An Address

ON THE

NATURAL HISTORY OF ULCERATIVE COLITIS AND ITS BEARING ON TREATMENT.*

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THE proved value of serum treatment in tropical bacillary dysentery makes it important that the active bacterial agents in ulcerative colitis should be known. It is the very type of disease which should yield to serum or vaccine treatment. The site of infection is localized, there is no general infection, and the symptoms are mainly local and exhaustive, though partly toxæmic. If it is not cured in an early stage, nothing remains as a rule but such crude measures as colostomy and ileo-sigmoidostomy. The necessity for bacterial treatment holds good, whether the primary organism concerned should ultimately prove to belong to the dysenteric, paratyphoid, *coli* or pyogenic group. Nothing can be done until the natural history of the disease is understood.

The pedigree of the disease can be traced back for nearly 300 years. It was then called dysentery, or bloody flux. In the seventeenth century epidemics were common in this country. There were sometimes 4,000 deaths a year from "bloody flux." These epidemics usually occurred in the fly season, but sporadic cases were met with also in the spring and winter. In the eighteenth century, probably through a safer disposal of excreta, epidemics became less common. In the nineteenth century they nearly disappeared in the open, except in Ireland, but they persisted in certain institutions, Millbank Penitentiary and various asylums being the chief offenders.

At the present time small outbreaks still occur in asylums. They still occur also on a small scale in the open, and the evidence is almost conclusive that both in these small epidemics and in asylum outbreaks the disease is spread by direct transference of infected material from person to person. Thus a small epidemic (Carver) arose in and around the Great Northern Central Hospital, in which children and adults were equally infected. In 1900 a small outbreak (Cautley) occurred in a London barracks. On one staircase lived 13 women and 30 children. Of the adults, 3 were infected and recovered; of the children, 6 were infected and 4 died. Both these outbreaks occurred in the fly season. In August and September of 1901 an epidemic occurred at Aldershot, and of the civilian population between 170 and 180 persons were attacked, of whom 38 died. All ages were affected, but of the 38 deaths 28 occurred under the age of 5, and 3 over the age of 65. This mortality-rate of about 27 per cent. is identical with that of Japanese dysentery before serum treatment was adopted. The reporting medical officer of health states that flies were very numerous at this time.

This same decline of the epidemic and persistence of the sporadic disease are to be noted all over Europe, except in the south-eastern fringe, where epidemics still occur. The sporadic case is still with us, just as Sydenham described it, and it has never altered its form. His description of the disease in 1669 may be applied word for word to the condition as we now see it. One sentence may be quoted, because I believe that a non-necrotic "dysenteric diarrhoea," such as he alludes to, is still to be recognized: "With these slimy motions appear streaks of blood, though not always; sometimes, indeed, there is no passage of blood whatever from first to last. Notwithstanding, provided that the motions be frequent, slimy, and attended with griping, the disease is a true bloody flux or dysentery." Though a few cases of dysentery are specified in the Registrar-General's report, this separate heading has only appeared in the last few years, and the bulk of our cases are probably buried with the 20,000 annual deaths from diarrhoea.

When the epidemic disease became insignificant, the sporadic case ceased to attract much attention, and it eventually acquired the new name of "ulcerative colitis." For the moment I think this is a better name than

"dysentery," and there should be no reversion to the original name, unless and until it has been shown bacteriologically that this disease belongs to the dysenteric group.

THE CLINICAL EVIDENCE.

This disease comes before us in varying guise, as a short severe illness, and as a long illness continuous or intermittent. To these three forms I think must be added a simple non-necrotic diarrhoea, often the precursor of a more severe attack. The difference between these various forms is not a matter of symptoms and physical signs. These are constant. The difference rests mainly on the duration of illness and partly on the mode of onset, and in both these respects this disease presents greater variation than does bacillary dysentery.

In considering a series of 85 cases (for about three-fourths of which I am indebted to my colleagues at St. Thomas's Hospital) one question is kept in view—namely, Are all these cases of the same nature, or are different diseases mixed under one name?

If an answer to this question can be given it will allow a definite though weak presumption, that an organism known to be causal in one case is the cause of all the others, and an attempt at appropriate treatment will follow. At the same time, the subsidiary question may be considered as to how far all or any of these cases resemble or differ from the bacillary dysentery of tropical countries. In all these 85 cases the disease was acquired in this country.

A.—The Acute Continuous Disease.

Among these 85 cases (of whom 41 died and 44 survived) we find instances both among the deaths and the survivals which, to my mind, so far as symptoms go, are identical with bacillary dysentery. I think, if the following cases occurred in a tropical country, no one would think twice about the diagnosis.

CASE I.

Man aged 59. Sudden onset of diarrhoea, with cramp in legs, and abdominal pain, mostly in right iliac fossa. Vomited three times. Stools five to six a day, much blood and mucus. Slight fever, 99-101° F. Hiccough. Tongue became red, glazed, and dry. Pulse 132, failing rapidly. Death on twenty-third day. *Post mortem*: Colon ulcerated from end to end; ulcers ovoid with swollen rounded edges, separated by strands of sodden mucosa, sometimes confluent over large tracts, mostly extending down to muscular coats, a few to peritoneum. No disease elsewhere. From splenic blood after death *Bacillus coli* and *Bacillus proteus* grown.

CASE II.

Woman aged 31. No previous attack. Sudden onset of rectal pain and passage of blood. Continuance of hæmorrhage and profuse offensive discharge, with little faecal matter. Slight fever. Death on thirty-eighth day. *Post mortem*: Ulceration of whole colon and rectum; in caecum only a few polypoidal islets of mucosa remained; no disease elsewhere.

Two similar cases ending in recovery may be quoted, in one of which the serum agglutinated Shiga's bacillus.

