SYMPTOMS AND PATHOLOGY
OF A CASE OF
ACUTE INFLAMMATION OF THE MUCOUS
MEMBRANE OF THE ILEUM
FROM CLIMATIC CAUSES.

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THE case which is recorded in the following paper is that of a patient attended by Dr. Thin, who had known and seen him occasionally for a period of twenty years. A post-mortem examination was made after death, from an acute illness, by Dr. Martin, and the viscera were prepared by Dr. Wethered, and examined microscopically by Dr. Wethered and Dr. Thin.

Dr. Thin is responsible for the clinical history of the case. The pathological histology has been jointly studied by Dr. Thin and Dr. Wethered.

The patient died from a purely climatic disease, which

is certainly uncommon, looked at from the clinical aspect. Pathologically the authors have not been able to discover an account of exactly similar changes.

The patient was a strongly built, healthy, muscular man, *æt.* about 40, of excellent constitution and of remarkable bodily and mental vigour. He had spent about twenty years in different parts of China, during which time he visited England on several occasions, and during these visits it was observed that he enjoyed excellent health.

In October, 1888, when in the north of China, he began to suffer from occasional attacks of diarrhoea. He spent the winter travelling in more southern parts of China, the diarrhoea occurring at regular intervals all through the winter, although it was never severe. Returning to the north of China in the early spring of 1889, he received a severe chill, which was followed by fever. During March, April, and May the fever frequently recurred, the diarrhoea became worse, and in June both the fever and diarrhoea became persistent.

Medicinal and dietetic treatment failing to give any permanent benefit he went to Shanghai, where the diarrhoea abated under a diet of beef juice, but the fever remained. Having lost forty pounds in weight in four months he was ordered home, and during the voyage across the Pacific he lost five pounds more. In the meantime he had become very weak, and was sent to hospital at San Francisco in a state of great prostration, and still suffering from fever and diarrhoea.

After being forty-two days under treatment, twenty-one of which were spent in bed, he was able to continue his journey. He continued to improve rapidly, and after three months his strength was completely restored. He had gained thirty-six pounds in weight, and with the exception of an occasional loose morning stool considered himself quite well, and when we met him in April he seemed in perfect health.

The first symptom of indisposition occurred on the

15th of May, when diarrhœa, disturbed digestion, and loss of appetite followed a chill. Four days afterwards, finding these symptoms continue, he consulted Dr. Thin, and complained of abdominal malaise and irregular action of the bowels. He had no fever; the heart, kidneys, and spleen were healthy; there was no tenderness over the liver, the area of hepatic dulness being only very slightly in excess of normal. The tongue was of a dark red colour, cracked and furrowed, but quite free from fur.

He exposed himself freely to cold, caught a fresh chill two days afterwards, and after suffering very severe distress and fever for two days, during which time he took, at his own instance, castor oil twice, and several fifteen-grain doses of quinine, he sent for Dr. Thin, who found him in bed looking extremely distressed and ill, in profuse perspiration, with a temperature of 103° . He stated that he had suffered for two days from fever, profuse diarrhœa, and much retching. Another dose of quinine was administered, after which the fever disappeared for twenty-four hours. The following day, however, fever again set in, the temperature reaching 104° , with much nausea, and a continuance of profuse diarrhœa. After twenty-four hours' fever the temperature fell to 98° (on May 26th), and it remained normal for four days (until May 30th), with a slow full pulse, but during these four days the nausea, retching, diarrhœa, and general abdominal pain continued, the bowels acting four to five times daily. After these four days of apyrexia the temperature again rose to 103° on May 30th, and the febrile condition remained persistent till he died, three and a half weeks afterwards, on the 25th of June.

We believe the chief features of the case will be more readily understood if we deal with the most important symptoms separately, instead of describing the condition from one day to another.

1. *The fever.*—The chill which he received on the 21st of May was followed by a severe rigor and fever. After two days of a temperature varying from 102° to

103° the temperature remained normal for twenty-four hours, when it rose again as high as 104°, but again subsided to normal after a day's fever, and the patient remained for four days with a normal temperature. Then on the ninth day of illness the temperature rose to 103°, and he had a febrile temperature from that day until he died, twenty-five days afterwards. There was a daily rise, which usually took place at night, sometimes slightly exceeding and sometimes not quite reaching 103°, the daily minimum being usually a little over 101°. It fell slightly on June 20th, when he began to pass blood from the bowels, and rose again the day before his death.

