CHRONIC STENOSING REGIONAL ENTERITIS SURGICAL PATHOLOGY AND EXPERIENCE IN SURGICAL TREATMENT*

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In 1934, two years after the original description of regional ileitis by Crohn, Ginzburg and Oppenheimer,[1] our first opportunity to operate on such a case arose. In the following 14 years, we have operated on 30 patients with regional enteritis or ileocolitis. In conjunction with the Department of Gastroenterology of the Graduate Hospital, we have carefully followed the progress of these patients. With the passage of time, we have had a splendid opportunity to appraise the results of the therapy of the earlier cases. The immediate results were very encouraging. However, with longer and more adequate follow-up, it became evident that the good results were not always permanent. We were forced to reoperate upon many of these patients because of recurrences or progression of the disease. Others manifested clinical or roentgenographic recurrences, but were maintained by intensive medical regimens. These recurrences took place, in spite of the fact that we employed a very radical operative approach and performed resection of the diseased bowel whenever possible.

Since the description of the disease by Crohn *et al.*,[1] and the histologic description by Hadfield,[2] very little has been added to our understanding of the etiology or pathogenesis of regional enteritis. A review of the pathology as we have seen it might therefore be of interest. From our observations of the gross and microscopic pathology, we believe that regional enteritis, ileocolitis, and regional colitis are manifestations of the same disease in different segments of the intestine. This does not include ulcerative colitis which first involves the sigmoid or rectum in 95 per cent of the patients[3] and is a different entity clinically and pathologically.

In our series, we have seen five types of the condition classified as to location. They are: regional duodenitis, jejuno-ileitis, terminal ileitis, ileocolitis and regional colitis. In four patients, the lesions have been confined to the jejunum or ileum (not terminal). Eight patients had involvement of the terminal ileum. Fifteen cases were examples of ileocolitis. In two patients, the site of involvement was limited to a segment of the colon, and in these there was no disease in the sigmoid-rectum characteristic of distal ulcerative colitis. In one case, the duodenum was involved in a process which grossly resembled chronic stenosing regional enteritis.[4] To our knowledge, a lesion of this nature in this area has not been reported previously.

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We have recognized three phases of this condition: the acute, the chronic and the chronic with complications.

The mimicry of acute appendicitis by regional enteritis is well known. We have operated upon patients for acute appendicitis and found the appendix normal, but the ileocecal area involved in the acute phase of regional enteritis. In one, the serosa of the distal ileum was markedly hyperemic; its texture was fine granular; the subserosal tissues were edematous; and the glands in the adjacent mesentery were enlarged and hyperemic. Appendectomy did not relieve this patient of her symptoms, and roentgenographic survey a month later confirmed the presence of ileocolitis.

The abdomen in the acute phase usually contains a small amount of free fluid. This may be serosanguineous, clear, or turbid, depending upon the presence of exudate. The site of involvement may be any of the four previously described. The serosal vessels are injected and the bowel is fiery red and the serosa is covered with a thin fibroplastic exudate. The diseased loops "stick" together with thin friable, fibrinous adhesions and the wall of the bowel is definitely edematous. The mesentery of the involved segment is hyperemic and moderately edematous, and its surface seems to "weep" fluid. The mesenteric glands are enlarged and congested, though the degree of enlargement varies, and some may attain a diameter of 2 cm. The color of the glands ranges from pale pink to deep red or a violaceous hue. In some instances, these enlarged glands are confined to the mesentery of the diseased segment of intestine; in others, they may be widely scattered throughout the entire mesentery from its base to its bowel attachment. We have not observed the acute phlegmonous type with perforation as described by Homb.[5]

Histologic descriptions of the acute phase have been few because resection of diseased bowel is not attempted at-this time. Homb[5] describes the picture as an infiltration of all layers by inflammatory cells: lymphocytes, leucocytes (many of them eosinophilic), large mononuclear and plasma cells. This is characterized by an enormous edematous thickening of the submucous coat and dilatation of the vessels is noted. The mucosa in this stage may be intact, or shallow ulcerations filled with mucopurulent debris may be present, though usually small.

In one patient, we made a preoperative diagnosis of subsiding acute appendicitis and found, at laparotomy, an acute ileocolitis which appeared to be subsiding. The lesion was resected contrary to our usual practice. When the bowel was opened, three large ulcers were found, just proximal to the ileocecal valve, the smallest of these measuring 1 cm. in diameter and the largest 2 cm. The edges were not overhanging; the bases were shallow and filled with mucopurulent exudate; and the mucosa between was hyperemic and markedly edematous. No evidence of involvement of the subserosal lymphatics was present.

