ing anæmic 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 administration of the simplest food in small quantities at regular intervals. I generally prescribe 1 ounce of milk and lime water every hour with the following mixture:

Sulphate of magnesium	40 grains
Sulphate of iron...	2 ,,
Diluted sulphuric acid	15 minims
Peppermint water to	1 ounce

three times a day. The milk and lime water, if borne without pain and vomiting, as is almost invariably the case, is increased 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 admission 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 anæmia 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 the first instance, half an ounce may be given, or if there be only pain without vomiting, a mixture of bismuth and soda may be substituted for that of iron and magnesia.

In those cases which have recently suffered from hæmatemesis it is desirable to give nothing by the mouth until forty-eight hours have elapsed after the vomiting of blood has stopped, and during that time I feed them by the following nutrient enema 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 irritability of the rectum, twenty to thirty drops of laudanum may be added. While the hæmatemesis 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 she wishes. If necessary, to relieve pain or to keep the patient quiet, I order a hypodermic injection of $\frac{1}{8}$ to $\frac{1}{4}$ gr. of morphine.

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 importance 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 have suffered in health from an insufficient nutrition, and have entered a vicious circle in which the anæmia 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 of the utmost importance to prove to your patient that she can take ordinary food. It is also very desirable 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 mixture 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 successful.

A BRONZE statue of the late Dr. William Pepper, was recently unveiled at Philadelphia, and at the same time the Free Museum of Science and Art was formally opened, and transferred to the University of Pennsylvania. The building and the site cost over 600,000 dollars, towards which Mrs. Pepper gave 50,000 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 cottages can be rented. The temperature is said to be very 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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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[1] and which were described by one of us in association 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 the year 1898, and in the beginning of the year 1899. They were 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 Commission 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 guinea-pigs, which were carried about from place to place for the purpose of keeping them continuously under observation. 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 results 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 weakening 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 prepared 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 vaccine 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 vaccine 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.

STATISTICS.

The statistical material which is presented below has been compiled from information furnished by officers of the Royal Army Medical Corps actually in charge of troops in the various stations. This information has been supplemented by reports received from the commanding officers of the various inoculated regiments.

