CHLOROFORM WITH PLenty OF AIR.

The rapidity and depth of this fall is directly dependent upon the concentration of the chloroform, so that if care is taken to give the chloroform with plenty of air it is possible to obtain anæsthesia with very little fall of pressure, for the heart is very little affected by blood containing only a small amount of chloroform. On the other hand, administration of chloroform with plenty of air, continued after complete anæsthesia has been produced, does ultimately overpower the respiration, although the heart is beating sufficiently well to maintain the blood pressure at a fairly good level.

These statements are well illustrated by an experiment on December 11th, 1890 (Fig. 11),²¹ where chloroform was administered to a rabbit continuously for a long period of time by dropping it on to a cloth placed round the head of the animal in a conical shape, so as to leave a free opening for air about two inches in diameter. Every now and then the part of the cloth upon which the chloroform was poured was brought closer to the nose and mouth of the animal, and the moment of bringing the chloroform nearer and of removing it again was noted on the kymograph paper. In the tracings *a*, *b*, *c*, *d*, *e*, *f*, Fig. 11, samples of the respiration and blood-pressure curves are given at various times throughout the experiment; as stated already, chloroform was steadily administered during the whole time.

In Tracing *a*, taken before the administration of chloroform at 3.34 we see: mean blood pressure, 64; pulse rate per minute, 222; respiration rate per minute, 30. The chloroform was then placed on the cloth, and the effect of bringing the chloroform nearer and removing it further tried for a number of times. An example of the effect produced is given in Tracing *b*, showing the inhibition of the respiratory movements, the slowing of the pulse, and the rise of blood pressure owing to the stimulation of the trigeminal and pharyngolaryngeal nerves, when the chloroform is more concentrated; immediately the cloth is removed further from the nose the blood pressure returns to its normal condition, and the slowed respiration gradually quickens up to its previous rate. This experiment was repeated again and again with similar results.

The effect of the continuous administration of chloroform in this way for 14 minutes is given in Tracing *c*, taken at 4.48, where we see: mean blood pressure, 67; pulse rate per minute, 218; respiration rate per minute, 31. Further continuation of the same experiment shows that the inhibition of the respirations and the slowing of the pulse when the chloroform is brought nearer to the nose become less marked; and, finally, after 3.56—that is, 22 minutes after the beginning of the experiment—the blood pressure and the respirations remained absolutely unaffected when the chloroform was brought close to the nose. At the same time, it was noticed that the corneal reflex was entirely abolished.

Tracing *d*, at 3.57, shows the absence of any effect upon temporary concentration of the chloroform, and we see: mean blood pressure, 69 mm.; pulse rate per minute, 204; respiration rate per minute, 42. It is noticeable that at this period, when all reflexes were abolished and the animal was in a condition of complete anæsthesia, the blood pressure was not lower than before the commencement of the experiment, and the only sign of the action of the anæsthetic is to be found in the quicker respiration.

At 3.58 the respiration rate per minute had increased to 46, the pulse tracing and respiration both remaining absolutely regular. At 3.59 the respiration was 45 per minute, at which it remained till 4.1, the mean blood pressure being then 62 mm. Both respiration rate and blood pressure continued steadily to diminish, and at 4.3, when Tracing *e* was taken, we see: mean blood pressure, 50 mm.; pulse rate per minute, 218; respiration rate per minute, 37. At 4.5 the respiration rate was 35; at 4.7, 31; at 4.8, 29; and at 4.9 the respiration had ceased. The termination of the experiment is shown in Tracing *f*, in which is seen the diminishing force of the diaphragm contractions, with the final rate, and we see: mean blood pressure, 48 mm.; pulse rate per minute, 126; respiration rate per minute, 24.

It is noticeable in this case, as in others (Figs. 1, 2, and 3),²²

how markedly the muscle strip of the diaphragm elongates when the respiration is failing. This points strongly to the conclusion that the respiratory centre possesses a distinct tonic influence on the diaphragm muscle, so that the failure of its action causes a loss of tone in the muscle as well as a diminution in the strength of each contraction. The pressure of 48 mm. at the time when the respiration ceased is not very low for a rabbit, and, indeed, the heart continued beating well for a considerable time, and then, by means of artificial respiration, the animal was easily recovered, and both blood pressure and respiration became normal, as is seen in Fig. 1, Tracings *a* and *b*, which represent the final ending of the experiment.