CASE III.

Man aged 25. No previous attack. Onset of diarrhoea slight at first, then more severe with abdominal pain; stools five to six a day, offensive, slimy, with streaks and clots of blood; genuine tenesmus; fever for one week. Treated with bismuth and Dover's powder. Apparently complete recovery; duration about six weeks. Subsequent history unknown.

CASE IV.

Woman aged 41. Sudden diarrhoea; stools every fifteen minutes at first, with straining and genuine tenesmus and pain on defaecation, most stools containing red blood. Tongue red and dry. Temperature normal. Treated with bismuth and opium and creolin irrigation; quickly improved, and was discharged apparently cured on the fortieth day of illness; subsequent history unknown. Her serum (1 in 100) agglutinated Shiga's bacillus at once. It is highly probable that this was a case of bacillary dysentery. It is noteworthy (cp. later evidence as regards dysenteric diarrhoea) that she stated that she had a similar but slighter attack three months previously and recovered completely.

Out of this series of 85 cases, 20 may be described as being of this "short, continuous type," which so closely resembles bacillary dysentery. A picture of the condition in the British case comprises a sudden onset, sometimes with constitutional disturbance, diarrhoea (up to twenty or more stools a day), the passage of mucus and blood, the blood being red, in considerable quantity, or

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mixed with inflammatory exudation to form reddish-brown or black liquid stools, severe gripping pain in connexion with defaecation, and in some cases true rectal pain and tenesmus, fever in nearly 50 per cent, and signs of toxæmia in the severe cases, dry tongue, parching of mouth, and rapid wasting.

B.—The Chronic Disease, Continuous and Intermittent.

As regards the remaining 65 cases, I think it may be said with truth that in all of them there occurred at one time or another a phase of the illness, during which phase this same close resemblance to bacillary dysentery was maintained. But it was a phase only (sometimes an opening, often a terminal, scene), and if this phase is put on one side, it must be confessed that in their general course these 65 cases bear little resemblance to the acute cases already described and to the majority of cases seen in tropical countries. The mere duration of the illness might lead one at first sight to think that we are dealing with some disease which is met with only in temperate climates. If we look at a rough table of duration we see something in chronicity of disease that is rarely, if ever, met with in the tropics.

In 30 of these 65 cases the illness was continuous from first to last, with little or no tendency to intermission or improvement. In 15 of these (fatal cases) death occurred:

In the third month...	...	...	in 3 cases
In three to six months	...	...	in 2 "
In six to eight months	...	...	in 2 "
In eight to ten months	...	...	in 2 "
In ten to twelve months	...	...	in 2 "
In eighteenth month	...	...	in 1 "
In two to two and a quarter years	...	...	in 3 "

In the 15 patients who left hospital alive only the minimum duration of illness can be given, because though they survived it is doubtful if many can be said to have reached a cure. The duration was:

Two to six months...	...	...	in 3 cases
Seven to twelve months	...	...	in 4 "
One to one and a half years...	...	...	in 3 "
Nearly two years	...	...	in 1 "
About three years	...	...	in 2 "
Five to six years	...	...	in 2 "

But this wide departure from the usual type of bacillary dysentery becomes wider still when we consider the remaining 35 patients. In these the story is often of immense duration. These cases must be described as "intermittent" or "relapsing," or as "comprising a series of separate attacks" with a decided tendency to cure, but always falling short of a complete cure. Of these 35 patients, 11 who died contributed a history of twenty-one attacks of diarrhoea, generally (cp. Sydenham's description) but not always associated with the passage of blood previous to the final and fatal attack which brought them into hospital. The 24 who survived gave similar histories of great duration. Thus 18 contributed a history of thirty-seven previous attacks, 5 gave a history of "several" previous attacks, and 1 stated, I believe with truth, that she had had an attack nearly every August for sixteen years.

C.—Dysenteric Diarrhoea.

Thus we have the concept of a long, intermittent diarrhoeal disease running over many years (eighteen years in one case, over five years in many cases), and probably these 35 patients may be fairly stated to have had seventy or eighty previous attacks of diarrhoea between them. As a rule, these early attacks are less severe (cp. Cases v and xiii), and severity increases with recurrence. It is probable that in some of them there is no actual ulceration. They are analogous to slight cases of bacillary dysentery which proceed no further than a superficial catarrhal inflammation. If they are reckoned, as I think they should be, as part of the unit "ulcerative colitis," then this disease becomes much more common than is generally supposed. I think that any case of sudden violent diarrhoea in this country that runs into a second or third day, especially if there is no sign of affection of stomach or small intestine, should be regarded with suspicion, and if blood and mucus are passed I think the case must be put into this group.

An example of this recurring disease may be given

which shows how far we have travelled from the usual picture of a bacillary dysentery as seen in tropical countries. It shows also how the early attacks of dysenteric diarrhoea which often precede a final severe attack may be regarded lightly, and how a cure may be recorded under any kind of haphazard treatment which much later events may disprove.

CASE V.

Governess, aged 34, liable to diarrhoea (that is, several slight attacks) for eighteen months. Last attack was longer and more severe, she passed blood and mucus, had considerable abdominal pain, and was admitted into hospital in April, 1896. In two months she seemed to be cured, and she was discharged in June. She remained well till September, when the same symptoms returned, and she was again admitted in October. After one month of treatment she seemed to be well again, and she remained well till April, 1897, when the symptoms returned, hæmorrhage being severe, and she was readmitted in May. Treatment now had little effect, and in September left colostomy was performed without benefit. In January, 1898, ileo-sigmoidostomy was performed with success, but in April an attempt was made to close the colostomy wound, and she died three days later from general peritonitis. *Post mortem* there were found a large ulcer in the long axis of the splenic flexure, and a similar ulcer in the iliac colon, with some patches of grey scar tissue around it. No disease of colon past or present, above the splenic flexure. The total duration of illness was two years.