We desire here to express our acknowledgments of the

Corps in which Inoculations were done.	Station where Troops were Quartered.	Period of Observation.	Numbers under Observation.		Cases of Enteric Fever.				Deaths from Enteric Fever.				Information Received from	Remarks.
					Inoculated.		Uninoculated.		Inoculated.		Uninoculated.			
			Inoculated.	Uninoculated.	Number.	Per Cent.	Number.	Per Cent.	Number.	Per Cent.	Number.	Per Cent.		
West Riding Regiment	Bangalore	December, 1898, to Sept. 22nd, 1899	223	753	1	0.5	8	1.0	0	0	2	0.25	Lieutenant R. W. Clements, R.A.M.C.	Case in inoculated reported to have been so mild as to render diagnosis somewhat difficult.
Bangalore garrison (includes above)	,,	December, 1898, to Sept. 22nd, 1899	276	1859	2	0.7	49	2.6	0	0	—	—	Major A. Peterkin, R.A.M.C.	The additional case in inoculated reported to have been extremely mild.
York and Lancaster Regiment	Agra	January, 1899, to May 15th, 1899.	172	Say, 900	*1*	—	20	2.2	0	0	4	0.4	Lieutenant-Colonel Routh, R.A.M.C.	Case in inoculated occurred eight days after inoculation. Number of uninoculated not communicated.
D Battery Royal Horse Artillery	Umballa	January to October, 1899.	105	63	1	1.0	0	0	1	1	0	0	Major Blakeley Russell, R.A.M.C. Lieutenant H. S. Wilson, R.H.A.	Battery had recently landed in India and had lost 1 case by enteric fever. The 63 uninoculated were for the most part men who had been long in India.
2nd Batt. Gordon Highlanders	Umballa and various Hill Stations	January, 1899, to August 13th, 1899	397	614	1	0.2	17	2.8	0	0	—	—	The late Colonel Dick-Cunyngham, V.C. Major Blakeley Russell, R.A.M.C. Captain H. P. Johnson, R.A.M.C. (Solon).	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 very mild attack of typhoid.
North Staffordshire Regiment	Umballa and Sabathu	January to July, 1899	317	Say, 700	5	1.6	14	2.0	1	—	1	0.1	Captain G. Stanley Walker, R.A.M.C. (Sabathu).	Numbers of uninoculated not communicated. The inoculated man is said to have succumbed to uræmia.
2nd Queen's Regiment	Rawal Pindi	January to September, 1899	203	756	1	0.5	10	1.3	0	0	1	0.1	Major J. Maher, R.A.M.C.	There was also a case of enteric fever in a man inoculated in 1897
Somerset Regiment	Rawal Pindi and Upper Topa	January to September, 1899	233	727	3 / *2*	2.1	13 / 4	2.3	0 / 0	0 / 0	2 / 2	0.5	Major Maher, R.A.M.C. (Rawal Pindi). Major Zimmermann, R.A.M.C. (Upper Topa).	66 men who had previous entries for enteric fever have been deducted from the number of uninoculated.
3rd Batt. Rifle Brigade	Rawal Pindi	January to September, 1899	205	693	0	0.0	15	2.2	0	0	2	0.3	Major Maher, R.A.M.C.	42 men who had previous entries for enteric fever have here been deducted from numbers of uninoculated.
11th Hussars	Meerut and Chakrata	January to September, 1899	234	357	2 / 1	1.3	10 / 0	2.8	2 / 1	1.3	4 / 0	1.1	Major S. J. Rennie, R.A.M.C. (Meerut). Colonel Dempsey R.A.M.C. (Chakrata).	—
South Wales Borderers	Meerut and Chakrata	January to September, 1899	41	1069	0 / *3*	—	1 / *19*	1.9	0 / 0	— / —	0 / *3*	0.3	Major S. J. Rennie, R.A.M.C. (Meerut), Colonel Dempsey (Chakrata).	—
3rd Hussars	Lucknow	February to November, 1899	303	281	*4+5*	1.3	16	5.7	—	—	—	—	Major S. Macdonald, R.A.M.C. (Lucknow).	Four men who had previously suffered from enteric fever have been deducted from the number of uninoculated. The cases among the inoculated include 5 cases (2 fatal) which were admitted into hospital within nineteen days of inoculation.
Scottish Rifles	Lucknow and Ranikhet	February to November, 1899	177	591	2	1.1	10	2.3	—	—	—	—	Major S. Macdonald, R.A.M.C.	30 men who had previously suffered from enteric fever are excluded from numbers of uninoculated.
			31	71	0		4		—	—	—	—	Lieut.-Col. P. Ellis, R.A.M.C. (Ranikhet).	
Royal Scots	Poona	January to November, 1899	172	Say, 850	0	0.0	11	1.2	—	—	2	0.2	Lieutenant-Colonel Blennerhassett, R.A.M.C. Lieutenant H. Herrick, R.A.M.C.	Number of inoculated in regiment has not been communicated.
Totals* ...	—	—	2,835	8,460	27	0.95	213	2.5	5	0.2	23	0.34	—	—

* 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 whom 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 in the various hill stations.

The whole of the information which has as yet come to hand with regard to the results of the series of inoculations referred to above, is summarised in the table on p. 123.

Taken as a whole, the statistical material given in the table, though it cannot, from the nature of the case, be assumed to 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 that 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, individuals. It was in every case 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 the protection which it was hoped would be 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 unseasoned soldiers to volunteer for inoculation.

Read in the light 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 above. 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 gauged by the fact that the sole case of typhoid which occurred in the battery was a case which occurred in an inoculated man.[2] The following were the circumstances under which the inoculations were done. The battery in question had only arrived from England a few months previous to 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 more than half of the battery, including most of the men who had come out from home, volunteered for inoculation. 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 fact that one case of enteric occurred in the 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 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 soldiers who had been taken over from the battalion 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 they are considered in connection with the circumstances which have just been detailed.

