ANTITYPHOID INOCULATIONS.

[Jan. 20, 1900.

ing anemic gastralgia and gastric ulcer in precisely the same way.

TREATMENT.

It is a rule which I would commend to your attention that in the management of stomach disorders obstinate vomiting should be treated by absolute rest in bed and the administra-
tion of the simplest food in small quantities at regular inter-
vals. I generally prescribe 1 ounce of milk and lime water
every hour with the following mixture:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Sulphate of bismuth</td>
<td>40 gr.</td>
</tr>
<tr>
<td>Sulphate of iron</td>
<td>2 gr.</td>
</tr>
<tr>
<td>Diluted sulphuric acid</td>
<td>15 minims</td>
</tr>
<tr>
<td>Peppermint water</td>
<td>1 ounce</td>
</tr>
</tbody>
</table>

three times a day. The milk and lime water, if borne without
pain and vomiting, as is almost invariably the case, is in-
creased every day or every second day up to 4 ounces every
hour, and afterwards the diet is gradually increased by the
addition of bread and milk, minced chicken, and minced
mutton at intervals, so that about twenty-one days after
administration the patient is usually able to eat the ordinary
house diet of the hospital. After this has been taken for two or
three days the patient is allowed to get up, and at the end of
a month is sent to a convalescent home. When the anemia is
marked the mixture may be supplemented by pil. ferri, 5 gr.
or more three times a day. Should the patient not be able to
tolerate so much milk and lime water in this instance, half an
ounce may be given, or if there be only pain without vomit-
ing, a mixture of bismuth and soda may be sub-
stituted for that of iron and magnesia.

In those cases which have recently suffered from hemato-
emesis it is desirable to give by mouth the following
forty-eight hours after the vomiting of blood has
stopped, and during that time I feed them by the following
nutrient emesis given every four hours: one egg beaten up
with one teaspoonful of brandy, and made up to 4 ozs. with
milk. Should there be any irritable quality of the rectum, twenty
to thirty drops of laudanum may be added. While the hemato-
emesis persists, I place an icebag upon the epigastrium,
although I am by no means certain that it does any good;
and I allow the patient to suck small pieces of ice if he
wishes. If necessary, to relieve pain or to keep the patient
quiet, I order a hypodermic injection of ½ to 1 gr. of mor-
phine.

It is of great importance to see that the patient is able to
eat ordinary food with comfort before she leaves the hospital,
and I always try to impress upon each one the im-
portance of continuing to do this after she returns home.
Many of these patients have been dieting themselves for so
long a time, and have become convinced, partly as the result of
injudicious advice, partly from their own experience, that
they cannot eat the same food as other people, that they
suffered in health from an insufficient nutrition, and have
entered a vicious circle in which the anemia is kept up by
want of food, so that the predisposing cause persists, and
recovery is impossible until the circle is broken; it is therefore
the utmost importance to the patient that she can take ordinary food.
It is also very de-
sirable that she should continue to take iron for some time
after leaving the hospital; and I may perhaps be allowed to
mention that the dose of sulphate of magnesium in the mix-
ture should be adjusted to the needs of each case, and may
be very properly increased or diminished at different times as
required.

These simple rules are all that I wish you to remember in
connection with the treatment of ulcer of the stomach, and
I hope I have proved that they are as safe as they are suc-
cessful.

A BRONZE statue of the late Dr. William Pepper, was re-
cently unveiled at Philadelphia, and at the same time the Free
Museum of Science and Art was formally opened, and trans-
ferred to the University of Pennsylvania. The building and
the site cost over 600,000 dollars, towards which Mrs. Pepper
gave 200 dollars.

Efforts are now being made to develop some of the more
favoured parts of Jamaica as resorts for invalids. One of the
most recent is the opening up of Malvern, in the Santa Cruz
mountains, where a hotel has been opened, and where cot-
tages can be hired. The climate is generally equable, the extremes being 64° and 75°, and the climate
generally well adapted for cases of catarrh and bronchitis.

REMARKS

ON THE

RESULTS WHICH HAVE BEEN OBTAINED BY
THE ANTITYPHOID INOCULATIONS

AND ON

THE METHODS WHICH HAVE BEEN EMPLOYED
IN THE PREPARATION OF THE VACCINE.

BY

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M.D.,

and

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Before proceeding to summarise the more important results
which have been obtained up to date by the application of the
antityphoid inoculations, which were inaugurated at Netley in
July, 1896, and which were described by one of us in associa-
tion with Major D. Semple, R.A.M.C., in January, 1897, it
will be well to explain in a few words the conditions under
which the inoculations, whose results are reported below,
were undertaken.

CONDITIONS UNDER WHICH THE INOCULATIONS WERE
PERFORMED.

The inoculations in question, with the exception of the
inoculations at Poona, which were undertaken by Colonel W. J.
Fawcett, R.A.M.C., were done by one of us while on service
in India with the Indian Plague Commission in the end of
1895, and in the beginning of 1896. They were
also done among the British troops in a series of military
stations which lay along the route which was followed by the
Commission during its tour of inquiry. Owing to the fact
that very little time was available before starting from
England, no sufficient supply of antityphoid vaccine could be
laid in before departure. It was therefore necessary to
manufacture vaccine en route during the intervals which
occurred in the course of the sittings of the Plague Commis-
sion in Calcutta and Agra respectively. In these places the
resources of local laboratories, presided over in the one case
by Dr. Nield Cook and, in the other case, by Mr. Hankin,
were in the most generous manner placed at disposal for the
purpose of making the vaccine. The vaccine was standardised
on guineas-pigs, which were carried about from place to place
for the purpose of keeping them continuously under observa-
tion. Inasmuch as the bottles of vaccine had to be opened
repeatedly for the purpose of drawing off the material, and
inasmuch as it was not possible to carry about an incubator
to verify the continued sterility of the vaccine, this last was
resterilised at 60° C. previous to undertaking each new series
of inoculations.