The danger, then, of chloroform administration consists (1) of causing a serious fall of pressure owing to weakening of heart from too great a percentage of chloroform in the air, which, combined with the action of the chloroform on the respiratory centre, in its turn causes failure of respiration; and (2) cessation of respiration after long administration owing to keeping on the chloroform, although given with plenty of air, too long a time after complete anæsthesia has been established.

ON HAFKINE'S METHOD OF VACCINATION
AGAINST ASIATIC CHOLERA.

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THE subject of M. Haffkine's anticholeraic vaccinations has already been treated of in the BRITISH MEDICAL JOURNAL, notably in an able paper by Mr. Hankin. In response, however, to a kind suggestion from the Editor, and in view of the great importance of the matter, we propose to give further details of M. Haffkine's method of vaccination as demonstrated by him at Netley during the past week. We gladly avail ourselves of this opportunity to express our sense of gratitude to him for his kindness in coming to Netley for this purpose.

It may perhaps conduce to clearness of exposition if we present the facts of cholera vaccinations in their relation to certain broad generalisations which have been made in connection with the subject of microbial infective processes.

Microbial infections are conveniently subdivided into "septicæmias" and "intoxications." In the case of the former the bacteria multiply freely in the blood and produce their poisons there. In the case of the latter the micro-organisms do not proliferate in the blood, but bacterial poisons become absorbed into the system from some point—generally a point on the inner or the outer surface of the body—at which the bacteria have effected a lodgment. Asiatic cholera belongs to the latter class of infective diseases, for the specific organisms which set up the disease are strictly confined to the alimentary canal. They are never found in the tissues, and they are very rapidly killed off when they are artificially introduced either into the blood or into the hypodermic tissue. For these reasons we may characterise the system as "bacteria proof" with respect to the specific organisms of Asiatic cholera. On the other hand, both experiment and clinical observation establish that the system is acutely susceptible to the poisons which are generated by the comma bacilli in the intestine. In view of the above facts, it will readily be understood that immunity against cholera can only be brought about by rendering the system "poison-proof" (*gift-fest*) with respect to the poisons of the cholera bacillus.

M. Haffkine's method of anticholeraic vaccination consists in such a process of chemical vaccination. The protection against cholera is brought about by acclimatising the system first to a weak cholera poison (first vaccine), and afterwards to a strong cholera poison (second vaccine). For adequate protection it is essential that this second vaccine should consist of the strongest obtainable cholera poisons.

²¹ BRITISH MEDICAL JOURNAL, January 28th, 1893, p. 169.

²² BRITISH MEDICAL JOURNAL, January 21st, 1893, p. 108.

We shall return to this matter later on in connection with the preparation of the anticholeraic vaccines. The object which M. Haffkine's vaccination has in view is to enable the system to tolerate such quantities of cholera poisons as might be expected to be absorbed from the intestine during the interval which elapses between the invasion of the alimentary canal by the comma bacillus and the natural elimination of that bacillus, which invariably takes place when convalescence becomes established after an attack of cholera. It is to be noted that M. Haffkine's vaccination does not aim at the impossible task of establishing a complete tolerance for an indefinitely large quantity of cholera poisons. It is indeed evident that if no reaction took place on the part of the cholera patient the cholera bacillus would not be dislodged from the intestinal canal, and its indefinite multiplication there would give rise to such an enormous amount of cholera poisons that it would be hopeless to attempt to cope with them. Under such circumstances the vaccinated patient would succumb with the same certainty as the unvaccinated patient, though he might hold out for a few hours longer. Seeing, however, that the system possesses this power of reaction to the invasion of the cholera bacillus, it would probably suffice for all practical purposes if a sufficient tolerance of the cholera poison could be induced to enable the system to put forth its whole reactive power. This, therefore, is the object aimed at in M. Haffkine's method of anticholeraic vaccination. The utility of the method will evidently entirely depend upon whether the tolerance of the cholera poison which can be induced in man by means of M. Haffkine's method is adequate to tide over the critical hours which supervene upon the outbreak of choleraic symptoms. This is a question upon which only actual clinical experience can decide. In the meantime, it is evident that a trial of the method ought to be made if the following three propositions can be established: (1) That the principle of the proposed vaccination is theoretically sound; (2) that the method confers a very high degree of tolerance upon animals; (3) that the vaccinations upon man are innocuous. We have already endeavoured to establish the first of these propositions. With regard to the second, we might have recourse for our facts to the published experiments of Haffkine, Iawein, and Tamacheff, in which it has been demonstrated that guinea-pigs vaccinated according to Haffkine's method acquired a tolerance to as much as sixteen times the lethal dose of cholera virus. Instead of doing this we propose to give the protocol of an experiment which we performed with M. Haffkine's kind assistance, with a view to satisfy ourselves that tolerance of the cholera virus could be established by M. Haffkine's method of vaccination. The experiment itself was as follows:

GUINEA-FIG 1.—Vaccinated with carbolised first vaccine on January 17th, 1893; vaccinated with carbolised second vaccine on January 20th, 1893; inoculated intraperitoneally with 1-6 tube of exalted virus January 23rd, 1893. Result: Died on morning of January 25th, 1893.

GUINEA-FIG 2.—Vaccinated with carbolised first vaccine on January 17th, 1893; vaccinated with carbolised second vaccine on January 20th, 1893; inoculated intraperitoneally with 1-8 tube of exalted cholera virus on January 23rd, 1893. Result: Alive and thoroughly recovered from cholera inoculation on January 24th, 1893.

GUINEA-FIG 3.—Vaccinations and cholera inoculation exactly the same as in the case of Guinea-pig 2. Result: Alive and thoroughly recovered from the effect of cholera inoculation on January 24th, 1893.

CONTROL ANIMALS.¹

GUINEA-FIG 4.—Received an intraperitoneal injection of 1-8 tube of exalted virus on January 23rd, 1893. Result: Dead by next morning.

GUINEA-FIG 5.—Received an intraperitoneal inoculation of 1-16 tube of exalted cholera virus on January 23rd, 1893. Result: Dead by next morning.

GUINEA-FIG 6.—Received an intraperitoneal inoculation of 1-32 tube of exalted virus on January 23rd, 1893. Dead on morning of January 25th, 1893.

It will be seen that in this experiment the lethal dose for the vaccinated guinea-pig was more than five times as large as the lethal dose for the unvaccinated guinea-pig (1-6 tube as compared with 1-32 tube). Further, it will be seen that almost complete tolerance had been established by these vaccinations for four times the lethal dose of cholera virus (1-8 tube tolerated by the vaccinated guinea-pigs as compared with 1-32 tube lethal for the unvaccinated guinea-pig).

In view of these striking results, it is evident that M. Haff-

kine's vaccinations do establish a high degree of tolerance for cholera poison in the case of guinea-pigs. M. Haffkine has shown that a similar tolerance for the exalted cholera virus can be established in the case of rabbits and pigeons.

With regard to our third proposition, which deals with the innocuousness of the cholera vaccinations on man, we need not do more than refer to the fact that M. Haffkine has already performed some fifty vaccinations on man without producing anything more than a general sense of *malaise* and a certain amount of local oedema and tenderness round the seat of the vaccination. It is perhaps worth mentioning in this connection that minute and detailed observations on these subjects were made by each and all of M. Haffkine's "patients." With regard to the dose of cholera poisons which is inoculated subcutaneously in man, M. Haffkine has, in the absence of clinical observations upon the subject, in all cases employed the doses of virus which he found would convey a high degree of tolerance in guinea-pigs. These doses, as will be explained further on, consist of one-sixth to one-eighth of the emulsion prepared from a single day's growth of cholera on a standard tube of agar-agar, kept at a temperature of 35° C.

Having thus described the principles of M. Haffkine's system of vaccinations we have to pass on to the *technique* connected with the preparation of the vaccines and the actual vaccinations.

PREPARATION OF ANTICHOLERAIC VACCINES.

These vaccines consist of emulsions of attenuated and of "exalted" cholera cultures. They may consist of emulsions either of living cholera bacilli (living vaccines) or of emulsions of cholera bacilli which have been killed by the action of dilute carbolic acid (carbolised vaccines). The living vaccines present the advantage of possessing a more powerful vaccinating power. The carbolised vaccines on the other hand present the advantage of being perfectly safe to handle or leave about. Further they appear not to be appreciably impaired by keeping. They could thus be sent out for use from any central bacteriological laboratory.