In another patient of this class who recovered, for a time at any rate, Shiga's bacillus was agglutinated.

CASE VI.

Man aged 31. Four years ago had several short attacks of abdominal pain, vomiting, and diarrhoea, sometimes with passage of blood. Then occurred an interval of three years of good health. In February, 1906, another severe attack, stools four to five a day, occasional blood, much mucus, great loss of weight, no fever, occasionally sick. He apparently recovered completely in three months, but the subsequent history is unknown. Shiga's bacillus was agglutinated by his serum, dilution 1 in 20 giving good diffuse clumping in one hour, 1 in 50 slight clumping in one hour, 1 in 100 no reaction.

D.—The Acute and the Chronic Disease.

We have now before us, then, the single attack proving fatal in three to six weeks, and the long continuous or recurring illness (or series of attacks) often tending to increase in severity, and spread over two to eighteen years. Are the short attack and the long illness separate forms of disease, or is this wide illness a single unit with great variation in duration?

To my mind the evidence, so far as clinical study can go, is in favour of unity. Between the temporary diarrhoea with or without bleeding, the short fatal illness, and the long recurring illness, clinical evidence shows no differentiating feature except the mere duration. They cannot be separated into two or more groups. There is a perfect gradation from the illness of thirty days to the long illness of many years, and there is no break. At any time in the long illness, as will be shown, there may supervene an acute attack which may rapidly prove fatal. The early attacks in the long cases are often severe enough in themselves. They differ in no particular from the short single attack which proves fatal except in their lesser severity, and in any one of them with a little less luck the patient might have died, and so have converted a potential long illness into an actual short fatal attack (cp. Case xiii).

If it is granted that we are dealing with a single unit, how does it compare with tropical bacillary dysentery? Is there anything in tropical countries which resembles our long-continued home-grown disease? It is clear that such a long-continued illness is at any rate not very prominent in the minds of experienced writers on tropical dysentery, but it is present. Of Japanese dysentery Shiga states that the duration is four to eight days in the light cases, and three to six weeks in the serious ones, and that in fatal cases death usually occurs in two to three weeks. But he adds, without any details, that the disease may become chronic, with a tendency to relapse, and he speaks of this as "a subsequent disease in which we cannot find the dysenteric bacillus." Davidson describes chronic dysentery as being a direct persistence of an acute attack, or a persistence by relapse, or a chronic disease from the first. As regards the ending of such a case, he says that "the patient after months or years of suffering dies of exhaustion or is carried off by some intercurrent disease."

I think we may take it, therefore, that the great variation in duration of the British disease is not without parallel in the experience of the tropics. There remains, however, the striking difference between the United Kingdom and tropical countries as regards the relative proportional frequency of the short case and the long case; the latter bulk largely with us. I expect they form 70 to 80 per cent. of our cases. In the tropics they form a small minority. But they may be more common than is generally supposed. As a matter of fact we often see such cases returned from the East, and they present just the same difficulties with regard to treatment, medical and surgical, as our native product.

Two examples of long-continued tropical dysentery for comparison with the British disease may be given:

CASE VII.

Soldier, aged 30. Went to India in 1895; dysentery there in 1898. For next four years liable to attacks of diarrhoea. In 1902 to South Africa, where second severe attack occurred. Liable to diarrhoea since. In December, 1904, having left the army and become a meat-porter in the Old Kent Road, he had a third severe attack, stools hourly, mucus and blood passed, tenesmus, prolapse of rectum, abdominal pain during and after defaecation. Improved considerably, but in February, 1905, a fourth severe attack occurred, which continued, off and on, till April, 1905, when he was admitted into hospital. He had lost 3 st. in weight in four months. Ulceration of rectum could be seen with speculum. Stools now two to four a day, containing abundance of polymorphonuclear leucocytes and generally visible blood. No amoebae found. Temperature normal. Under medicinal treatment and irrigation he improved considerably, regained a little weight, and left on June 28th to resume work. Subsequent history unknown. Reckoning from the start (as with our British cases), the duration up to date is about seven years. He was certainly not cured when he left hospital.

CASE VIII.

Man aged 38. In 1898 he had his first attack of dysentery on board ship off the East Coast of Africa. In succeeding years in this country he had slight recurrences. In 1905 he had another severe attack in Rhodesia, and he has been liable to diarrhoea ever since, with passage of blood and severe griping. In April, 1906, he was admitted into hospital. A culture from stools yielded only *Bacillus coli* and an atypical bacillus of this group. With medical treatment and twelve injections of *Bacillus coli* serum he improved considerably, and left in August. Three weeks after discharge he was as bad as before, with constant pain and haemorrhage. He returned to hospital, and a right colostomy was performed. A period of comparative peace ensued, though a blood-stained discharge from rectum continued until August, 1907. A course of irrigation with silver nitrate was then tried; it was badly borne and proved useless. Two unsuccessful attempts at ileo-sigmoidostomy were made in 1908. There can be no doubt that at this date, ten years after the first attack of dysentery, the colon is still ulcerated.

E.—The Haemorrhagic Disease (Lower Segment Type).

From a study of the mode of onset a point is extracted, which is more likely to have a differentiating significance than the mere duration of the case. In 10 of these cases simple bleeding from the colon preceded the diarrhoea and all other signs of colitis. Of these 10 patients 6 died and 4 survived, though I doubt if they were cured. In 2 of the fatal cases there was actual constipation with the haemorrhage, so that aperients were necessary. In 2 cases haemorrhage continued off and on for about eighteen months, in another case for twelve months, and in the others for days, weeks, or a few months before diarrhoea began. In all of them, however, diarrhoea and all the symptoms with which one is familiar in the more usual form of ulcerative colitis, set in sooner or later, and the condition of the colon after death did not differ from that found in the patients who began their illness in the more orthodox diarrhoeic way.