These particulars will suffice to show that the inoculations
were undertaken under conditions which were very far from
ideal. In particular there is reason to suppose that the re-
sults obtained (this applies notably to the results of the
inoculations done in Meerut and Lucknow, which came last
in series) may have been unfavourably influenced by a weaken-
ing of the vaccine brought about by repeated resterilisation.

CHARACTER OF THE VACCINE EMPLOYED.

The vaccine material which was brought out from England
consisted of lysolised (1 per cent. lysol) four-week-old cultures
of a virulent typhoid bacillus. These cultures had been pre-
pared about twelve months previously. They had been
sterilised by an exposure to a temperature of 60° C. The
quantity of culture which was employed for each inoculation
varied between 0.5 and 0.75 c.cm. This last was the minimum
quantity which was fatal to 100 grams of guinea-pig. This vac-
cine was employed in inoculations done in Bangalore and Agra.

The additional vaccine material, which was either prepared
at Calcutta and Agra, or which was afterwards sent out from
Netley, consisted of virulent typhoid cultures which had been
grown for twenty-four hours on nutrient agar at a temperature
of 37° C. These cultures also were sterilised for the most
part at 60° C. In some cases, however, a higher sterilising
temperature was employed. The quantity of this agar vac-
cine which was inoculated varied between 0.3 and 0.5 c.cm.
This last quantity corresponding approximately to the quan-
tity of culture which grew on one square centimetre of agar surface. Measured by its effects on guinea-pigs, this quantum was considerably less toxic than the quantum of broth culture which was spoken of above.

Both varieties of vaccine gave, in the doses in which they were employed, fairly severe reactions on man. Unfortunately, it was not in any case possible to undertake two successive inoculations.

### Corps in which Inoculations were done

<table>
<thead>
<tr>
<th>Corps in which Inoculations were done</th>
<th>Station where Troops were Quartered</th>
<th>Period of Observation</th>
<th>Numbers under Observation</th>
<th>Cases of Enteric Fever</th>
<th>Deaths from Enteric Fever</th>
<th>Information Received from</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Riding Regiment</td>
<td>Bangalore</td>
<td>December, 1898, May 1899</td>
<td>223</td>
<td>753</td>
<td>1.55</td>
<td>Lt. R. W. Clements, R.A.M.C.</td>
<td>Case in inoculated reported to have been so mild as to render diagnosis somewhat difficult.</td>
</tr>
<tr>
<td>Bangalore Garrison (includes above)</td>
<td></td>
<td>December, 1898, May 1899</td>
<td>276</td>
<td>1859</td>
<td>0.7</td>
<td>Major A. Peterkin, R.A.M.C.</td>
<td>The additional case in inoculated reported to have been extremely mild.</td>
</tr>
<tr>
<td>York and Lancaster Regiment</td>
<td>Agra</td>
<td>January, 1898, to May 1899</td>
<td>172</td>
<td>823</td>
<td>1.2</td>
<td>Lieutenant-Colonel South, R.A.M.C.</td>
<td>Battery had recently landed in India and had lost 1 case by enteric fever. The 65 uninoculated were for the most part men who had been long in India.</td>
</tr>
<tr>
<td>D Battery Royal Horse Artillery</td>
<td>Umballa</td>
<td>January to October, 1899</td>
<td>105</td>
<td>614</td>
<td>1.3</td>
<td>Major Blakeley Russell, R.A.M.C.</td>
<td>The case assigned to inoculated was in a man whose name is not to be found on the rolls of inoculated. He is said to have had a mild attack of typhoid.</td>
</tr>
<tr>
<td>2nd Batt. Gordon Highlanders</td>
<td>Umballa and various Hill Stations</td>
<td>January, 1899, to August 1899</td>
<td>397</td>
<td>614</td>
<td>1.7</td>
<td>Captain G. Stanley Walker, R.A.M.C. (Sabol).</td>
<td>Numbers of uninoculated not communicated. The inoculated man is said to have succumbed to uremia.</td>
</tr>
<tr>
<td>North Staffordshire Regiment</td>
<td>Umballa and Sabathu</td>
<td>January to July, 1899</td>
<td>317</td>
<td>823</td>
<td>1.3</td>
<td>Major J. Maher, R.A.M.C.</td>
<td>66 men who had previous entries for enteric fever have been deducted from the number of uninoculated.</td>
</tr>
<tr>
<td>2nd Queen's Regiment</td>
<td>Rawal Pindi</td>
<td>January to September, 1899</td>
<td>203</td>
<td>756</td>
<td>1.3</td>
<td>Major Maher, R.A.M.C. (Rawal Pindi).</td>
<td>42 men who had previous entries for enteric fever have been deducted from numbers of uninoculated.</td>
</tr>
<tr>
<td>Somerset Regiment</td>
<td>Rawal Pindi and Upper Topa</td>
<td>January to September, 1899</td>
<td>223</td>
<td>777</td>
<td>1.7</td>
<td>Major Zimmermann, R.A.M.C. (Upper Topa).</td>
<td>Four men who had previously suffered from enteric fever have been deducted from the number of uninoculated.</td>
</tr>
<tr>
<td>3rd Batt. Rifle Brigade</td>
<td>Rawal Pindi</td>
<td>January to September, 1899</td>
<td>205</td>
<td>693</td>
<td>1.5</td>
<td>Major S. J. Rennie, R.A.M.C. (Meerut).</td>
<td>The cases among the inoculated include 5 cases (2 fatal) which were admitted into hospital within nineteen days of inoculation.</td>
</tr>
<tr>
<td>11th Hussars</td>
<td>Meerut and Chakrata</td>
<td>January to September, 1899</td>
<td>234</td>
<td>357</td>
<td>1.3</td>
<td>Colonel Dempsey R.A.M.C. (Chakrata).</td>
<td>30 men who had previously suffered from enteric fever are excluded from numbers of uninoculated.</td>
</tr>
<tr>
<td>South Wales Borderers</td>
<td>Meerut and Chakrata</td>
<td>January to September, 1899</td>
<td>41</td>
<td>1069</td>
<td>1.4</td>
<td>Major S. MacDonald, R.A.M.C. (Lucknow).</td>
<td>Number of inoculated in regiment has not been communicated.</td>
</tr>
<tr>
<td>3rd Hussars</td>
<td>Lucknow</td>
<td>February to November, 1899</td>
<td>303</td>
<td>282</td>
<td>1.5</td>
<td>Major S. MacDonald, R.A.M.C. (Ranikhet).</td>
<td></td>
</tr>
<tr>
<td>Scottish Rifles</td>
<td>Lucknow and Ranikhet</td>
<td>February to November, 1899</td>
<td>177</td>
<td>593</td>
<td>1.1</td>
<td>Lieutenant-Colonel Bienenbassett, R.A.M.C. (Ranikhet).</td>
<td></td>
</tr>
<tr>
<td>Royal Scots</td>
<td>Poona</td>
<td>January to November, 1899</td>
<td>172</td>
<td>850</td>
<td>1.1</td>
<td>Lieutenant-Colonel Bienenbassett, R.A.M.C. (Ranikhet).</td>
<td></td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td><strong>2,823</strong></td>
<td><strong>8,860</strong></td>
<td><strong>27.05</strong></td>
<td></td>
<td><strong>123</strong></td>
</tr>
</tbody>
</table>