When the chronic phase of this disease is reached, the gross picture changes. The involved bowel is thickened and stiff, and it has been adequately described as "hose-like." The serosal surface may be covered with a fibro-

plastic exudate as seen in the acute phase, but often this has become organized into thick fibrous tissue which is contracted and stenoses the bowel. A striking feature is the overgrowth of the mesenteric fat on the serosal surface, which tends to encircle the diseased segment of small bowel; and frequently none of the antimesenteric border is visible in the area of greatest involvement. We have not observed this in the colon. The bowel proximal to the stenotic area may appear to be entirely normal, or, if some obstruction exists, it will be dilated. The change can be an abrupt one. Usually this proximal bowel is hyperemic for a few inches orad and has some sticky exudate on its serosal surface.

Palpation of the involved area in a classic case reveals a "rubbery" or "boggy" feel, with marked thickening, and the lumen seems absent. This can be compared to the normal, soft, velvety feel of the bowel above. In Crohn's original description, this was most marked in the ileum adjacent to the ileocecal valve; however, we have observed marked involvement in other portions of the jejuno-ileum or colon. We have seen as many as five different areas of involvement in a single patient, each separated from the other by normal ileum. The occurrence of these so-called "skip areas" is well recognized.

The mesentery of the diseased bowel is usually thick, edematous, and rubbery. The mesenteric vessels are not visible, and in cases with extreme thickening, the pulsations may not be palpable. The nodes are almost always enlarged as in the acute phase, and they are discrete, soft and fleshy.

When the bowel is opened, the mucosa appears hemorrhagic, the villi edematous and bulbous, and this hypertrophy gives a "cobblestone" appearance to the mucosa. The hypertrophy may be so marked that the mucosa is polypoid. Varying amounts of mucosal ulceration and destruction are present and the ulcers are often shallow, discrete and contain a dirty grey necrotic exudate. These ulcers tend to occur on the mesenteric side of the lumen, but we have seen them at any location on the wall. In the areas of greatest ulceration, the induration and cicatrization of the bowel wall are most marked. There may be regions of attempted healing of the mucosal defects, and here the mucosa is atrophic, flat and glistening.

The thickening of the bowel is tremendous and gives rise to a marked narrowing of the lumen. Grossly, all coats are thickened but the submucosa shows the greatest increase. As one passes up the bowel, there is a progressive enlargement of the lumen and decrease in breadth of the wall. The limits of the overgrowth of the antimesenteric fat often coincide with a termination of the mucosal ulceration and bowel thickening.

The chronic stage may be complicated by the presence of obstruction, peritonitis, abscess formation and fistulas. Obstruction has its origin in contracture of the stenotic areas, and dilatation and edema of the proximal bowel is noted. Peritonitis of the spreading type from a free perforation has not occurred in our series; the extreme thickening of the submucosa probably forms a strong barrier against rapid perforation of an ulcer. Perforations usually occur late in the course of the disease and are walled off to form a

localized abscess. Burrowing into the mesentery is common. This abscess, together with the involved ileum and mesentery, forms a rather firm inflammatory mass which may be in the pelvis or along the vessels in the iliac fossa. These abscesses may perforate into adjacent bowel loops that are matted together and result in internal fistulas, and these may invade any of the hollow visci; in one case, an ileosigmoid fistula was present. These fistulas may burrow externally through the abdominal wall.

The appraisal of the extent of colonic involvement in ileocolitis has not been easy in many of our patients. At times, the terminal ileum and cecum show distinct evidence of advanced disease, but there is no abrupt termination of the process in the colon when external examination is made. There may be a slight suggestion of congestion and edema of the wall of the colon with no involvement of the mesentery, yet when this colon is opened, its mucosal surface may abound with small ulcerations. This was met with in one of our recent cases.

The colon that is extensively involved will show the same thickening and contraction of the wall as is seen in the small intestine, and fibroplastic or fibrostenotic exudate may appear on its serosal surface. In our experience, the mesentery is not as thick and edematous; it often is firm and shortened due to fibrosis. The presence of visibly affected glands varies, and in several of our patients with advanced colonic disease, only minimal lymph gland involvement was noted. In one case of ileocolitis, the right half of the colon was much more destroyed than was the terminal ileal segment, yet the lymph glands in the mesentery of the small intestine manifested the greatest enlargement and inflammation.

The complete classical picture of the gross pathology is not present in every case. It should be stressed that many variations occur and are a source of confusion in the determination of the limits of the disease. Perhaps this contributes to the high rate of recurrence following resection because the lesion is not always completely eradicated. For example, some cases do not show marked thickening and narrowing of the bowel, but have a soft, flabby wall with no diminution in the size of the lumen, and serosal exudate may be entirely lacking. One may see great thickening of the mesentery with little or no overgrowth of fat on the serosal surface of the bowel. Lymphadenopathy may range from minimal to widespread. Furthermore, the picture in the chronic stage may be complicated by a superimposed acute exacerbation of the process.

