branches, had been punctured by a fragment of the metallic cover of the bullet. A silk ligature applied just above the hole in the artery cut through the softened vessel, and severe haemorrhage recurred. With considerable difficulty a thick silk ligature was passed around the vessel 1 in. proximal to the former ligature—that is, well within the bony pelvis. Both branches of the artery were next ligated, also with thick silk. The deep hole, reaching down to the point of ligation of the gluteal artery, was then filled with ether, the rest of the wound washed with the same, and gauze soaked in ether was used as a dressing.

The patient was removed from the theatre in a very feeble condition, and during the next twelve hours his temperature never rose above 96.8° F. For several days I suffered acute anxiety, fearing a recurrence of the secondary haemorrhage, and wondering what might happen to three thick septic silk ligatures at the bottom of the infected wound. The ether, however, did its work splendidly, and the wound cleaned and closed with remarkable rapidity. Nothing was ever seen of the silk ligatures, and on the thirty-fourth day the patient proudly informed me that he had "walked halfway down Bond Street."

CASE II.

A soldier, during a bayonet charge at Ypres, had the misfortune to be wounded almost simultaneously by a German bullet from the front and by British shrapnel from the rear. The latter wound was extraordinary in that the lowest 4 in. of the posterior wall of the recto-anal canal were blown away, leaving a cavity into which a closed fist could be easily introduced. On admission to Charing Cross Hospital the patient's condition was deplorable, and the stench from the wound was so horrible that the poor fellow told the ward sister that "he was not fit to be put into a clean bed." The vilely septic wound was washed at first twice, and then once, daily with ether. At the end of a month, during which time the pulse and temperature had been practically normal, the wound had healed, and, to my astonishment, a fair degree of continence of faeces has been secured. This was, I think, the dirtiest wound I have ever seen.

CASE III.

A soldier sustained a severe shrapnel wound of the soft parts of the leg. Washing with ether was the sole treatment employed in this very foul wound. Within two days the large infected surface had begun to clean, and rapid healing ensued.

Gunshot Compound Fractures.

I have not employed ether in the treatment of gunshot compound fractures to anything like the extent that I originally intended. It has, however, been used in six cases. The treatment adopted has been to enlarge, whenever necessary, the often small wound in the skin and soft parts down to the seat of fracture. The open wound has then been daily filled with ether, which has been allowed to evaporate. The results in all cases have been excellent, and I regret that I have not made more frequent use of the method. One merit of ether in the treatment of infected wounds deserves mention, namely, its action in dissolving fat, shared, to my knowledge, by no other antiseptic agent.

I desire to express my best thanks to Mr. C. J. Marshall, M.D., B.S.Lond., Surgical Registrar to Charing Cross Hospital, for his careful notes of the cases that were in my wards in that institution. The value of Mr. Marshall's notes is enhanced by the fact that the majority of these patients were under his immediate observation when he was my house-surgeon. I am also much indebted for notes of cases to Mr. E. P. Stibbe, resident medical officer to the Victoria Hospital for Children, to Dr. Whittingdale of Sherborne, and numerous other medical friends.

Before I conclude I desire to take this opportunity to refer to the "iodine treatment of wounds." I do so for the reason that I believe the paper on "Sterilization of the Skin by the Use of an Alcoholic Solution of Iodine," by my colleague Mr. W. S. Fenwick and myself, was largely responsible for the now almost universal employment of this method, and during the past few months some of my friends have said to me, "I am treating gunshot wounds with your iodine method." I beg to state emphatically that I have never recommended this use of iodine. I consider it painful, inefficient, and deserving of condemnation. Two of my friends who sustained large flesh wounds agreed that their worst recollection of this awful war was the brush with which the iodine solution was daily applied to their wounds, and my experience has been that many of the most septic wounds that have come under my care have been those which had been painted with iodine. Three soldiers, questioned by me regarding the amount of pain caused by ether, agreed that "it stung a bit for rather less than a minute."

The daily instillation of a drachm of ether into the bladder in an aggravated case of *Bacillus coli* cystitis, consequent upon a bullet wound of the cauda equina, markedly improved the condition and caused no pain to the patient.

BIBLIOGRAPHY.

- Jeanneret, L.: *Revue médicale de la Suisse romande*, 1913.
Morestin: *Bulletins et mémoires de la Société de Chirurgie de Paris*, February, 1913.
Murphy, John B.: *Surgical Clinics*, 1912 and 1913.
Témoign: *Bulletins et mémoires de la Société de Chirurgie de Paris*, May, 1913.
Waterhouse, H. F.: *Virchow's Archiv*, 1890.
Waterhouse, H. F., and Fenwick, W. S.: *Lancet*, April 4th, 1910.

THE ACTION OF ETHER ON CERTAIN MICRO-ORGANISMS.

