J. F. Watkins

SUMMARY
A small outbreak of dysentery due to a sulphonamide-resistant Sh. sonnei is described. The treatment with oral streptomycin is discussed. Rapid elimination of a symptomless excretor, oral anti-biotic therapy and isolation of the patients limited the extent of the disease.

REFERENCES

SALMONELLA PARATYPHII BO AGGLUTININ LEVELS IN PARATYPHOID B FEVER

BY
Formerly Major, Royal Army Medical Corps*
Specialist in Pathology

The sera described in this paper were taken from 107 proved cases of paratyphoid B fever and 38 undiagnosed cases of pyrexia occurring over the same period during an outbreak in the Royal Sussex Regiment in the Canal Zone, Egypt, in 1952. None of the patients received chloramphenicol or any other antibiotic during the course of their illness. All had been immunised with T.A.B. vaccine.

MATERIALS AND METHODS
Sources of sera. Sera from the following sources were examined:

1. Proved cases: total in outbreak: 107
   Cases providing at least one sample: 100
   Cases providing two samples at intervals: 44
2. Clinical enteric fever cases: total in outbreak: 38
   Cases providing at least one sample: 29
   Cases providing two samples at intervals: 18

"Proved cases" were patients from whose stools or blood Salmonella paratyphi B was isolated at least once by standard methods. "Clinical enteric" cases were patients from the same unit who had pyrexia during the outbreak and from whose blood or stools no pathogenic organisms were isolated in spite of repeated examinations. Control sera were selected at random from samples sent for routine W.R. investigation. Cases providing W.R. sera were clinically well and belonged to other units, in which no enteric infections were occurring at the time.

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Serum was collected from clotted blood left overnight at 4° C. and was stored at 4° C. until titrated.

*Titration of sera.* Doubling dilutions of serum in 0.9 per cent saline were made from 1 in 10 to 1 in 320 in 3 in. × ½ in. tubes, leaving 0.5 ml. in each tube. 1/40 ml. of concentrated standard BO suspension containing $8 \times 10^9$ organisms per ml., supplied by The David Bruce Laboratories, was added to each tube. A saline control and the same positive serum control were included in each batch of titrations. Tubes were incubated at 37° C. for two hours, then placed at 4° C. overnight and read next day after standing at room temperature (20-22° C.) for one hour. The end point was taken as the last tube showing agglutination visible to the naked eye. Paired sera were always titrated in the same batch.

**RESULTS**

*Distribution of serum titres in the first two weeks after onset of illness.* The results from all samples taken during the first two weeks are compared in Table 1. The following facts emerge:

Table 1. *Percentage distribution of anti-BO titres in sera taken in the first two weeks of illness, and in control W.R. sera.*

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of sera</th>
<th>Serum Titre</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;1/10</td>
</tr>
<tr>
<td>Proved cases</td>
<td>104</td>
<td>0</td>
</tr>
<tr>
<td>Clinical enteric</td>
<td>39</td>
<td>5.5</td>
</tr>
<tr>
<td>W.R. sera</td>
<td>32</td>
<td>15.5</td>
</tr>
</tbody>
</table>

(a) There was no titre less than 1/10 in proved cases, while several clinical enteric and W.R. sera were below 1/10.

(b) The distribution curve in proved cases shows a peak at 1/40, while the curve of titres in clinical enteric cases is shown to the left with its peak at 1/20.

(c) The highest titre in the W.R. sera was 1/80. This indicates that a single serum titre of 1/160 or more from a suspected case may support a diagnosis of paratyphoid B.

(d) No conclusions can be drawn from a serum titre of 1/80 or less in an immunised person during the first two weeks of illness. That is, a patient with a serum titre as low as 1/10 two weeks after onset could nevertheless be suffering from paratyphoid B.

*Over-all antibody response in proved cases.* Fig. 1 is a scatter diagram in which all the serum titres from proved cases have been plotted against the days after onset on which the sera were taken. The diagram shows no tendency for higher titres to be obtained later in the disease, so that in this outbreak there was, over all, little or no rise in antibody level. Serial antibody determinations on individual patients were not made, but the results of paired serum titrations suggest that in most individuals little or no rise in titre occurred.
Value of paired sera in retrospective diagnosis. Table 2 shows the presence or absence of a rise in titre in paired sera from proved and clinical enteric cases. All except four of the first sera in each pair were taken in the first week of illness. The second sera were taken at times ranging from two to six weeks after onset. There was no significant difference in the proportions showing a rise in proved and clinical enteric cases. In proved cases only 20 per cent showed a rise of two tubes in titre. If a rise of two tubes or more is taken to indicate infection, 80 per cent of proved cases gave a negative result.