2. *Nausea and retching*.—From the first day of the attack, on the 21st May, until the day before his death, nausea was more or less persistent, not being much felt for hours at a time if nothing was swallowed, but always evoked to some extent, even by swallowing fluids. Retching was a prominent symptom during the whole illness, and could only be kept in check by very small quantities of fluid being swallowed at a time. Milk was nearly always vomited, even when taken in the smallest quantities, and even thin water arrowroot was not borne. The only nourishment that the stomach could receive was very small quantities of the juice of raw meat, or one or two teaspoonfuls of concentrated chicken broth. Any attempt to assuage the incessant thirst by drinking fluids usually brought on severe vomiting.

3. *Diarrhœa*.—Diarrhœa began with the sudden onset of the illness on the 21st of May, and continued until the end. During the first two days the diarrhœa was very frequent, but afterwards the motions were usually four to six daily. They were passed without pain or straining. The character of the stools remained the same from the beginning until within a few days of his death, when they contained fluid and coagulated blood. They were quite fluid, not very copious, of a dark brown colour, somewhat resembling dark mahogany. This colour never varied

throughout the illness. They had a sickening though not very intense odour, but the smell was not fæcal. They contained nothing resembling fæces from beginning to end. On June 20th, five days before his death, dark blood-clots were observed in the motions. These increased in quantity until the amount of blood lost by the bowel was considerable, and this bleeding undoubtedly hurried on the catastrophe.

During the first days of the illness he complained of some abdominal pain, but the tenderness was not great: in its subsequent course there was at times a sensation of uneasiness, scarcely approaching to pain, felt more or less during the whole time, but on some days it was scarcely noticed, and pain was certainly not a prominent symptom. On firm pressure over the bowels, particularly in the umbilical region, some pain or uneasiness was evoked, but the tenderness to pressure was not marked. On very firm and hard pressure on the lower edge of the liver slight pain or uneasiness was also produced, but this again was not a marked symptom.

The appearance of the tongue varied very little from the first, remaining of a dark red, and free from fur.

His mind continued clear and unclouded until within a few days of his death. Simultaneously with the hæmorrhage from the bowels he had short intervals of slight wandering, scarcely approaching delirium, followed by intervals of clearness.

He closely observed his symptoms, and reasoned from them very clearly.

In the third week of the illness he came to the conclusion that recovery was very improbable, and shortly afterwards gave himself up as being hopelessly ill, being much impressed by the continued febrile condition, and incapacity to take or retain food.

During the whole course of the malady there was not only an entire absence of appetite, but the foods usually given to invalids were almost invariably rejected. Digestion, as we shall immediately see, seemed to be entirely

suspended. Emaciation, which was not rapid, progressed steadily until the end. The pulse was, considering the severe nature of the symptoms, never very quick, the patient naturally having a slow pulse. It was only the day before his death that it rose above 100, when it rapidly increased till it reached 140 about ten hours before his death.

In this account of the illness we have purposely omitted any reference to the treatment by drugs and by diet, in order that the clinical picture might be less disturbed ; but before remarking on these two points it will be convenient to record what the patient told us concerning his acute illness in San Francisco.

The attack that he had there was evidently of the same nature as that from which he eventually died, the chief symptoms being retching, passage of dark-coloured fluid motions by the bowels, abdominal uneasiness, and fever. It was found at San Francisco that milk could not be borne, the food on which he eventually recovered there being pure beef juice squeezed from raw meat, of which he took from five to six coffee-cupfuls a day. During his last illness it was also found that milk could not be borne, producing invariably more or less sickness, and that which was not vomited appeared in the stools as white cheesy coagula. Yolk of egg was tried, and passed undigested in the motions. Raw white of egg in water was rejected. Thin barley water was given him for his thirst, water arrowroot was also given when the temperature was at its lowest. Raw beef juice was freely and persistently tried ; he had also freshly prepared beef and chicken jelly, and occasionally whey. These were given in the very small quantities which the stomach tolerated, and seemed to produce no effect on the colour or consistence of the intestinal discharges.

