THE EARLY HISTORY OF TYPHOID VACCINATION*

BY

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WHEN General Hilton-Sergeant asked me to give one of the evening lectures this session, I thought it might be of interest to recall some of the early work on typhoid vaccination. I realize that to many of you it must be more familiar than it is to me, and you may think it presumptuous of an outsider to discuss in this building work which was carried out almost entirely by members of the Army Medical Services. I hope, however, that what I have to say will be as fresh to some of the younger members of the Royal Army Medical Corps as it was to me when, for reasons which some of you will know, I became specially interested in it about a year ago. For the past seven years I have been closely associated with a series of field studies into the value of another bacterial antigen— whooping-cough vaccine—and am perhaps in as good a position as anyone to appreciate the difficulties which had to be overcome, and the amount of effort which went into the field work, in the early studies of typhoid vaccines.

It is convenient to define the early history of typhoid vaccination as that of the period between 1896 and the beginning of the 1914-18 war, and for the purpose of this lecture to confine the story to the work on vaccination done in Britain and in the British Army.

* Based on a lecture given at the Royal Army Medical College on 14th January, 1954.

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PREVALENCE OF TYPHOID FEVER IN THE LATTER HALF OF THE NINETEENTH CENTURY

It is difficult for us to appreciate now the importance of the enteric fevers in the fifty years before vaccination was introduced, but it is necessary to have some understanding of this and of the increasing interest in the epidemiology of the disease before discussing vaccination. In the civil population in England and Wales in 1870 there were about 500 deaths per million of the population. In 1880 there were about 300 deaths per million, and in 1890 about 200 per million. You will notice that though the rates were very high they were falling before the end of the century and, as you know, the rapidity of the decline increased until in the early 1920’s they became negligible. In the armed services during war time and in peace time in foreign stations at the turn of the century the incidence of enteric was far greater than in civil life; in the Spanish-American War of 1898, for instance, one in five of the 100,000 officers and men engaged were recorded as having developed enteric fever, and 1,600 of the recorded cases were fatal. The incidence was probably very much greater than the official figures suggested. When Vaughan (1899) and his colleagues made an investigation they found that, in order to cover up the true position, many of the cases were being diagnosed as other diseases. In one regiment all the deaths were ascribed to dengue, and in another 15 per cent. of the deaths were said to have been due to “indigestion.” Yet on making serological examinations Vaughan found evidence of recent enteric infection in almost every case of prolonged pyrexia.

When reading about enteric fever in the second half of the nineteenth century one can see how the emphasis slowly changed from descriptions of methods of treatment to reports on investigations into the sources and modes of spread of infection. After Budd’s paper in 1856, reports on water-borne outbreaks began to appear and by the end of the century were frequent. One of the earliest was the description of the outbreak in Lausen in Switzerland in 1872, when about 130 of the 780 inhabitants of the village developed typhoid between August and October. All the cases were in persons who used the public water supply. This outbreak is of interest not only because it was one of the first water-borne outbreaks to be reported, but also because of the very careful studies which were made to establish the source of infection. The water supply came from a well at the foot of a hill. On the other side of this hill was a valley through which ran a stream believed by some of the villagers to have a subterranean connection with the well in the village. As three cases of enteric had occurred in June and July in peasants living near this stream, the story of the supposed connection became important. Some 1,800 lb. of salt were poured into the stream and three hours later an increased salinity was detected in the village water supply, so that the water supply could have been contaminated from the apparently remote stream.

Water-borne outbreaks in this country were reported from Caterham in 1897, Worthing in 1893 and Maidstone in 1897. The details of these will be...
known to many of you and need not be described. In the United States of America one of particular interest occurred in Pennsylvania in March-April, 1885, when 1,000 of the 8,000 inhabitants of a town were affected and 114 cases were fatal. So explosive was this epidemic that at its height over 100 cases a day were being diagnosed. As with Snow's investigations on cholera, the differential distribution of the cases between one source of water supply and another yielded important information. For example, in a street where all the houses on one side had a public water supply and all those on the other side had private wells, the cases were confined to those who lived on the public water supply side. The source of infection in this instance was a man who lived near the stream from which the water supply came and who had had typhoid in January, three months earlier. His excrement had been thrown on to the banks of the stream, where it remained frozen until March; with the thaw the whole accumulation of infected faeces from the case was washed into the stream and thence to the water main.

