

in any other way, and since taking to charting the pulse in all these cases I find that one has a much better idea of how the disease is going on. (Chart 2.)

Treatment.

It must be admitted that the treatment of acute carditis is very disappointing. Salicylates, which so effectually control the temperature and joint manifestations of acute rheumatism, seem to exert little or no influence on the heart inflammation. It is, however, well to administer them to keep the general rheumatic process in check. Sodium iodide has been advocated; I have not found it efficacious. For the restlessness and anxiety, especially of pericarditis, small repeated doses of opium are certainly useful. In order to limit dilatation of the heart and to control the pulse-rate digitalis has often been employed, but opinions as to its usefulness are very diverse. Sturges regarded it as "worse than useless," whereas Sutherland⁵ found that it had a striking effect in lessening the rate of the heart. My own experience has been that its effects are very variable. In some cases it slows the heart; more often it seems to be without influence.

In pericarditis various external applications to the heart have been tried. The late Dr. D. B. Lees was a great advocate of the ice-bag, but although it may quieten a tumultuously acting heart it is difficult to believe that it has any other effect. Blistering appears to be of little value, except perhaps in those rare cases where præcordial pain is pronounced. Leeching has supporters, but children stand loss of blood badly, particularly in the presence of the usual anæmia; blood-letting should therefore be reserved for cases with sudden engorgement of the right side of the heart and great dyspnoea, where it may be of capital value. Some form of specific treatment is wanted which will attack the microbe of acute rheumatism or its toxin directly, but so far no such treatment is forthcoming. I have tried in a few cases the effect of a vaccine prepared from cultures of streptococci taken from rheumatic nodules excised under local anæsthesia and from the blood of the heart post mortem, but without any appreciable benefit.

Prolonged rest is the best means at our command for controlling acute carditis. Here, again, the pulse chart is of great value for estimation of the length of rest required. So long as the pulse curve is slowly falling, strict rest in the recumbent position should be enforced. If the curve appears to have "touched bottom," and has remained stationary for a few days, one may cautiously begin to relax the strictness of the regime of rest, always being prepared to reinforce it if the pulse-rate is unfavourably affected. It is astonishing how unstable the heart is in many of these cases. Even the introduction of an extra pillow or the slightest excitement or emotional disturbance may produce a notable and not evanescent acceleration of rate.

The treatment of carditis, then, offers few opportunities for active intervention—rest and patience are chiefly required, and too active therapeutics may do more harm than good. In this connexion it is well to recall the story told by Dr. Sturges of a practitioner who was expressing his regret to a consultant that he had not recognised the presence of pericarditis in a case of rheumatism that they were seeing together. "Don't apologise," said the consultant, "if you had recognised it you might have treated it!"

⁵ Quart. Jour. of Med., 1919, xii., 183.

THE LATE DR. G. W. H. TAWSE.—Dr. George Watson Hackney Tawse, who died recently at Whitehaven, aged 55, was a distinguished graduate of Aberdeen University, where he obtained the M.B. and C.M. degrees with highest honours in 1891. For a time he acted as house surgeon to Sir Alexander Ogston, who was then professor of surgery at the Aberdeen University, but afterwards went to Whitehaven, where, prior to entering general practice, he obtained an appointment at the West Cumberland Infirmary. To this institution he was hon. surgeon at the time of his death.

AGGLUTININS IN NORMAL SERA FOR SOME MICRO-ORGANISMS OF THE PARATYPHOID GROUP.

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DURING the past few years certain members of the paratyphoid group of micro-organisms have come into prominence as giving rise to disease of an enteric nature in human beings.^{1 2 3 4 5} Agglutination reactions play an important part in the diagnosis of infections with members of this group of bacteria; it therefore seems desirable to have precise information of the proportion of the general population whose serums possess the power of agglutinating these bacilli and of the titres at which they react. These facts ascertained, we shall know the value of the agglutination reaction for diagnostic purposes, and can appreciate its limitations. In this investigation the three organisms dealt with have been *B. enteritidis* (Gaertner), *B. aertrycke* (Mutton), and *B. paratyphosus* C (Hirschfeld). The majority of serums have also been tested against *B. typhosus* and *B. paratyphosus* A and B. Inclusion of these latter organisms allows certain deductions to be drawn as to the extent to which the agglutinating powers of the serums for the three organisms under investigation are due to group agglutination; it is also useful as a means of a presumptive division of the cases into those which have received typhoid inoculation and those which have not.