The microscopic appearance of the bowel wall in chronic stenosing regional enteritis has been most adequately described by Hadfield.[2] He has stressed the thickness of the submucosal coat as being directly proportionate to the thickness of the bowel wall, and has stated that hypertrophy of the muscular coat is inconstant and variable in degree and is usually prominent only in the late stages of the disease. The submucosal lesion is characterized by hyperplasia of the lymphatic tissue and an obstructive lymphedema, the former being

non-specific in type. He emphasized the replacement of the germinal centers making up a nodule of lymphadenoid tissue by a marked proliferation of the reticulo-endothelial cells. In the middle of these cell systems, Langhans' type of giant cells are often seen. These clear-cut giant-cell systems resemble miliary tuberculosis without caseation. The same picture is noted in the available lymph glands. As mucosal ulceration progresses, secondary inflammation occurs, and the giant-cell systems may be obscured by a secondary lymphadenitis characterized by diffuse inflammation and fibrosis.

In some of our cases, the mucosal lesion has been striking. Aside from the superficial ulcerations with diffuse cellular exudate and secondary inflammation of the craters, other changes of the mucosa are noted. Mucosal hypertrophy is often a prominent feature and this is particularly marked in the villi, where hyperemia and new blood vessel formation may be seen. Regions of interstitial hemorrhage may be evident, and fibroplastic activity is present in the mucosal layer, which may be in degree enough to amount to frank scar formation.

This histologic picture has not been limited to the small intestine and its mesentery in our cases of ileocolitis. We have identified the same lesion in the colon and its mesentery. The hyperplasia of the lymphoid tissue is not as marked as in the terminal ileum because of the progressive decrease in the amount of lymphoid tissue in the submucous coat of the colon from the cecum caudad.

In considering the surgical treatment of this disease, it is necessary to define the stage of the pathological process: that is, the acute or the chronic phase with or without complications. A remission of the acute stage can often be obtained by rigorous medical management if an abscess or obstruction has not developed. Even when these complications arise, there is occasionally a subsidence of the acute phase while the patient is being prepared for operation. A regression of the acute stage is not always followed by stenosis or other sequelae. Some do not progress to obstruction, abscess formation or fistulization. It is in this category that we believe rigorous medical management, as outlined by Bockus,[6] may have as much in its favor as surgical intervention. No operation should be attempted in a patient known to be in the acute stage of this condition without complications.

In the cases that simulate acute appendicitis, exploration is advisable to rule out a pathological process in the appendix. If the appendix is found to be normal, and an uncomplicated acute ileocolitis exists, it is best to terminate the procedure. Many believe that removal of the appendix under these circumstances is often followed by fistulas because the disease is actually present in the cecal wall and is not recognized. Because of the likelihood of remission and the lack of preparation of the patient, we do not advocate resection of the lesion during this stage. In fact, three of the 17 cases reported by Pugh[7] were of this type and all subsided after laparotomy without definitive surgery. If the picture is complicated by an abscess, drainage is necessary.

In the surgical management of the chronic stage, two types of operation are employed. One consists of resection of diseased bowel and primary anastomosis. The other procedure is a transection of the ileum above the site of the lesion and anastomosis of the normal ileum to the colon distal to the lesion. The ileal stump just above the lesion can be closed or it can be brought out through a stab wound as a mucous fistula to act as a safety-valve if the terminal ileum is partially obstructed.

TABLE I.—*Results of Radical Resection*

Total number of resections		24
Operative deaths	2	
Cases followed less than 1 year	7	
		9
Cases closely followed from 1–14 years	15	
Number of proved recurrences	11	
Recurrence rate	73%	

In our earlier experience with this disease, we assumed that wide excision of the involved ileum or colon would result in a cure. A long segment of terminal ileum approximately two feet above the level of the disease and the proximal half or two-thirds of the colon were usually resected. In two patients, all of the ileum and right half of the colon were removed. The mesentery was excised as close as possible to its base. It was often impossible to remove every vestige of thickened mesentery and involved lymph glands without endangering the blood supply to the remaining bowel. We thought that removal of the diseased bowel would allow the process in the remaining mesentery to subside. An early favorable response to this type of operation caused us to continue with the method of attack; however, later follow-up observations revealed that recurrences took place after the most radical resections.

TABLE II.—*Time Elapse Between Resection and Recurrence*

	Number of Cases
1–2 years	5
2–3 years	3
3–5 years	1
5–10 years	2
Total	11

Resection of the diseased bowel was performed in 24 of the patients with two deaths—an operative mortality of 8.3 per cent. Five of the resections have been followed for less than a year and should be excluded from the series when results are considered. This is important because all but one of our recurrences took place after one year had elapsed. One patient died of malnutrition one month after operation, and another patient was committed to an asylum and lost for follow-up purposes. There remain 15 patients who

have been carefully followed from one to 14 years. Eleven recurrences, based on clinical and roentgenographic examination, have taken place in those 15 cases—a recurrence rate of 73 per cent. (Tables I and II).