2. It must further be borne in mind in connection with the statistics which have been given above that the inoculations were, in certain cases, undertaken in the actual presence of a typhoid epidemic. These were the conditions in the case of the Gordon Highlanders at Umballa, and, more particularly, in the case of the 3rd Hussars in Lucknow. In the case of the Gordon Highlanders, 30 cases of enteric had occurred during the three months which had elapsed between the arrival of the regiment from England and the institution of the inoculations. In the case of the 3rd Hussars, some 10 deaths from enteric fever had occurred 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 epidemic it was only to be expected that some of the inoculated 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 nineteen days after inoculation. In 2 of these cases 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.

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, must now amount to several hundreds, there have, so far as we have been able to ascertain, been only 5 cases of enteric fever. Those that have come to my knowledge include 2 cases in the subalterns of the South Wales Borderers (of whom 6 were inoculated), and 1 in the subalterns of the Queen's Regiment in Rawal Pindi (of whom 10 were inoculated). A further case occurred in a subaltern at Quetta, and a fifth case occorred in a subaltern of the Royal Army Medical Corps at Kirki. All these are reported to have been very mild cases.[3] In the 2nd Gordon Highlanders, while no cases of enteric occurred 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.

Before briefly summarising 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" (*a*) before inoculation, and (*b*) after inoculation. These lists, compiled six months after the date of inoculation, show that of 121 men who had previously suffered from "fever and ague," 111 declared themselves to have been quite free since, the remainder declaring themselves to have been practically free. Only 2 men who had not previously suffered from "fever and ague" declared themselves to have suffered slightly since. In view of these statements, the question as to whether any protection against malarial fevers is in reality afforded by an injection of a dead typhoid culture may, in spite of the *a priori* improbability of such being the case, perhaps be deserving of attention.

Before dismissing the question of these results, we may, though we are not certain that it is not premature to do this, turn for a moment from the scientific to the practical aspect of these inoculations. With regard to this last, it will suffice to point out that even on the assumption that no greater amount of protection could be conferred in the future than that which appears to have been conferred in these preliminary inoculations, the result obtained would in the aggregate be a significant one. Taking the figures just as they stand in the summary of the table, assuming, in other words, that there would be a reduction of cases from 2.5 per cent. to 0.9 per cent., and a diminution of mortality from 0 35 per cent. to 0.2 per cent., such as is evidenced above, and calculating on the figures 1800 and 460, which represent in round numbers the average number of cases and deaths from enteric fever in the British army in India as deduced from the figures for the last three years, there would, on the assumption that the whole army, or the susceptible portion of it, were inoculated, be an annual saving of over 1,000 cases of enteric and of nearly 200 lives.

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 asepticity 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 inoculation is giving its best results. This said, 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 cultivate 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 cultivations 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 $2\frac{1}{2}$ 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.

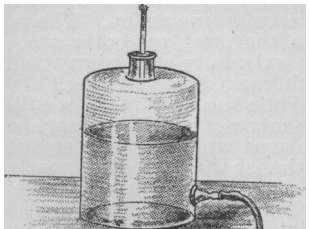

Fig. 1.—Cultivation flask.

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 minute 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.[4] 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.

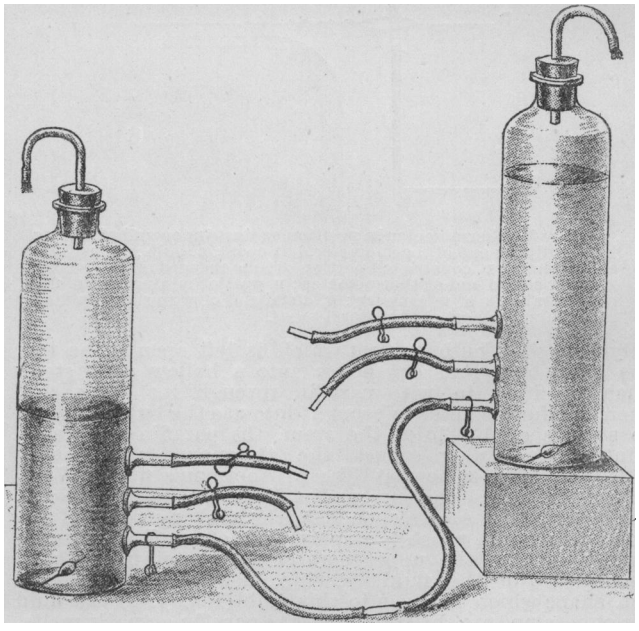

Fig. 2.—Large jars connected together for the purpose of mixing the vaccine. Paraffin thermometers which have sunk are shown at the bottom of each mixing jar.

