is an agent, the tendencies and results of which must be fully taken into account in the clinical surgery of the young. This necessity arises from the fact that in the instances I have adduced, and in others that could be mentioned, various deformities are developed because conditions have arisen which have interfered with or superseded the law of conformity to type, under the regulating influence of which growth normally takes place. When this is recognised it at once becomes apparent that treatment, if it is to be successful, must be guided by the principle of removing as far as possible the disturbing influence, whatever it may be, that is at work, and substituting for it those conditions by which normal growth shall be promoted to the greatest available extent. Nor, I think, can any principle be named which rests on a sounder foundation, or which in the true sense of the term is more directly conservative. Many forms of treatment which are properly named conservative are conservative in only a limited or qualified degree, for, although under the circumstances they undoubtedly secure the safety or promote the advantage of the individual concerned, they do so only by the sacrifice of parts or organs, the loss of which involves more or less serious disability or inconvenience; while in the cases to which I have been alluding the surgeon, recognising in growth one of the most strongly operative of all the manifestations of life, and observing the marvellous results which are produced by its agency, makes it his endeavour to ascertain the conditions which are most favourable to it, and does his best to secure their full effect. It would not be difficult to mention plans of treatment which have done violence to Nature and her methods, and which have inevitably led to failure and disappointment, for *Nature non imperatur nisi parendo*. But the subject I have discussed may suffice to remind us of one of the chief rules of practice, that under which the surgeon makes it his object to act as the strict disciple of Nature, and renders himself ancillary to her work.

NOTES AND REFERENCES.

¹ *Origin of Plant Structures*, by the Rev. George Henslow. 1895, p. 136.
² *Loc. cit.*, p. 190. ³ *Loc. cit.*, p. 180. ⁴ *St. Bartholomew's Hospital Reports*, vol. xxx, p. 223. ⁵ This subject has been fully discussed by Mr. Jonathan Hutchinson, jun., in his able and instructive lectures at the College of Surgeons on Injuries to the Epiphyses and their Results. ⁶ Henslow, *loc. cit.*, p. 204. ⁷ *Diseases of the Joints and Spine*, 1895, pp. 272 et seq.

THE CROONIAN LECTURES

ON THE

CHEMICAL PRODUCTS OF PATHOGENIC BACTERIA
CONSIDERED WITH SPECIAL REFERENCE
TO ENTERIC FEVER.*Delivered before the Royal College of Physicians of London,*

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LECTURE III.

THE PRODUCTION OF THE POISONS OF THE TYPHOID BACILLUS
IN ARTIFICIAL CULTURE OF THE MEDIA.

Two different kinds of media were employed in which to grow the bacillus. Ordinary peptone broth was used to determine the presence or not of secretory products of the bacillus; and broth containing no peptone but mixed with some proteid solution—either blood serum, alkali albumin made from the spleen, or an extract of lymphatic gland—in order to determine the presence of digested products of the bacillus. In some cases, liquid blood serum sterilised at 60° C. was used without the addition of broth. The virulent bacillus grows well in ordinary peptone broth, but the growth in solutions containing much proteid is very much less exuberant. This is especially the case with sterile blood serum, and most commonly the bacilli, after growing for a time, sink to the bottom in clumps and cease growing, although they are still alive and active. It grows much better in a solution containing a small proportion of alkali albumin, but still not nearly so well as it does in broth. The object of growing them in the presence of proteids was to test whether there

was any digestive action of the bacillus. In one experiment, two test tubes were filled about 3 inches deep with liquid blood serum, which was rendered semi-solid by heating at a temperature of 65° to 70° C. The medium was translucent, and one of the tubes was inoculated with the bacillus, the other being kept as a control. It was observed that the bacillus rapidly grew in the medium, spreading through all parts of it, but that no liquefaction indicative of digestion occurred during incubation, which lasted 102 days. When grown in a liquid medium, however, containing a small proportion of alkali albumin, and especially alkali albumin made from splenic pulp, the virulent bacillus had a slight digestive action, although a very insignificant one. Thus in one experiment, after the bacillus had grown thirty-two days in such a medium, it was found that the solution gave a distinct biuret reaction with copper sulphate and potash, and that the alkali albumin was beginning to be changed into albumoses. This digestive action, although slight, is explanatory of the albumoses found in the spleen in cases of typhoid fever.

POISON FORMED IN PROTEID SOLUTIONS.

