at the isolation of bacteria and the preparation of vaccines. His opinion, therefore, as to the dosage of the vaccines is often taken only from what he has learnt from someone else, and it may be extremely fallacious.

A Successful Result with Vaccine Therapy.

When the microbes are exposed to the full effect of the antibacterial substances elaborated as a result of the injection of vaccine, then the result should be rapid and favourable. When, on the other hand, the microbes are enclosed in inflammatory tissue and in tissue where, as a result of the inflammation there is a greatly diminished blood and lymph supply, they will be partially sheltered from the antibacterial substances and the result will be much slower and less certain. Where the microbes are contained in some necrosed material such as a slough or sequestrum, it is unlikely that the antibacterial substances which may be produced will have any influence on the bacteria which are so hidden, although they may limit the infection and prevent its spread to the surrounding tissues.

It follows from this that in incipient infections a rapid success may be obtained, but where the infection is of old standing and the circulation through the infected focus has become impeded success will only be obtained after a long series of immunizing doses, while in cases where there are sloughs or collections of pus success with vaccines will only be obtained after the sloughs have been removed or the pus has been evacuated by surgical means.

When a vaccine is given for *prophylactic* purposes it is not to be expected that the immunity will be absolute. Even when an individual is highly immune he may receive such a large dose of a virulent organism that infection will result. It is doubtful whether a vaccine will ever be produced which will confer such immunity that the individual is resistant to the strongest infection. The vaccine will, however, confer immunity to a moderate infection, so that a disease like typhoid fever, instead of assuming epidemic proportions, will occur in an inoculated community only in a few individuals here and there who have either received an enormous infection or whose immunity may have been temporarily reduced by privation or other cause.

CLINICAL APPLICATION.

I now wish to discuss the vaccine treatment of some of the conditions which are common in general practice.

Catarrhal Infections of the Respiratory Tract.

I will commence with these first, because at this season of the year they are very much in evidence, and secondly, because in no conditions is the practitioner likely to achieve greater success with vaccines.

The bacteriology of the whole respiratory tract is roughly the same, and the three microbes which are most commonly in evidence in infections of this region are the pneumococcus, streptococcus, and Pfeiffer's bacillus of influenza. There are others, such as the *Micrococcus catarrhalis*, *Bacillus septus*, Friedländer's pneumonia bacillus and staphylococcus, which are at times found, but infections with these are not so common.

In all these catarrhal infections of the respiratory tract we must bear in mind that we are all constantly being exposed to infections with one or other of these microbes as the number of carriers is legion. It was shown during the war that when there was an epidemic of cerebro-spinal meningitis—which is caused by an organism which inhabits the respiratory passages—there were among the people of the infected camps a very large number of carriers. During the influenza epidemics it was shown that in some communities more than half the population were harbouring in their respiratory passages the pneumococcus and Pfeiffer's bacillus, while it is probable that nearly all of us constantly have pathogenic streptococci in the mouth and post-nasal spaces. It is evident, therefore, that every one is being very frequently brought into contact with these microbes which are responsible for the catarrhal conditions, and there is no doubt that we have all acquired a certain amount of immunity. It is common knowledge that individuals vary enormously in their susceptibility to these infections; some people hardly ever get colds, others are constantly picking them up.

When we examine these "colds" bacteriologically we find that while some individuals (and these are in the minority) get many "colds" which are always caused by the one microbe, others (the majority) are infected by one microbe at one time and by another at another time. The same is seen in many cases of chronic bronchitis. The flora is not constant, but one microbe may be there for a time and then it will disappear and its place will be taken by another. This varying flora makes the treatment of respiratory conditions more complicated, but it has had one good effect as regards the vaccine treatment by the practitioner, and that is that it has caused the mixed polyvalent vaccines to be introduced. For routine vaccine therapy practice where many patients have to be dealt with, and where there is not the opportunity of having extensive bacteriological investigations done on each patient, these polyvalent mixed vaccines have met with very great success.

When a sputum is sent to the laboratory from a case of chronic bronchitis, often there is found a very mixed flora, and it is extremely difficult to say which is the infecting organism and which of the organisms are merely growing saprophytically. In such cases better results are very often obtained with the mixed stock vaccines than can be got with autogenous vaccines. There is no doubt that in the period before the influenza epidemic, in very many cases of chronic bronchitis, Pfeiffer's bacillus was missed in the examination of the sputum; it is not very easy to see in a stained specimen of sputum, and the methods of cultivation were very indifferent, so that in very many cases autogenous vaccines were made which did not contain this, which was probably the most important part of the infection.