* The totals for the number of men under observation are arrived at by excluding the first and the penultimate rows of figures. This first row of figures is excluded, inasmuch as it is included in the figures of the second row; the penultimate one because it is included in the previous row. The totals for the number of cases are arrived at by excluding from consideration the figures printed in italics. These represent cases which were incubating typhoid fever at the time of inoculation. The percentages of deaths are calculated not upon the whole number of inoculated and uninoculated, but on the numbers of these regarding both the necessary information as to the issue of the attacks is available.
kindly assistance which was afforded, not only in carrying out the inoculations, but also in the task of collecting these statistics. This last task has not been free from difficulty owing, among other things, to the fact that the various regiments are, in the hot season, broken up into detachments which are dispersed over the whole of the province of Oudh, and it only now and then that the detachment could be either complete or free from errors, would appear to show conclusively that a certain measure of protection was conferred by the inoculation of the quantities of dead typhoid culture which have been specified. In appraising the amount of protection from the data which are given, the following facts must not be lost sight of:

1. The inoculated men in the above units were, taken as a whole, in practically every case men who were much more likely to contract typhoid than the uninoculated men; for, in practically every case, the inoculated consisted to a large, and sometimes to a preponderating, extent of young men who had only recently come out to India, while the uninoculated consisted to a very large extent of older and more seasoned, in other words, of less susceptible, men. Such a result is pointed out in the preliminary lecture, in which the facts regarding the antityphoid inoculation were laid before the men, that the young and susceptible newcomers were more particularly in need of protection than it was afforded by the inoculations. The commanding officers and the company officers, further, in many cases used their influence to get, so far as this was possible, all the young and seasoned soldiers to volunteer for inoculation.

2. The same thing holds true of the inoculations done in the 2nd Battalion of the Gordon Highlanders. Here again we have a body of inoculated consisting in predominant part of men who had just come out from home, while we have a body of uninoculated in which there was a large element of seasoned officers who had been taken over from the battalions which had just returned to England. The figures given in the table for this regiment, which are already very favourable to inoculation, become much more strikingly so when these are considered in connection with the circumstances which have just been detailed.

3. Lastly, it is to be borne in mind that the results given above apply to men as distinguished from officers. In the case of officers no accurate statistical materials are available, as the conditions under which individual officers live differ very considerably. From India, up to the present, among a number of inoculated officers who, counting only the subalterns, are, after the first few months, not only free, but also in the future, cases of enteric fever. Those that have come to my knowledge include 2 cases in the subalterns of the South Wales Borderers (of which regiment no inoculations were done), 2 in the subalterns of the Queen’s Regiment in Bombay (of which regiment no inoculations were done). A further case occurred in a subaltern at Quetta, and a fifth case occurred in a subaltern of the Royal Army Medical Corps at Kirk. All these are reported to have been very mild cases. In the 2nd Gordon Highlanders, while no cases of enteric affected among the inoculated officers, who numbered (the list containing the names of the inoculated officers in the regiment has been mislaid) some 10 or 12, 2 cases, both fatal, occurred among uninoculated officers.

