LOCALIZED CHRONIC ULCERATIVE ILEITIS

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For the last twenty-five years and during the last decade particularly, there have been sporadic reports in the literature of cases loosely classified under the heading granulomata of the intestine.

Until 1909, when Heinrich Braun referred to a case previously reported by him and collected reports on several other cases, the condition was practically disregarded in both Europe and America. Probably many cases of intestinal granulomata had been seen prior to this time; in fact some had been reported. But the majority of such cases were relegated to a pathological discard under such headings as tuberculomata, malignancies and the granulomata of syphilis, and their true nature never questioned or studied.

In 1909, Braun, pointing out the importance and difficulty of differentiating these intestinal granulomata from neoplasms of the intestine, collected six cases (including two of his own) of this type. The granulomata were situated at various places in the large intestine and the majority caused obstructive symptoms. In most cases a mass could be felt. In none of the cases was the etiology apparent. In 1920, Tietze[6] reviewed all literature on this type of case and added to it several cases of his own. Moschcowitz and Wilensky,[5] in 1923, reported four cases, in one of which the terminal ileum was involved. In 1925, Coffen[4] added a case to the literature and cited previous cases as reported by Braun, Moschcowitz and Wilensky. In 1931, Mock[3] described ten cases of granulomata and, in 1932, Golob[2] reported another case, discussed the subject further, and made some suggestions as to its etiology.

The etiology of the condition is exceedingly obscure. Many cases of granulomata are found apparently arising around a foreign body. Mock believes that they are usually due to a low-grade infection. Golob cited a case in which he believed the presence of a duodenal ulcer with its "constantly irritating influence over the ileocæcal region" might have been a predisposing factor.

Until 1932 no attempt had been made to differentiate a specific entity from the types of cases which had previously been reported. They were simply called intestinal granulomata, and they were found throughout the large intestine, in the omentum and occasionally involving the terminal ileum and proximal cæcum. In 1932 Crohn and his co-workers[1] isolated from this mass of heterogeneous granulomata a specific entity which they called "regional ileitis." In a review of the work by Tietze and Mock they were unable to find a report of a case which approached the picture which they had discussed. In one case reported by Moschcowitz and Wilensky, however,

there was a close resemblance to the type of case they classified as regional ileitis.

Regional ileitis, as described by Crohn *et al.*, is a disease which clinically suggests ulcerative colitis. It is characterized by fever, diarrhœa, and emaciation and eventually leads to intestinal obstruction requiring surgical interference. In all cases a mass is present in the lower right iliac fossa. In all cases the terminal ileum is alone involved. The process begins at the ileocæcal valve and extends upward, involving the ileum usually for a distance of from 20 to 30 centimetres. Often there are fistulæ leading to adjacent segments of the colon and occasionally to the anterior abdominal wall. The etiology of the condition is unknown.

Characteristically, the pathology is as follows: The inflammatory process begins at the ileocæcal valve and usually involves 20 to 25 centimetres of the distal ileum. It is most pronounced at the valve, the process becoming less severe and gradually shading off into normal intestine, proximally. The submucosal, and to a less extent the muscular, layers of the bowel show hyperplastic and inflammatory changes. The walls are thickened, the lumen made smaller. The adjacent mesentery is greatly thickened and fibrotic.

The formation of fistulous tracts into adjacent loops of bowel (sigmoid, cæcum, colon) is common. These fistulæ are preceded by slow perforations giving rise to walled-off abscesses which, if drained, result in intractable fæcal fistulæ.

Microscopically the picture is one of non-specific inflammation and proliferation. In many cases the mucous membrane is destroyed and often replaced by an atrophic layer of epithelium. Giant cells are occasionally seen. They are interpreted by Crohn to be due to a foreign-body reaction to minute particles of vegetable material entrapped in lymphatics during the process of healing.

In half of the cases reported by Crohn, previous appendectomy had been done. It is pointed out that in cases in which no appendectomy had been done, the walls of the appendix showed inflammatory change but the mucosa was normal.

The disease is limited to young adults. Males are more often affected. The disease lasts over months or years. Diarrhœa, fever, loss of weight and anæmia are almost constant features. The temperature is usually intermittent with periods of remission. It rarely goes higher than 103° F. The diarrhœa is the chief complaint. Two to four stools a day of varying consistency, but always containing mucus and often blood and pus, are usually the case. Tenesmus is always lacking.