If the non-virulent bacillus is grown in a solution containing digestible proteid instead of peptone, a poison is formed which has an action like that of the poison formed in broth. Thus, in one experiment the bacillus was grown in a 1 per cent. solution of serum alkali albumin in broth for twenty-nine days, at the end of which time it was filtered and the filtrate concentrated, and the proteid separated by alcohol. Some amount of digestion had taken place, as the solution gave a biuret reaction. The solid product obtained was injected in two doses (about 0.3 g.) on successive days into the marginal vein of the ear of a rabbit. Following each injection there was a marked lowering of the temperature and a subsequent rise, but not to the average normal temperature of the animal for some days. Some bodily depression was observed on the first two days of the experiment, and there was a loss of body weight, but there was no diarrhoea; and the animal subsequently completely recovered.

In another experiment the non-virulent bacillus was grown in a solution of alkali albumin made from the splenic pulp, but without adding broth. One flask was filtered after forty-five days, and 10 c.cm. of the filtrate were injected in two doses on successive days into the marginal vein. After the first injection there was only a very slight rise of temperature, which, however, was more marked after the second injection. The animal showed no particular symptoms except a gradual loss of weight, which amounted to 235 g. at death on the twenty-eighth day of experiment. The *post-mortem* examination revealed no naked-eye change in any of the organs or tissues of the body. No cultivations were obtained from the heart's blood; the heart muscle showed no fatty degeneration, and there was no degeneration of the peripheral nerves. Another culture was filtered after fifty-nine days' incubation, and 12 c.cm. were given in two doses on successive days, also into the marginal vein. There was a well-marked rise of temperature after each injection but no diarrhoea was produced, and there was only a slight loss of weight, which was recovered from. The animal died in twenty-four days, and no cultivations were obtained from the heart's blood, liver, spleen, or peritoneal cavity. There was subcutaneous hæmorrhage in patches in front of the thighs and the caudal region, and the peritoneum contained about 1 cm. of clear fluid. There was no peritonitis, and the organ showed no naked-eye change.

The results of growing the non-virulent bacillus in a proteid solution show that the poisons excreted are of the same nature as that formed by the virulent bacillus in broth. The digestion which takes place in the proteid solution is extremely slight, and the toxic body is thus mainly an excretion of the micro-organism.

Although the toxic products are developed in the presence of digestible proteids, yet they are most evident when the bacillus is grown in peptone broth. In one experiment the broth was inoculated with the typhoid bacillus obtained from the spleen of a case of enteric fever, but before it had been made virulent by passage through animals. The growth was allowed to continue for eleven days, and the broth was filtered through a Chamberland filter. Two injections into the marginal vein were made on successive days.

The first injection of about 3 c.cm. resulted in the lowering of the temperature and the production of diarrhoea soon after the injection. The second injection, also of 3 c.cm., produced but little effect, and on the three subsequent days no appreciable change occurred in the animal. On the sixteenth day of the experiment the animal was found to have lost 170 g. in weight, and to have some degree of fever, which, however, did not reappear. It lived for twenty-four days, gradually losing weight until at death it had lost 235 g. At the *post-mortem* examination there was no obvious lesion found in any of the organs of the thorax or abdomen; the intestines were normal, and cultures made from the heart's blood and the peritoneal cavity were sterile, showing that there was no bacterial infection. The heart muscle, examined after staining with osmic acid, showed degeneration of most of the fibres, there being loss of striation with longitudinal fibrillation and fatty granules in the muscle cell. This experiment shows several points which will be brought out more fully later on: (1) That a poisonous substance is present in the broth apart from the bacillus itself; (2) that this body produces a lowering of temperature and diarrhoea, as well as a loss of weight; and (3) that at death there was distinct degeneration of the cardiac muscle.

The broth culture from the same stock of bacillus was more poisonous, and produced a more profound effect if the incubation lasted twenty-five days. Thus a rabbit received a single dose of 6 c.cm. of the broth filtrate after twenty-five days' growth. The initial effect of this injection into the venous system was a rise of temperature (the maximum being attained in two hours and a half) and a rapid fall, during which there was profuse diarrhoea, with collapse and laboured breathing. This period of depression lasted some hours, and on the next morning was succeeded by a febrile rise, which continued during the whole of the day. On the following day the temperature was somewhat irregular. Subsequently no great change in the temperature was noticed. The weight fell rapidly up to the fourth day of the experiment, when the animal had lost 120 g. Subsequently, however, it regained part of the weight; and at death, on the twenty-sixth day of experiment, the loss was only 35 g. from the original weight. No naked-eye changes were observed on *post-mortem* examination; no cultures were obtained from the organs of the body. The heart muscle showed slight signs of degeneration.