Here one person was sufficient to defile a water supply which came from a mountain stream draining almost uninhabited territory. It is said that this outbreak greatly stimulated the people of North America to safeguard their water supplies. Both there and in this country methods for the provision of safe water and the safe disposal of sewage began to be rapidly applied. In fact, there may have been at this time too much concentration on contaminated water supplies, for, though they were the commonest cause of large epidemics, we now know that there are many other modes of spread. Vaughan (1899) noted this in his investigation of the Spanish-American War epidemics and came to the conclusion that water played a very minor part in the spread of infection in American army camps. He considered that the main sources were the fouling of the ground with faeces and urine and the abundance of flies in the camp areas.

**Typhoid Vaccination**

It is against this background of growing knowledge of methods of spread that we have to consider the history of typhoid vaccination.

The idea that a killed culture of typhoid bacilli might induce immunity to the natural disease came to Wright after a discussion with Haffkine, who had used a somewhat similar method against cholera. Wright and Semple (1897) made their first injections in 1896 and published their report in the following year. Pfeiffer and Kolle are thought to have established priority, however, by their publication in 1896. Wright and Semple employed a diluted broth culture heated to 60°C for five minutes and made careful observations on the antibody production in several of the men whom they injected. They compared the properties of the serum of the inoculated with serum from convalescent patients, and observed that the properties of the sera from the two sources were similar. They suggested that the agglutinating power of the sera could be used as an index of immunity, though they were careful to point out that agglutination was not necessarily the only or the most important factor in immunity.

As is well known, there were sometimes considerable local and general
reactions after the injection of these early vaccines. Cameron (1896-7) gave a
good description of the reactions which occurred after he himself was injected
in the loin. Three hours after the first dose he had local swelling and pain, with
reddenning of the lymphatics up to the axilla and down to the groin. Later he
found his axillary and inguinal glands enlarged and tender. The second dose
was followed by a rigor, severe headache, malaise and muscle pains for forty-
 eight hours. On examining his serum he found the agglutination titre had
increased, and he concluded that if the injections prevented typhoid fever the
temporary pain and discomfort were worth enduring.

Wright (1900) used his opportunities as a member of a Plague Commission
in India in 1898-9 to inject some 4,000 soldiers in the Indian stations he visited.
He used broth cultures of a virulent strain killed by heat and preserved with
1 per cent. lysol. The volunteers were generally the younger soldiers recently
out from England, in whom, as you know, the incidence of infection was usually
highest. He noted that some of the reactions were severe. So far as I can
make out, only one dose of vaccine was given. The information on the sub-
sequent history of the men was collected by many regimental medical officers,
and in some units the results were said to be good, while in others they were
inconclusive. An interesting feature of these trials was that Wright was unable
to take sufficient vaccine with him from England and during his tour he prepared
fresh batches. These batches were tested for toxicity in guinea-pigs, and as
the stay of the Commission at each station was short the test guinea-pigs had
to be carried along with the Commission so that Wright could gauge the toxicity
of the newly-prepared vaccines. Wright was unhappy about the sterility of
his vaccine and at each station he resterilized all his stock by heating it to 60° C.
before he used it. I doubt if any immunologist would now expect one dose of a
typhoid vaccine repeatedly heated to 60° C. to give any degree of protection.
Wright, however, and others also, considered the results were encouraging, and
in the South African War which began soon afterwards he and Leishman
prepared vaccine, and supervised the administration of it to about 100,000 men.

It was thought that the South African War experience would settle con-
clusively the value of vaccination, for, as you know, enteric fever was rife
during the whole campaign. In a mean annual strength of 208,000 men, 10 per
cent. per annum were admitted as cases and about 1.5 per cent. per annum died
of the disease.