The Common Cold.—The mixed stock vaccine (0.2 c.cm.) should be given immediately the "cold" is noticed, and in a certain number of cases the attack will be aborted. Even when the cold has developed, the vaccine will generally cut short the attack, and especially the last stage, when there is a profuse muco-purulent discharge from the nose without constitutional symptoms. The vaccine also seems to prevent the infection spreading down to the bronchi. With the common cold, however, the chief value of the vaccine is in prophylaxis. In people who are susceptible to colds the anticatarrhal vaccine should be given in the

autumn in three doses—0.25, 0.5 and 1 c.cm.—and during the winter monthly doses of 1 c.cm. may be given. It has been common experience that by this means people can be kept free from colds who, without the vaccine, were having one attack after another during the winter.

Bronchitis.—The bacteriology of bronchitis is roughly the same as that of the common cold, and very often the attack begins with a cold. If the infection is simple, an autogenous vaccine may be made, but usually the mixed stock vaccine does all that is necessary. Doses of from 0.25 to 1 c.cm. of the mixed vaccine for colds or of the anti-catarrh vaccine are given at intervals of from three to seven days, and after the first one or two doses the patient notices the improvement. The condition usually improves rapidly up to a point at which it gives little trouble to the patient, and when this stage has been reached, if larger doses are given monthly the infection gradually disappears.

Influenza.—By this term I mean the acute epidemic influenza and not the catarrhal conditions which are loosely called influenza by the public. During the recent epidemics vaccines have proved of very great benefit both in the prophylaxis and in the treatment of the complications of this disease. The primary cause of the infection is obscure. There are two schools: one holds that Pfeiffer's bacillus is the primary infection, and the other that the nature of the infection is yet unknown. There is not the slightest doubt, however, that Pfeiffer's bacillus, together with the pneumococcus and streptococcus, is responsible for the complications of the disease, and it is to them that the bronchopneumonia which caused the mortality was due. Exact figures as regards the influence of the vaccine on the epidemic were not easy to obtain, but a very interesting and important communication was published by Sir William Leishman, on the results in the military camps in England during the last wave of the epidemic, which showed that the incidence of the disease was reduced from 47.3 to 14.1 per 1,000 and the mortality from 2.25 to 0.12. Even allowing a very considerable margin of error, these figures are quite enough to prove that the vaccine was of enormous benefit in reducing the mortality. The vaccine which was used in these experiments was one which only contained a small dose of Pfeiffer's bacillus, and it has now been modified, so that it is more than likely that with the new vaccine the results would be even better than is shown by Sir William Leishman's figures. As regards the composition of the anti-influenza vaccine, there are many different combinations on the market containing varying proportions of the three microbes which are involved. Of these different vaccines, I think that the best combination is the one which we prepare at St. Mary's Hospital, which contains 500 million Pfeiffer's bacillus per cubic centimetre, with 1,000 million pneumococci and 100 million streptococci. The Ministry of Health vaccine contains a smaller dose, and especially a smaller dose of the pneumococcus, and is really a compromise between the old army formula and the St. Mary's Hospital formula. It has been shown, especially by Lister in South Africa, and by the American army authorities during the war, that very large doses of pneumococcus can be given with impunity and that better immunity followed these larger doses than was obtained with the smaller ones.

Treatment.—It has been the experience of many practitioners that small doses of one of the anti-influenza or anti-catarrh vaccines was of very great benefit in the treatment of the bronchitis and bronchopneumonia which followed influenza. Doses of about 0.1 c.cm. of the prophylactic vaccine were given immediately and repeated in twenty-four hours if the temperature still remained high.

Pneumonia.

During recent years great advances have been made in the treatment, and more especially the prophylaxis, of pneumonia by means of vaccines.

In 1913 Sir Almroth Wright published results showing that among the natives employed on the mines in South Africa the administration of vaccines had a very definite effect in reducing the incidence of and mortality from lobar pneumonia. He also showed that vaccine given in the incubation period not infrequently aborted the attack—this latter observation proving that the administration of pneumococcus vaccine was not followed by any prolonged