During the first week of his illness quinine had a decided and marked effect in reducing the temperature. It was continued, usually in full doses, until the last week of his illness, but latterly with less effect. No quinine

being given from the 19th to the 22nd, it was found that the temperature was on an average one degree higher ; and on being again administered, the temperature immediately fell to what it was before. The distressing nature of the symptoms appearing to depend largely on the fever, the quinine was usually given in doses of five grains, as much as twenty grains being sometimes given daily.

When it was found that full doses of quinine failed to reduce the temperature, four grains of antifebrin at once lowered it and produced great relief ; but the depressing effect of this drug was so marked that it was discontinued. As soon as the symptoms of hæmorrhage from the bowels appeared ergot was given, usually in the form of hypodermic injections of ergotin, but without producing any apparent results.

Occasionally moderate doses of laudanum were tried, without producing any effect on the diarrhœa. During the last week of his illness, when the distress became more aggravated, hypodermic injections of morphia were administered, without, however, producing very happy effects. Death occurred from exhaustion, accompanied by distressing nervous symptoms, on the 25th.

The general points to be noted in the case appear to be that for about a period of thirty-three days there was an apparent almost entire, if not entire, suspension of the digestive functions ; the absence of anything like fæcal matter in the fluid intestinal discharges ; and persistent fever (with an intermission of low temperature, lasting for four days) after the first three days of his illness. The tendency to nausea and occasional retching persisted the whole time. Abdominal uneasiness, although never severe, was hardly ever absent.

On account of Dr. Wethered's absence from town the post-mortem examination was made by Dr. Sidney Martin, whose report is as follows :

Æt. 41. Date of death June 25th, 1890. Date of examination, June 26th, 1890. Weather mild, wet. Rigidity slight.

General appearance.—Body emaciated but not extremely. Very little subcutaneous fat. Muscles slightly developed. No œdema.

Heart.—Pericardium, no excess of fluid. No pericarditis. Valves and endocardium normal. Muscles pale, otherwise normal.

Lungs.—Pleuræ not adherent; no excess of fluid. Lungs slightly congested posteriorly, otherwise normal.

Abdomen.—No ascites or peritonitis.

Liver.—Slightly enlarged; substance pale and rather soft (slightly fatty). On upper surface in the substance of the right lobe is a wedge-shaped mass about the size of a large bean; pale red on section, firm; it has more the appearance of a vascular growth than of an infarct.

Spleen.—Enlarged slightly, soft, diffuent. Near surface of spleen are three masses similar to that found in liver, one quite round; size of a large pea to a small horse-chestnut; largest is wedge-shaped. Masses are dark red, firm, not caseating; somewhat resemble recent infarcts.

Kidneys.—Not enlarged; capsule not adherent, surface smooth. Cortex not diminished. Substance pale, firm (anæmic).

Stomach.—Contains mucus and bile-stained food; no blood. Mucous membrane normal.

Small intestine.—The mucous membrane of the jejunum is bile-stained (green); in the upper part it is for the most part normal, showing two or three superficial erosions size of a split pea. The mucous membrane of the lower part of the jejunum is pigmented in dots, giving the "shaved beard" appearance (chronic inflammation).

The mucous membrane of the ileum and of the large gut is covered with dark brownish-red and liquid blood, which stained the surface of the gut. On washing the blood away the mucous membrane presents a worm-eaten appearance along the whole course of the ileum to the cæcum. This sinuous ulceration does not go deeper than the mucous membrane; in some places there are discrete

erosions size of a split pea. The ulceration increases as it descends the ileum. The mucous membrane is thickened generally, but the other coats of the gut are not affected.

Large intestine.—Just at the entrance of the vermiform appendix the mucous membrane of the cæcum is thickened and slightly eroded. There are about ten superficial ulcers in the large intestine; five are grouped together. None is larger than half an inch long and a quarter of an inch broad. Their edges are sharp-cut, not thickened, and the base formed by the lower layers of the mucous membrane and by the subcutaneous coat. The mucous membrane is not generally thickened; one or two of the ulcers appear to be in the solitary glands.