When the results came to be analysed no agreement on the value of vaccina-
tion could be reached. There were many reasons for this, unconnected with
the method of preparation of the vaccine. Sometimes only one dose was given,
sometimes two doses were given. The recording of the injections was unsatis-
factory, and the investigator had to depend on the soldier's statement. As
can well be imagined, the South African War soldier was often unable to
distinguish between injections of typhoid vaccine and the inoculation of vaccine
lymph. Further, the diagnosis was frequently in doubt and no clear distinction
could be made between typhoid fever and paratyphoid fevers which were
common in South Africa, though paratyphoid bacilli were not included in
the vaccine. Leishman himself stated more than once between 1907 and 1910 (see, for example, Leishman, 1910) that it was impossible to say whether the inoculated and uninoculated men in South Africa had been exposed to the same degree of risk, and that no satisfactory evidence of the value of vaccination was obtained. Karl Pearson (1904) and Sir David Bruce (1905) made extensive investigations into the available figures and came to similar conclusions. Pearson stated that “[The results] fall into that range of intensity which would justify suspension of the operation [vaccination] as a routine method.” Bruce was of the opinion that “the general statistics are not sufficiently extensive or exact to permit of any conclusions being drawn as to the utility of Wright’s anti-typhoid inoculation.” Five years later, in his address as President of the United Services Medical Society, Bruce was much more downright and said: “Anti-typhoid inoculation was in vogue during the last South African War, but it proved useless.” Wright and others did not agree with the criticisms, and Wright and Pearson conducted an informative and sometimes acrimonious correspondence in the British Medical Journal for 1904.

Because of these critical reports, because of occasional severe reactions, and because of fear of the “negative-phase”—which fear appears to have been unfounded when a suitably small dose was given—an anti-typhoid committee under the chairmanship of C. J. Martin was set up to investigate the problem further. Leishman was the active member of this committee, and the Report (1912) reveals how much hard work he and his colleagues in the Army Medical Services at home and abroad carried out in the laboratory and the field between 1904 and 1909.

This Report is still considered to provide authoritative evidence on the value of typhoid vaccination in the field. It is quoted in the 1946 edition of Topley and Wilson’s Principles of Bacteriology and Immunity and by Sloan Miller (1951). Along with it are usually mentioned the favourable comments by Greenwood and Yule (1915), who analysed the results in a series of papers read at the Royal Society of Medicine.

The Report is in two parts. Part 1 deals with laboratory experiments on the methods of preparation and testing of vaccines in the laboratory. From the information gained in the laboratory experiments it was decided that the best vaccine was a saline suspension of typhoid baccilli killed by heating to 53°C for one hour and preserved with 0.5 per cent. lysol. Part 2 of the Report is a record of the plan and results of the field studies, and no one who has read it can fail to be impressed with the scope of the investigation and the magnitude of the effort required for its execution.

Plan of the Field Studies

In order to test the vaccine exhaustively, the Committee decided that between 1904 and 1908 a specially appointed medical officer should be attached to each regiment of cavalry or infantry and each brigade of artillery about to go on foreign service. Each medical officer was instructed:
The Early History of Typhoid Vaccination

(a) To accompany the unit to which he was attached on all changes of station for three years.
(b) To inject volunteers in the unit before and after it left Britain.
(c) To keep records of the men injected and of the number of cases in the injected and uninjected.
(d) To carry out agglutinin tests on definite and doubtful clinical cases.
(e) To attempt to confirm the cases by the isolation of the infecting organism.

Twenty-four units, mainly in India, were included in the investigation, and they were observed for 4-46 months after arrival at their foreign stations.

Results:

At the dates of the final reports from the medical officers engaged in the studies there were, in round figures, 10,000 men in the injected group and 9,000 men in the uninjected group. Fifty-six cases occurred in the injected and 272 cases in the uninjected, giving attack rates per 1,000 men of 5.4 in the injected and 30.4 in the uninjected. The difference was highly significant when statistical tests were applied. In the Committee's opinion the difference could only be attributed to the preventive effect of the injections, and they recommended that anti-typhoid vaccination should be extended immediately to all members of the forces. This recommendation was carried out on a voluntary basis, and on this voluntary basis it still continues.