The more virulent the bacillus the more toxic becomes the broth. Thus, after growing for eleven days, the bacillus was killed by chloroform, and the broth mixture centrifugalised, the clear broth being used for the injection; 5 c.cm. were injected in two doses on successive days (2 c.cm. and 3 c.cm.). An initial depression of temperature followed by fever was observed after both injections, and the animal died in twelve days, with no naked-eye change in the organs of the body, which gave no bacterial growth. There was a very well marked degeneration of most of the muscle fibres of the heart. These results may be taken to illustrate the action of the clear broth without the bodies of the bacillus—that is, of the chemical poison which is present in solution in the broth.

ACTION OF BROTH WITH THE BODIES OF THE BACILLUS.

The toxic action of the bodies of the bacillus itself was tested by killing the bacillus with chloroform. When the culture was sterile, the chloroform was removed *in vacuo*, and the liquid used for injection. In one experiment a thirteen-days-old culture was used, and 4 c.cm. injected into the marginal vein of the ear. There was a great fall of temperature in two and a half hours, and this low temperature continued the whole of the first day of experiment; also on the second day, and on the morning of the third day the mercury of the thermometer would not rise, and the animal died. Soon after the injection there was a slight diarrhoea. During the subnormal temperature the animal became increasingly weaker, the fur becoming ruffled, although there was no diarrhoea. The loss of weight in the two days of experiment was 180 g. There was no naked-eye change in any of the organs, and the blood was sterile. This experiment may be taken as showing the profound effects following the injection of the poison. The great depression of temperature, however, observed in this experiment is not the only effect to be produced. In some of the experiments with a weaker poison no depression ensued, but a

well-marked rise of temperature. Thus 3 c.cm. of a broth culture (seven days' growth) killed with chloroform were injected into the marginal vein of the ear of a rabbit. There was a considerable rise of temperature to over 106° after the injection, which continued during the whole of the following day and the day after. On the fourth day the temperature partly regained the normal limit, and continued afterwards normal. There was a loss of weight up to the seventh day, after which the animal recovered. In this experiment no diarrhoea was produced, and no symptom except that of fever and loss of weight.

In two or three other experiments with the broth and the bodies of the bacillus these features were noted, but there was not infrequently an initial fall of temperature, succeeded by a prolonged rise, and diarrhoea for a longer or a shorter period, was a fairly constant symptom. There is no doubt, then, that the retention of the dead bodies of the bacillus in the broth renders it more poisonous. The effect on different animals varies somewhat. In one experiment 4 c.cm. took two days and a-half to kill; in another experiment 4 c.cm. of the same stock caused death with lowering of the temperature in three hours and a-half. There is also some individual peculiarity in the animals as regards their resistance against the poison.

THE EFFECT OF HEAT.

The effect of high temperature on this poisonous liquid containing the bodies of the bacillus was tested in order to see whether the toxic substances were sensitive to heat or not. In one experiment the broth with the bodies of the bacillus was heated to 60° and 64° C. for ten minutes; 4 c.cm. were injected into the marginal vein and death occurred, with lowering of temperature and diarrhoea, in 2 hours and 20 minutes. This death was more rapid than in the control experiment with the same amount of broth unheated. As marked was the effect of exposing the broth to a higher temperature before injection. Four c.cm. of a broth mixture heated at the boiling point of water for five minutes were injected into the marginal vein, and death, with profuse mucoid diarrhoea, occurred in 2½ hours. This experiment may be compared with a similar one in which the same amount of broth, but unheated, was injected into another animal, which lived for 2½ days with a great depression of temperature. It may be said, therefore, that this degree of heat not only does not destroy the poison which is in the bodies of the bacillus, but actually brings out its effects. It may be that the heat breaks up the bodies and liberates the poison inside, and after heating some of the bodies of the bacilli may be observed disintegrated under the microscope.

There is no evidence from the experiments that there are two kinds of poison, one extracellular or secreted by the bacillus, and one intracellular, with different actions. The toxic properties of the broth from which the bacilli are separated by means of the Chamberland filter are practically the same, although not so pronounced, as those observed when the broth contains the bodies of the bacillus as well; and this is not an unimportant point, inasmuch as some have made a distinction between the intracellular and the extracellular poisons of pathogenic micro-organisms.