The authors state that perirectal abscesses, condylomata and peri-anal fissures are never found since the colon and rectum are not involved.

Vomiting, accompanied by pain and visible peristalsis, is present in the stenotic cases. The pain is dull and cramp-like and may be fairly general in the lower abdomen or localized in the right lower quadrant. Occult blood is found in the stools. The white count is usually normal but may be slightly elevated.

The authors list characteristic findings in the physical examination as follows:

(1) A mass in the right lower quadrant. (2) Evidence of fistula formation. (3) Emaciation and anæmia. (4) Evidences of previous appendectomy. (5) Evidences of intestinal obstruction.

The disease may be divided into four types, according to Crohn. In one type the disease simulates acute appendicitis. There are signs of acute intra-abdominal inflammation with an elevation of temperature and leucocyte count, tenderness in the lower right quadrant and occasionally a mass in this area. If operation is done at this time, the terminal ileum is greatly thickened, red, blotchy and surrounded by œdematous tissues. Peri-appendicitis is present, and occasionally one finds an abscess. In another type symptoms of ulcerative enteritis with colicky abdominal pains, diarrhœa, and elevated

temperature predominate. Loss of weight, anæmia, and general weakness are characteristic of the later phases of this type. Clinically it passes slowly into the stenotic type of the disease. In the stenotic type, which is the most common, the symptoms are those of small bowel obstruction of varying degree. Cramps, borborygmus, occasional vomiting, and constipation may be present. In the last type the outstanding feature is the presence of persistent fæcal fistulæ. These fistulæ follow an attempt to drain what are thought to be appendiceal abscesses. Fistulæ, it is pointed out, may develop after the original drainage wound has been healed for several months.

In the röntgenographical examination two observations are of value in the diagnosis. Because of the clinical resemblance of this disease to ulcerative colitis, a barium enema is usually first given. This examination is negative because the disease stops at the ileocæcal valve. A barium meal, however, usually denotes a fluid level in the terminal ileum and delayed motivity in this region. In the stenotic type the delay is pronounced.

Regional ileitis is to be differentiated from ulcerative colitis, ileocæcal tuberculosis, fibroplastic appendicitis, carcinoma of the terminal ileum, Hodgkin's disease, actinomycosis, sarcoma, intestinal or mesenteric tuberculosis and non-specific proctitis.

The treatment of the condition is primarily surgical. Medical treatment is palliative and supportive. Resection of the diseased segment leads to a cure of the condition in all patients surviving the operation.

Case Report.—A man aged thirty-nine was admitted to the Billings Hospital September 19, 1932, on the service of Doctor Palmer complaining of diarrhœa of four years' standing, intermittent abdominal cramps, loss of 49 pounds in four years. Until five years ago he had been entirely well. He then developed a diarrhœa and had as many as fifteen or sixteen thin, watery stools daily. He averaged from six to eight stools daily. This diarrhœa persisted intermittently, with occasional remissions lasting from several days to a month, until his entrance to the hospital. Occasionally there was tenesmus associated with this diarrhœa, and though there was mucus in nearly all the stools, no blood or pus was ever seen. During the remissions, the stools were usually of a normal consistency; however, there were always at least two movements daily. The diarrhœa occurred without relation to the type of food eaten or to the activity of the patient. Associated with this diarrhœa, were abdominal cramps which were partially relieved by defecation and enemata, and an almost constant, dull, aching pain in the lower abdomen, which frequently radiated to the right loin.

The patient's family physician sent him to a nearby hospital for observation. While there gastro-intestinal X-rays were taken, gastric analysis made and stools examined. After three days the patient was discharged, told that there was nothing organically wrong with him, and put on a low-residue diet of milk, cereals, *etc.* He adhered to this diet for six weeks with no relief.