The process of preparation of these vaccines may be treated of under two headings—preparation of cultures of attenuated and exalted cholera bacilli, and preparation and preservation of the vaccines prepared from the above cultures.

METHOD OF PREPARING AN ATTENUATED CULTURE OF CHOLERA BACILLI.

Such a culture could doubtless be prepared in many different ways. Probably most of the cultures which have been grown for some time on artificial media in our laboratories would be found attenuated, but up to an uncertain point only. M. Haffkine has employed a method in which the cholera bacillus is grown in media which are continually aerated with air at a temperature of 39° C. When cholera bacilli have been grown under these unfavourable conditions for some time they become so weakened that they cause a local oedema instead of a necrosis when they are injected into the subcutaneous tissue of a guinea-pig. It is important to note that when the cholera bacillus has been thus attenuated it may be grown indefinitely in agar tubes without regaining any of its lost virulence. A cholera which has been found suitable for employment as a first vaccine may therefore be propagated indefinitely by transplanting it at intervals upon fresh nutrient media.

METHOD OF PREPARING A CULTURE OF "EXALTED" CHOLERA BACILLI.

The cholera which is obtained in Nature, that is, from the evacuations of cholera patients, is generally not sufficiently virulent to provide an effective second vaccine. In order to obtain a sufficiently exalted virus for his purpose, Haffkine grows the cholera bacillus in the peritoneal cavities of a series of guinea-pigs. As each guinea-pig of the series dies, the fluid which is found in its peritoneal cavity is removed. It is afterwards transferred to the peritoneal cavity of another guinea-pig, and so on through a series of twenty or thirty animals. It is evident that the difficulty of keeping the peritoneal fluid of these animals perfectly free from contamination during such a series of "passages" must be very great. The danger of contamination is threefold: (1) The bowel may

¹ Note, all these animals were of larger size than the vaccinated guinea-pigs.

be wounded in making the intraperitoneal injections; (2) bacteria may be introduced into the peritoneal cavity from the surface of the skin when the needle is pushed through; (3) there may be a defect in the sterilisation of the instruments and vessels employed in conveying the peritoneal effusion from one guinea-pig to another. The methods which are adopted to minimise the risks of such contamination will become apparent in the course of the description of the operations.

In order to start the series, that is, to inoculate the first guinea-pig, we may have recourse to any ordinary pure cultivation of the cholera bacillus. Standard tubes of these cultures are prepared by inoculating the whole surface of nutrient agar with the cholera bacillus. The test tubes employed are some 15 centimetres in length. Of these 15 centimetres, 10 centimetres are occupied by the sloping surface of the nutrient agar. The inoculated tubes are placed in an incubator at 35° C. for twenty-four hours. Two or more of these standard tubes are to be prepared for the inoculation of the first guinea-pig. Proceed then as follows: Take the determined number of standard cholera tubes, and further provide yourself with the following apparatus: (1) a sterilised glass pipette (*vide* Fig. 1), (2) a tube of sterilised broth, (3) a cautery,

Fig. 1.

Fig. 2.

Fig. 3.

(4) a pair of curved scissors, (5) a guinea-pig of, say, 300 to 400 grs. in weight. Having these things within easy reach, proceed with a little (say 3 c.c.) of the sterilised broth to make a suspension of the cholera bacilli growing on the sur-

face of the agar tubes. This may be done with stout, straight platinum wire, mounted on a glass rod which has been drawn out to the same thickness as the platinum wire. Contamination of the tube is to be carefully avoided by holding it in a horizontal position.

The guinea-pig is now placed under the influence of ether, and while it is held by an assistant the hair is cut short over the central part of the abdomen. The cautery is now heated to a full red heat, and a small portion of the skin of the lower part of the abdomen is cauterised. It is not necessary to carry the cautery through the whole thickness of the skin; it is sufficient to destroy the superficial horny layer. Now break off the tip of your sterilised glass pipette with a sterilised forceps, and suck up the emulsion into the pipette. The point of the pipette may now be pushed through the burnt portion of skin into the peritoneal cavity, without the slightest risk of carrying living bacteria from the skin into that cavity, or of injuring the intestine.