Mesenteric glands.—Not enlarged.

The specimens were placed for a few hours in alcohol, and then transferred to a 2 per cent. solution of bichromate of potash. After an interval of about six weeks they were embedded in celloidin, and the sections stained in hæmatoxylin and eosin.

Microscopical examination of the tissues thus prepared showed that there was nothing in the condition of the liver, spleen, stomach, jejunum, or heart of a markedly abnormal character. The pale wedge-shaped masses described by Dr. Martin in the liver and spleen were found on microscopical examination to consist of localised dense small cell infiltration around the vessels. We regard them as the first stage of a congestion that would have led to the development of pyæmic abscesses had the patient lived longer. The mucous membrane of the large intestine was found to be perfectly healthy. This remark of course applies to the gut as a whole, and not to the few superficial ulcers close to the cæcum.

The histological changes, as well as the naked-eye appearance, showed that the disease was essentially, and it may be said almost exclusively, an acute process in the mucous membrane of the ileum.

The changes in the ileum were found in the following stages.

No traces of the villi were seen in any of the sections, the free surface being composed of a seam, more or less deep, of a granular material, which was coloured a uniform brick-dust colour by eosin, and in which no cellular elements were stained.

At the parts least affected, Lieberkühn's crypts seemed in the deeper parts to be unchanged. Towards their extremities the epithelial cells were difficult to make out, being rebellious to the action of the staining fluids used; but they did not seem broken up. Towards the free surface they became lost in the layer of finely granular material which covers the surface of the mucous membrane.

In the next stage observed the crypts are shorter than usual; the lumen distended with a clear somewhat glutinous-looking substance in which fine granules are scattered. The epithelial cells are more or less broken up and vacuolated. The shortened crypts soon end in a thicker and better marked layer of the finely granular material previously referred to. This condition may be described as an atrophic condition of the epithelial structures involving a certain amount of shrinking and destruction.

A more advanced stage was best seen in the intermediate parts between the slightly affected crypts and the eroded or superficially ulcerated parts. In this stage the outlines of the crypts could still be traced by the rows of disintegrated and partially destroyed epithelial cells. The nuclei of the epithelium in this stage refused to take on any stain, and the crypts were in an advanced stage of destruction and disintegration, being lost in the surrounding and covering granular layer previously alluded to.

The last stage is that of erosion, or superficial ulceration. All traces of epithelium or crypts are gone, the free surface being composed of a thick layer of the granular material referred to. In the deeper parts of this layer leucocytes commenced to be made manifest by the action

of dyes, and in the deepest parts of it they were present in dense groups.

When the whole thickness of the ileum was examined, it was found that small-cell infiltration was present unequally in the submucous layer, very dense in the parts which were eroded, and partially and unequally in the parts which were less affected. Nothing remarkable was observed in the subperitoneal layer or the muscular coats. Under the eroded parts a certain amount of cell infiltration was present around some of the vessels in the inner muscular coat.

In some sections in the subserous layer, which was not specially congested, or the seat of any infiltration, large ovoid cells were seen, with granular protoplasm well stained, exactly similar to cells frequently seen in tissue undergoing repair, or in rapidly developed soft fibrous tissue in certain pathological conditions. These were possibly indicative of reparative changes that had followed the patient's recovery from the acute illness which he had in San Francisco.

In comparing the clinical symptoms with the naked-eye and microscopical pathological appearances, we believe we are justified in coming to the conclusion that we have had to do with an acute inflammation of the mucous membrane of the ileum supervening on imperfect recovery from a previously acute attack.

From the history given by the patient it seems clear that the first appearance of the disease was insidious and not attended by fever. After lasting for some months the process became subacute, and was attended by fever. On the subacute condition there developed a highly acute process, from which complete recovery took place, leaving, however, a susceptibility which, under the influence of accidental causes, led to the development of a second very acute and fatal attack.