In about August of 1928 he went to a clinic where, after eight days of observation, he was told that he had a fissure in ano. He was advised to rest in the country, eat a normal diet and take retention enemata of warm olive oil twice daily. This advice was followed, the patient remaining in the country for one month. At the end of this time he had experienced no relief. He sought the advice of another doctor in Chicago and remained under his care for three months. During this time the treatment was purely dietary with the exception of enemata given night and morning. After three months of this treatment, during which the patient felt somewhat relieved, he developed an ischiorectal abscess. This was opened and the physician stated that it was due to a fistula and that it would heal spontaneously. The drainage persisted for three months and finally the patient went for treatment to a sanitarium which specialized in rectal disease. During all this time the diarrhœa and abdominal pains persisted intermittently. After eight operations the patient was discharged as cured so far as the fistula was concerned. He went home for about two months. When he left the hospital he felt much better and was having only occasional cramps and diarrhœa. About two months

later, however, the diarrhœa and pains grew worse and he again went to a clinic for examination and treatment.

Before entering the clinic he noticed that he felt feverish. During his five weeks' stay he ran a temperature of from 98.6° to 103° F. The fever persisted until about ten days before his dismissal. While in the clinic the patient developed frequency (about every thirty minutes), burning, and nocturia. He was cystoscoped and told that his urinary symptoms were due to mechanical causes. The urinary difficulties lasted until about three weeks after his dismissal from the hospital.

The patient was told on entering the clinic that a mass could be felt in his rectum and that it could be seen in X-ray examination. Colonic irrigations were instigated and diathermy treatments given. The patient states that as a result of this treatment he felt much better. The diarrhœa and pain disappeared and he gained in weight. He was discharged from the hospital and told to continue the diathermy and irrigations. This he did until January, 1932. After leaving the clinic the diarrhœa and abdominal pain recurred but were neither so severe nor so frequent as before. The patient discontinued the diathermy. After a brief period, pain and diarrhœa became more severe. He again tried diathermy, this time with no relief. He entered this hospital in August, 1932, for observation and treatment.

His past history, with the exception of that which has already been given, was largely irrelevant. His best weight five years ago was 210 pounds. One year before entering the hospital he weighed 143 pounds. He had lost 20 pounds in the last six weeks.

It was brought out in the history that his attacks of pain were much worse at night and that a bowel movement only partially relieved them. Associated with the abdominal pain there was a right lumbar pain, which, though less severe than the cramps, lasted long after they had ceased. In addition to the complaints of diarrhœa, pain, and progressive weakness and loss of weight, the patient stated that for several months he had had frequency of six to eight times a day, nocturia of two times, and dribbling and incontinence which had been growing progressively worse for the last six weeks.

He was a fairly well-developed, fairly well-nourished white male who looked at least five years older than his stated age, and who was not acutely ill. The physical examination was essentially negative except for the following findings:

Heart.—There was a soft systolic murmur over the aortic area which was transmitted up the neck. The heart was otherwise normal.

Abdomen.—The abdominal musculature was well developed and somewhat spastic. There was some generalized tenderness all over the lower abdomen. The entire abdomen was tympanitic. No fluid was found on percussion nor were there any areas of definite dullness. The bowel was distended and vigorous peristalsis was seen to occur at five-minute intervals.

During a typical attack of pain the spasticity of the muscles of the lower right quadrant increased enormously and a definite swelling could be seen in this area. At the same time visible peristalsis occurred and then, accompanied by much rumbling and gurgling, the mass diminished in size and, together with the spasticity of the overlying musculature, disappeared.

Rectal examination revealed the scars of previous operations. At the upper edge of the prostate a large, irregular mass was felt which did not seem to involve the rectal wall. The mass was not ballotable.

Proctoscopic examination revealed a sudden narrowing of the lumen of the rectum at about 12 centimetres as if from pressure from without. The proctoscope could not be manipulated beyond this point.

Laboratory Findings.—Blood: hæmoglobin 92 per cent. Sahli; red blood cells 4,490,000; white blood cells 6,500; differential polymorphonuclears 57; large leucocytes 2; small leucocytes 34; mononuclears 4; eosinophiles 4; basophiles 0. Blood Wassermann and Kahn negative. Urine negative except for 5 to 10 white blood cells per high powered

field on two out of six examinations. Stools negative for blood and mucus on all examinations.

The patient remained on the medical service for nine days after his entrance into the hospital. During this time a gastro-intestinal X-ray was made.

X-ray Report.—Colon fluoroscopy August 22, 1932. With enema the colon fills easily and completely from the rectum to the tip of the cæcum and after vigorous manipulation through the abdominal wall the barium enters the ileum in a fine stream. The appendix is not seen.