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-

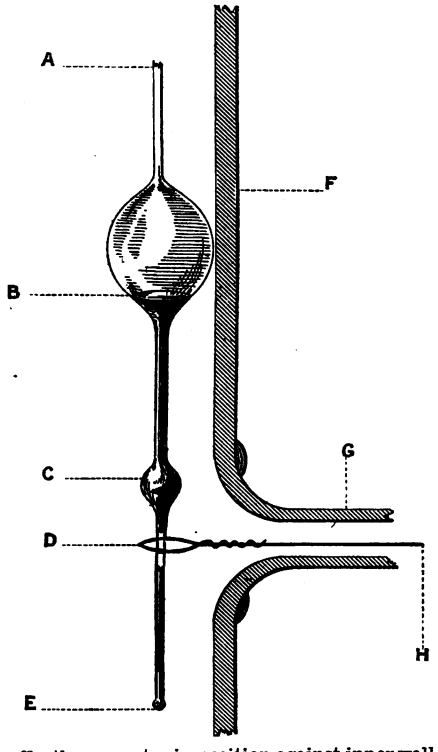

Fig. 3.—Paraffin thermometer in position against inner wall of mixing jar. A, Upper end of thermometer, left open; B, bulb; C, fusiform enlargement; D, constricted portion of tube engaged in wire snare; E, lower sealed end of thermometer; F, wall of mixing jar; G, upper lateral tube of mixing jar; H, 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, C), 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 so 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 fitted up, previous to sterilisation, a noose of fine brass wire is passed in through the rubber tube which is connected 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, G). 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

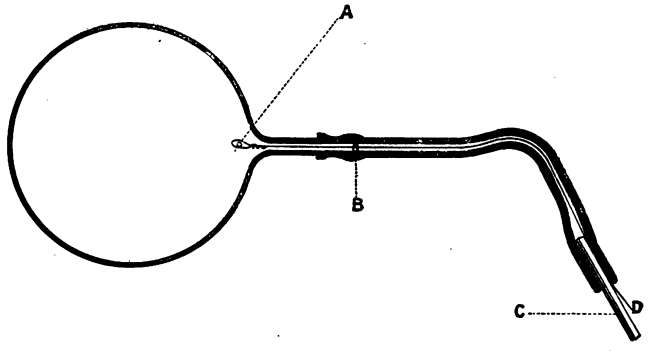

Fig. 4.—Transverse section of mixing jar at the level of the uppermost lateral tube, showing method of fixing the paraffin thermometer. A, Noose of brass wire engaging the constricted part of the stem of the thermometer: B, end of lateral tube; C, glass rod plugging the end of the rubber tube; D, free end of the wire clamped in position by the rod C.

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.[5]

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 connects the two tubes. The needle of a syringe which has been filled with undiluted carbolic acid is then inserted into the lumen of the tube at a point between the clamp and the glass nozzle which was referred to above. The syringeful 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 mixture 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 effected, samples of the vaccine are withdrawn in 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 Kitasato flask fitted with a length of 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 Kitasato flask is connected up with the series of mixing jars which contain the vaccine and the antiseptic is throughly 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 each case superadd to the determination 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, F).