I know nothing of such a stealthy haemorrhagic mode of onset in tropical dysentery, but I suppose it is possible that both this unorthodox beginning and also the large relative proportion of chronic cases as compared with acute cases in this country can be explained in the same way up to a certain point. The severity of the disease and the degree of toxæmia vary with the site of disease in the bowel. This is clearly the case in bacillary dysentery. Shiga speaks of an "ascending" and a "descending" dysentery. In the majority of tropical cases the disease begins in the rectum and iliac colon, and remains localized there or ascends thence. In a small proportion it begins in the caecum and descends. This latter form presents the more severe results, and a still graver intoxication ensues when the lower end of the ileum is also affected,

and the disease then as regards toxæmic symptoms may approximate to enteric fever. The higher the site of disease, the more severe and general are the symptoms; with a lower site they are milder, and the results are more local.

There is evidence to show that this variation in the site of the disease, with a corresponding variation in the severity of the symptoms, occurs in British ulcerative colitis as in tropical dysentery. In Case v a relapsing illness of two years occurred, but the patient was never gravely ill, and might have recovered. *Post-mortem* examination showed that the disease had never extended upwards above the splenic flexure. It was a lower segment disease from first to last, there was no great toxæmia, and death was accidental.

This may be contrasted with Case i, in which the disease was of the upper segment type, "pain in the caecal region" was the earliest symptom, the illness was grave from the first, intoxication was severe, and death took place on the twenty-third day.

Far apart as these two cases seem, I see no reason for thinking that they are not of the same nature, considering that in Japanese dysentery, a disease of known uniform causation, there is noted the same variation of severity with the segment of colon affected. If in Japanese dysentery, as is frequently the case, the infection remains limited to the rectum and lower colon, the symptoms are mild and the prognosis is favourable. The following three cases may be interpreted as examples of long continuance of lower segment infection with preservation of fair health, followed by sudden rapid extension to the upper segment ending in death:

CASE IX.

Woman aged 37. In 1902 she began to pass blood and slime with loose stools. The haemorrhage persisted with loose but not frequent stools, and in January, 1903, she was admitted into hospital. So local did the disease seem to be, that a shallow abrasion just above the sphincter was cauterized and an ulcer 2½ in. from sphincter on posterior rectal wall was excised. In March, 1903, she was again admitted for fissure in ano. All through this year and for six months of 1904 she continued to pass blood and mucus from time to time, but was never laid up. In the autumn of 1904, that is, at least eighteen months after the first appearance of blood in the stools, a sudden change occurred. Diarrhoea set in with considerable abdominal pain. She wasted rapidly. Stools up to sixteen a day. Slight fever. Colostomy was performed in November, 1904, irrigation employed, and she improved considerably. Pain and diarrhoea ceased, but as usual in such cases blood and mucus were occasionally discharged per rectum. In August, 1905, an attempt to perform ileo-sigmoidostomy resulted in fatal peritonitis. *Post-mortem* the colon was found to be uniformly ulcerated from end to end. I think it is probable that up to the autumn of 1904 her infection was limited to rectum and pelvic colon.

CASE X.

A solicitor's clerk, aged 22. Had never been out of England, and had had no previous illness. In 1902 a brother was invalided home from South Africa convalescing from enteric fever. Soon after his arrival this patient acquired enteric fever. He made a good recovery, but stated that he always had some trouble with his bowels afterwards, an irregularity with constipation predominating, and the passage of mucus. This may or may not have any connexion with subsequent illness. About a year later this became more marked, and he began to pass small quantities of dark blood in most stools. This bleeding continued from December, 1904, to May, 1906, but during these eighteen months his general health remained good, there was no pain or diarrhoea, aperients were often necessary, and he actually continued at work, though his weight gradually fell from 10½ st. to 8 st. On May 11th, 1906, I think an upward extension occurred. He had a sudden attack of severe pain with diarrhoea, considerable haemorrhage, and the passage of "slime and shreddy stuff." This persisted, and he became extremely anaemic and feeble. On May 31st right colostomy was performed and irrigation carried out, but he died on June 23rd. The colon was very thin and rotten, and so completely ulcerated from end to end that only a few polypoidal tufts of mucosa remained. In this case we see two parts—(1) eighteen months of lower segment disease and haemorrhage; (2) six weeks of disease of upper colon not to be distinguished from tropical bacillary dysentery.

CASE XI.

A lady, between 50 and 60 years of age, noticed blood in her motions in May, 1890, but she had no pain or diarrhoea. This haemorrhage soon ceased, and she seemed to be quite well. In the following October, however, diarrhoea and abdominal pain set in. The diarrhoea was severe, over twenty stools a day being noted, a good deal of blood was passed, and there was great tenesmus. She died five or six weeks later. The colon was ulcerated from end to end, and the undermining was very

marked, some ulcers being spanned by bridges of surviving mucosa.

CONCLUSIONS.

I think (1) that the great variation in the duration of the illness, and the fact that in some few cases simple colic haemorrhage may for a long time be the only sign of disease, do not necessarily require that we should regard these cases as separate forms of disease, distinct from the dysenteric diarrhoea and from the short fatal illness, which so closely resembles bacillary dysentery, and (2) that both points may be explained on the ground of primary localization in the lower segment of the colon.

THE BACTERIOLOGICAL EVIDENCE.

