percentage with the Wassermann of no less than 92.44 per cent. (Sachs and Georgi, 1920).

The most recent advance is that of Dreyer and Ward (1921), who follow in principle the method of Sachs and Georgi, but prefer as antigen, on the ground of greater stability, one recommended by Bordet and Ruelens (1919) for Wassermann tests. To this antigen, which, according to Bordet and Ruelens, can itself be flocculated in the presence of luetic serum, Dreyer and Ward add cholesterol. They claim that with a stable antigen and a refined technique involving the quantitative expression of all degrees of flocculation, the test so conducted can lend itself to accurate standardization in terms of standard units.

Time and experience on the large scale will show how far this claim is justified and compatible with practicability in the hands of average workers, whose power to translate visual impressions into arithmetical language is notoriously variable. In treated cases particularly, the superiority of quantitative readings in flocculation tests over the purely qualitative evidence of the Wassermann would be warmly acknowledged, and it is to be hoped that the extensive parallel series which we understand are in contemplation may furnish important information on this point.

The above sketch is concerned solely with methods based on the mutual interaction of organic colloids and takes no account of the various and, on the whole, unsatisfactory tests which involve merely the precipitation of serum globulins by electrolytes.

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RESIDUAL VACCINES IN ACUTE BACTERIAL DISEASES.

BY

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WHEN a dose of any vaccine is administered the extent of the resulting general reaction is beyond control. In chronic disease and where prophylaxis is intended it is possible to adjust the dose so that the reaction, if any, is small and therefore negligible. But cases which are acutely ill may, and usually do, react violently to a dose which would cause only trivial malaise in the other types of cases. The reason for the lack of control lies in our inability to gauge the effect before administration.

Another objection less frequently heard is to the effect that the patient is already "full of toxins," and any addition is not likely to improve his state. The argument is so plausible that its hypothesis is overlooked and suffered to pass unquestioned. The patient is not "full of toxins" until he is moribund; and since that is a clinical estimation, the lethal amount of toxin may have been reached before or after the patient is estimated to be in that condition. The objection also appears to presume that the human organism is a kind of pot into which a fixed amount of toxin may be poured. In any case the criticism misses the mark as far as residual vaccines are concerned, for they contain neither toxin nor endotoxin. It is evident that lack of control is the real bugbear, and I believe that the system about to be described is one which goes some way towards meeting the difficulty.

The treatment of acute sepsis does not permit delay, consequently it is not justifiable to wait for the preparation of

an autogenous vaccine. A stock vaccine may be below an autogenous in efficiency, but the prospect of success in a given case would be placed in far greater jeopardy by two or three days' delay before commencing treatment.

To be generally useful a stock vaccine must contain the organisms that are most likely to cause such conditions as septicaemia, pyaemia, peritonitis, cellulitis, and large carbuncles associated with grave toxic disturbance. Two vaccines were therefore prepared: the first contained equal numbers of the streptococcus, pneumococcus, staphylococcus, and diphtheroid bacillus; the second contained the colon bacillus instead of the pneumococcus—in other respects it was the same as the first vaccine. A certain degree of discretion is needed to decide which of the two is the more suitable in a given case, but as a simple guide it may be said that the first is intended for all purposes except septic conditions of the abdomen and pelvis, in which the second will be found more generally useful.

A stock vaccine was frequently required in the out-patient department, and the opportunity was taken to note the largest dose that most walking chronic cases could tolerate without a general reaction. A minority showed a reaction with this dose, but they were ignored because it is impossible to assess individual idiosyncrasy on a graduated scale.

The vaccine was next tried with acute cases, starting with very small doses, and increasing them as experience demonstrated their lack of effect. A dose was ultimately reached which was capable of producing marked clinical improvement without causing any discernible clinical reaction. This was true of the great majority; a small minority reacted with undesirable intensity, and the problem they presented still awaited solution. The dose was one-third that of the corresponding dose in the chronic cases, and was approximately 80 millions of the mixed organisms. It will be observed that the vaccines were standardized upon a physiological basis. This method is, in the author's opinion, more exact than the counting methods, which are notoriously only accurate, as far as can be discovered, to within about 40 per cent. This dose, suitable for acute cases, was termed the standard dose.

The solution of the difficulty presented by the minority was found in a close study of the clinical manifestations of the effects of the vaccines. The following facts emerged:

- A general reaction in an acute case will be seen, if at all, in six to ten hours after injection.
- An improvement will make itself evident in nine to eighteen hours.
- It will be admitted that, if two doses of a vaccine are given within a few minutes of each other, the effect will be as if one dose equal to the sum of the previous two had been given. It was found that this rule invariably held good for all periods up to twenty-four hours, and was commonly true up to forty-eight hours.