It may be remarked that it is well to place the point of the pipette at right angles to the skin, and to work it through the abdominal wall by a gentle boring motion. The suspension of cholera bacilli can now be blown in. Lastly the pipette is withdrawn and any drop of fluid which may have exuded from the wound is got rid of either with the point of the heated cautery or simply by washing with an antiseptic.

The guinea-pig so operated on will die within 24 hours. It will then be necessary to proceed almost at once to remove the serous exudation which has taken place into the peritoneal cavity, as any prolonged delay might lead to a contamination of the fluid with putrefactive bacteria. The method of operation is as follows: The guinea-pig is tied out on a suitable board and the hair over the exposed ventral surface is thoroughly moistened with water to prevent dust or germs flying about when the skin is cut through. An incision is then made through the skin from the pubes to the root of the neck, and four other incisions are carried outwards at right angles from the extremities of this median incision. The skin is then reflected from the whole anterior surface of the body. This preliminary operation is done with non-sterilised instruments, as there is no danger of contaminating the peritoneal fluid through the intact muscular parietes. The actual opening of the peritoneal cavity must, however, be done with the most stringent precautions. The instruments employed are three pairs of dissecting forceps and a pair of ordinary scissors. These are placed in a suitable vessel, and are boiled for several minutes. In the meantime the lines of the proposed incision must be thoroughly cauterised to remove any possible source of contamination. This is done by branding a line half an inch wide in the shape of a capital T on the front of the abdomen. The cross stroke of the T runs transversely across the abdomen, about the level of the ensiform cartilage. The instruments may now be removed from the boiling water, in turn as they are required. During the manipulations the operator must keep the instrument in his hand, and not allow it to come in contact with any non-sterilised object, or with the non-cauterised parts of the dead body, in order to avoid any contamination. The muscular walls are divided along the lines of cauterisation, care being taken not to wound the intestine, then the flaps of the muscular wall are to be turned back to the right and to the left. In making the incisions the blade of the scissors, which had been held ventrally in making the first incision, is to be held ventrally throughout, as the dorsal blade may have become contaminated.

When the flaps have been reflected, the coils of intestines are seized between the blades of a sterile pair of forceps, and are thrown over upwards and to the right. Before doing this a sterilised pipette similar to that previously employed (Fig. 1) has been taken, and its point has been broken off with a sterilised forceps. This pipette is now held in the mouth, and the peritoneal fluid is carefully aspirated into it from the iliac fossæ, in which it will have lodged. The whole of this fluid is now introduced into a sterilised test tube. The plug of cotton wool is replaced, and the test tube containing the peritoneal fluid is placed in an incubator at 35° C, in such a position as to expose the greatest amount of surface to the atmospheric air. The tube is kept in the incubator for a period of some eight or ten hours, or even more. The object of this manoeuvre is to allow of a proliferation of the comma

bacilli in the peritoneal fluid in the presence of oxygen. A similar intercalation of an interval, however, short of an aerobic growth has been found essential for the perfect development, even of such strictly anaërobic bacteria as the *clostridium butyrocum*. After a sufficient interval has been allowed for such growth the exudation fluid is introduced into the peritoneal cavity of a second guinea-pig in exactly the same manner in which the original emulsion was introduced into the first guinea-pig.

In choosing a guinea-pig for the next in the series the following indications must be strictly attended to. If the amount of peritoneal fluid obtained from the previous guinea-pig is large this will be indicative of a considerable amount of resistance on the part of the guinea-pig. In such a case the comma bacilli present in the exudation will be comparatively few, and it will be necessary to choose for the next in series a guinea-pig of somewhat smaller size. The question of size is of importance as an index of the degree of resistance on the part of the guinea-pig. Where the amount of exudation fluid is small it will be found to be swarming with comma bacilli. In such a case a guinea-pig of somewhat larger size is employed for the next in series. In this manner the cholera bacilli are passed through a series of from twenty to thirty guinea-pigs, while their virulence becomes gradually exalted at each "passage." The bacilli are considered to have attained their maximum exaltation when further "passages" cease to shorten the period which elapses between inoculation of the virus and death of the guinea-pig. The exaltation which can be obtained by this means is so great that a specimen of cholera which was only lethal for a guinea-pig in a dose amounting to two standard agar tubes has, in M. Haffkine's hands, become lethal for guinea-pigs in doses of 1-32 to 1-64 of a tube.