The work of the Army Medical Department to the effects of antityphoid inoculation, it may be permissible to refer to the fact that our attention has been called from several different quarters to the possibility that the antityphoid inoculation may confer a certain protection against malarial fever. In the case of one particular regiment, we have been furnished by the commanding officer with lists personally prepared by the company officers giving with respect to each inoculated man particulars as to whether he had suffered from “fever and ague” in the future, and 23 men not inoculated, while no case occurred in the uninoculated; it is rather the fact that a battery consisting in large part of men newly arrived from home has, in the eleven months subsequent to the institution of the inoculations, only had one case of enteric.

The summary of the above facts, many of the results appear under a much more favourable aspect than that in which they appear on a mere inspection of the figures given in the table. Thus, for instance, in the case of D Battery, Royal Horse Artillery, a consideration of the facts will show that the results of inoculation are not fairly comparable with that the sole case of typhoid which occurred in the battery was a case which occurred in an inoculated man. The following were the circumstances under which the inoculations were done. The battery in question had only arrived from England a few months previous the date of inoculation. On the previous day the battery had lost its first man from enteric fever. Owing to this and other favouring circumstances, the cases of enteric fever, including most of the men, had not gone home for furlough, and so the battery was protected. Those who did not volunteer for inoculation consisted in large part of seasoned men who had been transferred to this battery after its arrival in India. In view of this it will be manifest that the fact which deserves notice here is not so much the unusually low rate of cases of enteric as the fact that no case occurred in the uninoculated; it is rather the fact that a battery consisting in large part of men newly arrived from home has, in the eleven months subsequent to the institution of the inoculations, only had one case of enteric.

In the interval of a few months which had elapsed since their arrival in India. In like manner a few cases of typhoid were occurring in the York and Lancaster Regiment at Agra at the time of inoculation. In conformity with the fact that inoculations were done in these cases in the presence of a typhoid patient, we are surprised that only 1 case of the inoculations would prove to have been incubating typhoid at the time of the inoculation. This turned out to be the case in the 3rd Hussars, 5 cases of enteric—occurring among the inoculated men—being admitted to hospital within the first nine months after inoculation. In the case of the 3rd Hussars, it is quite certain that there was a definite history of the men having been ill previous to inoculation. One similar case occurred among the inoculated in the York and Lancaster Regiment within a few days after inoculation. These cases have been distinguished by italics in the above table, and they have not been reckoned in the general summary of cases contracted subsequent to inoculation.

The total number of deaths from enteric fever in the 3rd Hussars, some 10 deaths from enteric fever had occurred in India.
PREPARATION OF VACCINE.

Having thus briefly considered the statistical results of the first large batch of inoculations which have been done among the troops, we may pass to consider certain questions in connection with the technique of preparing and sending out the vaccine.

These questions seem to us to have a very considerable importance, inasmuch as it is manifest that the best results will only be obtained from a system of inoculation, when, on the one hand, the perfect asepsis of the vaccinating material, and when, on the other hand, the accurate standardisation of the vaccine shall have been secured. It will only be when this last desideratum has been secured, and when the results obtained by the inoculation undertaken with different quanta of vaccine shall have been studied, that it will be possible to be sure that the antityphoid inoculations have been careful to exist and we may proceed to consider the above-mentioned questions of technique.

Virulence of the Typhoid Organism which is employed in the Preparation of the Antityphoid Vaccine.

The virulence of the micro-organism which is employed in a vaccination process would appear to be of absolutely fundamental importance only in cases where the vaccinating material which is employed consists of a living culture of micro-organisms. We have there, on the one hand, to guard against the introduction into the organism of an over-virulent culture, and we have, on the other hand, to guard against the introduction of a culture whose virulence is so low that it will be unable to activate itself in the organism and to produce there that quantum of toxins which will call forth the production of a sufficiency of immunising substances. These considerations do not directly apply in the case of antityphoid inoculation where the vaccinating material consists only of dead bacteria and of the specific poisons which have been elaborated by these bacteria in the course of their cultivation on artificial media. None the less, inasmuch as toxin-producing properties probably do, in the case of the typhoid bacillus, stand in some relation to the virulence of the cultures, we have been careful to employ only virulent cultures in the preparation of our anti-typhoid vaccine. The virulence of our cultures has been kept up by a series of intraperitoneal passages through guinea-pigs.

Medium Employed for Cultivation of the Typhoid Bacillus.

After experimenting with various culture media we have not found any which offers distinct advantages over the ordinary 1 per cent. peptone broth. The most luxuriant cultures appear to be obtained when the medium which is employed has been accurately neutralised.

 Cultivation Flasks.

We have found it convenient for the purpose of cultivation to employ flasks of some 2½ litres capacity of the pattern shown in Fig. 1. These flasks are, as will be seen, furnished with a lateral tube, to which is fitted a piece of perfectly sound vulcanised rubber pressure-tubing. The orifice of this last is blocked with a piece of glass rod, and is fitted with a pinch cock (see figure) in such a manner that the distal end of the tube remains free from fluid. The advantages which are associated with the employment of cultivation flasks fitted in this manner are the following:—

The flasks can easily and rapidly be inoculated by puncturing through the pressure tubing with the needle of a syringe which has been filled with a pure culture of typhoid. In doing this, as a precaution against the introduction of contaminations, the outside of the tubing is first sterilised by the application of undiluted carbolic acid. After withdrawing the needle the puncture hole can readily be sealed up. To do this the carbolic acid is first washed off with alcohol followed by ether, a drop of rubber solution is then pressed out from the flamed orifice of a collapsible tube of rubber solution, such as is supplied by any bicycle agent for mending punctures in pneumatic tyres. Further advantages which are associated with the use of these flasks are (a) the possibility of withdrawing samples at any time with a view to controlling the purity of the cultures, and (b) the possibility of transferring, without exposure to the air, the contents of the cultivation flasks to the larger jars (Fig. 2) which are employed in the processes of preparation which are described below.

