and enteritis," which demand "more than a human hecatomb" from child life every week in the late summer and early autumn year by year, are bracketed with "other diseases of the digestive system"; while "puerperal fever (septicæmia), &c.," are followed by "other causes incident to childbirth."

Now, it will be observed that every one of these diseases undoubtedly belongs to the class of the acute infections, and the infecting agent in the first two of them, at all events, has long since been identified and isolated. And even in the case of summer diarrhoea the active part played by Shiga's bacillus as a causative agent can hardly be questioned at the present day. Further, is not "puerperal fever" universally acknowledged to be due to sepsis caused by sapræmia or septicæmia—forms of toxæmia which in the International List are grouped with tetanus and tuberculosis? Surely small-pox, measles, and scarlatina might just as well be included with "diseases of the skin and cellular tissue," or influenza, diphtheria, and "croup" (which last term should be expunged from any scientific list of diseases) with "diseases of the respiratory system," or enteric fever with "diseases of the digestive system." "Typhus," again, has disappeared from the International List as printed in the English Weekly Return, but it has very properly been retained among "other epidemic diseases" by the Registrar-General for Ireland.

The point, however, which I wish in particular to make is that the transference of such unquestioned acute infections as cerebro-spinal fever, pneumonia, diarrhoea, and puerperal fever from their rightful position under the heading "epidemic diseases," places a formidable stumbling-block in the path of sanitary reformers and medical officers of health. The hands of the State Medicine clock are being put back a quarter of a century at least—to pre-notification days. For when sanitary authorities are asked to add such and such a disease to the schedule of the Notification and Prevention of Infectious Diseases Acts, they will answer: "Oh! the Registrar-General holds that this disease is one of the respiratory system, that other is an affection of the digestive system."

In Ireland on March 31st, 1910, the provisions of the Infectious Disease Notification Act of 1889 had been adopted in 142 out of 158 rural districts, and in 83 out of 95 urban districts. Throughout Great Britain the Act has long since been in force. Writing as a resident in Ireland, I cannot but regard with concern a modification in the list of causes of death which will probably delay (for it cannot ultimately prevent) the including among notifiable diseases under an Act which is now almost universally adopted in the United Kingdom of such death-dealing, yet preventable, maladies as pneumonic fever and epidemic diarrhoea.

I am, Sir, yours faithfully,

JOHN W. MOORE, M.A., M.D., D.P.H.

Dublin, Jan. 16th, 1911.

(1871) Dub., F.R.C.P. Irel.

ABBOTT AND WIFE v. RYALL.

To the Editor of THE LANCET.

SIR,—I have seen a cutting from one of the morning papers misrepresenting the answers given to certain questions put to me in a law court last week. My object in writing to you is to make it clear that in my answers the word "anxiety" was only employed in relation to the giving of "instructions" (for after-treatment and observations of results) to "subordinates."

The case was an important one for our profession, and one of the chief points upon which it turned (*vide* the summing-up) was the matter of the instructions given by the doctors to the nurses, and the deductions made by them from the report of the nurses as to the result of the carrying out of those instructions. I was in the witness box more than half an hour, being examined, cross-examined, re-examined, and then questioned by the judge. The two reports which I have seen were brief epitomes. That in the *Times* is a fair one, and demonstrates that that reporter clearly understood the matter in question to be one of "instructions" given by a surgeon to a nurse—his nurse—the nurse he had taken to the case. The word essential to the proper understanding of the questions and answers with which this note is concerned is "subordinate."

I was asked whether "the surgeon would before leaving the case give instructions to his subordinate," and I replied

"Yes." Then to a further question, of detail as to examining and reporting the result of an enema given with the intention of bringing away the swab from the bowel, I said, "As this case shows that is one of our greatest anxieties." And with this statement surely everybody who is used to the after-care of abdominal operations will agree.

I ask you to publish this explanation in case any of your readers may have seen only the second, the unfair and misleading, epitome to which I refer at the beginning of this letter; for in attempting to boil down into one the many questions and answers upon a technical point it misses entirely the matter at issue; and, what is far worse, it at the same time insults my profession and myself by substituting for the word "subordinate" the words "patient's medical adviser."

That this substitution was effected by some reporter who is quite incapable of conveying, even if he can grasp, the technical points involved in the evidence is proved by his senseless jumbling of terms in the preceding paragraph.

I am, Sir, yours faithfully,

Jan. 17th, 1911.

ALFRED D. FRIPP.

A METHOD OF SERUM DIAGNOSIS FOR TUBERCLE.

To the Editor of THE LANCET.