Method of Test.

The majority of serums tested have been sent to the laboratory for a Wassermann reaction, and it was only possible to obtain accurate information regarding previous antityphoid inoculation in about a third of them. The tests were carried out between January and September, 1921; we have tested over 1000 serums against these various organisms. The serums were chiefly obtained from the venereal department, from patients in the hospital wards suffering from diseases other than enteric, with a few from members of the laboratory staff. The majority were from people between the ages of 18 and 60, nearly twice as many were from males as females. The emulsions were kindly made for us by Dr. G. S. Wilson. Three batches of emulsion for each organism were made in all. The first 300 serums were tested against the first batch, the second 300 against the second batch, and so on. Each batch before use was tested against a high titre homologous serum to find out whether the use of a reduction factor would be necessary in changing from one emulsion to another. The emulsions were standardised to contain approximately 750 million bacilli per c.cm., and 0.25 per cent. formalin was added to preserve them. Dreyer's technique has been employed with the slight modification of using calibrated instead of dropping pipettes, and the results are returned in titres instead of units. No attention has been paid to agglutination occurring below a dilution of 1/20.

The result of testing 1000 serums against these organisms was that the various types were agglutinated by the following percentages of serums: *B. typhosus*, 29; *B. paratyphosus* A, 17; *B. paratyphosus* B, 23; *B. paratyphosus* C, 8; *B. aertrycke* (Mutton), 16; *B. enteritidis* (Gaertner), 11; giving standard agglutination at a dilution of 1/20 or higher.

As regards *B. paratyphosus* C, the percentage was calculated from 700 cases only, for the following reason. The first 300 serums tested produced only one capable of agglutinating *B. paratyphosus* C. Of the second 300, however, it was agglutinated by 6 per cent. of the serums, and of the remaining 400

it was agglutinated by 9 per cent. of serums. A possible explanation of this result is that the batch of emulsion used for the first 300 serums, although agglutinating to full titre with its homologous high titre serum, was not coagglutinated by serums containing para. B agglutinins, whereas the second and third batches of emulsion (made after several subcultures) responded to a para. B serum.

Andrewes⁶ and others have shown that an emulsion of para. C, although agglutinating to full titre with its homologous serum, may only be coagglutinated by a para. B serum after several subcultures. If this be the explanation it is a possibility that the one serum agglutinating *B. paratyphosus* C in the first batch of emulsion came from a subject who had received inoculation with this organism—a measure carried out on the Salonica front. He also agglutinated *B. typhosus*, *B. paratyphosus* A and B, but we were unable to get in touch with him to ascertain details of his inoculations.

As far as we know, the only work of this kind that has been published is a report on the agglutinating properties of certain serums against a particular strain of *B. enteritidis* (Gaertner) by O'Farrell in 1916.⁷

As a result of his investigation he came to the conclusion that typhoid inoculation had no effect on the agglutinating power of a serum against the particular strain of *B. enteritidis* (Gaertner) he was testing. However, his uninoculated cases numbered only 32, and furthermore his tests were performed before the triple vaccination became general, so the results are hardly comparable with those presented here.

Difference of Results in Inoculated and Uninoculated Persons.

In the present investigation it soon became apparent that serums coming from inoculated subjects were more likely to agglutinate *B. enteritidis* (Gaertner), *B. aertrycke* (Mutton), and *B. paratyphosus* C than those obtained from uninoculated persons, as one would expect. If we now compare the results of serums from persons known to have received inoculation with typhoid vaccine or T.A.B. with serums from persons known to be uninoculated, the difference is seen to be very striking. (Table I.)