No effect is more marked or more constant in the action of the poison than the production of diarrhoea, which, with the more active poison, is very profuse, lasting a varying time—sometimes hours, sometimes a day—and consists in the passage of liquid motions, with mucus occasionally, but no blood at any time. On a *post-mortem* examination of an animal dying with this diarrhoea, characteristic appearances are almost invariably found. The stomach may be full of undigested food, the caecum and colon contain liquid faecal matter, but the greatest change is in the small intestine, which is full of a slightly turbid, sticky fluid, containing but little food and no bile. This liquid is simply a solution of mucin, which may be separated by precipitation with acetic acid. The mucous membrane is a little soft on the surface, and there is a very large increase in the number of goblet cells. The Peyer's patches were not apparently altered. The changes described by Sanarelli in the Peyer's patches of the intestines have not been observed by me. The loss of weight is also a constant symptom, and the more virulent the poison the more marked is it seen. It is also in this case progressive. With a smaller dose of the poison, however, the initial

loss of weight is regained. No naked-eye change is produced by the poison in the organs of the body.

The effect of the poison, when the death of the animal is slow, in producing degeneration of the muscle fibre of the heart, is well marked. The heart was never found in a state of advanced fatty degeneration, but rather in the earlier stage, in which there is loss of transverse striation of the fibre, with the appearance of longitudinal fibrillation and the presence of numerous granules in the fibre, staining more or less black with osmic acid.

BACILLUS ENTERITIDIS GÄRTNER.

The experiments with this micro-organism were conducted in the same manner as those with the typhoid bacillus.

A culture was kindly sent to me by Dr. Durham, which gave the reactions previously described as characteristic of the bacillus. It differs from the typhoid bacillus in the fact that it causes gas formation in glucose-agar or glucoselatin; but, like the typhoid bacillus, it does not coagulate milk, and it forms but little or no indol in broth. The original culture of the bacillus worked with was toxic, as 5 c.cm. of a two days' old broth culture injected into the peritoneum of a guinea-pig killed the animal in under twenty-four hours. The virulence of this bacillus was increased by passage through animals in a manner similar to that which has been described with regard to the typhoid bacillus; that is, some of the peritoneal exudation from the first animal that died being injected into the peritoneal cavity of a second guinea-pig, and from the second into a third, and so on. The death of each animal occurred, as a rule, in under twenty-four hours. The dose was gradually lessened until a small loopful of an agar culture injected into the peritoneal cavity killed the animal. In the series of experiments the intraperitoneal injections caused the exudation of a highly albuminous fluid containing numbers of bacilli. In the earlier cases there was also an exudation of leucocytes; later on, however, these disappeared. Occasionally there were a few flakes of lymph on the surface of the peritoneum, but only at the early stage of the series of inoculations. At no time was there any exudation of blood. During the series cultivations were made from the peritoneal fluid of each animal to test the purity of the growth, to see whether the bacillus kept its characteristics, and also to study the distribution of the micro-organism in the body. It was found that the growth was always typical and pure, and that when the bacillus became virulent it was found always distributed throughout the organs of the body, being obtained from the heart's blood, the spleen, the liver, and the kidneys and peritoneal cavity in pure cultivation. In this respect the presence of the bacillus of Gärtner in the various organs of the body was more constant than that of the typhoid bacillus. The peritoneal fluid was highly toxic. Thus, in one experiment in which the bacilli were killed by means of chloroform and removed by subsequent centrifugalising, 3 c.cm. of clear peritoneal fluid injected into the marginal vein of a rabbit weighing 470 g. caused death in an hour and a-half, the temperature rapidly falling in half an hour from 102° to 97.4°. The peritoneal fluid filtered through porcelain is not so toxic as the unfiltered, from which the bacilli have been removed by centrifugalising. This filtered peritoneal fluid was found to produce fever when injected into the marginal vein of the ear of the rabbit, but when given in two doses of 1.5 c.cm. and 1 c.cm. it did not cause the death of the animal nor any particular symptoms except a rise of body temperature.

GROWTH OF THE BACILLUS IN BROTH.