Before we accept the findings of the Committee it is necessary to examine the methods used in the collection of the information and to decide whether the conclusions were fundamentally sound, for no statistical test can be considered valid if the information on which it is based has been subject to error, however unforeseeable that error may have been.

The criteria which from recent experience are necessary for a strictly controlled study may be briefly defined as follows:

1. The men to be injected and the men to serve as controls must be chosen so that when considered as groups they are alike in every relevant respect.
2. The groups must be subject to the same risk of exposure.
3. The two groups must be observed with the same thoroughness over the same period.
4. The clinical diagnosis of disease in the two groups must if possible be confirmed by objective means such as the isolation of the infecting organisms.
5. Neither the observers nor the subjects observed should know until the end of the investigation whether a particular person belongs to the test or the control group.

These criteria were not satisfied in the 1904-1908 studies: the importance of some of them was not recognized, and others—for example, the isolation and
TABLE I.—UNITS 1 TO 7

<table>
<thead>
<tr>
<th>Unit</th>
<th>Date of arrival abroad</th>
<th>Period of observation (months)</th>
<th>Strength on arrival at the foreign station</th>
<th>Strength at the end of the trial</th>
<th>Number of cases</th>
<th>Attack rate per 1,000 men (1)</th>
<th>Attack rate per 1,000 men (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dec. 1904</td>
<td>42</td>
<td>Injected 106 Not injected 777</td>
<td>Injected 198 Not injected 815</td>
<td>12</td>
<td>61</td>
<td>113</td>
</tr>
<tr>
<td>2</td>
<td>Oct. 1905</td>
<td>46</td>
<td>Injected 130 Not injected 446</td>
<td>Injected 460 Not injected 160</td>
<td>18</td>
<td>39</td>
<td>138</td>
</tr>
<tr>
<td>3</td>
<td>Dec. 1905</td>
<td>31</td>
<td>Injected 46 Not injected 310</td>
<td>Injected 202 Not injected 128</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Sept. 1906</td>
<td>34</td>
<td>Injected 211 Not injected 388</td>
<td>Injected 377 Not injected 257</td>
<td>4</td>
<td>11</td>
<td>19</td>
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<tr>
<td>5</td>
<td>Oct. 1906</td>
<td>34</td>
<td>Injected 90 Not injected 618</td>
<td>Injected 540 Not injected 214</td>
<td>2</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>6</td>
<td>Oct. 1906</td>
<td>33</td>
<td>Injected 149 Not injected 789</td>
<td>Injected 589 Not injected 321</td>
<td>5</td>
<td>8</td>
<td>34</td>
</tr>
<tr>
<td>7</td>
<td>Nov. 1906</td>
<td>31</td>
<td>Injected 62 Not injected 996</td>
<td>Injected 311 Not injected 797</td>
<td>1</td>
<td>3</td>
<td>16</td>
</tr>
</tbody>
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|     |                       |                                |                                            |                               |                |                                |                                |
|     |                       |                                | 794                                        | 4,324                         | 2,677          | 2,692                          | 42                             | 223                           | 16                            | 83                            | 53                            | 52                            |

(1) Based on the number of men in each group at the end of the trials (the method of calculation used by the Committee).

(2) Based on the number of men in each group at the beginning of the trials (the method used by Greenwood and Yule).

Identification of the organism—were difficult to carry out. In some cases a bacteriological diagnosis was made. In many, reliance was placed on serological tests, the results of which in injected men are still difficult to interpret. In those days it was also difficult to distinguish between typhoid and paratyphoid infections by serological examinations.