TABLE I.

Organism.	Known uninoculated.		Known inoculated.	
	Number of serums tested.	Percentage agglutinating.	Number of serums tested.	Percentage agglutinating.
<i>B. paratyphosus</i> C ..	148	4	126	23
<i>B. aertrycke</i> (Mutton) ..	181	10	149	32
<i>B. enteritidis</i> (Gaertner) ..	181	4	149	24
<i>B. typhosus</i> ..	181	3	149	89
<i>B. paratyphosus</i> A ..	181	Nil	149	58
<i>B. paratyphosus</i> B ..	181	4	149	71

The practical points of interest emerging from this table are: (1) Among the uninoculated population 10 per cent. of people will probably agglutinate *B. aertrycke* (Mutton) and 4 per cent. are likely to agglutinate *B. paratyphosus* C and *B. enteritidis* (Gaertner), giving standard agglutination at a titre of 1/20 or higher; (2) among people who have received T.V. or T.A.B. a year or more previously there will be found between 20 and 30 per cent. who will agglutinate *B. paratyphosus* C, *B. aertrycke* (Mutton), and *B. enteritidis* (Gaertner) at a dilution of 1/20 or higher. It may be mentioned that the uninoculated cases gave no history of a previous enteric infection or history of food poisoning.

As so many more males than females received typhoid inoculation in the war, when we compare the results according to sex we should expect a preponderance of the males to agglutinate these organisms.

This we find to be the case, thus:—

Percentage of 276 serums from males.	Percentage of 165 serums from females.	Organism agglutinated.
42	5	<i>B. typhosus</i>
28	2	<i>B. paratyphosus</i> A
39	7	<i>B. paratyphosus</i> B
11	3	<i>B. paratyphosus</i> C
23	15	<i>B. aertrycke</i> (Mutton)
11	5	<i>B. enteritidis</i> (Gaertner)

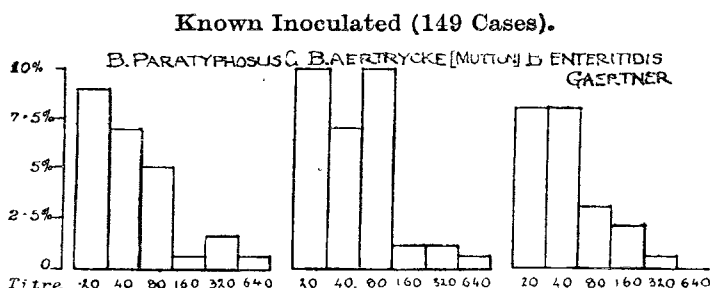
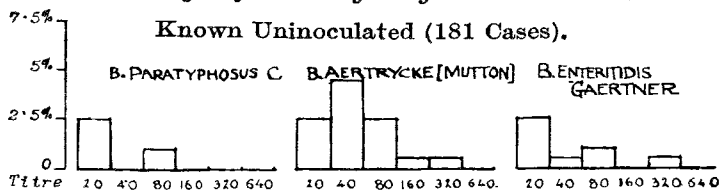
If we now take only the cases known to be uninoculated we find, with the exception of *B. typhosus*, a slight preponderance amongst females, if 61 cases be thought a sufficient number for purposes of comparison, thus:—

Percentage of 111 males known to be uninoculated.	Percentage of 61 females known to be uninoculated.	Organism agglutinated.
4.5	1.5	<i>B. typhosus</i>
Nil	Nil	<i>B. paratyphosus</i> A
4.5	4.9	<i>B. paratyphosus</i> B
4.3	5.6	<i>B. paratyphosus</i> C
9.9	10.9	<i>B. aertrycke</i> (Mutton)
3.6	7.8	<i>B. enteritidis</i> (Gaertner)

This is of interest in view of Captain T. R. Ritchie's work.⁸ He found a higher percentage of positive results in females than in males when performing similar tests with *B. typhosus* and *B. paratyphosus* A and B.