The experiments done in this way were precisely similar to those performed with the typhoid bacillus. The virulent Gärtner bacillus was grown in broth for twenty-two days and the culture was not filtered, but the bacillus was killed by chloroform. Experiments were performed with the clear broth after centrifugalising, and with the turbid broth, that is with the broth *plus* the bodies of the bacilli. Each animal received the same dose, namely, a single dose of 4 c.cm. into the marginal vein. The result of the injection of the clear broth was a continued and marked depression of temperature during the day of experiment, the temperature next day again rising to normal. There was diarrhoea soon after the injection of the poison, and there was a progressive loss of weight. A similar dose of the broth, *plus* the bodies of

the bacilli, caused a more marked depression of temperature, which lasted till the following morning and most of the following day. Here also there was diarrhoea and a progressive loss of weight. The effect of heat on the broth *plus* the bodies is seen in the two following experiments. Thus the same dose (4 c.cm. of the mixture) heated to 60° C. for 10 minutes caused a depression of temperature which was very great and ended in death in 4½ hours. This animal also showed diarrhoea. A similar dose heated to 100° C. for ten minutes produced also a very great depression of temperature which lasted to some extent, on to the next day. There was well-marked diarrhoea and great loss of weight. It is thus seen that the characteristic action of the toxic products of the Gärtner bacillus are very like those of the typhoid. There is present in the broth from which the bacilli have been removed a poison which causes a great depression of temperature, and this poison is also present in the bodies of the bacillus, and has an action similar to that of the poison obtained from the typhoid bacillus, namely, it produces diarrhoea and loss of weight.

Like the poison of the typhoid bacillus the virulence of a broth culture containing the bodies of the bacillus is increased by heating the solution at 60° C., so that—as seen in the experiments just quoted—whereas 4 c.cm. of the unheated mixture did not cause death; when heated to 60° for ten minutes, death occurred in 3½ hours, with great lowering of the body temperature. Heating to 100° C. for the same time gives a greater effect than the non-heated mixture, but does not produce death in the same way as when the mixture is heated to only 60°. The effect of heat appears to be to break up the bodies of the bacillus, so that the poison is liberated, making the liquid more toxic.

When grown in a proteid solution containing alkali albumin or serum proteids Gärtner's bacillus causes some amount of digestion with the formation of albumoses. This is more marked than is the case with the typhoid bacillus, although the digestion is still far behind that which occurs in the case of the bacillus diphtheriæ and the anthrax bacillus. One result obtained is interesting, inasmuch as the bacillus coli also produces it, namely, that when grown in Marmorek's fluid Gärtner's bacillus produces a partial precipitation of the proteid in the form of a gelatinous clot. In strong solutions containing serum this result, however, was not observed, and it was not so constant as with the bacillus coli.

BACILLUS COLI COMMUNIS.

There is one important difference between this bacillus and the two other forms we have considered (the typhoid and Gärtner's bacillus), this is the fact that it is one of the causes of putrefaction of the proteids; it forms indol, for example, in proteid solutions; it is found in foul water, in soil, and it is a constant habitant of the intestines, being found in that region soon after birth. After death it sometimes penetrates the different abdominal organs, and is one of the causes of the putrefaction of the body. These characteristics therefore mark it sharply off from the two other micro-organisms. There are no doubt many different forms of the bacillus coli which differ in minute particulars; some, for example, forming hardly any indol, others coagulating milk slowly. Without, however, entering into the different forms which this bacillus may assume, or into a discussion as to whether they are all modifications of the same form, I may say that the bacillus I worked with was one which was obtained from the spleen in a case of typhoid fever, and which no doubt came originally from the intestinal tract. The virulence of the bacillus coli, as obtained from the intestines, varies considerably, and several observers have described an exaltation and an increase in the numbers of the bacillus in the course of cases of typhoid fever. The bacillus I obtained from the spleen was more virulent than the stock cultures of the bacillus which I had in the laboratory, and which were obtained from different sources; its virulence was readily increased, much more readily than was the case with the typhoid bacillus, and much more readily than with Gärtner's bacillus. Six c.cm. of a fourteen-days-old broth culture injected into the peritoneal cavity of a large guinea-pig, caused death in under twenty-four hours; 4 c.cm. of a broth culture of the peritoneal exudation of the first guinea-pig was injected into the peritoneal cavity of a second, and killed the animal in under twenty-four hours. In the succeeding experiments 2 c.cm. of the peritoneal fluid were

found to kill, 0.5 c.cm. was fatal at the fifth inoculation, and at the sixth it was found that 0.25 c.cm. and 0.1 c.cm. killed the animals under twenty-four hours. At this stage the virulence of the bacillus was considered sufficiently exalted for experiments to be performed. Throughout, the cultures obtained from the peritoneal fluid were pure, and always gave the typical reactions of the bacillus coli. The results of the injection of the bacillus into the peritoneal cavity were markedly different from those obtained from the injection of the other two bacilli, mainly in the fact that the effusion was bloodstained, more so at first than later on, when the bacillus became more virulent. The bloodstaining was not due to the exudation of corpuscles, but to the colouring matter of the blood being dissolved in the liquid, which was highly albuminous. Numerous petechiæ were also observed, beneath both the peritoneum and the mucous membrane of the ileo-cæcal region and cæcum. No peritonitis was observed at any time. The toxic products of the bacillus were investigated by growing it in broth and in proteid solutions.