Period during which the Cultures are Incubated.

The flasks, after having been inoculated, are transferred to an incubator, which is kept at blood temperature. The cultivation is continued for from fourteen to twenty-one days. After the expiration of that period, there is little if any further proliferation of the bacteria.

Mode of Fitting up the Mixing Jars in which the Cultivations are Sterilised by Heat.

After the purity of each flask has been ascertained by culture, the contents of the cultivation flasks are transferred to the larger jars (Fig. 2). This transference is undertaken first with a view to mixing together the contents of a series of cultivation flasks, so as afterwards to standardise them in bulk; secondly, it is undertaken with a view to eliminating the possibility of the vaccine becoming spontaneously reinoculated with living bacilli after it has been exposed to heat. This possibility would exist if there were to be found on the sides or neck of the flask, when it is transferred to the water bath, any typhoid bacilli which had been rendered by desiccation less sensitive than they would otherwise be to the heat which is there brought to bear on them.

Before describing the process of transferring the typhoid culture from one flask to another, and the subsequent processes of heating and mixing, it will be necessary first briefly to describe the manner in which the larger "mixing" jars are fitted up.

As will be seen from Fig. 2 the lateral tubes are fitted with vulcanised rubber pressure tubing. The ends of the two lower rubber tubes are fitted with glass nozzles, which are plugged with cotton wool. A clamp is further placed on each tube. Through the lowest of these lateral tubes the contents
of the cultivation flasks are introduced into the mixing jar. The upper tube is appropriated to a paraffin thermometer, which is employed for the purpose of notifying the point at which the internal temperature of the typhoid culture has reached 60° C. The principle and the mode of using these thermometers require a word or two of explanation.

**Principle and Mode of employing the Paraffin Thermometers.**

This will readily be understood from a consideration of Fig. 3, which represents the thermometer in position in the mixing jar. It will be seen that the thermometer consists essen-

![Diagram](https://via.placeholder.com/150)

**Fig. 3.—Paraffin thermometer in position against inner wall of mixing jar.**

A, Upper end of thermometer, left open; B, bulb; C, fusiform enlargement; D, constricted portion of tube enganged in wire snare; E, lower sealed end of thermometer; F, wall of mixing jar; G, upper lateral tube of mixing jar; H, distal end of wire snare passing through uppermost of the lateral tubes.


tially of a glass bulb or float which is left open at the top. This glass bulb runs out below into a hollow glass stem, which is filled in with paraffin through its lower end. When the thermometer is brought into use the bulb floats on the surface of the fluid, the stem, the paraffin receptacle, acting as a sinker causes the thermometer to stand up in the fluid somewhat like a fisherman's float. When the temperature of the surrounding fluid rises to 60° C. (or to such other point as corresponds to the melting point of the particular paraffin which is employed), the paraffin is pressed upwards against the upper part of the containing bulb by the pressure of the fluid. Owing, however, to the fusiform shape which is given to this bulb (Fig. 3, b), the fluid cannot pass up into the stem until the paraffin actually melts. As soon as this occurs the fluid enters the upper bulb or float and the thermometer sinks to the bottom. These thermometers having been devised, the only difficulty which presented itself was that of disposing matters as to allow of the thermometer being sterilised in situ. This object is effected by sealing up the lower end of the thermometer (Fig. 3, e) so as to prevent the paraffin escaping during the process of sterilisation. The further problem of snapping off the sealed end of the thermometer without opening up the sterilised jar is satisfactorily solved by the following device. When the jar is being filled up, previous to sterilisation, a noose of fine brass wire is passed in through the rubber tube which is con-


tected with the uppermost lateral tube of the mixing jar. This noose is brought up to the neck of the jar, and the sealed capillary end of the thermometer is engaged in it in such a manner that the noose fits into a constriction which is marked in the diagram (Fig. 3 d). The noose is now drawn gently home until the thermometer becomes fixed, as is shown in the diagram opposite the orifice of the upper lateral tube (Fig. 3, o). It only remains to fasten the free extremity of the wire. This is done by inserting a piece of tightly-fitting glass rod into the end of the tube in such a manner as to engage the wire between the rod and the wall of the tube (Fig. 4). This done, a rubber bung, which is perforated by a glass tube plugged with cotton wool, is inserted into the neck of the jar and is tied in tightly. The jar is now ready for autoclaving.

**Method of Killing off the Cultures and of Mixing Together the Contents of a Series of Cultivation Flasks.**

When the jar has been autoclaved, and when the bung has afterwards been duly luted with sterilised paraffin, the subsequent procedure is as follows: A cultivation flask is taken in hand, the end of the attached rubber tubing is sterilised in the flame, and the glass rod which blocks the orifice is withdrawn in an aseptic manner. At the same time a flame is passed over the outside of the glass nozzle which is fitted into the lowest of the three lateral tubes of the mixing jar, and the contained cotton-wool is aseptically withdrawn. This done, a connection is established between the two tubes, the clamps are withdrawn and the fluid passes out from the cultivation flask into the mixing jar. As soon as a certain amount of fluid has entered the mixing jar, and at any rate before the fluid has reached the level of the uppermost lateral tube, the pressure tubing which is attached to this side tube is gently pulled. This causes the wire noose which is round the capillary end of the paraffin thermometer to snap this off by a guillotine action. The released thermometer then drops into the fluid, ready for use. The glass rod is now removed, the extremity of the brass wire grasped with a forceps, and withdrawn from the tube.