The incidence of infection in inoculated volunteers was compared with that in uninoculated non-volunteers, and such a method of comparison would not now be accepted as valid as volunteers, by the fact that they have volunteered, must differ from those who have not volunteered. Pearson considered this factor of the greatest importance, and suggested in 1904 that in studies of this kind only half the volunteers should be injected and that the incidence of disease in injected volunteers should be compared with that in uninjected volunteers. If this had been done, some criticisms would have been prevented. On the other hand, Greenwood and the members of the Anti-Typhoid Committee believed that both volunteers and non-volunteers in the same unit were exposed to the same risk of infection. There is no means now of determining the effect of the method employed on the accuracy of the results, but experience has shown that it is one which frequently leads to false conclusions on the efficacy of a vaccine. In one unit in the investigation (Unit 1, see Table I) the incidence of disease in the volunteers was similar to or greater than that in the non-volunteers. The volunteers were injected with the "old-type" vaccine killed by heating at 60° C. for five minutes, which the investigators considered less effective than
the “new-type” vaccine used for the injections in the other 23 units. If it is accepted that the old-type vaccine was less effective than the new type, these results could be taken to indicate that at least in some units the risks of infection in the two groups were similar.

The next point of importance to be considered is whether the men in the two groups were kept under observation for the same length of time. If 100 uninjected men were observed for twenty-four months and 100 injected men were observed for only six months, it is not unreasonable to suppose that more cases might occur in the uninjected than in the injected, because the uninjected presumably had a greater chance of being exposed in two years than the injected had in six months. In some of the units, particularly those which were included in the early part of the study, many of the men were injected towards the end of the trials and were in the injected group for a few months only, though they might previously have been in the uninjected group for about two years. Greenwood and Yule were aware of the influence of this procedure on the results and they compensated for it by relating the numbers of cases, not to the numbers of injected and uninjected men at the end of the study as was done in the Report, but to the numbers in each group at the beginning. As men were moved from the uninjected to the injected group during the study, the numbers in the injected group were less and in the uninjected group were greater at the beginning than at the end, so that calculation of attack rates on the numbers in each group at the beginning favoured the uninjected. By this method of calculation the attack rates were for the injected 8 per 1,000 men and for the uninjected 23 per 1,000 men—a threefold difference compared with the sixfold difference given in the original report. The differences obtained by Greenwood and Yule’s method were still significant. If, however, the units are divided into three groups according to the date on which the observations began (before the end of 1906, during 1907, and after the end of 1907), as has been done in Tables I, II and III, we find that in the first seven units (Table I) there is no difference between the injected and uninjected if the rates are calculated on the numbers of men in each group at the beginning of the period of observation. There is, however, a difference in the incidence in injected and uninjected men in the units listed Tables II and III. The lack of difference in the units in Table I may be due to the test being too stringent, for it is evident that, in contrast to the later units, comparatively few of the men in the earlier units had volunteered to be injected by the time they arrived at their foreign stations. On the other hand, it is clear from the records of Unit 2 (Table I) that the attack rate in the uninjected of 600 per 1,000 men, based as it is on the number of men not injected at the end of the study, was due in great part to the fact that by the end of the study only 160 of about 600 men were left uninjected. It is impossible to determine from the report at what stage of the observations the uninjected men in the early units began to volunteer to be injected, though one of the factors which influenced the men was the occurrence of typhoid. It is, for example, stated that “this [obtaining volunteers] was found to be an easier task when the unit in question was actually serving in a station where
enteric fever was present.” In these circumstances men injected during or after an outbreak could only have been among those not suffering from the disease, and they may not have owed their subsequent immunity to the injections—they may have already had a natural immunity derived from a sub-clinical

<table>
<thead>
<tr>
<th>TABLE II.—Units 8 to 14</th>
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<tr>
<td>Unit</td>
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<td>8</td>
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<tr>
<td>13</td>
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<tr>
<td>14</td>
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<tr>
<td></td>
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ATTACK RATES

<table>
<thead>
<tr>
<th>Injected</th>
<th>Not injected</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6</td>
<td>14.2</td>
</tr>
<tr>
<td>3.5</td>
<td>12.3</td>
</tr>
</tbody>
</table>

(1) Based on the number of men in each group at the end of the trials (the method of calculation used by the Committee).

(2) Based on the number of men in each group at the beginning of the trials (the method used by Greenwood and Yule).