GROWTH OF THE BACILLUS IN BROTH.

An early experiment was done with a culture which was not extremely virulent, and which was grown in broth for twenty-three days. The broth was then filtered through a Chamberland filter, and 8 c.cm. of the sterile filtrate were injected in two doses on successive days into the marginal vein of the ear of a rabbit weighing 1,090 g. The initial effect of the first injection was a fall of temperature in about two hours, which lasted over four hours, the total fall of temperature being 5.8° F. The result of the second injection on the following day was practically *nil*, but on the third day the temperature was subnormal. It then began to rise gradually, and there was some degree of fever on the fifth, sixth, and eighth days of experiment, which was markedly increased on the ninth day. On the tenth day there was a fall, and a subsequent rise on the eleventh day, after which the temperature of the animal became practically normal. The animal steadily lost weight during the first two days of experiment, 100 g. the first day, 38 g. the second day, the weight remaining stationary on the third, fourth, and fifth days of experiment, after which it slowly regained its normal. The animal exhibited no other symptom; there was no diarrhœa, and complete recovery took place. This result shows that the poisonous products which are formed in the broth by the bacillus coli have the initial effect of reducing the temperature of the body as well as weight, and that subsequently there is a reactionary rise of temperature, which remains at a febrile point for several days.

Other experiments were done with the broth cultures in the same way as those done with the typhoid bacillus and with Gärtner's bacillus—namely, after a period of eighteen days' incubation, the bacilli were killed with chloroform, and the injection of the clear broth obtained by centrifugalising, and of the broth with the bodies of the bacilli, was performed in different animals. In the first experiment, 4 c.cm. of clear broth were injected into the marginal vein of a rabbit, weighing 720 g. In two hours and a-half the temperature had fallen 2°, and there was slight diarrhœa. In four hours and a-half there was a further fall of 2.5°, and the temperature altogether remained subnormal for over five hours. On the next day it had regained its normal limit, though the animal continued to lose weight.

In the second animal a similar dose of 4 c.cm. of the broth containing the bodies of the bacillus was injected into the marginal vein. The temperature fell about 1.5° in two hours and a-half, after which it began to rise slightly, and during the whole of the next day the temperature of the animal was febrile. In an hour and a-half after the injection there was slight diarrhœa, and the animal lost 70 g. in twenty-four hours. The temperature remained at about the normal level till the fifth day. On the seventh day it had fallen, and there was slight diarrhœa. On the eighth day there was a fall to 98° F.; and on the ninth day, when death occurred, the temperature was below 95°. The total loss of weight was 210 g. These results were compared with the results of injecting a similar dose of the same stock of broth containing the bodies of the bacillus, but which had been subjected to heat. In the first of these experiments the mixture of broth and bodies was heated at 60° C. for ten

minutes. The result of the injection was the cause, in a very short time, of a febrile rise of temperature, which lasted the whole of the day, and was present in the morning of the following day; the temperature then gradually fell to the normal. In an hour and a quarter after the injection there was profuse diarrhœa, and the animal lost somewhat in weight during the first two days of experiment. In another experiment a similar dose was given, after being heated to the boiling point of water for ten minutes. In less than an hour after the injection profuse diarrhœa was observed, and the temperature rapidly fell, the total fall being 7° F. The animal died in six hours.

It is seen from these experiments that the clear broth—that is, the broth not containing the bodies of the bacillus—produces a fall of temperature and loss of weight with some diarrhœa, and that a similar dose of the broth with the bodies of the bacillus causes some lowering of temperature and a reactionary febrile rise; and that the effect of heating the mixture of broth with the bodies of the bacillus is to increase the poisonous activity of the solution; so that when the mixture was heated to 100° C. it proved fatal to the animal in six hours, with great lowering of temperature. The explanation of this appears to be that the action of heat causes the discharge of the poison which is present in the bodies of the bacillus.

1. The type of action of the poison of the bacillus coli appears to be the same as that of the other two bacilli investigated, in some cases producing a great fall of temperature, and in other cases a rise of temperature.