Stomach fluoroscopy August 23, 1932. Barium given yesterday is scattered throughout colon. Oral barium is taken without difficulty. The œsophagus and stomach are entirely normal except that the latter is in high transverse position with a posterior bulb. (Figs. 1 and 2.)

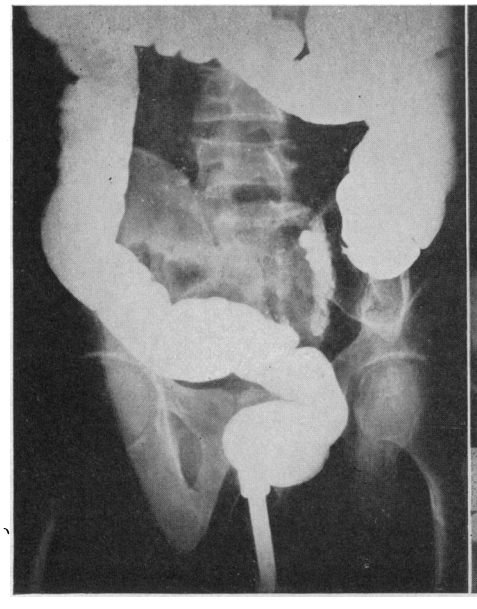

FIG. 1.

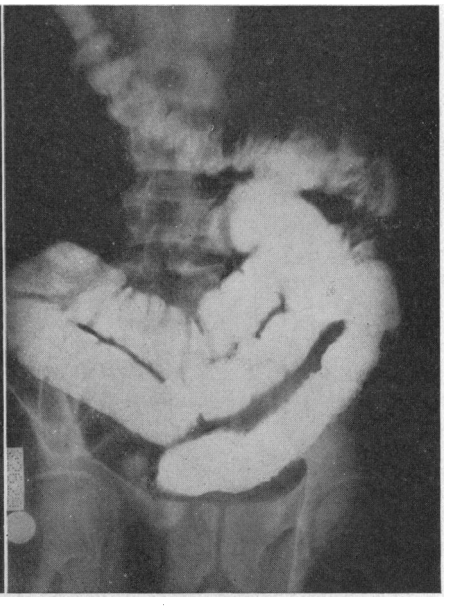

FIG. 2.

FIG. 1.—Barium enema five days before operation showing sharp retention of barium at ileocæcal valve.
FIG. 2.—Barium meal four days before operation, twenty-three hours after ingestion. Note enormous dilation of terminal coils of ileum with typical stepladder arrangement. Stoppage of barium at a point near the ileocæcal valve.

Serial No. 3. Abdomen: Patient prone, six hours after the ingestion of the oral barium. The stomach is empty. The coils of small intestine contain most of the barium and appear enormously dilated. Small amounts are also seen in the colon.

Serial No. 4. Twenty-three hours after ingestion of barium. There is still considerable retention of the barium within the small intestine. Barium is also seen in the cæcum, transverse and descending colon.

Serial No. 5. Approximately forty-eight hours after ingestion of oral barium. The barium has now almost completely left the small intestine and is within the colon. Obviously there is delayed emptying time of the small intestine with marked dilation of it. We have not been able to demonstrate a mass within the gastro-intestinal tract though we can infer the presence of something within the abdomen causing a partial obstruction to the passage of the barium meal. The impression resulting was of a mass (?) within the abdomen causing delayed motility of barium through the small intestine.

While on the medical service the patient was given tincture of belladonna and

deodorized tincture of opium in an effort to relieve his symptoms. Further study of the case was interrupted about a week after the patient's entrance into the hospital by the rapid onset of alarming signs of acute intestinal obstruction which seemed to be located at the ileocæcal valve which had previously been shown to be strictured.

Operation August 27, 1932. Ethylene anæsthesia. Dr. Andrews. Through a right-rectus incision an enormous mass of matted, indurated bowel was discovered in the cul-de-sac. This was freed by finger dissection and the pocket from which it was taken packed with gauze. The mass was then delivered outside the abdomen and found to be composed of terminal ileum. The appendix and cæcum were grossly normal. The ileum, together with its mesentery, was enormously thickened for a distance of about 8 inches above the ileocæcal valve. The ileum above this mass was markedly hypertrophied due to the obstruction. Scattered throughout the mesentery were large, indurated glands, some of which fluctuated. Exploration of the abdominal cavity revealed no signs of tuberculosis. It was therefore decided that the intestinal pathology was due to a low-grade pyogenic infection in the terminal ileum.