These three items taken together offer a simple method of dealing with the matter.

Since the lengths of time in (a) and (b) are appreciably shorter than in (c) it is possible to give a fraction of the standard dose, then observe its effect, and if neither reaction or improvement occurs the second fraction can be administered next day. Any reaction following this second fraction is either very mild or, more frequently, so small as not to be recognizable clinically. After the first dose has been completed, in one or two portions, no further vaccine should be given for at least four days; it is better to wait five or six.

The system is very simple in operation and gives such reliable results that there is some danger of it generating a belief that the clinician is working with a remedy of very feeble potency, and that he can do as he pleases upon occasion. When a first fraction produces no result of any sort and the second a marked improvement without visible reaction there is a temptation to "continue" the benefit by giving a third fraction on the third day. If this is done the resulting general reaction may be very disconcerting, and although permanent harm has not ensued, for a few hours the aspect of the patient has been such as to deter me from any further excursions in the same direction.

It is not every case that needs a second dose, or a second fraction of the first dose. The first dose is frequently sufficient to be a turning point in the course of the disease, enabling the patient to recover without further stimulation.

The rapidity with which improvement can show itself throws an interesting light upon the question of a "negative phase" in connexion with this type of vaccine. The patient's tolerance to a second dose is not established for some four or five days after the first dose, and during that time he is

abnormally sensitive to the vaccine, yet the clinical change for the better appears in a much shorter time, and we may therefore only conclude that the patient's general resistance does not coincide with his resistance at the focus of infection. This is demonstrated in a remarkable manner in cases of large carbuncles accompanied by grave toxic symptoms. The disappearance of the slate-blue colour round the lesion and its replacement by a bright red erythema is a striking change that occurs in a few hours. A possible explanation is that the first antibodies produced by the vaccine are all removed from the circulation as quickly as they are formed by some process of concentration at the site of infection. Whether the inflamed tissues in that area play an active or a passive part in this fixation of the antibodies is a matter of speculation at present.

The following cases are the first few treated with the vaccine, and nearly every one illustrates some point discussed above. The cases have not been "selected," but are a true consecutive series.

Case 1.—Aged 26. Septic finger due to running dirty scissors into it. Next day, small pustule, lymphangitis, and axillary adenitis. The finger was fomented and the lymphangitis disappeared, but swelling of the whole digit commenced. Serum only on incision. General lassitude. Vaccine given on seventh day. Next day the swelling was rapidly subsiding; there was distinct tenderness at the point of original injury. Pus visible that evening; on incision, a large quantity escaped and there was complete relief from pain. Next day, a clean granulating surface, which was completely healed on the fourth day after administration of vaccine.

Case 2.—Aged 11. Streptococcal peritonitis, apparently idiopathic. Abdomen opened, drain inserted: prognosis hopeless. Vaccine given twenty-four hours later, up to which time the patient was moribund and apparently dying. Heroin failed to calm the patient. Six hours after vaccine was given the patient went quietly to sleep, temperature and pulse fell, the former several degrees, and the case made an uneventful recovery.

Case 3.—Pyæmia; purulent arthritis of right elbow with abscesses in axilla and groin. Temperature 100° to 102.2° , pulse 100 to 120. Vaccine given. The next day the temperature was still swinging, but on the down grade. A second dose was given four days later, and temperature and pulse settled finally on the tenth day.

Case 4.—Aged 11. Acute osteomyelitis of spine and infection of canal. Prognosis hopeless. Vaccine given on the sixth day at 11 a.m. That evening the temperature rose half a degree, but the next morning was down one degree; the pulse fell from 140 to 110. The patient was operated on that afternoon, and died early next morning.

Case 5.—Carbuncle of hand, involving half of palm, index finger, and back of hand; acute toxic symptoms and swelling of arm; tissues blue-grey in appearance. Prognosis very serious. Vaccine given; no reaction, but tissues had lost blue colour within twelve hours; the carbuncle was surrounded by deep scarlet erythema, hot to the touch; toxic symptoms much less. Not content with this a second dose was given next day, and caused an alarming reaction for a few hours; then all passed off. A large slough separated on the eighth day, and a clean granulating surface was left which healed rapidly.

Case 6.—Infant aged 8 months. Furunculosis and toxæmic absorption; sleeping badly. Vaccine given and child taken home. Next day there was great improvement; the child slept well from then onwards. The mother volunteered the statement that the lesions had changed colour from blue to red. No sign of a general reaction. No further treatment needed.