negative phase such as sometimes follows typhoid vaccination. At the time that Sir Almroth Wright's observations were made it was not appreciated that pneumococci differed among themselves as regards their antigenic properties, but soon after it was shown by Dochez and Gillespie that pneumococci could, by immunological methods, be split up into several groups more or less definite. These observers found that there were three definite groups of pneumococci, and besides these there were a number of cocci which did not fall into these groups, and these they made a conglomerate group which they designated Group 4. It was shown that a vaccine of a pneumococcus of Group 1 would protect against an infection of Group 1 but not against the other groups; Group 2 vaccine would protect against Group 2 but not against Group 1, and so on. Lister, who continued Sir Almroth Wright's work in South Africa, ascertained which were the common types of pneumococci causing pneumonia on the Rand, and he prepared a mixed stock vaccine containing all the types, which he administered to the natives in large doses with wonderful effects as regards the prevention of the disease. The table given below, which is taken from Lister's work, refers to the incidence and mortality of pneumonia on one of the large mining compounds where there was a native population of something like 15,000 men, and it will be seen that whereas the incidence

Table showing the Pneumonia Returns of one of the South African Mines for the Years 1908 to 1913, also for the Experimental Period from November, 1916, to October, 1917, inclusive.

Year.	Incidence per 1,000.	Mortality per 1,000.
1908	70.71	14.17
1909	104.85	17.97
1910	153.54	28.97
1911	128.98	26.94
*1912	67.68	19.96
*1913	31.75	4.80
†1914	—	—
†1915	—	—
Experimental period, November, 1916, to October, 1917	4.67	0.86

* During these years the inoculations were carried out in accordance with the principles advocated by Sir Almroth Wright and his associates.

† No record on account of war conditions.

of pneumonia before vaccine therapy was instituted was 70 or more per 1,000, it dropped during the year when Lister was giving his vaccine consisting of mixed types of pneumococci to about 4 per 1,000. The effect on the mortality from the disease was even more striking, as this dropped from about 20 per 1,000 to 0.86. There can be no question from these figures that pneumococcus vaccine is of extreme value as a prophylactic, and if further evidence was required it is furnished in the various reports from the camps of the United States army during the war. Pneumonia was one of the great scourges of the American camps, but by the use of vaccines the incidence and mortality from this disease was much reduced.

As regards the treatment of lobar pneumonia with vaccines it is much less easy to obtain reliable figures owing to the great variations which are observed normally in the course of the disease. Wright's observation that the disease can be prevented by inoculation during the incubation period shows that large doses of the vaccine can be given with safety and without producing a negative phase, and a number of reports have been published showing that the administration of vaccine shortened the disease and hastened the crisis. It must be remembered, however, that when the lung is consolidated there is a very large amount of tissue swarming with pneumococci through which the circulation is greatly impeded, so that even if a certain amount of immunity is produced the immune bodies will have difficulty in obtaining access to the seat of infection. There seems to be no doubt that the administration of vaccine aids the resolution of the pneumonia and hastens recovery.

Whooping-cough.

This disease is caused by Bordet's bacillus, but very soon after the onset there appear, just as we see in influenza, Pfeiffer's bacillus and pneumococcus. For the treatment of the disease, therefore, a mixed vaccine should be given. The technical difficulties of isolating Bordet's bacillus make it almost imperative in practice to use a stock vaccine, and such a vaccine should contain all three of the bacteria mentioned above. This vaccine is very little toxic, so that even for small children comparatively large doses (1,000 or 2,000 million) can be given, and it is well to repeat the doses every two or three days instead of at the longer periods which are common with the other vaccines.

The administration of the vaccine cuts short the attack and prevents complications.

It is for prophylactic purposes that the whooping-cough vaccine will be found of greatest value to the community. Either a simple vaccine of Bordet's bacillus may be given or a mixed vaccine of this bacillus combined with Pfeiffer's bacillus and pneumococcus. Three doses of the vaccine should be given at intervals of a week, and it has been found that in some communities of children whooping-cough has been almost wiped out by this means. I should strongly advocate prophylactic vaccination in institutions where there are aggregated together numbers of children, and also in families where one of the children has become infected.

Chronic Rheumatic Conditions.

I include under this heading rheumatoid arthritis, fibrositis, neuritis, sciatica, myositis and similar complaints. These all seem to take their origin from some chronic infection, which is usually streptococcal. The site of the infection is usually in the mouth or the intestine, and the streptococcus which is responsible is very different from the *Streptococcus pyogenes*, which is the causative agent in acute septic infections such as erysipelas or acute septicaemia; it is of very much less virulence, so that it may infect a portion of the body for years without causing more than slight inconvenience. It is because of this that infections of this type are allowed to persist, maybe, for many years, and it is often only when some serious result, such as rheumatoid arthritis, is seen that any attention is paid to the original infection. A common history of a patient with rheumatoid arthritis when she comes to the out-patient department is that she had bad teeth for years, and when she consulted her doctor she was told to have all her teeth out. This was followed by only temporary improvement, after which the arthritis progressed as before. On examination of such a patient's stools, it will in all probability be found that there is an enormous preponderance of streptococci, and more especially of streptococci of the mouth type. Doubtless the infection commenced in the mouth, but some of the streptococci which were being continually swallowed escaped destruction by the gastric juice and bile and established themselves in the intestine, where they had continued to flourish.