2. Heating the dead bodies of the bacillus suspended in the broth culture fluid increases the toxicity of the solution, as in the case of the other two bacilli, but in the case of the bacillus coli it requires a temperature of the boiling point of water to effect this; whereas with the other two micro-organisms such a temperature rather diminishes than increases the toxic action. Altogether the mode of action of the poisonous products of the bacillus coli is more irregular than with the other two bacilli, not only as regards its lethal, but also as regards the irregular kind of fever and after-fever produced.

GROWTH OF THE BACILLUS IN PROTEID SOLUTIONS.

As with the other bacilli, very different forms of proteid solution were used as culture medium, liquid serum, serum diluted with salt solution, serum diluted with broth, alkali albumin in broth and Marmorek's fluid. The general result obtained in these culture media was that the bacillus coli digested the proteids present, and produced an abundance of albumoses (a much greater quantity than the typhoid bacillus and Gärtner's bacillus), so that at the end of a month's incubation of such a culture, a brilliant biuret reaction was obtained. The digestion of proteids by the bacillus coli is not nearly so marked as it is with the anthrax bacillus or the diphtheria bacillus. A more remarkable effect was observed in the fact that after the bacillus had been growing in a proteid solution for some time, it precipitated the proteid in the form of a clot, and this occurred more particularly in the solutions of diluted serum and in Marmorek's fluid. The results were compared with a control flask which was not inoculated, and which was kept in the incubator alongside the cultures. The precipitation of the proteid in the form of a gelatinous clot was not constant, although it occurred in the majority of cases. It did not appear to be due to any increased acidity of the culture medium, produced by the growth of the bacillus in it, inasmuch as no such increase of acidity was present, the liquid remaining alkaline. The phenomenon appears to be a special action of the growth of the bacillus coli. In some solutions Gärtner's bacillus produced the same result. Thus five flasks were prepared containing about 100 c.cm. of Marmorek's fluid, which is a mixture of 1 part of ascitic fluid with 2 parts of broth. Two flasks were inoculated with the bacillus coli, two were inoculated with Gärtner's bacillus, one was kept as a control. In fourteen days a copious and soft clot had formed at the bottom of all the four flasks, the liquid in the control flask remaining limpid and unclotted. In none of the similar experiments with the typhoid bacillus was any clot or precipitation of the proteid observed, so that this serves as another distinction between the typhoid bacillus and the two other bacilli. The clotting of the proteid solution is of interest in connection

with the experiments of Stillmark, who found that the substance ricin, which is obtained from the seeds of the castor-oil plant, and which will be discussed later on, also produces a clotting in proteid solutions, especially serum. Stillmark used it as an argument in favour of the ferment nature of the toxic body, ricin.

PROFESSIONAL RECOLLECTIONS OF A VISIT TO CANADA.*

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THE President, after thanking the Branch for the honour which had been done him by electing him to that office, offered a hearty welcome once again to the annual gathering in the Norfolk and Norwich Hospital. He then gave some professional recollections of a visit to Canada and the United States, which he had made in the autumn of last year in company with Mr. Burton. The pleasure and profit was materially increased by the privilege of acting as one of the delegates of the East Anglian Branch. Mr. Robinson referred to the meeting of the British Association for the Advancement of Science, held at Toronto, which had afforded an opportunity of visiting that beautiful city under very auspicious circumstances. The opening address of the President, Sir John Evans, dealt with the subject of the Antiquity of the Human Family and the Scene of its Infancy, which was always of special interest to the medical profession. He also indicated the general argument of Sir William Turner's address, a full account of which was published in the *BRITISH MEDICAL JOURNAL* last autumn. To those, he said, who had not escaped altogether from the fetters of old traditional beliefs, these two addresses brought some help and comfort, since they showed that that which related to chronology of the earth and its inhabitants in remote ages, as recorded in sacred history, might after all not be so far from the truth, and that the adaptation of the structure of the human body to produce a being capable of taking a distinctive positive position in the universe superior to that which any other organism could assume established the conception of the dignity of man in nature and the association of the human form with the idea of a divine Creator. Mr. Robinson then referred to Professor Michael Foster's address to the Section of Physiology which was published in full in the *BRITISH MEDICAL JOURNAL* of August 21st, 1897. Professor Foster's remarks, Mr. Robinson observed, almost seemed to foreshadow a time when the knowledge of the nature and origin of nerve power and the means for its proper direction and control would enable us to correct many of the deviations both of structure and function from the normal and even retard decay. Passing on to the annual meeting of the British Medical Association in Montreal, Mr. Robinson said that the arrangements were all that could be desired, and that the special fitness of the McGill University with its numerous museums and lecture rooms in close proximity to the city made the working of the Sections especially easy.