When the contents of a cultivation flask have passed into the mixing jar, the clamp belonging to the mixing jar is replaced upon the rubber tube at a point somewhat nearer to the jar than the glass nozzle which was referred to above. The syringe full of carbolic acid is then driven through the tube into the cultivation flask. This done, the cultivation flask may be disconnected without risk. The next cultivation flask in the series is now taken in hand in the same manner. When the process of filling in the mixing jar has been completed, the side tubes are blocked with pieces of sterilised glass rod. These are luted with rubber solution.

The next proceeding is to transfer the mixing jar or jars to the water bath. This is to be done without delay, and the jars are to be carried in such a manner as to avoid all splash-
ing up of the vaccine on to the sides and neck of the jar. The water bath must be deep enough to allow of the water coming well over the shoulder of the mixing jar. This last is not to be filled within 2 inches of this level. If the jar, when it is introduced into the water bath, is found to be buoyant, it is weighted down by passing a heavy leaden collar round its neck. The jars having been securely placed in position, heat is applied to the water bath, and the condition of the thermometers in the separate jars is noted from time to time. This is best done by lowering a piece of ordinary looking-glass below the surface of the water in the water bath. The heating is continued for 10 to 15 minutes after the paraffin thermometers have sunk.

The next step is to mix the contents of the whole series of mixing jars so as afterwards to obtain for standardisation a representative sample of the whole brew of vaccine. The mixing is effected by connecting up the mixing jars with each other by means of their rubber tubes (Fig. 2). These rubber tubes are of such length as to allow of any one of the jars being freely raised above or lowered below the level of its companion jars. By these means complete mixing of the contents is readily effected. In cases where the mixing jars are so full as to place a difficulty in the way of the satisfactory mixture of their contents, an additional empty sterilised mixing jar is introduced into the circuit. Mixture having been duly accomplished, samples of the vaccine are taken, the manner described above in connection with the control of the purity of the contents of the cultivation flasks. As before, the sterility of the samples of vaccine is tested by introducing them both into tubes of broth and into tubes of nutrient agar.

After this has been done further samples of the vaccine are drawn off for the purpose of determining the strength of the vaccine. An addition of antiseptic is now made to the vaccine with a view to preserving it against risk of subsequent contamination. We have found that an addition of one-tenth of its bulk of a 5 per cent. solution of lysol or carbolic answers this purpose very well. A simple method of making this addition is to take the required quantity of water and to sterilise it in a Kitisato flask fitted with a hot vulcanised pressure tubing. After sterilisation the appropriate quantity of carbolic acid is introduced by puncturing through the pressure tubing. After solution has been effected the Kitisato flask is connected up with the series of mixing jars containing the vaccine and the antiseptic is thoroughly mixed up with the vaccine. We have found that it is inexpedient to add undiluted carbolic acid directly to the vaccine, inasmuch as it causes the bacteria to run together into large masses.

Process of Standardisation.

The problem as to how to obtain an absolutely accurate standardisation of a bacterial vaccine is still unresolved. We propose in another communication to dwell on certain facts bearing on this question, which we have elicited in the course of a very considerable number of experiments made with a view to resolving this problem. For the present it will suffice to detail the process of standardisation as it is actually carried out by us.

In each case we estimate the strength of the vaccine in two different ways. We determine, by a process which is described below, the degree of opacity of each sample of vaccine. We take it that in the opacity we have a criterion of the number of undissolved bacteria which are contained in the unit of volume. We in such cases approximate to the estimation of the opacity of the vaccine a direct test of the toxicity of the dead culture. This last test is carried out by the subcutaneous inoculation into guinea-pigs of measured quantities of the sterilised vaccine.

Method of Determining the Opacity of a Sample of Antityphoid Vaccine.

After casting about in many directions for a method of determining the opacity, which could be carried out without the assistance of any complicated apparatus, we have devised the following method, which is of very easy application, and which seems to us to give very accurate results.

Description of the Method.

We take, in the first place, a definite test object. We have selected as suitable for this purpose a system of alternate dark and bright lines, such as can easily be constituted by gumming two strips of black paper 0.5 cm. wide, at distances 0.5 cm. apart, transversely across an ordinary microscopic slide (Fig. 5, r).

Fig. 5.—Diagram of a microscope arranged for the estimation of the opacity of the vaccine. A, top of the body of the microscope, and point from which readings may be taken on the scale; B, plane glass cemented on the end of an old objective; C, plane glass at bottom of vaccine receptacle; D, plane mirror by which the image of the test object is thrown up through the vaccine to the eye at A; E, "live box," serving as receptacle for vaccine; F, test object.

Having thus obtained our test object we have to determine what is the minimum thickness of the stratum of vaccine which will, when interposed between two plane glass surfaces, suffice to effect the obliteration of our pattern of lines. With a view to making this determination we set up our test object in the window, at a distance of 1.5 metre from a microscope which has been dismantled of all its lenses. By means of the plane mirror we then reflect up the pattern of lines upon the transparent lower surface of a receptacle containing the vaccine, which is placed on the stage of the microscope. We have improvised a suitable receptacle out of an inverted "live box" (Fig. 5, c). Any similar receptacle which has opaque walls and a floor of plane glass would serve equally well. We have next to make provision for lowering into the pool of vaccine a plane glass surface in such a manner as to displace a stratum of fluid of such thickness as to allow of the pattern of lines just becoming visible through the layer of vaccine. Further, we have to make provision for measuring the exact thickness of this interposed layer of vaccine.