Case 7.—Acute appendicitis, large burst abscess, and peritonitis in a female aged 40. She appeared to be doing well for three days after operation, then became worse—abdomen distended, anxious facial expression, wound drain diminished, temperature and pulse rising. Vaccine given, with prompt improvement within sixteen hours; there was profuse outpouring of pus. The patient looked much better, and distension disappeared. A second dose was given forty-eight hours later. Prompt reaction caused the patient to feel very unwell, and for a few hours the medical attendant had grave doubts as to her recovery. Next day she seemed better than ever, and eventually made a complete recovery.

Case 8.—Phagedænic primary sore of penis; widespread septic infection of groins; advanced pyorrhoea. The patient was in a filthy personal condition. Streptococcus isolated by blood culture. Vaccine given on two occasions without clinical benefit; no reaction at any time. Ulcerative endocarditis found at necropsy.

Case 9.—Acute osteomyelitis in a patient aged 10. Bone opened up and drained, but temperature remained for seven days after operation at about 103° , with no sign of subsiding. Vaccine given, and temperature fell to 98° six hours later, and was 97° in another eight hours.

Case 10.—Pyæmia. Patient was ill three weeks before vaccine was given. No reaction or benefit after both fractions of the first dose, so a week's interval was allowed to elapse before giving a second dose. Again no reaction or improvement, so another week's interval was ordered. The third dose was then given, with the same result. All three doses were the same size.

Case 11.—Primary sore of penis with severe balanitis, becoming gangrenous in one part. Vaccine caused a small slough to separate,

with total disappearance of the surrounding swelling, and left a small clean sore. No sign of a general reaction.

Case 12.—Subacute cellulitis of leg. Chronic indurated area which was subject to periodical acute exacerbations. Vaccine cleared up the condition promptly. No general reaction observed.

Case 13.—Streptococcal septicaemia. Patient had been ill for fourteen days when residual vaccine was first given. A previous dose with the common toxin-containing vaccine produced a reaction which lasted several days and from which no good result was derived. The first dose of the author's vaccine produced no result of any sort, and a second dose four days later also failed to make any impression. The temperature remained at about 105° all the time. The patient died four days after the second dose was administered.

These cases cannot be called promising from the standpoint of collecting a good "record" of results, but the author has acted in accordance with the belief that a remedy can only be tested thoroughly when it is given an opportunity to fail as well as to succeed. In no instance was there the smallest sign of an undesirable result due to the vaccine.

One fact is very clear: vaccine treatment can cure when other remedies have been tried and have failed, but the best results can only be expected when the vaccine is given as early as possible in the disease. It cannot be expected to resuscitate those with the death rattle already in their throats, although on occasion it seems to have come tolerably near to it.

The most important feature of all these cases is that in no case where the fractional dose system was followed did any alarming general reaction occur. The cases demonstrate the author's main contention: it is possible to administer a vaccine to a patient suffering from acute sepsis in such a manner that the vaccine is under control and the individual susceptibility of the patient prevented from causing a disastrous reaction. The system in brief is:

1. The largest dose that most chronic walking cases can tolerate without a general reaction is ascertained.

2. One-third of this dose is called the standard dose, and is administered to an acute case in two halves.

3. If after the first fraction there is neither a general reaction nor improvement, the second fraction should be given within twenty-four hours.

4. If the first dose requires both fractions, the amount of the dose should be considered to be that of the sum of the two fractions.

5. The second dose should not be given for at least four days after the completion of the first dose, and can be of the same size as the first or increased by not more than 20 per cent. If a result has been obtained with the first dose, it is doubtful if an increase of amount in the second is of much advantage.

6. It is as well to prepare two stock vaccines—one containing the streptococcus, pneumococcus, *Staphylococcus aureus*, and Hoffmann's bacillus; the other having the colon bacillus substituted for the pneumococcus, but otherwise the same as the first vaccine.

The author is much indebted to Mr. Roy R. Kerr, F.R.C.S., for providing some of the cases, and most particularly for his close clinical observation, which was largely instrumental in furnishing the facts upon which the system of dosage advocated has been built.

THE PARASITOLOGY AND CLINICAL ASPECTS OF MALARIA IN ANTIGUA.

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THERE has not, hitherto, been any investigation into the parasitology of malaria in Antigua. The following observations, based on a record of 300 positive blood films, may be of value in providing an accurate indication of the nature of the infection with which we have to deal. Of the 300 positive films which were analysed 61 per cent. showed *Plasmodium falciparum* (malignant tertian), 28 per cent. *Plasmodium malariae* (quartan), and 11 per cent. *Plasmodium vivax* (benign tertian). The predominant infection, therefore, is *Plasmodium falciparum*.

The form of parasite most frequently found was the young form, but it is worthy of note that the classical signet-ring form was conspicuous by its rarity. The majority of young parasites seen were in the tenue form. In most cases in