cient nutriment to enable the typhoid bacillus to grow through the walls of the filtering candle.

Experiment III.—The same form of apparatus was employed as before, and the mantle was filled with sterile barrack sewage largely diluted with distilled water. The dilute sewage was found to have the following composition, expressed as parts per 100,000: Total solids, 7; chlorine, 0.3; oxygen absorbed (Tidy, 4 hours), 1.1; free ammonia, 0.1248; albuminoid ammonia, 0.2016; nitrites, absent; nitrates (NO_3), 0.926. The dilute sewage was inoculated with a subculture of the *B. typhosus* employed in the former experiments; filtration was then carried on daily, the amount filtered being replaced by sterile sewage so that the filtering candle was never allowed to become dry or exposed to the air. The broth in the flask remained perfectly clear for nine days, but on the morning of the tenth day of filtration a slight turbidity was noticed. A loopful of the turbid broth was removed and planted out on agar.

The growth which resulted was found to be a pure culture of *B. typhosus*. The results of the agglutination and cultural tests exactly corresponded with those of the *B. typhosus* introduced into the mantle. In this experiment the typhoid bacillus was not supplied with as much nutriment as in the two former experiments, and it appeared to require nine days to grow through the walls of the filtering candle.

Experiment IV.—In this experiment sterilised surface water from a ditch was placed in the mantle. The water on analysis gave the following results, expressed as parts per 100,000: Total solids, 44; volatile solids, 16; chlorine, 6.2; free ammonia, 0.526; albuminoid ammonia, 0.60; oxygen absorbed (Tidy, 4 hours), 2.2; nitrites, absent; nitrates (NO_3), 1.005. The water in the mantle was inoculated with a loopful of an agar culture of *B. typhosus*, and filtration was then carried on daily as in the previous experiments. The broth in the flask remained perfectly clear for eight days, but on the ninth day distinct turbidity was noticed.

A loopful of the turbid broth, when examined as before, was found to contain a pure culture of *B. typhosus*.

Experiment V.—This was simply a repetition of Experiment II, a new No. 12 bougie and a fresh sample of sewage being employed. The results of the chemical analysis of the barrack sewage, after sterilisation, were as follows: Total solids, 55; chlorine, 0.5; free ammonia, 8.28; albuminoid ammonia, 5.07; oxygen absorbed (Tidy, 4 hours), 6.4; nitrites and nitrates, absent. The mantle was inoculated with a loopful of an agar culture of *B. typhosus*, and filtration carried on as in the previous experiments.

The typhoid bacillus was found in the filtrate on the fifth day. The available organic matter was much greater in this experiment than in III and IV, and the bacillus only required four days to grow through the walls of the candle.

Experiment VI.—The same form of apparatus was employed, a new No. 2 candle being fitted into the mantle. A specimen of water collected from a reservoir in Netley was sterilised, and then analysed. The results obtained were as follows, expressed in parts per 100,000: Total solids, 18; chlorine, 3.3; free ammonia, 0.00816; albuminoid ammonia, 0.0158; oxygen absorbed (Tidy, four hours), 0.5; nitrites, nil; nitrates (NO_3), 0.8. This water was placed in the mantle, and inoculated with an agar culture of *B. typhosus*. Filtration was carried on as in the previous experiments, and the broth in the Kitasato flask remained perfectly sterile until the ninth day, when slight turbidity was noticed. A loopful of the turbid broth was planted out on agar, and tested in the usual manner.

A pure culture of *B. typhosus* was obtained.

Experiment VII.—The same water was used for this experiment, which was conducted in exactly the same manner as Experiment VI, a new, sterile No. 12 candle being employed.

The typhoid bacillus appeared in the filtrate on the ninth day.

Experiment VIII.—Candle, No. 10, fixed in a large glass mantle, was attached to a large Kitasato flask with the usual precautions. Sterile reservoir water was placed in the mantle, inoculated with *B. typhosus*, and then filtration carried on as in the previous experiments.