From the clinician's point of view tropical bacillary dysentery is a unit of disease. So it will remain. It presents some differences as regards degree of toxæmia and duration, but these differences are small as compared with those noted in the British disease. Bacteriology, however, shows that it comprises several groups, each of which is dependent on a definite specific organism separable by agglutination and by sugar-fermenting reactions. Probably there are three or four such groups. The two varieties of Shiga and Flexner certainly account for the dysentery of Japan, China, the Philippines, and the West Indies. One or other of these varieties has been so often isolated from cases of dysentery and even of non-necrotic diarrhoea in temperate climates—for example, America (Flexner), Germany (Kruse), France, Austria, and Holland—that its general causal connexion is highly probable. But it must be noted that these observations have been mostly made in institutional epidemics, and not on the sporadic cases which we are considering. *B. dysenteriae* has, however, been found in sporadic cases in Philadelphia.

The range of *B. dysenteriae* has been recently extended. It seems to be proved that the ubiquitous Shiga and Flexner varieties are the chief cause of the diarrhoea of children in New York, both in summer and winter, the Flexner variety predominating, both varieties sometimes co-existing. To this pair Hiss and Russell added a third, which differs from Shiga's bacillus only in fermenting mannite. A fourth variety, such as was found in children by Wollstein, must be recognized, which ferments saccharose, maltose, and dextrin. Shiga tentatively adds a fifth variety.

Now it may be taken as highly probable that the small epidemics which still occur in asylums in this country are also dependent on *B. dysenteriae*. Eyre found Shiga's bacillus in 6 out of 10 cases. McWeeney isolated Flexner's bacillus from 1 case. Boycott found Flexner's bacillus in 17 out of 19 cases. But investigation of our sporadic cases hangs fire and is inconclusive. From 1 case only, so far as I know (acute case of a child), has Flexner's bacillus been isolated in this country (Marshall). Saundby has reported 2 cases from which Hewetson is said to have obtained Shiga's bacillus, but as regards the first of these the identity must be disallowed.

Sporadic disease is more difficult to investigate than an epidemic. Cases commonly reach the chronic stage before examination is possible. Even in the acute asylum cases it is seen that the specific bacillus was not isolated from every case examined. Eyre states from his further observations that in cases of chronic asylum dysentery (which probably corresponds to the bulk of our sporadic cases) *B. dysenteriae*, if present, is so outnumbered by *B. coli* and other intestinal saprophytes as to render its isolation a matter of extreme difficulty.

Further, we have Flexner's observation that even in tropical bacillary dysentery the faeces do not contain *B. dysenteriae* in such numbers as to make it possible to recover them as readily as from the intestinal mucosa, and that a scraping from the rectal mucosa will yield *B. dysenteriae* when it has not been found in the faeces. This is confirmed on all sides. Once outside the crypts and substance of the mucosa, it is quickly overgrown by saprophytes.

Consequently the following results of examination of "faeces" in ulcerative colitis at St. Thomas's Hospital are of little or no value. In 6 chronic cases *B. coli* was thus obtained: Pure in 2 cases, with *B. proteus* in 2 cases, with *Streptococcus faecalis* in 1 case, with this organism and *B. pyocyaneus* in 1 case. In 4 other cases the stools were examined for *B. dysenteriae* with a negative result.

Now as regards scrapings from the intestinal mucosa, Dr. L. S. Dudgeon has kindly examined 2 cases for me.

CASE XII.

Man aged 34. In May, 1908, began to pass blood, with a continual ache about the sacrum. A week later diarrhoea set in, five or six stools a day, generally containing blood, with griping, fever, and loss of weight. He lost ground until November, when improvement began. In January, 1909, he had regained 1½ st. in weight, and was passing one or two fairly well-formed stools daily without blood. Though he appeared to be convalescent, I doubt if he was cured, and his rectum remained very red and moist, and it bled unnaturally on gentle scraping. Broth was inoculated with the scraping, and after four hours' incubation this was plated on Drigalski's and Conradi's media, and on MacConkey's lactose agar. *B. coli* was found on all plates. But the blue colonies on the former media and the white colonies on the latter consisted of bacilli which gave almost identical reactions. This bacillus was slightly but distinctly motile when emulsified in normal saline; it was agglutinated, dilution 1 in 20, in thirty minutes at room temperature by the patient's serum, but there was no reaction with dilution 1 in 50. It was Gram-negative. It fermented, with production of gas, glucose, maltose, mannite, glycerine, salicin. It did not ferment lactose, raffinose, cane-sugar, or dulcitol. No action on neutral red broth. Litmus-milk alkaline; no clot after several days. Peptone, no indol. Jelly, no liquefaction. Other colonies examined gave similar results, except that salicin was unaffected. In two rabbits inoculated intravenously and in two guinea-pigs inoculated intraperitoneally no results followed. This patient's serum did not agglutinate either standard typical Shiga's bacillus or the bacillus obtained from the next case, or *B. typhosus*.

CASE XIII.

Man aged 23. In June, 1908, he had his first attack. Sudden onset of violent diarrhoea, stools up to ten a day, some containing bright red blood, much slime, severe griping across lower abdomen. Under treatment this subsided; in three weeks he was beginning to improve, and in six weeks he was apparently well again, and his stools became normal and formed. In tropical countries this would have been called dysentery, but no bacteriological examination was made. On December 11th a second attack of the same kind began. Profuse diarrhoea, with blood and mucus, great rectal pain as well as general griping, vomiting, fever. This soon proved to be more severe than the first attack, and he began to lose weight. In January, 1909, his rectum was very red, granular, and moist, and it bled on the least touch. A high scraping plated direct on to MacConkey's lactose-agar gave the following results: The majority of colonies after twenty-four hours on two plates were white, the remainder red. These latter were true typical *B. coli*. The white colonies consisted of a bacillus, Gram-negative, non-motile. This bacillus fermented with production of gas, glucose, maltose, glycerine, mannite, and cane-sugar. It did not ferment lactose-broth (but formed acid and gas in lactose-jelly at 22° C.), salicin, raffinose, inulin, or dulcitol. No action on neutral red broth. Litmus-milk, very slight acidity, no clot, result permanent. With peptone, indol; jelly, no liquefaction. Patient's serum did not agglutinate either this bacillus, diluted 1 in 10, 1 in 50, or Shiga's bacillus. This bacillus was not agglutinated by serum of the preceding case.