In these objects can be readily achieved by removing the lenses of any old objective and by cementing on in the place of the front lens a disc of glass whose surfaces have been ground plane (Fig. 5, b). We screwed this transformed objective on to our microscope, and having, as said before, removed all the other optical parts, we rack down our plane glass objective into the pool of vaccine, until we find, on looking down the empty tube of the microscope, the point at which the pattern of lines is only just obscured by the interposed layer of fluid. We now set up a centimetre rule on the stage of the microscope, and take a reading of the height at which the microscope tube stands. This gives us a height corresponding to the upper surface of the stratum of interposed fluid.

We now have further to determine the height which corresponds to the lower surface of the interposed layer. We do this by racking down the body of the microscope until the lower
surface of our plane glass objective comes into contact with the plane glass surface which constitutes the floor of the vaccine receptacle. We now take a second reading of the height of the microscope tube, and by deducting this height from the height as determined at the first reading, we arrive at the thickness of the interposed layer of antiseptic fluid, which suffices to blur our test object. We may note in passing that by this method we take cognisance, not of the greater or less amount of light which is transmitted, but only of the degree to which the transmitted rays are deflected by the interposition of the bacterial particles. It is a matter of difficulty, given that time is available, to allow the bacteria to sink down to the bottom of the mixing jars and to decant off the clear supernatant fluid through the uppermost of the lateral tubes, in such a manner as to concentrate the vaccine to any desired degree.

Finally, we hasten to say that the methods of bottling the vaccine and of putting it up in sealed capsules.

**Bottling the Vaccine.**

In order to reduce to a minimum the possibility of any contamination occurring during this operation we have, after trying various other methods, devised the following method by which the vaccine is run from the large jars directly into small bottles without being at any time exposed to the air.

When the autoclaved bottles are cool the cotton-wool plugs are removed, the bottles are filled with the required quantity of the vaccine into guinea-pigs. We have generally employed for this purpose the completed carbolised vaccine, as we find that the small amount of antiseptic which is added does not sensibly affect the response in guinea-pigs. Inasmuch as the susceptibility of guinea-pigs is, like that of men, subject to considerable individual variations, we make it a practice to test the effect of each separate quantum of vaccine on a series which consists of at least two guinea-pigs. We generally begin with 5 guinea-pigs. The mixing doses of vaccine vary from 0.5 to 0.75 c.cm. We prefer, when possible, to employ for our toxicity-estimations guinea-pigs weighing 250 to 300 grams. When death occurs it may take place as early as twelve hours after the incorporation of the vaccine. As a rule, however, it does not take place till the second or third day.

The post-mortem signs usually found are the following: cedematous infiltration of the subcutaneous tissue the site of inoculation, marked congestion of the suprarenals, slight enlargement and congestion of the spleen, distinct enlargement and congestion of the Peyer's patches. Fluid is occasionally found in the peritoneum, pleura, and pericardium, and hemorrhagic patches on the surface of the lungs are frequently present. The intestines are also frequently filled with a watery contents. Of the water clear, with the passage of a brew of vaccine stands in close relation with its strength as determined by the estimation of opacity. The maximum toxicity of the vaccine which we have found our vaccine to possess is represented by a minimum lethal dose of 0.5 c.cm. per 100 grams of guinea-pig's body weight. The minimum toxicity of the vaccine which we have sent out is represented by a minimal lethal dose of 2 c.cm. per 100 grams of body weight. Where the toxicity of the vaccine is less than this, the method of determining it by inoculations on guinea-pigs would appear to be inadmissible, inasmuch as we find the 1 per cent. peptone broth (Witte's peptone), which we employ as a nutrient medium in the preparation of our antityphoid vaccine, is lethal to guinea-pigs in doses which little if at all exceed 3 c.cm. per 100 grams.

We propose to make the following observations, in order to reserve for a future publication the details of which may be of interest to the manufacturers of the vaccine.

**Determination of the Dose to be Employed on Man.**

In fixing the dose of each separate brew of antityphoid vaccine we have been guided in each case by a consideration of the results of each of the above methods of standardisation. Where, for instance, the opacity of the vaccine was great, and where the opacity, as determined by the cream, was represented by a minimal lethal dose of 0.5 c.cm. per 100 grams of body weight, we fixed the dose of vaccine at 0.5 c.cm. Where, on the other hand, the toxicity and the opacity test alike indicated that the vaccine was weaker, we have fixed the dose as high as 1.5 c.cm. We do not think it is necessary ever to employ larger injections than these, for, where we are dealing with a vaccine which is unduly poor in toxicity or which possesses a low opacity value, it is a matter of difficulty, given that time is available, to allow the bacteria to sink down to the bottom of the mixing jars and to decant off the clear supernatant fluid through the uppermost of the lateral tubes, in such a manner as to concentrate the vaccine to any desired degree.

Finally, we hasten to say that we have found the best results of this method of bottling the vaccine and of putting it up in sealed capsules.
the microscopic punctures in the rubber caps and to coat them with a protecting envelope of paraffin. For this purpose we again employ the solution of rubber which is sold for the purpose of repairing bicycle tyres. Before applying it, the remains of the antiseptic solution are first cleaned off by absolute alcohol, and then the rubber is freed from all traces of grease by means of ether. When the rubber solution has hardened, each bottle is further protected by coating the whole cap with paraffin, which has been previously raised to a temperature of 150°C. A paraffin with a high melting point is selected if the vaccine is to be sent to a tropical climate. In dipping the bottles into the melted paraffin it is well to immerse the whole cap, so that the paraffin may fill up the interspace between the base of the cap and the neck of the bottle.