The effect in such cases of the administration of vaccines, either autogenous or stock, has been that in almost all there is some alleviation of the condition, and in some there is apparently complete disappearance of the disease. In some few there is apparently no benefit, which is not surprising considering the difficulty in isolating the organisms from the intestine and the multiplicity of types of streptococci found there. Considering, also, that the source of the streptococci is the intestine, which is to all intents and purposes outside the body, it must be appreciated that the course of vaccine treatment must be long, and it is seldom that recovery will take place in less than a year. Owing to the multiplicity of types of streptococci in the mouth and intestine it is frequently better to commence treatment with a mixed stock vaccine such as the anti-rheumatic vaccine which we make at St. Mary's Hospital and which contains a very large number of strains of streptococci from rheumatic patients, and only to proceed with an autogenous vaccine if the stock vaccine fails. If this is done, only comparatively seldom will an autogenous vaccine be required.

Diphtheria Carriers.

Brownlie (*Lancet*, March 27th, 1920) showed that by the administration of a vaccine the diphtheria bacilli could be

got rid of in a very much shorter time than by any other means. Out of a series of 50 consecutive and unselected cases who received the vaccine in doses of 10 to 60 millions every four days 44 were free from bacilli after three doses, and all were free after eight doses of the vaccine. If these observations are confirmed it would seem that for public health purposes this vaccine of the diphtheria bacillus would be of the greatest value.

Other Conditions Suitable for Vaccine Treatment.

Vaccine therapy is applicable to very many conditions other than those on which I have touched, but time prevents my going into these. Local tubercle, acne, staphylococcal infections such as boils and carbuncles, streptococcal infections such as erysipelas or pyorrhoea, and many others have been successfully treated, and indeed vaccine therapy in these conditions seems to furnish the only direct means of combating the infection. Many publications have been made on these matters, and I need not weary you with recital of the merits of vaccines in these conditions which have been treated in this way for many years.

In conclusion, I wish to draw attention to the fact that patients may be inoculated with bacterial products not only from without, but also introduced into their circulation by some disturbance of the infected focus. It has been shown by means of blood examinations that any such disturbance is followed by a sequence of events which are the exact counterpart of those following the administration of vaccines by hypodermic injection.

It does not matter what form the disturbance takes—whether exercise, massage, forcible movement or the active hyperaemia induced by the application of a fomentation—the result is the same, the only difference being that, whereas the light forms of disturbance reproduce the effect of a small dose of vaccine, the more severe disturbances may be followed by the same events which follow a large dose of vaccine, and to which I have alluded above under the heading of "General Reaction"—namely, malaise, fever, or even collapse.

It follows from this that in the treatment of any patient by vaccines a satisfactory conclusion is only to be arrived at if this phenomenon of auto-inoculation is considered, and in most cases it is necessary that these auto-inoculations should be diminished or abolished by keeping the infected part as much as possible at rest by splinting or some other means.

In some conditions, such as phthisis, it is very difficult to control these auto-inoculations, and it is probable that the very indifferent results which have followed the administration of tuberculin in this condition in many cases have been due to this fact.

THE SEROLOGICAL CHARACTERS OF DISEASE-PRODUCING PNEUMOCOCCI.

BY

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RECENT investigations on several groups of micro-organisms, of which the meningococcus group may serve as an example, have proved the value of discrimination between disease-producing strains on the one hand and non-pathogenic saprophytes on the other. Such discrimination has been rendered possible by the general method of testing the agglutination reaction of a particular strain against specific serums, previously prepared by inoculation of rabbits with typical organisms from morbid lesions. By this means disease-producing micro-organisms have been gradually relegated to types.

The diversity of the clinical picture presented by pneumococcal pneumonia, the wide prevalence and severity of this disease, and the fact that the pneumococcus is a normal and usually harmless inhabitant of the upper respiratory passages, has suggested that distinct disease-producing types of the organism may exist.

Such has been shown to be the case by American workers at the Rockefeller Institute for Medical Research,¹