<table>
<thead>
<tr>
<th>TABLE III.—Units 15 to 24</th>
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<tbody>
<tr>
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<tr>
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<td>22</td>
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<tr>
<td>23</td>
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ATTACK RATES

<table>
<thead>
<tr>
<th>Injected</th>
<th>Not injected</th>
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<tbody>
<tr>
<td>1.8</td>
<td>7.5</td>
</tr>
<tr>
<td>2.3</td>
<td>6.2</td>
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</tbody>
</table>

(1) Based on the number of men in each group at the end of the trials (the method of calculation used by the Committee).

(2) Based on the number of men in each group at the beginning of the trials (the method used by Greenwood and Yule).
dose of infection before the injections were given. It is particularly unfortunate that the evidence from the first seven units is so difficult to interpret because 42 of the total of 56 cases observed in the injected men and 223 of the 272 cases observed in the uninjected men during the whole period of the investigation occurred in these units.

Only 14 cases in the injected and 49 in the uninjected occurred in the units which arrived at foreign stations after the end of 1906 (Tables II and III). Here the numbers of men in the injected and uninjected groups at the beginning and the end were more equal, and by Greenwood and Yule's method of calculation the attack rates in the two groups were 2.8 per 1,000 and 8.3 per 1,000—again a threefold difference in favour of the vaccinated. This is the same as Greenwood and Yule obtained by including all units in their calculations—but it is now shown to be based on a very small number of cases. Corrections for the duration of the observations therefore reduce the difference in attack rates between the two groups, but do not dispose of it.

The influence of other factors must now be taken into account. In the calculations it has been assumed that the same men were present in the units at the beginning and end of the study. This was by no means the case, for it is stated in the report that there were marked fluctuations in the strength of the injected and uninjected men from time to time due to postings, to and from the units, to time-expired men being discharged, to new arrivals from the United Kingdom, to sick men being admitted to hospital and to the many day-to-day changes which are common to all units in the Services. No method of analysis can take account of these changes, for no information on the numbers of men concerned or of the dates of their entry or exit is given.

The accuracy of the diagnosis must also be considered in some detail. It is stated that “Widal's reaction had been carried out in every instance” and that in a “large proportion of the cases the attempts which had been made to isolate the typhoid bacillus during life from the blood or excreta had been successful.” The difficulties in interpreting the agglutination reaction in injected men have already been mentioned, and no indication of the numbers constituting the “large proportion” from whom the organism was isolated or of their distribution between the injected and uninjected men is given.

Only in two units is there an indication. In Unit 9 all of seven cases in the uninjected were confirmed bacteriologically, and in Unit 14 the typhoid bacillus was isolated by blood culture from one case and a paratyphoid bacillus was isolated from another during the same outbreak. In the absence of information on the numbers of cases confirmed bacteriologically in the injected and uninjected it is permissible to have doubts about the invariable accuracy of the clinical diagnosis as the observers, especially those in charge of the units which entered the study in the later stages, were undoubtedly convinced that the vaccine was of value. In these circumstances it is difficult to rely upon the absence of unconscious bias on the part of the observers. They might, for example, have believed that a mild or atypical case could not have been typhoid fever if the patient had been vaccinated.
In these extensive studies, therefore, the value placed on the evidence that the vaccine was responsible for a threefold reduction in the incidence of typhoid fever in the injected men depends on the importance attached to the following points:

1. The injected men were volunteers and the uninjected men were not.
2. The diagnosis may not always have been accurate.
3. Men were transferred to and from units during the period of the study, but the numbers of men concerned and the time spent by them in the units is not known.
4. The observers believed that the vaccine was of value and may have been biased when diagnosing cases in injected men.

**Severity of Attack**

In the report information is given on the severity of the illness in the two groups, and it is concluded that 66 per cent. of the cases in the injected men were mild compared with 29 per cent. in the uninjected men and that 34 per cent. in the injected were severe or fatal compared with 71 per cent. in the uninjected. As the report describes the severity of the illness in only 202 of the 272 cases in the uninjected men, and as no information on the other 70 cases is given, the information on severity cannot be interpreted satisfactorily.