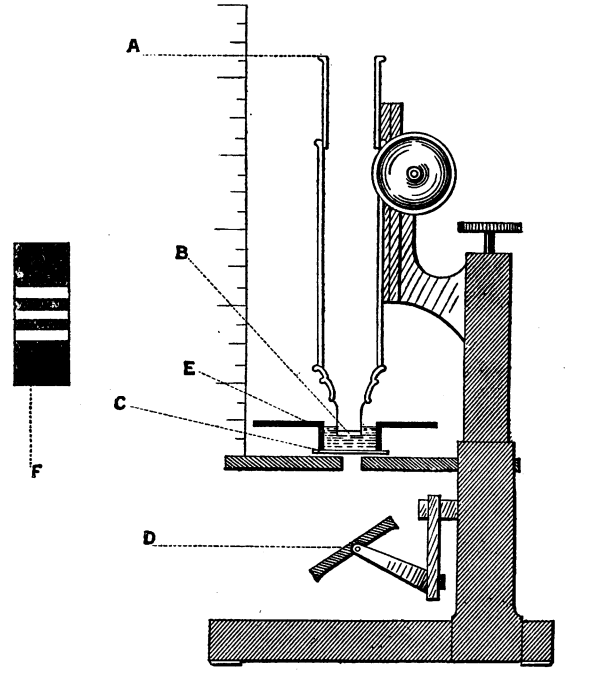

Fig. 5.—Diagram of a microscope arranged for the estimation of the opacity of the vaccine. A, Top of the body of the microscope, and point from which readings may be taken on the scale; B, plane glass cemented on the end of an old objective; C, plane glass at bottom of vaccine receptacle; D, plane mirror 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.

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 screw 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 vaccine which just suffices to blurr 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. Measured in this manner, the opacity of the antityphoid vaccine which we have prepared works out on an average as 1 cm. In other words, a layer of vaccine, 1 cm. deep, will obscure the detail of the test object. The highest value which we have obtained for this opacity is 0 65 cm. and the lowest has been 1.3 cm. It must be noted that the opacity of the vaccine is influenced by several different circumstances. It is obviously influenced in the first place by the solution of bacteria which gradually takes place as the vaccine is kept. It is further influenced in a very marked manner by the addition of the antiseptic. With a view to diminishing so far as possible the operation of these disturbing causes, we make it a rule to determine the opacity of the vaccine immediately after it has cooled down.

Method of Determining the Toxicity of the Typhoid Vaccine.

It has been explained above that, in addition to determining the opacity of each brew of vaccine, we resort also in each case to a direct determination of the toxicity of the vaccine by the subcutaneous inoculation of measured volumes 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 result obtained. 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 8 guinea-pigs, giving doses of 0.5, 0.75, 1 c.cm. and 1.5 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: œdematous infiltration of the subcutaneous tissue round the site of inoculation, marked congestion of the suprarenals, slight enlargement and congestion of the spleen, distinct enlargement and occasional congestion of Peyer's patches. Fluid is occasionally found in the peritoneum, pleura, and pericardium, and hæmorrhagic patches on the surface of the lungs are frequently present. The intestines are also frequently full of watery discharges. Generally speaking, the toxicity of a brew of vaccine stands in close relation with its strength as determined by the estimation of opacity. The maximum toxicity 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, as we have said above, to reserve for a future communication the discussion of the uncertainties which are thus imported into the method of standardisation.

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 toxicity, as determined on guinea-pigs, 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 bacterial elements, it is a matter of no 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 have to describe 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. We have satisfied ourselves that the bottles filled by the process now to be described retain their contents in a perfectly sterile condition for an indefinite period.

In the first place a number of small bottles, of a shape and capacity best suited to the requirements of the case, are plugged with cotton wool and autoclaved. Those which we have found most convenient have a capacity of 25 c.cm., but, for special purposes we also use bottles of other sizes, of not less than 10 c.cm. and not more than 75 c.cm. capacity.

When the autoclaved bottles are cool the cotton-wool plugs are replaced under antiseptic precautions by strong rubber caps, which have been soaked in a saturated solution of perchloride of mercury, and which have been specially made to fit each size of bottle. The use of these rubber caps, in preference to any form of cork or stopper, presents many advantages, chief among them being the fact that they admit of all fluids being introduced into or withdrawn from the bottle by means of a syringe and hypodermic needle—an obvious gain when we consider the danger of contamination which occurs every time a bottle is corked or uncorked.