In the next fortnight the patient went rapidly downhill, with great wasting, severe pain, raw tongue with aphthae, and parched throat. Right colostomy was therefore performed. A scraping made from the caecum and plated direct on to Drigalski's and Conradi's media and MacConkey's lactose-agar, gave only *B. coli*, abundant growth of *B. pyocyaneus*, and *B. proteus*. In spite of the diversion of faeces and irrigation, the patient died nine weeks after the commencement of his second attack. Only a small part of the colon could be obtained for examination—namely, the transverse colon and splenic flexure. Over the whole of this the muscular layer was exposed, only a few polypoidal fragments of mucous and submucous layers remaining. Such a fragment showed (1) infiltration of mucosa and submucosa, and to a less extent of the other coats, with small and large mononuclear cells, some plasma cells, a few eosinophiles, no polynuclear cells or basophiles; (2) thrombosis of capillaries and small vessels; (3) haemorrhagic oedema of muscular coats; and (4) bacilli, short and fat, long and thin, throughout the whole intestinal wall, an infective condition which accounts for the toxæmia and the failure of treatment. Such a fragment was seared and incised, and a scraping was plated direct on to MacConkey's lactose agar. Here again *B. pyocyaneus* and *B. coli* were obtained. But the predominant growth was a white colony consisting of bacilli, having much the same characters as the organisms grown previously from this patient's rectum and from Case XII. Two such white colonies worked out gave nearly the same results. It was a short, Gram-negative bacillus, non-motile in one case on agar and jelly, in the other case non-motile on agar but slightly motile on jelly. They gave no reaction with antidyenteric serum (Shiga). They fermented, with production of gas, dextrose, mannite, maltose, cane-sugar, lactose, and dulcitol. They did not ferment inulin or raffinose. They had no effect on neutral red broth and did not liquefy jelly. They both produced indol. With litmus milk one produced acidity with slight clot after several days, with the other milk remained alkaline for five days and was then decolorized.

Turning now to the agglutination reaction, we find some evidence in favour of the identity of ulcerative colitis with bacillary dysentery. Foulerton obtained the reaction with Flexner's bacillus in 3 cases, dilution 1 in 40, 1 in 100. Vedder and Duval record the same results with Shiga's bacillus. Vaillard and Dopfer found the reaction well marked, diluted from 1 in 20 to 1 in 300, in an outbreak at Vincennes. Hewlett obtained a positive reaction with Flexner's bacillus in 2 cases of asylum dysentery. In Boycott's cases a reaction with Flexner's bacillus was noted, sometimes with dilution up to 1 in 200 and 1 in 500, but Shiga's bacillus was unaffected. A multivalent anti-dysenteric serum agglutinated the bacilli, which he isolated, with a dilution of 1 in 1,000, and when so examined even 1 in 10,000. The Shiga's bacillus obtained by Eyre was immediately agglutinated by antidyenteric (Shiga) serum with dilution 1 in 200, and by the serum of another patient in similar dilution. In a woman under my care (Case iv) Shiga's bacillus was immediately agglutinated by her serum. In Case vi also the reaction was obtained, though in less dilution. In 5 of our chronic cases, on the other hand, there was no reaction with Shiga's bacillus, though Flexner's bacillus was not tested.

The agglutination test, therefore, leaves us in the same doubt as does the search for a specific bacillus. The case is nearly conclusive for asylum dysentery, it is suspicious for the acute sporadic case, and it fails entirely against our common chronic disease. Yet I think the clinical evidence must be taken to mean that our long-continued case is directly related in some way to our short fatal illness, and perhaps also to the acute asylum case. In such an instance as Case xiii, where the patient tided through a short severe attack of three weeks, only to relapse three months later and die after a second illness of nine weeks, we must conclude that both illnesses were of the same nature. This instance is only one of many. Now it may be taken as nearly certain that *B. dysenteriae* was not present in this second attack, or at any rate during the last five weeks of it. Was it present in the first attack or in the first four weeks of the second attack?

If the clinical evidence is considered to be strong enough to warrant the belief that the short illness and the long illness own the same origin (perhaps one of the organisms of the dysenteric group), it is possible that the relation between them may be explained on the hypothesis of a concurrent or consecutive action of organisms of the paratyphoid or *coli* variety, or of pyogenic cocci. *B. pyocyaneus*, also, may be an important factor. In the analogous intestinal infection of typhoid fever there is considerable evidence indicating concomitant failure of the normal intestinal protection against *B. coli* and pyogenic cocci. It is known that from tropical bacillary dysentery in a chronic stage *B. dysenteriae* can no longer be obtained, and, in such examples of tropical disease as Cases vii and viii, one can hardly doubt that the perpetuation of the disease is the work of common non-specific organisms. It may be that the chronic British disease is similarly a secondary non-specific ulceration, in which case the prospect of a generally applicable specific treatment becomes remote.

TREATMENT.