The broth in the flask remained perfectly sterile for ten days; on the eleventh day a growth appeared, which was found to be caused by *B. typhosus*.

Experiment IX.—A perfectly new No. 10 candle fixed in a mantle was employed. The mantle was filled with sterile barrack sewage, having the same chemical composition as that used in Experiment V.

On the fifth day of filtration the typhoid bacillus was found in the filtrate.

Experiment X.—The candle used in Experiment VI was removed from the mantle and thoroughly cleaned with a stiff brush; the metal delivery pipe was also thoroughly washed and flamed. The candle was then replaced in a sterile mantle, and the apparatus fitted up in the usual manner. Sterile reservoir water was then filtered through the candle; next day the broth in the Kitasato flask was found quite turbid.

The typhoid bacillus was easily isolated from the turbid broth. This result appeared to show that carefully cleaning a candle would not remove the *B. typhosus*, which had evidently penetrated into the interior of the filtering material, and then been washed through into the filtrate by the passage of the sterile water.

Experiment XI.—The candle used in Experiment VII was sterilised with boiling water, and then fitted up in a sterile apparatus. Sterile reservoir water was then filtered through the candle for eleven days.

The broth in the flask remained perfectly clear, and loopfuls withdrawn and planted out on agar produced no growth.

Experiments on the same lines were then made with Pasteur-Chamberland candles, fitted into glass mantles by

means of indiarubber bungs. The delivery pipe of the candle in each apparatus was connected by a short piece of india-rubber tubing, fitted with a pinchcock, to a Kitasato flask containing sterile broth. All the joints were then made watertight with melted paraffin wax. In the first experiment the mantle was filled with sterile broth, which was inoculated with a twenty-four hours' agar culture of *B. typhosus*. Next day the broth in the mantle was extremely turbid. Filtration was then commenced, 10 c.cm. of broth being filtered into the flask every day, and the amount filtered replaced by sterile broth in the mantle. After filtration for three weeks the broth in the flask was found quite sterile. One loopful of the broth from the mantle, however, contained a very large number of typhoid bacilli.

Trials were then made with other candles, fitted up in the same manner. Sterile barrack sewage, sterile sewage effluents, polluted ditch water, and reservoir water, repeatedly inoculated with large doses of *B. typhosus*, were filtered for three weeks, but no traces of the typhoid bacillus could be detected in the filtrates. The failure to pass through the filtering candle was not due to the death of the typhoid bacilli in the fluid contained in the mantle, as in each experiment one loopful of the fluid from the mantle, taken at the end of the trial, was found to contain a very large number of living typhoid bacilli.

The following conclusions appear justified:

1. Typhoid bacilli are not able to grow through the walls of a Pasteur-Chamberland candle, and if proper care be taken to prevent the direct passage of the bacilli through flaws in the material or imperfections in the fittings, the Pasteur-Chamberland filter ought to give complete protection from waterborne enteric fever.

2. Typhoid bacilli can grow through the walls of Berkefeld candles, probably owing to the larger size of the lacunar spaces and the consequently diminished immobilising and devitalising influences. The time required for the typhoid bacilli to traverse a candle varies between four and eleven days, and appears to be largely dependent on the nutriment supplied to the organisms by the medium in which they exist. In order to obtain complete protection from waterborne enteric fever, when employing Berkefeld filters, it is necessary to sterilise the candles in boiling water every third day.

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HÆMATURIA FOLLOWING THE ADMINISTRATION OF UROTROPIN.