The unknown cause of the disease which led to the death of this strong man was one that found the conditions of its development and activity in the mucous mem-

brane of the ileum; and did not find a congenial soil in any other part of the intestine; because, considering the healthy condition of almost the whole of the large bowel, we can only regard the limited affection of that gut near the cæcum as a very partial continuation of the disease dependent on the condition of the ileum.

A case previously published by one of us (see 'Brit. Med. Journ.,' June 14th, 1890) establishes the fact that in a peculiar, insidious, chronic climatic disease, unattended by fever, psilosis of the bowel, or "sprue," the mucous membrane of the ileum is the special seat of election of a morbid element; but these cases are conspicuous by the entire absence of fever.

It is possible, in the case we are now discussing, that from exceptional causes a similar affection of the ileum became, and continued, more or less acute; but if we were to look at it in this light, namely, that of acute congestion of the mucous membrane of the ileum, supervening on the early stage of psilosis, the case would require to be regarded as very exceptional. Favouring the idea that it was an exceptional acute condition of the usually chronic disease is the fact that anatomically the same portion of the gut was exclusively affected, and that in the early stages of the malady, before it had become acute; the patient—a highly intelligent man—identified his case as being similar to those described by one of us under the name of psilosis. In this case, however, there is no record of the peculiar condition of the mucous membrane of the mouth and gullet which is characteristic of the chronic wasting process.

Clinically it is to be observed that in this case the general symptoms of acute congestion of the mucous membrane of the ileum were retching, nausea, complete anorexia, and great thirst, the temperature ranging from 101° to 103° ; the discharge from the bowels of a dark-coloured fluid, in which there was no apparent trace of fæcal matter, absolute suspension of digestion, and steadily progressive emaciation.

The diseases from which it was necessary to distinguish it, and in regard to which a question of diagnosis naturally arose, were typhoid fever and a particular form of dysentery. From typhoid fever it was distinguished by the absence of spots and of tympanites, by the unclouded intellect, which remained perfectly clear until almost the end, when the patient was under the influence of morphia, and by the entire absence of the characteristic typhoid stools.

There is a form of dysentery in which, from the rapid destruction of the mucous membrane of the large intestine, almost from the beginning of the disease considerable quantities of a highly offensive dark-coloured fluid are poured from the bowel. The fluid of these dysenteric cases has somewhat of the tint of Condry's fluid, and is not so brown as the discharges were in the present case. Exhaustion rapidly takes place, and the patient dies long before the term reached in the case which we have described.

In the present case, the knowledge that the mucous membrane of the ileum was liable to be specially affected, the previous history of the case as given by the patient, and the exclusion of all other abdominal diseases known to us, led one of us to make the diagnosis of acute congestion of the mucous membrane of the ileum at the very outset of the illness, and he never saw any reason to depart from his view during its whole course—a view which, as we have seen, was completely borne out by the post-mortem examination.

In regard to the complete suppression of the digestive functions, whilst the whole of the intestinal viscera except the ileum were comparatively healthy, we would suggest that it is a question as to how far the functions of the anatomically unaltered digestive glands were suspended by a reflex effect produced by the congested mucous membrane of the ileum.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. iii, p. 165.)

DESCRIPTION OF PLATE VII.

Symptoms and Pathology of a Case of Acute Inflammation of the Mucous Membrane of the Ileum from Climatic Causes (GEORGE THIN, M.D., and F. J. WETHERED, M.D., M.R.C.P.).

FIG. 1.—*a*. Submucous layer.

b. Lieberkühn's crypt, very slightly obliterated at the free surface.

c. Remains of a Lieberkühn's crypt, destruction almost complete.

d. Dense small-cell infiltration of submucous layer under superficial ulceration.

FIG. 2.—Oblique section of a Lieberkühn's crypt showing breaking up of some of the epithelial cells. The cavity of the crypt is filled with a transparent glutinous-looking substance with granules.

a. Membrana propria of the crypt.

FIG. 3.—Section through one of the small ulcers showing the subperitoneal and muscular coats unaltered.

a. Subperitoneal coat.

b. Outer muscular layer.

c. Inner muscular layer, slight small-cell infiltration round some of the vessels.

d. Dense small-cell infiltration in the submucous layer.

e. Granular substance covering the free surface of the ulcer.