VACCINES AND VACCINE THERAPY.

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IT is impossible in a short article like this to give a full account of such a large subject as Vaccines and Vaccine Therapy. This would involve, to begin with, a discussion of the principles underlying this form of treatment and that, in itself, would take up too much space. We will therefore content ourselves with a superficial glance at the principles of vaccine therapy and after that the preparation of vaccines and their uses in the treatment and prevention of disease.

The best definition of the principles of vaccine therapy is that of Sir Almroth Wright, who says, "the fundamental principle of vaccine therapy is to exploit in the interest of the infected tissues the unexercised immunising capacities of the uninfected tissues." Let us now consider what this means. Some part of the body is invaded by micro-organisms, it may be the subcutaneous tissues, the lungs, the bladder or the intestines. These germs proceed to elaborate their toxins or poisons which are discharged into the body ; and by them, the symptoms of disease are produced. The body, at the infected part, does its best to repel these invaders and proceeds to produce antitoxins, or antibacterial substances which tend to neutralise the toxins or to destroy the invading germs themselves. In the great majority of cases, the tissues at the infected part are able to defend themselves and cure results, but, from time to time, the toxins gain the upper hand and the disease persists. With vaccine therapy, we endeavour to help the tissues to develop their own antitoxins or antibacterial substances in some healthy part of the body These antibodies then travel by the blood stream to the infected part and help to turn the tide in favour of the body. To supply the necessary stimulus to the healthy tissue, we inject bacterial vaccines which may be defined as the sterilised and standardised emulsion of any micro-organism. At first sight, one would imagine that the injection of a vaccine into the body would simply be placing more poisons into the system, and that thereby the body would have a harder task to perform, but this is by no means the case. To begin with, the germ is dead and therefore it cannot multiply and produce more toxins, and secondly, the injection is carried out on a healthy piece of tissue, which, if the dose of vaccine is correct, must undoubtedly win ; in which case, an excess of antibacterial substance is produced which passes into the blood and thence to the infected part. The body thereby gains victory over the invading germs ; we can see, therefore, that our great endeavour is to force the healthy tissues to declare in favour of the body instead of remaining passive and doing nothing.

We thus see how a bacterial vaccine can be used as a curative agent. They are also extensively used as prophylactic or preventive agents. The principles involved here are precisely the same as above. The dead micro-organisms are introduced into the healthy body and the tissues produce the antibodies in excess. This excessive production goes on for some time after inoculation and circulates in the blood till the special germ invades the tissues. The antibodies then come into action and the invading germ is killed off before it can do any damage. These vaccines do not produce immediate protection, in fact, after inoculation, there is a negative phase, short though it may be, in which the person is more susceptible than usual; but for practical puposes this negative phase may be neglected. The antibodies which are produced under the stimulus of inoculation are of many kinds and act in a variety of ways. It has been shown that, amongst others, "opsonins" are produced. These opsonins aid the corpuscles in the blood to deal with the bacteria. They are specific, *i. e.*, there is a different opsonin for each kind of micro-organisms and they act on the germs present, so that the white corpuscles can ingest and digest them. Sir Almroth Wright has devised a method by which the amount of opsonins in the blood can be measured. It depends on the power of the leucocyte to ingest bacilli. The ratio between the opsonins present in the injected individual to the amount present in the normal individual is called the "opsonic index." This index is of use as a control in the administration of vaccines because its increase or decrease after inoculation points to increased or decreased immunity. After an injection of vaccine, the opsonic index falls slightly and then begins to rise if the dose given is correct. When it reaches its maximum, a second dose is given and the index rises still further. The injections are then continued at suitable intervals so that the opsonic index continues at a high level. This means that there is a large increase of opsonins present in the blood, and as a result, that the body is highly protected against any specific disease according to the germ used for inoculation. This opsonic index, though theoretically of great value, is found wanting practically in many respects. It varies considerably in normal persons from time to time and also is extremely difficult to carry out in a satisfactory and reliable manner. For this reason, many medical men prefer to judge the result of vaccine inoculations by the amelioration in the symptoms or otherwise.