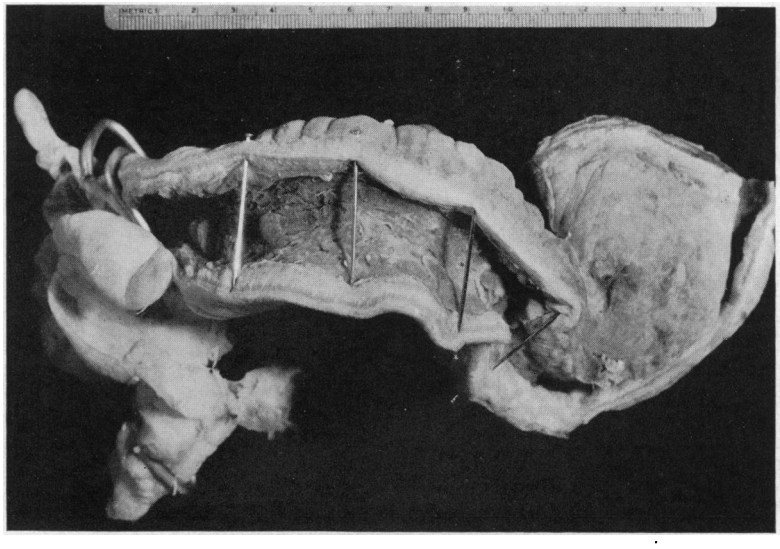

FIG. 3.—Photograph of excised specimen. Note enormous thickness of walls of terminal ileum and normal appendix and cæcum at bottom.

A Mikulicz exteriorization was made and a portion of the cæcum, together with the indurated ileum, was brought outside the abdominal wall and sutured in place. The abdominal wall was then partially closed around the loop of exteriorized intestine.

The next day, under nitrous-oxide anæsthesia, the terminal portion of the ileum and proximal portion of the cæcum were amputated with the actual cautery and a right-angle clamp applied to the spur. The walls of the ileum measured 3 to 4 centimetres in thickness and the lumen was about 1 centimetre in diameter. The wound was partially closed with interrupted silk sutures.

Pathological Report.—Gross.—The specimen is that of terminal ileum, appendix and proximal cæcum. The ileum is enormously hypertrophied and indurated. The attached mesentery is markedly thickened, indurated and hyperæmic and contains many hyperplastic lymph-nodes which display a reddish-gray pulp on cut section. The walls of the appendix and cæcum are slightly thickened.

On cut section, the walls of the ileum, particularly at its distal end, are seen to be enormously thickened and fibrotic (Fig. 3), the lumen being encroached upon. Near the ileocæcal junction the walls measure 3 to 4 centimetres in thickness while the lumen

is only 1 centimetre in diameter. The hyperplasia of the walls becomes gradually less marked proximally, and at about 25 centimetres from the ileocæcal junction the ileum is apparently normal. At various places near the ileocæcal junction, the mucosa is denuded and exhibits shallow serpiginous ulcers with low margins.

Microscopical.—The walls of the ileum are markedly thickened and œdematous. The mucosa is lacking in some areas with the formation of shallow ulcers with overhanging edges. There is a marked diffusive and focal lymphocytic infiltration of the submucosal layers, the normal lymph follicles are hyperplastic and the vessels are engorged. (Fig. 4.) The muscular layer is markedly hypertrophied and exhibits diffuse leucocytic infiltration. The serosa is covered by a thin layer of leucocytes and degenerating fibrin. No granulomas are present in any of the sections.