By W. W. C. TOPLEY, M.B., M.R.C.P.,

BACTERIOLOGIST TO CHARING CROSS HOSPITAL.

(From the Bacteriological Department of Charing Cross Hospital.)

In the preceding paper Mr. Waterhouse has reported the clinical results obtained by the use of ether in cases of various pyogenic infections. The following investigations were undertaken in order, if possible, to obtain some information as to the manner in which this substance acts.

THE BACTERICIDAL ACTION OF ETHER VAPOUR.

Bearing in mind that the body temperature is 2° C. above the boiling point of ether, and also that the area to be dealt with in such a condition as an infected peritoneum is large, it seems clear that the action of the ether vapour must play a large part in any results produced. An attempt was therefore made to determine the bactericidal action of ether in this state.

The method adopted was to bury a sterile 2 c.cm. ampoule in the lower part of an agar slope, so that the mouth projected above the medium. An even surface growth was obtained, the ampoule was then three-quarters filled with ether by means of a capillary pipette, and the mouth of the culture tube closed with a well-fitting rubber cork. Incubation was carried out at 37° C., and subcultures were made at intervals. The organisms were thus subjected to the action of saturated ether vapour at body temperature.

The organisms examined were as follows:

- B. coli*, 11 specimens.
Staphylococcus albus, 11 specimens.
Staphylococcus aureus, 7 specimens.
Streptococci, 9 specimens.
Pneumococcus, 3 specimens.
B. pyocyaneus, 7 specimens.

The results obtained show that ether vapour exerts a definite bactericidal action on all these organisms. The intervals after which subcultures remained sterile varied from one to forty-eight hours. The *B. pyocyaneus*, the *Pneumococcus*, the *B. coli*, and the *Streptococcus* appeared to be the most easily killed, since three hours' exposure sufficed to kill every specimen of the two former organisms, 8 out of the 11 specimens of *B. coli*, and 6 of the 9 specimens of *Streptococci*. The *Staphylococci* would appear to be more resistant; many specimens survived five hours' exposure, and 3 survived twenty-four hours. It is impossible to exclude the possibility that this difference in resistance may depend on a difference in the nature of the growth on agar rather than on any difference between the actual organisms.

THE BACTERICIDAL ACTION OF LIQUID ETHER.

An attempt was next made to determine how the action of ether in the liquid state compared with that of ether vapour. Considerable difficulty was met with, since it was found impossible to mix the ether and the organisms in such a way as to ensure even action. Many methods were adopted, but the only one which gave anything like uniform results was to mix a saline suspension of the organism (*B. coli*) with an equal quantity of ether by vigorous shaking in a sterile tube closed with a rubber cork. The ether rapidly separated after the shaking ceased; a sterile pipette was plunged through the ether layer and 0.1 c.cm. of the suspension was withdrawn and added to a tube of melted agar at 40° C. After being kept at this temperature for a few minutes to allow the complete

evaporation of any ether which had been transferred with the bacterial suspension, this was poured into a sterile Petri dish and incubated.

One experiment of this kind showed that, after one minute's shaking with ether, 0.1 c.cm. of the *B. coli* suspension, when plated in this way, gave rise to only two colonies after twenty-four hours' incubation. In a control plate, prepared with an identical amount of the same suspension which had been shaken for one minute without ether, the colonies were too numerous to be counted. After three minutes' shaking with ether, 0.1 c.cm. of the suspension yielded no growth. Further experiments gave approximately similar results. It is clear that in these experiments the ether may have caused the death of the bacilli either by exerting a direct toxic action or by extracting from them some essential constituent.

When ether was allowed to act on dry films of living organisms (*B. coli*) on sterile cover-slips, an exposure of four hours sometimes failed to kill completely, though in other experiments fifteen minutes' exposure sufficed for complete sterilization.

It would seem probable that the immiscibility of ether with watery fluids and its action as a fat solvent are important factors from this point of view, and that the efficacy of its bactericidal action will depend in no small degree upon the physical conditions under which it meets the organisms.

As regards the action of liquid ether on spore-bearing organisms only a very few observations have been made. In a single experiment small pieces of cotton-wool were soaked in a broth culture of *B. oedematis maligni*, and then dried at 80° C. The dried pellets were immersed in ether for periods varying from thirty minutes to twenty-four hours, and then dropped into tubes of glucose broth which were incubated anaerobically. Twenty four hours' immersion failed to prevent subsequent growth under these conditions.

THE TYPE OF PERITONEAL EFFUSION PRODUCED BY INJECTION OF ETHER.