The diseases in which vaccine-therapy has proved of the greatest value are those of a chronic localised nature, like acne, boils, &c. This is only natural. As already stated, when a germ invades the tissues, antibodies are produced which counteract the influence of the toxins.

Thus, this attack and defence goes on in the body which gradually gets more and more immune and finally the disease is cured. Frequently, however, from a variety of causes, the body is unable to cope with a particular infection. In a chronic case, the poisons produced by the bacteria are small in amount, hence the reaction of the body is equally small and the disease persists. We can then step in with our vaccines and stimulate some healthy part of the body to produce antibodies in sufficient amount to overcome the original infection. The doses of vaccine used must be appropriate in amount and the interval between the injections must be well timed.

Before proceeding further, let us now briefly summarise what has been said about vaccines and their action:—

1. Vaccines are standardised, sterilised emulsions of micro-organisms.
2. They are specific, *i.e.*, the vaccine of a particular germ is efficient against that germ only.
3. Vaccines act by stimulating normal tissues to produce antibodies which are carried in the blood to the infected parts where they help to neutralise the toxins of the invading germs.
4. The chief antibodies produced are opsonins which act on the micro-organisms and enable the white blood corpuscles to ingest and digest them.
5. The opsonic index is the ratio between the opsonins in the infected person and in the normal person. It is useful for measuring the degree of immunity.
6. Bacterial vaccines are of greatest value in chronic localised infections.
7. The inoculations must be carried out in carefully regulated doses and at well timed intervals.

Preparation of Vaccines.

The particular micro-organisms, from which the vaccine is to be prepared, is grown on a tube of agar or some other suitable nutrient medium. The growth is allowed to proceed for a certain time and at the end of that time, an emulsion of the organism is made with salt solution. This emulsion is then standardised by counting the number of bacilli in a certain volume of fluid. The method of counting is quite a simple one but space forbids a description of this method here. After standardisation is complete, the emulsion is then sterilised by heat or antiseptics. The vaccine is then bottled and labelled as containing so many bacilli per cubic centimetre.

Method of Inoculation.

Vaccines are usually administered by subcutaneous injection in the ordinary way. Administration by the mouth is uncertain as is also the rectal method. This, however, is a point of little importance as the subcutaneous method is quick, sure and simple. Sir David Semple recently tried some experiments with intra-muscular injection but found that this method was in no way superior to the subcutaneous method.

Uses of Vaccines.

Typhoid Vaccine.—This vaccine is of great value as a prophylactic against typhoid fever. Its use in the army in India and South Africa has proved this and it may be said that in an inoculated person, the risk of infection is diminished by a half and when he does contract the disease, the chance of mortality is also diminished by a half. Numerous instances could be quoted showing its undoubted value as a prophylactic. Typhoid fever is a particularly fatal disease to Europeans in India, and for this reason, everyone on his arrival into this country, should be inoculated against this disease. The best protection is obtained with two inoculations at an interval of 10 to 15 days. The second dose is double the first. There may be a slight constitutional disturbance after inoculation, but this very quickly passes off. Re-inoculation should be carried out every two years. This vaccine is also used in much smaller doses as a curative agent. Sufficient evidence, however, is not forthcoming to warrant any definite statement as to its routine use in the disease.

Plague Vaccine.—This consists of a dead culture of plague bacilli and its use as a prophylactic against plague is of great value. When a person is likely to be exposed to plague infection then he should be inoculated against the disease.

Staphylococcus Vaccines.—With this group of vaccines, vaccine therapy has gained its most brilliant successes. Staphylococci are the causal micro-organisms of abscesses, boils and many other septic lesions. Their vaccines can be used as prophylactics but their chief use is as a curative agent. There are many strains of this germ and for this reason, the standard vaccine may fail in its action. Now-a-days, the common practice is to prepare an "autogenous" vaccine, *i.e.*, the germ causing the particular lesion is isolated from the patient and grown in the usual way; so that the vaccine prepared contains exactly the same strain of germ as that causing the disease These vaccines, standard or autogenous are used in a great many conditions, of which the chief are boils, carbuncles, furunculosis, &c. In the case of acne, a special acne-bacillus has been shown to be the causal micro-organism and from it a special