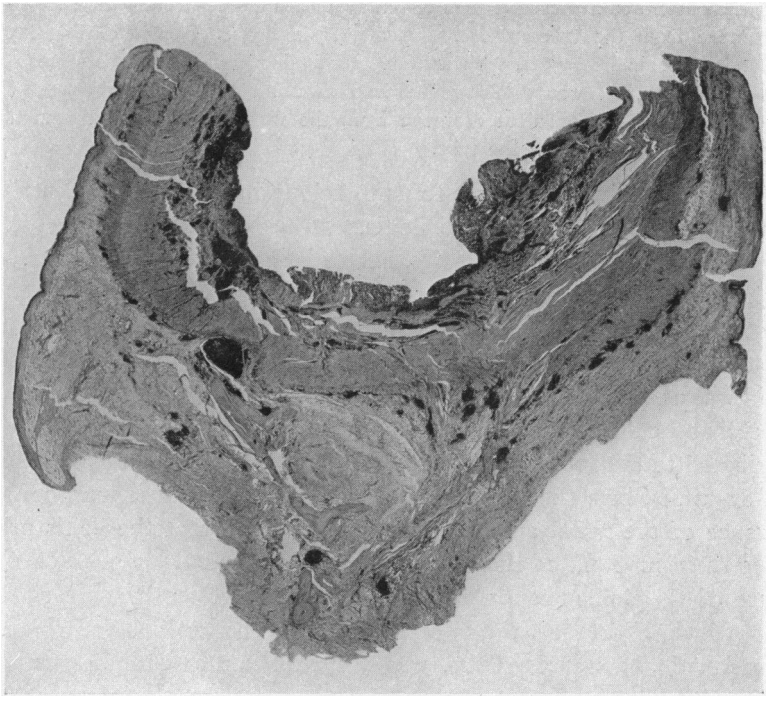

FIG. 4.—2x magnification of section through inflamed area, showing numerous ulcerations, hypertrophy and œdema of outer layers and marked focal collections of lymphocytes.

Sections from the appendix are essentially negative except for a thin layer of fibrinopurulent exudate over the serosa.

Following this operation the patient made a fairly rapid convalescence, his urinary symptoms entirely disappeared, and he regained his appetite and was relieved of all pain. The diarrhœa, however, persisted, probably due to the fact that all the irritated portion of the ileum had not been removed at the operation. The liquid ileostomy drainage was alkaline (Ph 8) and had a marked digestive action on the wound edges, which became excoriated and extremely tender. In an effort to neutralize this fæcal drainage, continuous irrigation with 1/100 N hydrocholoric acid was instigated. This was combined with continuous suction designed to carry away excess fæcal material and irrigating solution. The condition of the wound materially improved under this treatment. In addition to this persistent diarrhœa from the ileostomy there was marked infection

of the wound and considerable purulent drainage, possibly due to the breaking down of the mesenteric glands seen at operation.

It was not considered safe to attempt a closure of the ileostomy in the face of such marked infection.

On the twenty-fourth of October, about a month after the original operation, the patient, who had been up in a wheel chair for two days, suddenly developed all the signs of an acute intestinal obstruction with vomiting, distention, and marked visible persistalsis.

On the following day under ethylene anæsthesia, laparotomy through the old operative wound was done and revealed a fibrous band constricting the ileum just proximal to the ileostomy opening. This was divided, allowing material which had been dammed back in the ileum to well up in the field. A catheter was sutured into the ileostomy opening and the gut closed around it. The wound was then closed around the tube in layers.

Drainage from the tube persisted for about six days. The tube was then withdrawn and the wound strapped with adhesive tape. Healing took place almost by first intention. The patient was discharged November 20, 1932. At that time there was a very small amount of purulent drainage from the wound. There had been no fæcal drainage since the removal of the tube.

Discussion.—This case seems to us to belong in the category described by Crohn and called by him regional ileitis. It belongs in the type which they designate as stenotic. It differs from their cases in several respects. None of their cases had had rectal fissures or fistulæ, as had our case. Tenesmus was not one of the characteristic features of the cases they reported. Furthermore, the formation of fistulæ from the affected gut to adjacent colon or sigmoid was an important finding in their cases which was not present in ours. We feel that the differences between our case and the cases they described may be attributed to the fact that in our case the affected ileum was bound down in cul-de-sac. Since the history of the disease dates back well before the appearance of the rectal abscess, it may be assumed that the ileitis preceded the abscess formation. If this is true, it would seem entirely possible that the presence of this inflammation in the cul-de-sac could easily give rise to an abscess, which, if drained, would cause a persistent rectal fistula, which, as in their cases of abdominal fistulæ, was very difficult to cure because of the underlying inflammatory mass.