A sufficient number of bottles having been prepared in this manner, one of the mixing jars is now taken in hand. If the jar be connected in series with others, we must first disconnect it. This we do—as described before—by clamping all the rubber tubes in connection with it, then withdrawing the glass joints aseptically and replacing them by solid rods. In the case of the jar which is to be bottled off, the lowest tube of all is connected by means of a glass nozzle with a further length of sterilised rubber tubing fitted with a hypodermic needle. To the plugged air tube which passes through the top of the jar is now attached an ordinary hand bellows, such as belongs to any spray-producing apparatus. This is done with a view to accelerating by air pressure the flow of the vaccine as it passes out through the small bore of the hypodermic needle. In order to prevent the paraffin with which the rubber bung is luted from yielding to air pressure when this comes to be applied, it is well to coat over every part of the bung with a layer of collodion, which should be allowed to set before pressure is applied. The hypodermic needle is now withdrawn from the sterile test tube or antiseptic solution in which it has been resting, and we proceed to fill in the bottles. The first operation is to get up a slight amount of air pressure in the interior of the jar by working the bellows. This done the bottles are dipped in a strong solution of carbolic acid or lysol. A vent is now provided for the air, which will be displaced by the vaccine by piercing the cap of each bottle as it is dealt with by a very fine hypodermic needle, which has just been removed by means of a forceps from a vessel of oil at a temperature exceeding 100° C. (Fig. 6, p. 129). The clamp on the rubber tubing which leads off from the mixing jar is now taken off, and the pressure of the fingers is substituted for it. The flow of the vaccine is now under perfect control, the hypodermic needle is introduced through the cap into the bottle, and the vaccine is then allowed to flow in (Fig. 6). In this manner any number of bottles of vaccine can be quickly filled, without the fluid ever coming in contact with the external air. The contents of the mixing jar are shaken up from time to time during the course of the operation.

When the bottles have been filled, it remains to repai r

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 160° 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.

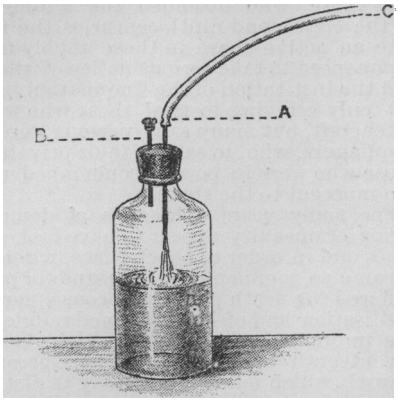

Fig. 6.—Method of filling small bottle from the mixing jar. A, Hypodermic needle connected with the tube C leading from the mixing jar; B, second hypodermic needle forming air valve.

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 undertaken, 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 of aseptically. They are then filled from a syringe 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.

NOTES AND REFERENCE.

[1] *Lancet*, September 19th, 1896. [2] The case in question was a somewhat anomalous one. 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. [3] In connection with the question of the results of the inoculations done on officers, reference may be made to a batch of twenty-two officers inoculated by Major Firth, R.A.M.C., on the troopship *Dilwara*, in October, 1897. It appears from inquiries which were instituted by Major Firth, which were supplemented by some further inquiries made by one of us, that none of these officers have suffered from enteric, whereas two uninoculated officers who came out in the same troopship have succumbed to that disease. [4] We have invariably found this rubber solution to be perfectly sterile. [5] 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 medical 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 Medico-Psychological Association 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.

Whatever may have been the causes 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 probably not in so marked a manner as among ourselves. Intoxication was not unknown to the ancient Egyptians, and without doubt exerted, 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. Doubts have been expressed as to whether 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 defection from his master and union with the Philistines was of no serious import. That the illness which separated the great 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.

Among the Greeks Ulysses is said to have feigned insanity when compelled to join the army against Troy. Bellerophon gave a name to melancholia—morbus bellerophonteus. Ajax, afflicted by madness at the instigation of Minerva, sword in hand attacks oxen in the dead hour of the night, and exhausts his maniacal passion upon them in mistake for men; and Hercules, who is said to have suffered from epileptic insanity, appears to have indulged in conduct which would in more modern days, in his own interest and that of the general public, have insured his speedy transference to some such establishment as that which is so conspicuous an object in the landscape as one enters Stafford by railway from the south.

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 first referred these diseases to the gods appear to have been just such persons as the conjurors, purificators, mountebanks and charlatans now