Of these 85 patients 41 died. Of the 44 survivors, many improved, but I doubt if more than 8 of them were cured. These figures, being drawn from hospital and consulting work, naturally only include the severe and chronic cases. In all the fatal cases the colon was examined after death, and in all these, except one (Case xvi) the colon was extensively ulcerated, such ulceration not being due to typhoid fever, tuberculosis, or other recognized cause.

Until specific treatment can be provided I do not think any dogmatic rules of treatment can be produced. I have nothing useful to say; but, looking back on the cases for which I have been responsible, I feel sure that lives might have been saved by an earlier recourse to colostomy. As regards serum treatment, there is no doubt that immune serum has a specific agglutinating action on each member of the dysenteric group. Vaillard and Dopfer, however, find that serum immunized with the Shiga-Kruse bacillus has a favourable influence on cases, whether they are due to Shiga's bacillus or to Flexner's bacillus. Shiga has made a serum covering three types. The Shiga-Kruse bacillus

alone is used by the Lister Institute for the manufacture of their serum. In France, Coyne and Auché have made a Shiga-Flexner serum, which is effective in infantile colitis.

I have used the serum of the Lister Institute freely in 5 cases, but I can offer no opinion as to its utility, for all the cases were chronic and various other methods of treatment were in force at the same time. The *coli* serum used in Case viii seemed to be beneficial. As regards *coli* vaccine, which was used in many cases, no obvious benefit can be noted. Case xiii had three doses of a vaccine of his own bacillus and of *B. coli* without benefit.

From the point of view of treatment, two classes may be considered.

(1) Dysenteric Diarrhoea.

A short, mild attack may yield to opium and bismuth, but in using these and such-like drugs we are only treating a symptom, and are relying on a natural resistance to the infection, which may or may not be forthcoming. It is clear that ipecacuanha has no specific influence on the disease. As regards Japanese dysentery, Shiga says of ipecacuanha that "it has a very poor place as a dysenteric remedy." In asylum dysentery, also, it appears to be useless. The general custom now is to use calomel, and I believe this to be the best line of treatment. Shiga gives 8 to 12 grains once or twice, or one dose of castor oil 3 to 5 drachms, or one dose of calomel followed by castor oil. In asylum dysentery also Gemmell found calomel beneficial. I prefer to give it in frequent small doses rather than a few heroic doses, and combine it with opium. Calomel, 1 or 2 grains, with opium, $\frac{1}{4}$ grain, can be given three or four times a day.

With the calomel treatment Shiga recommends simple enemata of 1 per cent. saline or soda solution for cleansing purposes (no astringent being permitted), with suppositories of opium, cocaine, or belladonna, and if there is much haemorrhage he applies an icebag to the abdomen and gives opium by the mouth.

Whatever temporary views we hold as to the nature of ulcerative colitis, I believe it is wise to use the serum of the Lister Institute in all acute cases. By its use Shiga states that "the course of the Japanese disease is shortened in those who recover, and lengthened in those who otherwise would die," and his figures show under its use a diminution of the mortality by about one-half (from 22 to 26 per cent., to 9 to 12 per cent.). The serum is bactericidal and antitoxic. I have given as much as 80 c.cm. in a chronic case in which recovery ensued, but it was combined with much other treatment.

(2) Acute and Chronic Necrotic Disease.

In the case which is severe from the first, and in which fever and toxæmia are considerable and widespread inflammation and necrosis of the mucosa are manifested by abundance of polymorphonuclear leucocytes and blood in the stools, the same line of treatment may be adopted. But if improvement is not quickly seen, we are face to face with a condition which may either prove fatal in the next few weeks or may tail off into the chronic and nearly incurable form. The question of local treatment, in addition to the use of serum, becomes imperative. It is easy to be too optimistic and to wait too long for cure. In genuine ulcerative colitis, as distinguished from the great functional and subinflammatory conditions of the colon with which it is often confounded and in which cures under any treatment are common enough, a deceptive appearance of health may be preserved for a time, while the disease extends upwards. Even a pure lower segment infection may quickly get out of control. We have to decide between irrigation per rectum, appendicostomy and irrigation, and colostomy with irrigation and the establishment of a free artificial anus. The right plan can only be settled by the degree of severity of the toxæmia and the probabilities as regards the extent of the disease in each individual case. From what I have seen, I have no high opinion of irrigation per rectum. I think irrigation by appendicostomy has advantages over rectal irrigation, but in no other respect has appendicostomy anything to recommend it. But looking back on many of these cases and on the condition of the colon after death, I believe that colostomy will prove to be the most life-saving proceeding

in the long run. It affords complete rest to the colon as well as efficient irrigation.

The irrigating fluids that may be used are innumerable. Silver nitrate, creolin, boric acid, argyrol, and tannin are often used. Among other things I have tried methylene blue (2 to 3 grains in a pint). In one stationary case under my care, milk, in which lactic acid bacillus had been incubated for twelve hours, was injected daily through an appendicostomy for a long time without obvious result. Similar milk I have given freely by the mouth and in large quantities by rectal irrigation without any apparent benefit. In my most successful case I used an emulsion of sulphur, 120 grains in 4 oz. of oil. This was thrown into the colon through an artificial anus every other day, and on the alternate days thorough sluicing with boric-acid solution was carried out. This was employed for seven weeks. With the same idea of using something that will adhere to the mucosa, Shiga has used enemata of gum arabic mixed with bismuth, gallate of bismuth, or iodoform.

That there is some natural tendency to cure is seen from the following case:

CASE XIV.

Man aged 66. In addition to a large number of recent ulcers, large and small, there were several bands and patches of cicatricial tissue, and about these parts the colon was thickened and narrowed. He died on the thirty-fifth day of his illness, but there was a history of previous attacks of diarrhoea. Colostomy was performed, but only just before death, and at too late a period to have induced the healing, and the scars were probably attributable to the earlier attacks.