SIR,—The object of my letter with regard to Captain V. B. Nesfield's communication on the serum diagnosis of tubercle was to point out that practically all persons—adults especially—have in their blood antibodies to the tubercle bacillus, and that, therefore, any method of diagnosis must be an accurate quantitative one. It is not a question of presence or absence, but of more or less. I believe I have found such a method by the application of a new principle—i.e., the estimation of the time in which complement absorption takes place with an emulsion of bacteria of definite strength under standard conditions. The process is simple and easy in execution, gives exact results, and is available for all cultivable organisms (though I have only used it at present for tubercle and typhoid), and I think it will be found of great clinical value as affording the simplest method for the application of the Bordet-Gengou reaction in diagnosis.

Captain Nesfield's method of gauging the strength of the emulsion by the appearance (i.e., by guess) is entirely inadequate where quantitative work is to be undertaken. For opsonic work it is different, for here a normal control is used in every case; and even here the careful worker will endeavour, by means of an orientating test, to get his emulsion as uniform as possible on each occasion. In a preliminary communication such as I was making I did not think it necessary to go into details, nor do I now; I may remark, however, that my standard emulsion is carefully sterilised, so that no "short, broad bacillus" can make its appearance, and that controls have been made to show that the disappearance of the complement is really due to specific absorption and not to destruction at the incubator temperature, which does not take place for a much longer period.

I have determined the amount of complement in the serum in a considerable number of cases by an accurate method, and have as yet found no connexion between the figures thus obtained, the amount of antibodies (as determined by the absorption time), and the opsonic index. The question as to whether free complement exists in the circulating blood or not has formed, as any of your readers who are interested in the study of immunity will know, one of the important controversies arising out of the subject, and Captain Nesfield will find an outline of the more important facts bearing on the dispute in my book on Immunity and Specific Therapy, where three pages are devoted to this question. I have also mentioned the fact that opsonin is absorbed along with complement in the Bordet-Gengou reaction, which I thought was now well known.

Captain Nesfield makes numerous definite statements which are entirely unjustified in the present state of our knowledge of the subject—for instance, that a patient suffering from tubercle must constantly be losing complement from intravascular deviation. There is no evidence that this ever occurs, and we should not expect it to do so if there is no free complement in the plasma. Again, he says that an excessive dose of tuberculin would probably reduce the complement in the blood and be a source of danger. I am aware that some

observers have found a diminution of the complement in the serum during anaphylactic shock, but this is not generally accepted, and even during a severe tuberculin reaction I have not found the amount reduced. Even if it were, there is no proof that it would be harmful. In my own measurements of the amount of complement in the different conditions I have found no relation whatever between the amount and the severity of the disease or any clinical indication. Lastly, he says that a falling opsonic index would at once show this and indicate danger. I am not prepared to say that there is no connexion between the opsonic index and the amount of complement, but if there is it is quite certain that it may be masked by other factors, and that a high index does not necessarily mean a large amount of complement, or *vice versa*.

In conclusion, may I point out that all hæmolytic observations on Hecht's method are liable to be vitiated by the fact that the amount of amboceptor is subject to variations, as yet unmeasured, and that this, as well as the variation in the amount of complement (which can be measured easily), renders accurate work impossible, or at least arduous in the extreme? I am, Sir, yours faithfully.

Jan. 16th, 1911.

W. D'ESTE EMERY.

RECENT VIEWS AS TO THE MECHANISM OF ANTISTAPHYLOCOCCAL DEFENCE.

To the Editor of THE LANCET.

SIR,—Amid so much that was interesting in Dr. F. W. Andrewes's Croonian lectures¹ it was disappointing to find how little attention the lecturer gave to the medical aspect of his subject. He told us that the new facts prove the immense importance of phagocytosis in pyogenic, and its lesser importance in non-pyogenic, infections; but, apart from this, I hardly remember a single practical application he has made of his discoveries. He has certainly not applied them to the solution of any of the more thorny problems which vex the practitioner in his daily association with infectious ailments. Perhaps, considering the nature of Dr. Andrewes's work, it could not well have been otherwise. In artificial infections local inflammations are much less prominent than they are in natural illness. To the intravenous inoculator of rabbits an infection comes to be little more than a useful starting point for a circulatory leucocytosis, whose source and fluctuations are to be examined in detail, but whose destination in the actual conflict with the bacteria may be left in a convenient vagueness. To the clinician, however, the sole interest of such researches lies in the light which they shed upon disease; nor, allowing for the extreme looseness of the parallel, is there any reason why the phenomena of animal infection should not be utilised for the purpose of illustrating human pathology. Looking at the experiments in this rather utilitarian way, I wish to consider how views which I outlined in a letter to THE LANCET of June 25th last are affected by Dr. Andrewes's and other recent work.