acne-vaccine has been prepared. It has been found that where the staphylococcus aureus is the causal organism in a lesion, the addition of some staphylococcus albus aids its action greatly and for this reason, a staphylococcus vaccine is practically always a mixed one, containing the autogenous vaccine and some staphylococcus albus vaccine. The dose of this mixed vaccine is about 250 millions of the aureus and 150 millions of the albus. The correctness of the dose can be estimated either by the opsonic index or by noting whether there is any improvement or not in the condition of the patient. Where an autogenous vaccine is used, the first dose must, of necessity, be more or less a shot in the dark but if the opsonic index rises after it, then it is fairly correct, while if it falls, then too much has been given and the second dose must be smaller. This vaccine may be given once a week or oftener.

Streptococcus Vaccine.—The streptococcus is a virulent type of micro-organism and is the cause of many serious conditions, such as erysipelas, puerperal fever, septicæmia, cellulitis, ulcerative endocarditis, and possibly, scarlet fever. It will thus be seen that there are here, as in the case of the staphylococcus, a great many strains of the germ. For this reason an autogenous vaccine may be prepared from the patient or a standard vaccine may be used. This standard vaccine is prepared from many strains of the streptococcus obtained from a variety of lesions and is used in any case of streptococcal poisoning, in the hope that one of the strains may be the correct one. These vaccines have been used in a variety of conditions, local and general; and there is no doubt that encouraging results have been obtained. They have been used also as a prophylactic against scarlet fever; there is no doubt that they are of value on this disease.

Bacillus Coli Vaccine.—The Bacillus Coli is the normal inhabitant of the intestine but it is resposnible for some inflamations of the bladder, kidneys and peritoneal cavity. It may also cause appendicitis and mucous colitis. Some very good results have been obtained by the use of these vaccines. This germ also has many strains and therefore an autogenous vaccine is most satisfactory. The dose is 5'15 millions at intervals of from 5-15 days.

Pneumococcus Vaccine.—This has been used in pneumonia and its various complications but definite statements cannot be given as to its value as a curative agent. It seems to be useful as a prophylactic and is given in doses of 10-15 millions every 36 hours.

Tuberculin.—This preparation was originally introduced by Koch in 1890, but it soon fell into disfavour as it was given in too large doses

and accidents occurred. Now-a-days its value in tuberculosis of various kinds is undoubted. This revival in its favour dates chiefly from our extended knowledge of opsonins and the opsonic index, and tuberculin has again taken its place as a valuable diagnostic and curative agent in tuberculosis. It is now known that formerly tuberculin was given in doses which were positively dangerous and the opsonic index has shown that tuberculin is a very poisonous substance and must be used with extreme caution. The tuberculin used now is prepared by macerating tubercle bacilli and adding distilled water to the mass. The mixture is then centrifuged and the upper layer so obtained is decanted off. The residue is again dried and treated as before and this process is repeated till no deposit remains. The fluids obtained from the various washings are added together and constitute new Tuberculin. In treating a case of tuberculosis, the initial dose must be very small and its effect judged by an estimation of the opsonic index or by variation in the clinical symptoms. It is then gradually increased. Koch's old Tuberculin is used in the diagnosis of tuberculosis and is of great value in this connection.

This closes now a very short account of the more common vaccines. Vaccine therapy is still in its early infancy but there is a promising future before it. Its proper application entails in the medical man a special knowledge of bacteriology and, as years go on, it will come to hold a most important place in general practice. Like everything else, it has its limitations but it has come to stay and will prove to be one of the most formidable weapons in fighting disease in the future.

ENTERIC FEVER.

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WE now come to the complications of enteric fever. These are rather numerous and embrace affections of almost every part of the body, but the majority are in the nature of clinical curiosities, and only three need be considered as of practical importance. The interesting feature of all of them is that the diagnosis has to be made by the nurse, as they all occur rather suddenly. Moreover, for any treatment to be of avail, prompt measures must be taken, so I will consider each in detail. They are three in number—namely, heart failure, hæmorrhage from the bowel and perforation of the intestine.

* Continued from p. 94.