Preliminary experiments showed that 1 c.cm. of liquid ether per kilogram body weight is about the maximum dose which can be injected with safety into the guinea-pig's peritoneum. A series of guinea-pigs received intra-peritoneal injections of this amount and were killed after intervals varying from fifteen minutes to nineteen hours. Without entering into details, it may be said that the injection produces a clear effusion, which does not attain its maximum amount for many hours, and is seldom very abundant. At no period does the fluid contain any large quantity of cells. Control experiments made by injecting normal saline always produced a more highly cellular though less abundant exudate. As regards the type of cell present, the endothelial cell predominates during the first two hours, up to which time the polymorphonuclear cells are relatively scanty, but they then rapidly increase at the expense of both the endothelial and small mononuclear cells, and in the nineteen hours' experiment they formed 88.4 per cent. of the cells present.

THE TYPE OF EFFUSION PRODUCED BY INTRA-ARTICULAR INJECTION OF ETHER.

Experiments were made on the knee-joints of rabbits. One cubic centimetre of ether was injected in each case, and the animals were killed and examined after periods varying from one minute to one week. These experiments showed that the absorption of ether is extremely rapid and the resulting effusion into the joint relatively small. No fluid could be detected in a shorter period than fifteen minutes after the injection, and no appreciable quantity was present after a shorter interval than six hours. The cells were always scanty, and, as in peritoneal experiments, cells of the endothelial type tended to predominate during the earlier period, but were replaced later by polymorphonuclear cells. The animals killed after one week showed perfectly normal joints.

THE EFFECT OF ETHER INJECTIONS ON EXPERIMENTAL PERITONEAL INFECTIONS.

A large number of experiments were performed, the animals employed in all cases being guinea-pigs.

The injection of ether almost always markedly increased the severity of the infection. This may, perhaps, be

explained by an increased rapidity in the absorption of toxins or bacteria, and it is noteworthy that in three instances a pure growth of *B. coli* was obtained from the heart's blood at *post-mortem* examinations made within a few minutes of the animal's death. It should be noted that the amount of ether which the guinea-pig will tolerate may well be too small to produce any beneficial result.

THE EFFECT OF ETHER INJECTIONS ON EXPERIMENTAL JOINT INFECTIONS.

Three similar experiments were performed; 1 c.cm. of a broth culture of the organism to be examined was inoculated into the knee-joint of each of two rabbits. One animal in each case received an injection of 1 c.cm. of ether five minutes later. The rabbits were killed after seven days in two experiments and after ten days in the third, and *post-mortem* examinations were at once made. Two experiments were performed with a strain of the *Streptococcus pyogenes* and the third with the *B. pyocyaneus*. The results were strikingly similar in all cases. Where bacterial culture alone had been injected the joint was found to be markedly swollen and to contain a considerable amount of pus. In the three animals which received ether in addition to the bacterial culture the joints appeared normal, save for the presence of a minute amount of white caseous material, which showed no structure in stained films. It is noteworthy, however, that streptococci were grown both from those joints which had been inoculated with the organism alone and from those which had received ether in addition.

DISCUSSION OF RESULTS.

Experiments made *in vitro* show that ether and its vapour have a definite bactericidal action, but it would be difficult to imagine anything in the nature of a complete sterilization of an infected peritoneum taking place, and both the clinical and experimental results indicate that nothing of the kind occurs.

The nature of the effusions produced by the injection of ether does not lend any support to the idea that an increase in the local leucocytosis is an important factor, since, as indicated above, the cells are always scanty. The various immune bodies which may be supposed to be present in the exudate are possibly more important, but it seems doubtful whether the ether would greatly increase the hyperaemia already present in an acutely inflamed serous membrane, or the amount of exudate in the corresponding serous sac.

Some recent investigations carried out by Gardner¹ have an important bearing on this subject. He examined a large number of peritoneal exudates for the presence of aggressins. He concluded that the aggressive action of such exudates increases proportionately with the multiplication and breakdown of bacteria, and suggests that such substances as ether and colloidal silver may act by killing the bacteria or inhibiting their growth, and thus lessening the output of aggressins.

Possibly a large proportion of the bacteria are directly killed by the ether and its vapour, possibly also organisms which have been modified but not killed are more easily destroyed by the tissues, and it should be noted that all the evidence seems to indicate that the toxicity of the ether to the body tissue is very slight. In this way the mass of infection would be greatly reduced, and this is probably a point of no small importance. These factors, combined possibly with some stimulant action, would in many cases turn the balance in favour of the tissues and against the bacteria.

Any possible action of the ether on the various remote body organs has not of course been considered.

It only remains for me to express my great indebtedness to Dr. S. G. Platts for his valuable assistance during the course of this investigation.

REFERENCE.

¹A. D. Gardner. Aggressins in Appendicitis and some other Varieties of Peritonitis. *Quart. Journ. Med.* 1914 Vol. vii, 325.

²In the seventy-seventh Legislature of the State of Maine, which met on January 6th, there are twelve medical members—five in the Senate and seven in the House of Representatives.