**Seventeenth Lanciers**

So far the trials have been described as a whole, but it is now necessary to examine the information about Unit 2 (17th Lanciers) in some detail. It has already been mentioned that the incidence in the uninjected men during the whole of the duration of the trial in this unit (see Table I) is of little value as recorded in the 1912 Report, but Captain Luxmoore’s report of the experience of the unit a few weeks after arrival at Meerut is of interest (Luxmoore, 1907). The men arrived early in October, 1905, and at that time 130 other ranks had received one or two injections and 360 were uninjected. (The figure for the uninjected is less than that in Table I, because I excluded a number of men who arrived in the unit in December after cases of typhoid had begun to occur.) The unit experienced an enteric outbreak which was clinically typical of typhoid fever and, though there was no bacteriological evidence, there was little doubt that the disease was in fact typhoid fever and not paratyphoid fever. The first cases occurred before the end of October, and by the end of December a total of 46 had been diagnosed. Only one of the cases was in the injected group and that was in a soldier who had received only one dose. The attack rate, therefore was 13 per cent. in the uninjected and 1 per cent. in the injected. If we were certain that the injected and uninjected men were exposed to the same risk, we should be justified in considering the results most promising. There are two points, however, which need to be considered. The first is that 17 of the cases occurred in a detachment of men who went on special duty for about a week to Delhi. Karl Pearson has said (see Maynard, 1908-9) that this may...
have been important, for if only uninjected men had gone to Delhi they might have been at greater risk. But from reading Captain Luxmoore's report of the outbreak I think it is reasonable to assume, taking into account the dates of onset, that at least some of the Delhi contingent were infected before they left Meerut. The second point is whether the injected men—who were of course volunteers—should be considered "similar in all respects" to the uninjected men who did not volunteer. The Committee's opinion and that of Greenwood and Yule on this point has already been stated, but no one can now be certain of the real answer. Karl Pearson considered that comparing volunteers with non-volunteers destroyed the value of the observations. There is no doubt that volunteers in the 17th Lancers were obtained with great difficulty. Colonel Leishman personally visited Edinburgh—where the unit was stationed before embarkation—and after obtaining what is described as the "cordial cooperation" of the colonel, he and Captain Luxmoore gave a series of lectures to the men and obtained the consent of between one-quarter and one-third of them. I was privileged recently to discuss the situation in the 17th Lancers with Captain—now Surgeon-Colonel—Luxmoore. He thought that the volunteers were representative of the unit except that most of them were the younger soldiers; the older men had heard of the severe reactions experienced by those inoculated in the South African War and had refused to be injected. As enteric has usually been commonest in the recently-arrived young soldier in India this is a point in favour of the validity of the results. My own impression is that the volunteers in this unit may have been more mindful of risks than the non-volunteers, especially as vaccination was commended by the Officer Commanding the unit and as nearly all the officers volunteered for inoculation (though they are not included in the analysis of the results). In this, the only unit where the conditions in the two groups was similar in most respects, the interpretation of the results depends on whether we believe that the injected volunteers were exposed to the same risk as the uninjected men. On this point there is room for different opinions.

Prevention of Spread of Infection in the Indian Army

It was on the basis of the results of the 1904-1908 studies that vaccination was offered to volunteers in the Indian Army, and this coincided with a reduction in the incidence of enteric fever. For example, between 1890 and 1899 the admissions per 1,000 men varied annually from 37 to 19; in the period 1900 to 1906 from 20 to 13; and in the years 1907-1912, when vaccination became common, the annual admission rates were respectively 13, 15, 8, 4, 2 and 2. How much of this decrease was the result of vaccination? I said at the beginning that vaccination against typhoid was introduced at a time when knowledge of the modes of spread was rapidly increasing. In 1902 and 1903 Koch and his co-workers in Alsace-Lorraine and other areas in south-west Germany, in their extensive efforts to control the disease, demonstrated for the first time conclusively that:

(a) The human host was the storehouse of infection;
(b) The life of the organism outside the human body was very short;
(c) Convalescent carriers were frequent;
(d) Some patients became chronic carriers;
(e) Some carriers had no definite history of a clinical attack.