Furthermore, the occasional tenesmus which our case had could also be attributed to the proximity of the ileitis to, and its consequent irritation of, the rectum.

The urinary symptoms, so outstanding a feature of our case, were certainly due to pressure and irritation of the bladder by the mass in the cul-de-sac.

Another feature of our case which was due to the position of the involved ileum is the fact that it might be easily confused with non-specific proctitis. In this condition a brawny, indurated mass outside the rectal wall is one of the outstanding features.

The absence of secondary anæmia in our case can possibly be explained by the remissions which our patient had had repeatedly during the course of the disease.

In all other respects the picture is certainly typical of the regional ileitis described by Crohn.

NOTE.—Since this report was written another case of localized chronic ulcerative ileitis has been seen and operated at this hospital. The patient, age twenty-eight, entered the hospital on June 9, 1933, complaining of a tender mass in the lower right quadrant which he had accidentally palpated five days before entrance to the hospital. Two and a half weeks before entrance he had noticed a dull ache which occasionally became a sharp pain in this same region. The pain was rhythmical in character, occurring at intervals of a half minute and lasting for from three to ten seconds. The patient was conscious of this pain for approximately two weeks following its first appearance. It continued during this period with about the same degree of severity. For four days before hospitalization the pain had become much less severe. At no time was there any associated nausea or vomiting, but on careful questioning the patient stated that for the past four years there was a tendency to diarrhœa in the morning. No blood had ever been seen in the stools.

On physical examination a mass about the size of a lemon could be palpated in the lower right quadrant. The mass was tender and freely moveable. Otherwise the physical examination was negative.

Fluoroscopy and X-ray plates revealed a definite filling defect at the ileocæcal junction which was not obstructive but was definitely tender to palpation.

On the basis of physical examination and X-ray findings a tentative diagnosis of neoplasm or granuloma of the cæcum was made. Because of the tenderness demonstrable both at physical and fluoroscopic examination the latter diagnosis was thought to be the more probable.

On entrance to the hospital the white blood cells were 10,000; red blood cells 4,900,000; hæmoglobin 85 per cent. (Sahli); pulse 100; temperature 98.6; urine negative.

On June 10, 1933, a laparotomy was done by Doctor Phemister through a right rectus incision and a hard mass found at the ileocæcal junction. Several large, indurated lymph nodes in the adjoining mesentery could be palpated, in a line extending medially and upward. The terminal ten centimetres of ileum and proximal fifteen centimetres of cæcum and ascending colon were resected and a side-to-side anastomosis made.

A frozen section at the time of operation was diagnosed as being suspicious of lymphosarcoma.

The patient made an uneventful recovery and was discharged two weeks following the operation.

The bowel resected at operation showed the following gross pathology: On opening into the lumen of the ileum the wall was found to be markedly thickened and a redundant portion of the mucosa extended for a distance of about one centimetre through the ileocæcal valve. A superficial longitudinal erosion of the mucosa of the ileum two and a half by one centimetre was found which ended sharply at the cæcum. The appendix was abnormally long and curved on its mesentery in a semi-circle but was otherwise grossly negative. A mass of enlarged lymph glands was present on the posterior medial aspect of the ileocæcal junction. The largest of these nodes measured two and a half centimetres across and the smallest eight millimetres. On cross section these nodes appeared homogeneously grayish white. The cæcum and colon were grossly normal.

Microscopically the picture is one of non-specific inflammation. The mucosal ulcer is shallow and has sharp margins. The mucosa adjacent to the ulcer and proximal to it for a distance of approximately ten centimetres is hyperæmic and infiltrated with polymorphonuclear neutrophiles. A markedly hyperplastic Peyer's patch appears at one margin. The wall of the ileum beneath and beyond the ulcer is two to three times its normal thickness and exhibits fibrosis with a marked diffuse and focal infiltration

consisting largely of round cells and polymorphonuclear neutrophiles in almost equal numbers. At a distance of six centimetres from the mucosal ulcer the serosa is moderately infiltrated in the same manner. This polymorphonuclear infiltration may also be seen at the tip of the appendix but does not extend through the muscularis or serosa. The cæcum and ascending colon are microscopically essentially normal. There is no evidence of tuberculosis or neoplasm in any of the sections examined.

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