The bottles are now labelled, each label giving the number of the vaccine, its date, and that on which its sterility was tested, the nature and amount of the antiseptic added, and the dose for an adult in cubic centimetres and minims.

To withdraw the vaccine from one of the bottles for inoculation it is only necessary to sterilise the cap in hot oil, or, better, in a hot antiseptic solution, and insert a sterile syringe — preferably graduated in tenths of a centimetre, and of a capacity of 5 c.cm. through the rubber cap. After the first puncture the needle is withdrawn and then reinserted and the syringe filled. The first perforation is made for the purpose of acting as an air valve to permit the entrance of air to replace the fluid withdrawn.

Should the entire contents of a bottle not be required at one time for the purpose of inoculating a series of persons, the cap may be again sterilised and the punctures sealed with rubber solution and paraffin as before.

With a view to providing for cases where isolated inoculations are expected to be required, the vaccine is filled into glass capsules, each containing a single dose. These capsules are very simply made by drawing out pieces of glass tubing in the flame. The tips of these are broken aseptically. They are then filled with a measured dose of vaccine, and are sealed up again in the flame. The contents are readily drawn off, after breaking off the tip with antiseptic precautions, by inverting the capsule over the end of the needle of a sterilised hypodermic syringe.

Instructions describing the method of drawing off the vaccine, the method of performing the injections, and detailing the clinical symptoms which may be expected to ensue, are sent out with the vaccine.

NOTE AND REFERENCE.

1 Lancet, September 15th, 1896. The case in question was a somewhat anomalous one, as it was the case of a man who, while in hospital for an injury to the foot, suddenly developed a high temperature and died within twenty-four hours. The post-mortem examination revealed ulceration of the intestine, which was diagnosed as typhoid ulceration. In connection with the question of the results of the inoculations done on officers, reference was made to a batch of twenty-two officers inoculated by Major Firth, R.A.M.C., on the troopship Bittern, in October, 1897. It appears from inquiries which were instituted by Major Firth, which were supplemented by a number of inquiries made by one of us, that none of these officers have suffered from enteric, whereas two un inoculants of a company and one of those taking out the same troopship have succumbed to that disease. We have invariably found this rubber solution to be perfectly sterile. If this precaution is neglected the contents of the flask may be found to drain away at this joint by capillary attraction.

Major-General Leonard Wood, who, as will be remembered, began his military career in the United States army, has now been gazetted Major-General of Volunteers, and appointed Governor of Cuba.

AN ADDRESS ON THE INSANE AND THEIR TREATMENT.

Delivered before the Staffordshire Branch of the British Medical Association.

By J. B. Spence, M.D.,
Medical Superintendent Staffordshire County Asylum, Burntwood, Lichfield; President of Great Britain and Ireland; President of the Branch.

The insane and their treatment have from the earliest times excited the sympathy and interest of all who felt for the afflicted and sorrowing of the human race, and many efforts are chronicled as having been made to alleviate the sufferings of those who in the distant past were supposed to be either possessed by evil spirits, or who were said by an old writer to be affected by a disease of the soul resulting from a special habit of body, producing in some simple ignorance, and in others madness, of which latter there are two kinds, namely, that arising from human disease, and the other from an inspired deviation from established custom.

Among the Greeks, as Lysias says, the cause which produced aberration of intellect in prehistoric days there is little doubt that two great factors with which we are confronted in this nineteenth century — drink and heredity — operated, though we attacks even in the days of Homer, that the disease of which Intoxication was not unknown to the ancient Egyptians, and without doubt existed, in conjunction with other vices, its baneful influence in the development of various forms of mental disorder; and heredity, while perhaps not so widespread in its influence as with us, claimed its due share in the causation of brain troubles. Ancient Egyptian papyri describe the existence of a condition similar to our senile decay, while the treatment of madness, or sadness as it was sometimes called, by the employment of music appears to have been recognised centuries before the time when the evil spirit from God was upon Saul, that David took a harp and played with his hand, so Saul was refreshed and was well, and the evil spirit departed from him.

Indeed, as early as the days of Moses the Children of Israel, in the event of any departure from the due observance of the commandments and statutes which were laid down for their guidance, were admonished, that "the Lord shall smite thee with madness," to say nothing of the long category of other troubles which the 28th chapter of Deuteronomy appears to delight in holding over the heads of possible delinquents. Peace was to be had to the madness which David was said to have feigned was not really an attack of epileptic mania, which Adam Clarke, the celebrated commentator, says was sent by God to save him from Achish, as one whose delusion from his master and union with the one which was of no ordinary kind, and of which David was separated at King Nebuchadnezzar from the company of his fellows for so long a period seems to have been one which not only affected his physical but also his mental state is generally admitted; and it is remarkable among other things for the fact that complete return to a healthy condition appears to have taken place after an illness of such a long duration, that nowadays one would give a more than doubtful prognosis as to the probability of complete recovery were one consulted under circumstances of a like nature.

Hippocrates, writing five centuries before Christ, says:

I see men become mad or demented from no manifest cause, and at the same time doing many things out of place. Who are the gods who cause these diseases to the gods appear to have been just such persons as the conjurors, purifiers, mountebanks and charlatans now