Some of the proved cases showed a fall in titre. The six pairs from proved cases showing such a fall all came from patients who were diagnosed by blood

Table 2. Alterations in anti-BO titre in paired sera from proved cases and clinical enteric cases.

<table>
<thead>
<tr>
<th>Category</th>
<th>Number providing paired sera</th>
<th>No change</th>
<th>One tube rise</th>
<th>Two tubes rise</th>
<th>One tube fall</th>
<th>Two tubes fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proved cases</td>
<td>44</td>
<td>19 (43%)</td>
<td>10 (23%)</td>
<td>9 (20%)</td>
<td>3 (7%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Clinical enteric</td>
<td>18</td>
<td>10 (53%)</td>
<td>4 (22%)</td>
<td>2 (11%)</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>
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culture only, although several stools were examined. Table 3 shows the days on which sera with a fall in titre were taken. Most of the second sera in this table were taken a long time after onset, so that the fall may represent a return to the original antibody level after an initial rise.

Table 3. Days on which paired sera with a fall in titre were taken.

<table>
<thead>
<tr>
<th>Category</th>
<th>Days after onset on which sera were taken</th>
<th>Change in anti-BO titre</th>
</tr>
</thead>
<tbody>
<tr>
<td>roved cases</td>
<td>Serum 1: 19, 5, 3; Serum 2: 37, 44, 41</td>
<td>Two tubes fall</td>
</tr>
<tr>
<td></td>
<td>Serum 1: 6, 3, 24; Serum 2: 11, 42, 47</td>
<td>One tube fall</td>
</tr>
<tr>
<td>Clinical enteric</td>
<td>Serum 1: 5, 8; Serum 2: 8, 35</td>
<td>One tube fall</td>
</tr>
</tbody>
</table>

DISCUSSION

The agglutinin titres in this series are similar to those recorded by others. Gardner & Stubington (1932) found anti-O titres of less than 1/400 to a formolised Salmonella typhi-murium suspension in 38 of 40 cases of paratyphoid B whose inoculation history was not known. Horgan (1932) found anti-BD titres from 0 to 1/125 one year after inoculation in healthy subjects. Downie & Fairbrother (1934) found anti-BD titres from 0 to 1/2,560 in 23 cases of paratyphoid B who were uninoculated or had been inoculated more than sixteen years previously.

The results presented here suggest that O agglutination with a single serum is of little value in the diagnosis of paratyphoid B. A single titre of 1/160 or more may be suggestive but is nothing more.

Paired sera were almost useless in diagnosis. Only 9 of 44 proved cases showed a four-fold rise in titre. Two of 18 clinical enteric cases had a four-fold rise in titre and might on this evidence have been added after the outbreak to the total of 107 cases proved by bacteriological methods. Fig. 1 might suggest that a more careful timing of serum specimens would give better results, but Mole (1948) found in serial Widal tests in typhoid and paratyphoid A in R.A.F. personnel that only 1 of 8 typhoid patients and 3 of 8 paratyphoid A patients showed a four-fold rise in titre. Both he and Dick (1945) concluded that the Widal test is of no value in the recently inoculated. No sera from patients suffering from diseases other than enteric were included in the figures presented here, but Wilson (1945) and others have reported non-specific rises in agglutinins to typhoid O and paratyphoid AO in inoculated subjects with non-enteric infections, though the frequency of a rise in titre was greater in enteric infections. Therefore even a four-fold or greater rise in titre is difficult or impossible to interpret.
The titres in W.R. sera, from personnel most of whom had been inoculated for the first time, or had received a booster dose within the preceding year, indicate a fairly high level of BO agglutinins in the normal military population.

It is impossible to assess the value of prophylactic inoculation from these figures, but it is worth noting that paratyphoid B in the Canal Zone was predominantly of a mild, enteritic type. Raettig (1950) produced evidence in Germany that prophylactic inoculation against paratyphoid B lowered the mortality significantly but had no effect on the morbidity of the disease.

The general mildness of the illness may account for the failure to show a clear-cut secondary response, but whatever the reason these results do not conform to the conventional idea of a rapid rise in anti-O antibodies in T.A.B.-inoculated subjects infected with organisms of the enteric group. Any rise in the first fortnight was very small, as Fig. 1 showed, so that protection appears to come from antibodies present as a result of inoculation and not from a rapid increase in antibody production after infection. This argument assumes that O antibodies detected by agglutination correspond to protective antibodies, an assumption which has not been completely proved.

SUMMARY

The results of paratyphoid BO agglutinations in 107 proved cases of paratyphoid B and 38 "clinical enteric" cases in an infantry unit are presented.

Routine BO agglutination on single or paired sera was of little value in diagnosis in this outbreak.

Cases over all showed little or no rise in antibody levels.

REFERENCES

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