The process of exaltation, even with the precautions described, is evidently complicated with a certain risk of contamination for the peritoneal fluid which has to be transferred from one guinea-pig to another through a long series of "passages." For greater security M. Haffkine has adopted the following method of controlling the purity of his cholera culture at its various stages. At each passage the peritoneal effusion is examined microscopically as a security against gross contamination. At the same time the point of a sterilised platinum needle is dipped into the peritoneal effusion. The needle is thus charged with a minimum of the exudation fluid, and a series of ten to fifteen parallel longitudinal lines are now scored on the sloping surface of a nutrient agar tube. The plug is replaced in the tube, and the same manipulation is repeated without recharging the needle upon the surface of a second agar tube. The tubes are then placed in the incubator, and are examined after twenty-four hours. By this time the bacteria which have been implanted have grown out into a series of discrete colonies, which are of course farther apart in the case of the last series of furrows. It is easy by this method to detect the intrusion of any foreign bacteria into the peritoneal exudation. The advantages of this system of control test tube inoculations is obvious, for not only are we enabled to detect the first trace of contamination in the peritoneal effusion, but we are able, in case of such contamination, to go back to the cholera bacilli of the penultimate "passage" instead of having to begin again at the original culture with which we started.

Having in this manner provided ourselves with a pure cultivation of attenuated and exalted² cholera bacilli, we may proceed to describe the preparation of the vaccines from these cultures. The process of preparing the vaccines is the same for both varieties of cholera bacillus.

PREPARATION OF THE VACCINES FROM THE CHOLERA CULTURES.

In order to prepare mass cultures for the preparation of vaccines a sterilised platinum needle is inoculated from a pure culture of the cholera bacillus, and the bacilli are distributed evenly in a thin layer over the surface of a standard agar

² Note.—These cultures of exalted cholera virus do not retain their virulence for more than ten days or so when they are grown on artificial media. After that period it is necessary to recur again to a certain number (from three to four) of "passages" in order to bring back the culture to its maximum of virulence.

tube; these tubes are placed in the incubator at 35° C. for twenty-four hours. At the conclusion of that period a sterilised pipette (Fig. 1) is taken, and a small quantity (2 to 3 c.c.) of sterilised broth is introduced into the agar tube containing the culture, and the layer of bacteria is scraped off from the underlying agar, and is beaten into a fine emulsion.

The emulsion thus prepared is aspirated into the pipette and is transferred into a sterilised V-shaped glass, which is covered up with a piece of sterilised filter paper. The quantity of emulsion thus obtained is drawn up into a sterilised syringe, and is then accurately measured. The contents of the syringe are emptied into another sterilised glass, and more bouillon is added to the latter, so as to make up a total quantity of 8 c.c. of liquid. By aspirating this liquid several times into the syringe and emptying it out again several times a uniformly mixed emulsion is obtained. The emulsion thus prepared constitutes the so-called "living vaccine." One cubic centimetre of this emulsion constitutes the quantity employed for the vaccination of a guinea-pig. The same dose is employed for a man.

It will readily be understood from what has been said in a previous part of this paper that the living cholera bacilli are rapidly killed off when they are introduced into the hypodermic tissue. The vaccine containing the living bacilli possesses greater immunising power than the next vaccine, the preparation of which we shall proceed to describe.

PREPARATION OF CARBOLISED VACCINES.

These vaccines are prepared in precisely the same manner as the living vaccines, except only as regards the fluid in which the emulsion of cholera bacilli is made. In the case of the carbolised vaccines this fluid consists of a 5 per cent. solution of carbolic acid, which has been sterilised³ before use in an autoclave (temperature of 115° C. for 15 minutes), and a tube of agar cultivation is diluted in 6 c.c. of liquid so as to make six doses of greater concentration than the living vaccine. Carbolised vaccines present the great advantage of containing no living cholera bacilli. They may also be preserved, apparently unimpaired, for some considerable time in sealed tubes.