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THE use of urotropin in enteric fever has been advocated of late by several authorities. Horton-Smith¹ urges the administration of 30 grs. daily in all cases throughout the whole course of the fever and during the first three weeks of convalescence, as first suggested by Richardson. In this way he considers it may be possible to prevent urinary complications in the patient, and also the spread of infection to others through the urine. He adds that, taken in such doses and during such a prolonged period, the drug produces no ill-effect beyond some urethral pain occasionally if the urine be allowed to become concentrated. Neufeld makes a similar plea, saying that urotropin is almost invariably well borne. Suter² states that doses of from 15 to 25 grs. a day can be given for weeks in succession. Mogh³ certainly reports a burning and pricking sensation in the bladder, increased strangury, and appearance of red blood corpuscles in the urine following the use of the drug in cases of cystitis of gonorrhœal origin; but he employed much larger doses than those recommended above, giving 6 grams (or 92.6 grs.) a day. It seems worth while, therefore, to record two cases of hæmaturia following the use of 10 grs. of urotropin three times a day. The drug, though of undoubted value, is not quite so free from injurious effects as has been thought.

CASE I.—Captain C., aged 33, who had been inoculated, was admitted on September 20th, 1900, suffering from enteric fever. He had been ailing for some weeks, and had been ill and delirious for four days before admission. He was given 10 grs. of urotropin in water three times a day. About two days later he complained of some pain and difficulty in micturition. On September 27th blood was passed in the last portion of the urine. On September 28th blood was seen oozing from the meatus; the urine was smoky in appearance and not scanty in amount. The administration of urotropin was stopped, and potassium bicarbonate and tincture of hyoscyamus given instead. A little more blood was passed the same evening. On September 29th there was no pain on micturition and no blood in the urine.

CASE II.—Lieutenant Y., aged 24, who had been inoculated, was admitted on September 21st, 1900, suffering from enteric fever. He had been ailing a few weeks, and had been ill in bed for two days prior to admission. He was given 10 grs. of urotropin in water three times a day. On September 27th he had some pain and difficulty in micturition. On September 28th blood appeared in the urine, actual clots being seen. The urotropin was stopped, and potassium bicarbonate and tincture of hyoscyamus were given instead. The next day the symptoms were much alleviated and soon disappeared.

The occurrence of hæmaturia in 2 cases admitted on successive days after urotropin had been given for eight days, and its rapid subsidence after the drug was stopped, is too striking to be a mere coincidence. Hæmaturia resulting from nephritis in enteric fever is not unknown,⁴ but in such cases urotropin appears to be beneficial. In my cases the bladder would seem to have been the source of hæmorrhage.

This untoward effect of urotropin cannot be common. Out of 82 cases of enteric fever treated at the Metropolitan Hospital during the last winter urotropin was given in 13. In one of these hæmaturia occurred, but the patient was taking turpentine at the same time.

Discomfort, which preceded the hæmaturia in both my cases, should be considered a danger signal when employing urotropin.

REFERENCES.

¹ Goulstonian Lectures, 1900, *Lancet*, April 14th, 1900. ² Suter, *Lancet*, February 23rd, 1901. ³ Mogli, *Il Politecnico*, January 19th, 1901. ⁴ Horton-Smith, *op. cit.*

A FATAL CASE OF HÆMATOPORPHYRINURIA.

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THE following case illustrates the necessity of care in the administration of sulphonal.

History.—A male patient, aged 33, single, one of those unfortunate people not obliged to do anything, consulted me for dyspepsia and giddiness. He fancied he could not sleep, and so had been in the habit for some years of taking hypnotics of different kinds, but chiefly sulphonal. A few days later he developed much pain and tenderness over the stomach, attended with nausea, vomiting, and constipation. He was at the same time slightly delirious at night (no drugs were taken), and he gradually passed into a condition resembling delirium tremens. The gastritis entirely passed off, and in ten days he was able to take a fair amount of food by the mouth. A few days from the onset of his illness it was noticed that his urine resembled port wine in appearance, and smelt like chlorodyne, while another specimen smelt like celery. The fœtor was most disagreeable and resembled that noticed in chronic renal disease.