We will now study the titres that have been encountered. (See Charts.)

Percentage of Cases giving Various Titres.



It should be noted that titres as high as 1/320 for *B. enteritidis* (Gaertner) and 1/640 for *B. aertrycke* and *B. paratyphosus* C have been met with. Some of these high titres have occurred amongst the inoculated, some amongst the uninoculated. None of the inoculated cases had received inoculation for less than a year previously, and some not for two or three years, so one can imagine that a recently inoculated subject might give a titre much higher than 1/640 for any of the three organisms under investigation. Owing to the small amount of serum available, absorption tests have not been carried out to ascertain which of the organisms in the triple vaccine give rise to the secondary agglutinins for the organisms under investigation, but if we study the serums that agglutinate *B. typhosus* only and do not agglutinate para. A or B, we have 63 serums of which: 4 per cent. also agglutinate *B. paratyphosus* C, 9 per cent. also agglutinate *B. aertrycke* (Mutton), and 7 per cent. also agglutinate *B. enteritidis* (Gaertner). Whereas, of those that agglutinate *B. paratyphosus* B only, and not *B. typhosus* or *B. paratyphosus* A, we have 34 serums of which: 29 per cent. agglutinate *B. paratyphosus* C, 67 per cent. agglutinate *B. aertrycke* (Mutton), and 6 per cent. agglutinate *B. enteritidis* (Gaertner). This seems to indicate that the paratyphoid C and aertrycke (Mutton) agglutinins are chiefly due to coagglutinins

derived from paratyphoid B, whereas the Gaertner agglutinins may apparently come either from *B. paratyphosus* B or *B. typhosus*.

In a serum giving heterologous agglutination, it may be taken as a general rule that the higher the titre for the homologous organism the more likely is the serum to give secondary agglutination for the organisms closely allied to it, and as the homologous titre becomes lower so will the power of giving rise to secondary agglutination usually become less.

Thus, for the sake of argument, if we assume that the para. C agglutinins in the inoculated are chiefly secondary to *B. paratyphosus* B, and we study the serums which agglutinate both these organisms we should expect to find the highest percentage of serums agglutinating *B. paratyphosus* C to occur amongst the serums giving the highest titres for *B. paratyphosus* B, and this percentage would gradually descend as the para. B titres became lower. On the other hand, if the para. C agglutinins were not secondary to *B. paratyphosus* B we should not expect to find a greater percentage of cases agglutinating *B. paratyphosus* C amongst those giving higher para. B titres than amongst those with lower ones. The results have been tabulated in this manner in Table II.

TABLE II.

B. typh. = Total number of cases agglutinating *B. typhosus*. B. aert. = Percentage of cases also agglutinating *B. aertrycke* (Mutton). B. para. A = Total number of cases agglutinating *B. paratyphosus* A. B. para. B = Total number of cases agglutinating *B. paratyphosus* B. B. para. C = Percentage of cases also agglutinating *B. paratyphosus* C. B. Gaert. = Percentage of cases also agglutinating *B. enteritidis* (Gaertner).

Titre.	B. typh. total.	B. aert. per cent.	Titre.	B. para. A total.	B. aert. per cent.	Titre.	B. para. B total.	B. aert. per cent.
320	41	41	320	8	50	320	12	58
160	55	38	160	17	52	160	34	58
80	78	32	80	37	43	80	79	44
40	56	19	40	53	39	40	61	37
20	37	29	20	32	18	20	43	32

Titre.	B. typh. total.	B. para. C per cent.	Titre.	B. para. A total.	B. para. C per cent.	Titre.	B. para. B total.	B. para. C per cent.
320	34	17	320	7	42	320	10	50
160	38	21	160	14	23	160	27	33
80	61	18	80	33	21	80	58	29
40	46	15	40	41	24	40	53	26
20	30	23	20	29	9	20	34	11