Let me recall that to Dr. Andrewes, as to most present-day authors, the main defence in staphylococcal infections is phagocytosis, while my letter was designed to show that in the furuncular group the chief danger, that from the spread of the local inflammation, is probably combated by antitoxin. In the first place, were leucocytes the chief defence in carbuncle we should expect a gradual arrest of the complaint, as they gradually got the upper hand of the bacteria. The fact that expansion goes on with no apparent diminution of rapidity suggests rather a new force brought suddenly to bear than the final effort of an agent that had been slowly wearing down the bacterial attack. Moreover, the time at which arrest takes place, some days at least from the onset, agrees well with the time required for the preparation of an antitoxic, and not so well with that required for the institution of a phagocytic, defence. Not only as regards defensive preparation, but still more from the point of view of the relative strength of the opposed forces, the time of arrest is unfavourable to the phagocytic theory. As there must be during the expansion of a carbuncle the same constantly increasing proportion of bacteria and toxins to defending leucocytes as I

have pointed out there is to defending tissues, arrest ought upon that theory to take place at the very beginning of the trouble, when defence is relatively strong in comparison with the attack, and not, as it actually does, at a stage when things are most favourable to the invading bacteria. Further, the likelihood of the leucocytes contributing materially to arrest will be the smaller the larger, we suppose, the number of them to be that are present in the first stage of carbuncle. A small leucocytosis might be thought insufficient to kill the bacteria. A large one would indicate the breakdown of the phagocytic defence in circumstances that were well suited to its effective exercise. On the evidence hitherto available one had imagined the number to be comparatively small. The relatively mild symptoms, the contrast, so much more marked than the common descriptions imply, between the characters of the swelling in the earlier and in the later stage, the kind of juice which can be squeezed from the section, all pointed to the probability of a rather small leucocytosis. Dr. Andrewes's experiments, however, suggesting a large early circulatory leucocytosis, make it almost certain that the part taken by leucocytes in the constitution of the early swelling of carbuncle is a large one, and so far are unfavourable to the phagocytic theory. Significant, too, in the present connexion is the recent surgical reaction against the theory, due partly to the disappointing results of the vaccination treatment, partly to a growing conviction as to the enormous anti-bacterial powers of the healthy tissues. The immunising functions of the leucocytes are now admitted to have been a good deal exaggerated, and to be still very imperfectly understood. Basing upon clinical experience, as the only safeguard against the like errors in future, we have to look for a theory which shall at once meet the difficulties I have enumerated, and escape a still more fatal objection to the current phagocytic doctrine to which I will come presently.

Obvious as are the above considerations, the force of some of them would clearly be lessened, were it permissible to regard the nascent leucocyte as having a higher defensive value than the ordinary circulatory one. The leucocytes formed in connexion with the bone-marrow changes, which occur some days after infection, might then be credited with an arrestive power which the first arrivals at the inflamed focus were without. While it is possible that in carbuncle such a higher arrestive power is actually exerted by the later-formed leucocytes, observation of the course of the complaint makes it extremely unlikely that the mode of arrest is phagocytic. Though no one has hitherto paid any attention to the facts tending to show the existence and successive neutralisation in carbuncle of at least two toxins, both the facts themselves and their bearing on the doctrine of immunity are sufficiently plain. The ultimate reason, which bars the phagocytic theory, is the circumstance that, under normal conditions—i.e., in carbuncle occurring in otherwise fairly healthy persons without complications—constitutional symptoms are met with chiefly in the period extending from arrest of the complaint onwards. The notion that we have to do with only one toxin will therefore imply that it can exert a disorganising effect on the tissues, when present in quantity, which produces little or no constitutional disturbance, and be without power to cause local damage, when in quantity capable of causing general symptoms of a quite noticeable order. Allowing then that an idea which involves an absurdity must itself be absurd, we seem driven to the alternative of admitting the toxic duality. But if in carbuncle two poisons are successively got rid of, clearly the neutralisation of the first cannot have been due to phagocytosis, for in that case the second must have ceased to be produced. In a word, the continued operation of the constitutional poison long after the tissue-destroyer has ceased to give trouble is a fairly obvious indication that the latter has been neutralised by an antitoxin.

Those who have had practical experience of infectious ailments will usually have no difficulty in admitting, as the preceding argument requires us to admit, that the constitutional symptoms of carbuncle are really toxic in character. In medicine, however, there are many different view points, and we read in the Croonian lectures without any surprise that the "chief clinical symptoms of infective disease depend on the work of defence." Dr. Andrewes nowhere says upon what particular defensive work they depend, but the plain inference is that it is the leucocytosis. There is nothing else in his analysis of the factors of immunity with

¹ Croonian Lectures on the Behaviour of the Leucocytes in Infection and Immunity delivered before the Royal College of Physicians of London by Dr. F. W. Andrewes, THE LANCET, June 25th (p. 1737), July 2nd (p. 8), 9th (p. 83), and 16th (p. 153), 1910.