State on Examination.—The urine contained no albumen, and the guaiacum test gave no sign of blood. The microscope showed nothing but a few crystals of uric acid. The spectroscope showed bands corresponding to those produced by hæmatoporphyrin. (See figure.) The radial artery was a little thickened, and the pulse, which was 80 per minute at the beginning of his illness, gradually increased to 180. He became tremulous, restless, and violent. This was succeeded by a vacant aspect and prostration, in fact, by general paresis, in which the sphincters participated. Although skillfully nursed, a bed sore formed over the sacrum. The temperature varied from 99° to 104°. The retina appeared to be normal. The patient could not swallow, but retained ample nourishment given through a nasal tube. The abdomen was sunken, and the diaphragm scarcely moved.

Four days before death general convulsions occurred, which were epileptic in character, and continued at short intervals till the end. During this time the patient was unconscious, quite pulseless, and a very feeble single heart sound, only audible at the lower part of the sternum, was all that indicated cardiac action. No urine was passed for forty-eight hours, and the bladder appeared to be empty. No headache was complained of all through the illness, which consisted of ten days of symptoms of acute gastric irritation, and two weeks with cerebro-spinal symptoms and progressive toxic paresis. No post-mortem examination could be obtained.

Hæmatoporphyrin has been observed in the urine in small quantities only where no sulphonal has been taken, as well as in the course of other diseases, namely, rheumatism, pneumonia, enteric fever, and peritonitis. In the sulphonal cases the symptoms are said to depend not so much on the direct action of the sulphonal itself as on chemical changes, almost certainly alimentary in the first place, and probably hepatic, of which the sulphonal has been the exciting cause.

Dr. Keith Campbell, who published a fatal case of hæmatoporphyrinuria in the *Journal of Mental Science* for April, 1898, where only 30 grs. of sulphonal had been taken in two doses, says that the pathological changes which produce this pigment are as yet obscure.

Professor Young, F.R.S., of University College, Bristol, and Mr. Stoddart, Public Analyst for Bristol, tell me that the spectroscope is the most reliable means of detecting hæmatoporphyrin in urine.

Dr. Stack, House-Physician to the Bristol Royal Infirmary, kindly undertook the investigation, and the accompanying chart (see figure) shows the result he obtained. Professor Stanley Kent, of University College, Bristol, and Bacteriologist to the Bristol Royal Infirmary, has kindly made the following remarks: "Hæmatoporphyrin as prepared in the laboratory exhibits two different spectra according to whether the solution examined is acid or alkaline in reaction.....When the bands of hæmatoporphyrin are visible in a pathological urine, the spectrum seen is not that of the acid modification of the pigment, such as would have been expected from the fact that the urine is an acid fluid, but that of the alkaline modification.....And a solution of the pigment showing the acid spectrum, if added to urine, at once changes its character, and shows the alkaline bands.....Another interesting point is that this pigment is iron-free, that it is probably produced from the pigment of the blood which contains iron, and that its appearance in the urine seems sometimes to be associated with derangement of the functions of the liver and spleen, organs normally concerned in the pigment metabolism of the body."

The epithelial cells in the cortices of the suprarenal capsules have been shown by Dr. W. F. Robertson to have undergone a marked degenerative change over numerous large areas, consisting of the replacement of the protoplasm by clear globules. These globules, which varied considerably in size, did not give a fatty reaction with osmic acid. There was no evidence of any tuberculous disease. These degenerative changes are evidently the same as those that are so commonly to be observed in the adrenal epithelium in various diseases. Yet it has been suggested that suprarenal extract should be given.

HIBERNATION OF ANOPHELES IN ENGLAND.

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SINCE the appearance of our *Studies in Relation to Malaria*,^{1 2} two publications have appeared relating to the hibernation of *Anopheles* in this country. I refer to the papers by Wright,³ and by Annett and Dutton.¹

That certain culicid larvæ are capable of living beneath the ice has already been noted by Gorham in the United States.