In two other cases (man aged 34, total duration of illness eight months; woman aged 24, total duration with intermissions five and a half years) the colon showed recent ulcers, healing ulcers, and scars of previous ulcers.

That this tendency to cure is increased by colon-rest is probably shown by the following cases:

CASE XV.

Man aged 39. Total duration of illness was two and a half years. Ileostomy was performed two years, and ileo-sigmoidostomy twenty months, before death. Death occurred from peritonitis arising from an attempt to close the artificial anus. Smooth white patches of scar tissue were found here and there in the colon, with active ulceration in pelvic colon and rectum—that is, below the point of anastomosis.

CASE XVI.

Man aged 34. His illness comprised a series of attacks (diarrhoea and haemorrhage), with intervals of fair health; total duration was two and a half years. Ileostomy was performed twenty months before death, and his death was due to peritonitis arising in an attempt to perform ileo-sigmoidostomy. The whole of the colon was much thickened and irregularly contracted, but no actual scarring could be recognized, and no ulceration was present.

The unpleasantness of an artificial anus can be mastered, and the patient who must use it is by no means a social outcast. The disadvantage lies in the fact that when the colon is out of use it undergoes progressive contraction, and it becomes surrounded by dense fibrous fat. So that after the lapse of a certain time (perhaps a year) both closure of an artificial anus and the performance of ileo-sigmoidostomy become difficult, dangerous, or impossible. A reference to the fatal cases in this series shows this.

In Case VII, already detailed as an instance of long-standing tropical dysentery, in which colostomy was performed in August, 1906, two separate attempts at ileo-sigmoidostomy were made in 1908. Both proved impossible by reason of the small size of the colon, and its embedding in dense fibrous fat. In fact, at one spot the colon seemed to have no lumen whatever.

While there are these difficulties before us, it is clear that the premature attempt to close an artificial anus before the colon ulceration is completely healed will be equally disastrous. In some extreme cases I believe that the loss of tissue is so deep and extensive that the colon can never be used again, and that either an artificial anus must be used to the end of life or an ileo-sigmoid anastomosis must be established, as to the difficulties of which the instances mentioned above give abundant testimony.

The following case is an instance of such a permanent artificial anus. The case, moreover, is a good example of the lower segment haemorrhagic disease.

CASE XVII.

Schoolboy aged 18. In November, 1903, he noticed a little blood in motions, but there was no pain and no diarrhoea. All through 1904 he passed a little blood from time to time. In December, 1904, there was a sudden extension of infection upwards; he was seized with severe pain, straining and tenesmus, with frequent (hourly at first) passage of liquid stools of blood and mucus. From this time he was confined to bed. During the first six months of 1905 there was almost daily haemorrhage with wasting and profound anaemia. In July, 1905, right colostomy was performed. He gradually improved, simply as a result of the non-use of the colon. Irrigation was tried at times, but never for long and never thoroughly. In January, 1909, he has taken his degree at a university; he can play tennis and bicycle for forty miles, and goes to dances; he looks and feels in perfect health; the artificial anus has acted continuously and well. But twice a day he passes per anum a little blood and mucus, so that we may take it that ulceration is still present even in such a contracted colon as he probably now possesses. By the way it is interesting to note that, in consequence of this complete exclusion of the colon, the ratio of ethereal sulphates to the total sulphates in his urine is as low as 1 to 39.

In another similar case in a woman an artificial anus was established in July, 1906, after one year's illness. In January, 1909, she remains in good health, but washes her colon out daily through the opening.

The matter, however, is not quite so hopeless as would appear from these cases. The following case shows that it is possible to obtain a complete cure by means of an artificial anus:

CASE XVIII.

Woman aged 47. She had had numerous attacks of diarrhoea and bleeding for sixteen years, the attack generally occurring in August and lasting about six weeks. In October, 1907, a similar attack began, but it was more severe, with profuse diarrhoea and great pain. She came under my care in November, 1907. A month of medicinal treatment and rectal irrigation had no effect. In December an efficient artificial anus was established. She received in four doses 80 c.cm. of antidyenteric serum. After trial of various other irrigating solutions she had 4 oz. of an emulsion of 120 grains of sulphur in oil injected into the caecum every other day, and a free irrigation with boric acid solution on alternate days. After seven weeks of this the result was rather flattering, and the discharge of blood from the rectum and "from the artificial anus" (the ulceration apparently extended up to the caecum) gradually ceased. In April, 1908, with the idea of re-establishing use of the colon, she was given small, steady doses of calomel. When formed stools were produced, in July, the artificial anus was closed successfully. In January, 1909, she remains well. In this case, and in some other equally chronic, I tried the effects of various diets, and I believe that if digestion is good a full mixed diet gives the best result.

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In spite of all the efforts of a powerful administration, the law of February 15th, 1902, for the notification of diseases in France has remained almost a dead letter owing to the passive resistance of the medical profession, which shelters itself behind the words of the Act imposing the duty on the medical practitioner of notifying the case as soon as he has "established his diagnosis," words which seem to be thought to leave the obligation so much a matter of discretion, that no serious attempt has been made by the authorities to secure the conviction of practitioners for failing to notify. The objection taken by the medical profession to the law as it at present stands is twofold—first, that it involves a violation of professional secrecy; and, secondly, that the obligation to notify is placed upon the doctor in the first instance instead of primarily upon the father or head of the family, with a secondary liability upon the doctor. The Prime Minister has stated in Parliament that he is quite willing to submit an amending Act in this sense, but only on the condition that the medical profession will "discontinue an abstention which is too general and mischievous to the common good." At present there does not seem much probability of the medical profession taking the initiative suggested by M. Clemenceau.