Among the topics so ably handled by the President in his address which revealed a new world to European climatologists, Mr. Robinson referred especially to the Muskoka Lake regions which he had been able to visit with Mr. Burton during the few days intervening between the two meetings. This region, about 100 miles north of Toronto in the highlands of Ontario, and at an altitude of 800 ft. above sea level, abounded in fine forests, while the climate was dry and the air pure and invigorating to those accustomed to the enervating influence of southern climates.

The region possessed remarkable climatic advantages for persons with phthisical tendencies, the death-rate being less than one-tenth of that which obtained in other parts of the province. A new sanatorium on the Muskoka Lake for the cure of incipient phthisis, with accommodation for 40 patients, was opened during Mr. Robinson's visit. It would be kept open during the winter, which, owing to the still bracing atmosphere, was not only tolerable but positively pleasant. The proprietor of the hotel at the north end of Lake Joseph

had come to the district forty years before from New York, where, as a young man, he had developed chest disease. He began life in a log hut, and the open-air existence suited him so well in spite of shortcomings in the way of food that he remained and prospered, and was now a hale and hearty man of 60. He was able also to mention the names of several men who had come from the States with lung disease in different stages who spent their lives, summer and winter, under canvas and prospered.

Mr. Robinson next passed in review the work of the various Sections of the annual meeting, and then referred to the hospitals in Montreal, dwelling especially on the splendid site occupied by the Victoria Hospital, the wards of which were replete with every modern improvement, while the complete arrangements for the clinical teaching of students and the excellent provision for the nursing staff left nothing to be desired. The active work carried on both in this and in the Montreal General Hospital in all departments was most apparent, and the numerous laboratory facilities for chemical and bacteriological investigation were a prominent feature. Mr. Robinson then mentioned some of the hospitals visited in the States; the St. Luke's Hospital at New York, erected under the auspices of the Vanderbilts and other prominent citizens, was quite an architectural feature with its white marble columns, its entrance hall, and its costly chapel. It was situated outside the city at the north end of Manhattan Island, it had a fine view of the Hudson, and though some years would elapse before the complete design of the building was finished, everything in connection with the building was of the best and most modern style. The Johns Hopkins Hospital at Baltimore, an older building on the pavilion plan, possessed wards so large and well ventilated that their atmosphere was preferable to the stifling heat outside. In all these hospitals the strictest antiseptic precautions were used.

In conclusion, Mr. Robinson said that all those who were present at the Montreal meeting would agree that it was quite out of the ordinary run of such gatherings. The presence of such a large number of the different races of English-speaking people, Americans, Canadians, and British, gave a novelty and charm to the proceedings to those visitors at any rate who had journeyed from this side of the water. Although no discovery of an epoch-making character was announced the work was satisfactory in quantity and quality, the addresses unusually interesting, and the lectures well attended and sometimes very lively. The organisation of the meeting was excellent, and nothing was forgotten or neglected to make things go smoothly, added to which the hospitality of the citizens in Montreal and the Dominion in general was worthy of the reputation of our Canadian fellow subjects. He would advise all those who could to go and see for themselves that Canada was alive, robust, and loyal, and wanted only plenty of English, Scottish, and Welsh immigrants to go and stop in the colony and develop the enormous natural resources of this grand and unfinished portion of Her Majesty's dominions.

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

A CASE OF MALARIAL ENTERIC FEVER.

A MAN, aged 20, contracted enteric fever by drinking water at a house in a marshy district where the disease was prevalent. The incubation period lasted about nineteen days.

The case ran an irregular, but not a severe, course until the twenty-seventh day, when, after a few days' improvement, the patient was seized with a severe rigor in the afternoon. This was followed by pyrexia and sweating, and the temperature rose to 105°. The following morning it had dropped to 100.4°, but the rigor was repeated about three hours later than on the preceding day, the temperature rising to 104°. He was given quinine in 2-grain doses every four hours, and there was no recurrence until a slighter seizure occurred after an interval of four days. During these four days the temperature had been generally subnormal and the pulse slow—95° and 51 beats to the minute being on one occasion recorded. A

* Abstract of an address delivered at the annual meeting of the East Anglian Branch.