Titre.	B. typh. total.	B. Gaert. per cent.	Titre.	B. para. A total.	B. Gaert. per cent.	Titre.	B. para. B total.	B. Gaert. per cent.
320	41	34	320	8	37	320	12	58
160	55	32	160	17	17	160	34	35
80	79	24	80	37	35	80	79	30
40	56	17	40	53	24	40	61	19
20	37	16	20	32	25	20	43	13

The results are such as would be expected if the agglutinins for *B. aertrycke* (Mutton), *B. paratyphosus* C, and *B. enteritidis* (Gaertner) had been produced in response to immunisation with T.A.B. vaccine. Examination of the table will show that the correlation is most striking between the agglutination of *B. aertrycke* (Mutton), *B. paratyphosus* C, and *B. enteritidis* (Gaertner) on the one hand, and *B. paratyphosus* B on the other. Since, however, a high titre for *B. paratyphosus* B is frequently associated with a high titre for *B. typhosus* and *B. paratyphosus* A among patients who have been immunised against all three organisms, we should expect the correlation to extend to these two organisms. This is obviously the case, but it is only in the case of *B. enteritidis* (Gaertner) that the correlation with typhoid agglutination is consistent throughout. Thus the results recorded in this table are in accord with the conclusions drawn from other

evidence, that the agglutination of *B. aertrycke* (Mutton) and *B. paratyphosus* C by the serum of inoculated subjects chiefly results from heterologous agglutination produced in response to immunisation with *B. paratyphosus* B, while the agglutinins acting on *B. enteritidis* (Gaertner) may be secondary to the specific agglutinins for either *B. paratyphosus* B or *B. typhosus*.

The conclusions, then, which may be drawn from this work would seem to be as follows:—

1. Amongst the general population a considerable proportion of individuals yield serum agglutinating *B. paratyphosus* C, *B. aertrycke* (Mutton), and *B. enteritidis* (Gaertner). This proportion is definitely higher amongst those who have received typhoid inoculation than amongst those not so treated, and therefore is much higher in males than in females.

2. Some evidence is brought to show that the agglutination of *B. aertrycke* and *B. paratyphosus* C is largely due to secondary agglutination from the paratyphosus B element of the triple vaccine, whereas *B. enteritidis* (Gaertner) seems to be coagglutinated both by the typhoid and paratyphoid B elements.

3. Titres as high as 1/320 and 1/640 for these micro-organisms may be encountered amongst individuals who yield no evidence of existing or previous enteric infection. So, for practical purposes, if a diagnosis is to be made on a single agglutination reaction the titre must be very considerably higher than 1/640 for these organisms. We shall probably be justified in regarding a titre of over 1/1000 as suggestive of infection with the organisms concerned, and a titre of over 1/2000 as strongly suggestive of the same conclusion, but in all cases it will be necessary, if an accurate diagnosis is to be arrived at, to perform repeated tests and to demonstrate that fluctuation in the agglutinin-content of the patient's serum which is now generally recognised as characteristic of infection with organisms of this group and which the studies of Dreyer and his associates have enabled us to follow with an accuracy hitherto unobtainable.

In conclusion, our thanks are due to Dr. W. W. C. Topley, at whose suggestion the investigation was carried out, for his kind advice throughout; to Drs. A. R. Berry, Henry Wilkinson, F. G. Rose, and S. D. Stewart for their help in performing the tests; and finally to Dr. B. Graves and others for supplying details regarding the inoculation states of the patients.

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THE COLLOIDAL BENZOIN REACTION IN THE CEREBRO-SPINAL FLUID.

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It has been known for some considerable time that the cerebro-spinal fluid presents certain specific alterations in syphilitic disease of the central nervous system. The number of mononuclear cells present is increased, the globulin content becomes augmented, and along with these the Wassermann reaction (W.R.), in the fluid, becomes positive in a large proportion of cases. It is known that the appearance of a positive W.R. in the blood is associated with certain changes in the physical state of the serum which are best brought out by this test, but which can also be demonstrated in more obvious fashion. The simple mixing of the serum with certain of the alcohol-soluble antigens in use in the test will result, in a large proportion of cases of syphilis, in the appearance