PRESERVATION OF CARBOLISED VACCINES IN SEALED TUBES.

The apparatus required for this purpose is extremely simple. A certain number of tubes are drawn out according to the pattern indicated in Fig. 2. The wider portion of tube which interrupts the stem of the capillary pipette is designed to hold the requisite dose (1 c.c.) of vaccine. Six of these "ampullary pipettes" are employed to hold the emulsion derived from each standard agar tube. The emulsion is simply aspirated into the tube with stringent precautions against contamination, and the capillary tube is then sealed in the flame at *xx*.

MODE OF INJECTING THE VACCINE.

For injecting the vaccine M. Haffkine employs a very simple form of hypodermic syringe, which is provided with a caoutchouc or elder pith piston (Malassez's or Strauss-Collin's syringe). This is taken to pieces and placed in boiling water for some minutes before use. Before transferring the contents of the vaccine tube to the hypodermic syringe the tube is carefully tapped with the finger nail to dislodge any sediment which may be clinging to the walls of the tube. One of the closed ends is then heated in the flame to sterilise it, and the tip is broken off with a sterile forceps. As the needle of the syringe is not long enough to reach to the bottom of the tube, the following ingenious expedient is resorted to to effect an aseptic transfer of the vaccine. The syringe is held needle uppermost, and the tube of vaccine is inverted over the top of the needle (*vide* Fig. 3). The contents are then simply aspirated into the syringe by gradually withdrawing the piston. No leakage of fluid takes place from the vaccine tube, as the upper extremity is still hermetically sealed. The vaccines are to be introduced into the hypodermic tissue, not into the depth of the muscles. The seat of election for the vaccination is under the skin of the flank halfway between the crest of the ilium and the

³ The carbolic acid solution must be sterilised in order to destroy any spores which the 5 per cent. carbolic acid would not be strong enough to destroy.

lowest rib. The inoculation of the first vaccine is made from three to five days before the inoculation of the second vaccine. When the first vaccine is inoculated into the right flank, the left flank is to be chosen for the inoculation of the second vaccine.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

CHOREA IN A BOY: NECROPSY.

A. M., aged 9 years, a tall, fair, anæmic boy, had well-marked bilateral choreic movements since the end of October. He had had no serious illness except whooping-cough, but had not looked well for the previous month. The immediate cause of the attack was thought to be a fall into a pond, after which he lay in a wood, wet, being afraid to go home. His father had had rheumatic fever three times. The boy remained in the same condition until December 21st, when he was unable to come up to the surgery, and for the last few days had been unable to walk. The lad was considerably weaker; the knee-jerks were not obtained, but the epigastric reflexes were present.

Examination of the chest revealed nothing definite. On December 24th slight cough and *râles* were present. On December 28th the jactitation had ceased, but the lad was much worse. Loud rubbing was heard over the præcordium, and moist *râles* over both lungs. He died on December 29th.

A *post-mortem* examination was made in the afternoon. Rigor mortis had commenced in the lower extremity; no subcutaneous nodules were found. The pericardium was rough and thickened, covered with fibrinous exudation, and contained a considerable quantity of turbid effusion. The heart was slightly hypertrophied, the muscle paler than normal but not friable. There were some very small vegetations on two of the aortic valves and less on the mitral; the right side was normal. There was evidence of broncho-pneumonia in both lungs; the brain and abdominal viscera were normal. The rarity of fatal cases makes this one of interest, although there is no fresh light thrown on the pathology of chorea.

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A CASE OF CHRONIC ANTERIOR POLIOMYELITIS WITH WELL-MARKED CUTANEOUS ANÆSTHESIA AND ANALGESIA.

THE association of cutaneous insensibility with analgesia in progressive muscular atrophy is sufficiently uncommon to warrant record. From the limited works of reference at my command I cannot find any mention of analgesia, a very prominent symptom in the case now to be described.

M. S., a Mahommedan, consulted me a few days ago, and after questioning and examination the following facts were elicited: About nine or ten years ago (present age 38) he noticed tingling sensations in the right thumb, and very soon after complained of weakness of the hand. Coexistent with this there was wasting of the muscles corresponding to the area over which the tingling was felt. This condition, with no other added symptom, gradually extended to the muscles ordinarily affected in this complaint, namely, those of the thenar and hypothenar eminences.