Semple and Greig (1908) were asked by the Government of India to make a similar investigation, and they published a most informative paper in which they demonstrated: (1) That a proportion of convalescent cases excreted the organism for long periods, sometimes intermittently; (2) that four outbreaks they investigated during their inquiry were due to carriers, two of them to carriers in cookhouses; (3) that nursing orderlies in enteric wards—who were seconded for nursing duties for six months and then returned to their (non-medical) units—could become temporary excreters or carriers with or without a history of a definite clinical attack, and were sometimes returned to their units while still excreting the organism.

As a result of their findings, which were probably well known in India before their paper was published, the methods for the prevention of the spread of infection in the Army in India were changed. Aldridge (1909) described the new methods. “Suspected cases are isolated in an observation ward, diagnosed cases in a special ward and convalescent cases in a separate ward.” The bowel and urine discharges of cases were placed immediately into disinfectant, and the water used for washing the sick was also disinfected. The sweepings of the wards were burned and the excreta of the cases boiled before being disposed of. Convalescent patients were sent to a hill station and examined regularly until negative and barrack-room bedding and latrines were disinfected. All the men in the same tent or barrack room as that in which the case occurred were segregated and inspected frequently for one month. Measures in all units included the periodical examination of food-handlers, the covering of food-stuffs with gauze and the substitution of cresol and water for dry earth in the latrine pans.

Firth (1911) mentioned that new arrivals in units were segregated for a period, and that between 1909 and 1910 the convalescent depot had detected 31 carriers among convalescent cases. Faichnie (1915) reported that for many years before the introduction of vaccines he had been impressed with the reduction of incidence which followed the adequate disposal of feces, for example by carefully supervised trenching, and thought the fall in incidence was associated with the lessening of the fly population. In support of his contention he quoted figures for the stations at Ambala, Nasirabad and Meerut where, after the introduction of adequate trenching and efforts to reduce the fly population, the incidence fell from about 30 per 1,000 (at which level it had remained for the previous twenty years) to between 2 and 5 per 1,000. There were many other reports telling of the activities of hygiene-minded medical officers about this time. One (Hayes, 1912) mentioned that in an outbreak in Reading the mops used in the urinals were also used to wipe the barrack-room table tops. Harvey (1915), speaking of earlier days, reported
that "There was no issue of latrine paper to soldiers. There were no facilities for washing hands in or near latrines. Pipes, mugs, clothes and rifles were all used in common."

**Purification of Water**

While latrines, carriers and food-handlers were receiving increased attention, the purification of water supplies by chemical means was also being investigated. Houston and McGowan had chlorinated the water supply as an emergency measure in an outbreak at Lincoln in 1905. Sims Woodhead (1910-11), Thresh (1909-10) and others had made investigations into the purification of water supplies by ultra-violet rays, ozone, hypochlorites and free chlorine in bleaching powder. In the summer of 1914 a change-over from the purification of water by filtration to purification by chlorination was being arranged in the Army, and by the autumn of that year all water supplies to the troops in France and in other theatres of war were being chlorinated.

This was in striking contrast to the water supply situation in the South African War, where instructions for boiling water were issued but little or no fuel for the purpose was provided, where the filter candles supplied invariably clogged or were broken soon after the arrival of the units in South Africa, where instructions on the dangers of failure to observe sanitary precautions were generally disregarded and where officers and men regularly drank foul water on the march (Simpson, 1910).

At the outbreak of the First World War, therefore, enteric was being attacked on three fronts—personal, unit and cookhouse hygiene; purification of water supplies; and anti-typhoid vaccination. It is not possible now to allocate to each the proper share of credit for the reduction in the incidence of enteric fever in war. It is unfortunate that the evidence for the true value of typhoid vaccination rested, as far as field studies were concerned at that time, on grounds which would now be considered only to be sufficiently hopeful to warrant further study by means of strictly controlled trials. Let me make it clear that criticism of the method by which the study was made in the field does not necessarily mean that the vaccine used then was ineffective. It does mean, however, that, unless supported by other good evidence, the favourable reports of the results apparently achieved in the 1904-1908 investigations should be accepted with caution.

**REFERENCES**