Both hands at present are typical instances of Duchenne's *main en griffe*. The muscles of the forearms are similarly and symmetrically affected, but notably the extensor and flexor carpi ulnares. The lower limbs are now a good deal involved, but not to the same degree as the upper. The solei and gastrocnemii have suffered mostly in the legs, and the condition of both feet is similar to the hands, with hammer-toes and flattened arches.

At the finger tips there is almost complete anæsthesia, lessening as the forearm is approached, until at the elbow sensation deviates but little from the normal. Coupled with the anæsthesia, and fading similarly towards the elbow, there is marked analgesia, so much so that on the dorsum of the hands, although well aware of the contact, a severe blow may

be dealt without pain; indeed, I think a fracture of the metacarpal bones might be effected without inconvenience to the patient. In both upper limbs the condition is identical. In the lower extremities the plantar reflexes are completely abolished, and analgesia with anæsthesia present, though to a less extent than in the upper. The cremasteric, epigastric, and abdominal reflexes are normal: the knee-jerk is unaffected, and there is no ankle-clonus. Though the disease is of nearly ten years' duration, there is no evidence of the muscles of the trunk being involved. Sexual desire is almost unabated and procreative capability unimpaired; two or three children have been begotten since the disease declared itself.

As to the diagnosis, the insidious onset and progressive character, with such unmistakable symptoms, indicates poliomyelitis of a chronic type. The points of interest about it are the analgesia, the apparent quiescence of the lesion, and the not inconsiderable severity of the disease in both upper and lower extremities without implication of the trunk. The patient states that all the symptoms are now as they were three or four years ago, and that he only consulted me on account of dyspeptic trouble, as he does not expect any amelioration of his present state. It is worthy of note that he has applied the faradic current to the atrophied muscles in an intermittent manner for several years, and undergone a prolonged course of treatment by Easton's syrup. Has the pathological change been arrested by the combined influence of the electricity and strychnine or is it a coincidence?

There is little doubt that in this case the posterior cornua are affected in some way in addition to the degeneration known to occur in the anterior, though it would be rash to venture a hypothesis as to the precise nature of the lesion. I examined for carefully, but failed to detect any evidence whatever of sclerosis in any form. Multiple peripheral neuritis may exist to complicate the chief disease, but it is so very unlikely that it may practically be eliminated; moreover, there is no history of anything to suggest any constitutional dyscrasia—syphilitic, alcoholic, gouty, rheumatic, or the like.

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FRACTURE OF FEMUR DUE TO MUSCULAR ACTION. THE case in the BRITISH MEDICAL JOURNAL of January 14th, 1893, reported by Mr. E. H. Jones, recalls a very interesting case I saw at the South Devon Hospital, Plymouth, which may be worth recording, owing to the supposed rarity of fractures due to muscular action, and to the way in which it proved fatal.

G. T., aged 42, a labourer of spare build, on March 24th, 1891, was wheeling a loaded barrow when he became conscious of a sprain in the region of the right knee. He went on with his work that day, but for the next few days stopped away from work, but did not lie up. On March 28th, whilst walking along a smooth pavement, he heard a sudden loud crack in his right hip, and would have fallen had he not been close to a lamp post. He was taken home on a barrow. On April 1st he was admitted to hospital under Mr. William Square. There was two inches shortening of the right leg, and the femur was broken across just below the great trochanter. There was some effusion into the right knee-joint. The bladder reached as high as the umbilicus, and a catheter drew off four pints of urine. He had had retention of urine for twenty-four hours after the accident, and after that dribbling. Before the sprain he had not suffered any pain in the legs, and was not conscious of anything wrong with the thigh until the sudden crack occurred. For three years he had not been able to hold his water properly, but had had no advice for it. There were no signs of scurvy, cancer, syphilis, scrofula, general paralysis, locomotor ataxy, or any other disease which might have predisposed to fracture.

From the date of admission the bladder condition was very serious, and, until the end, required the use of the catheter and washing out three times a day. The urine from the first was alkaline, and contained pus and mucus.

On April 13th, vomiting and delirium appeared. There was rapid emaciation, and the temperature fluctuated widely, indicating pyelonephritis. During May there was some im-