These discouraging results have caused us to modify our views; and in the past two years we have elected to use ileocolostomy with exclusion of the diseased bowel in six cases. The results of Garlock[8] and Colp[9] with this type of operation have been exceptionally good, and the surgical mortality from this operation is very low.

The cases of chronic stenosing regional enteritis which are classified as complicated are best treated by the short-circuiting and exclusion operation. The case with a large abscess walled off by adjacent loops of diseased bowel and complicated by an infiltrative process in the mesentery cannot be resected safely. Large obstructing inflammatory masses can also be treated by a side-tracking operation with less hazard. Similarly, when the diseased bowel is densely adherent to the posterior parietes or to the vessels along the lateral pelvic wall, it is unwise to attempt a resection. Internal and external fistulas are further indications for ileocolostomy with exclusion.

The six cases in which we performed this type of operation were all complicated ones. Two had had radical resections before but had developed recurrences. In addition, a gastro-jejunostomy was performed on the patient with duodenal involvement. Four of these remain symptom free after a two year follow-up. In one case, a transection of the terminal ileum and ileotransverse colostomy with exclusion was performed. One year later there was a definite recurrence in the ileum proximal to the anastomosis. She was reoperated upon and the ileum was transected above the site of the recurrence and anastomosed to the distal transverse colon. The distal stump of transected ileum was brought out as a mucous fistula. The inflammatory mass present in the right iliac fossa at the first operation had entirely disappeared. All gross evidence of disease in the excluded ileum had disappeared. This section of bowel was found to be soft and collapsed and the serosa was pale and shiny. No enlarged glands were present in the mesentery. The entire colon appeared normal. Six months after the second operation, her disease again became active, and roentgenographic study revealed a second recurrence at the anastomotic site. She was again explored, and the colon distal to the anastomosis was markedly involved. This is of interest because the process had previously been confined to the small bowel, but recurrence took place in the colon. An ileostomy was necessary to divert the fecal stream from the diseased bowel. She died three months later of inanition.

The presence of widespread mesenteric lymph gland involvement is an indication for the exclusion operation. Cases with extensive involvement of the small intestine or multiple "skip areas" should be treated conservatively. One of our cases was operated on by a surgeon well trained in the recognition of this process. Four skip areas were present in the ileum; therefore, he closed the abdomen without any surgical attack on the lesions. She was treated

medically for three years and finally died following our attempt to relieve a multiple obstruction. We believe that his keen judgment allowed this patient three years of uncomplicated survival.

Occasionally a case with involvement of the colon from the ileo-cecal area to the sigmoid is seen. In such a case, we elect to do an ileostomy well above the site of the disease in the ileum. If the lesion becomes quiescent and does not progress into the distal sigmoid, restoration of bowel continuity by ileosigmoidostomy may be attempted. It is wise to observe these cases for a period of two to three years before restoring the continuity of the bowel. One case had an extensive enteritis in the terminal ileum complicated by an obstructing mass adherent to the sigmoid colon. The sigmoid was involved by contiguity. An ileostomy was made above the lesion. He improved markedly, and three years later, he insisted that the ileostomy be taken down. At the second operation, the distal sigmoid was found to be partially obstructed by scar tissue. Therefore, the terminal ileum was anastomosed to the ascending colon, and a colostomy proximal to the sigmoidal obstruction was performed. We reasoned that a left-sided colostomy would be easier for the patient to care for than a high ileostomy, and the colon from the cecum to the sigmoid had been free of involvement. At the second laparotomy, it was noted that the excluded ileal segment which had been badly diseased, appeared normal. The mass along the sigmoid and the fistulous tracts had all disappeared. The only evidence of old inflammation was the contracted scar on the distal sigmoid colon. When the abdomen was opened at the second operation, the ileum proximal to the ileostomy appeared normal. However, after the slight trauma of inspection and palpation, the serosal surface became edematous and hemorrhagic. Therefore, a segment 35 cm. in length above the ileostomy was excised and the remaining ileum was anastomosed to the ascending colon. When this resected segment of ileum was opened, small mucosal ulcerations were noted and microscopy revealed the typical tubercle-like nodules in the lymphoid tissue of the submucosa. We believe that this man will have a recurrence at the anastomotic site.

SUMMARY

1. The surgical pathology of chronic stenosing regional enteritis as we have observed it has been reviewed.

2. In our early experience with this disease, we performed radical resection of the diseased bowel with the hope that a cure would result. In the ensuing years, recurrences took place in such a large percentage of the cases, that we are convinced that resection is no longer the procedure of choice.

3. The less radical procedure advocated by Garlock has accomplished as much, and even though we have had recurrences from this type of operation, it is attended with much less morbidity and mortality.

4. It is difficult to understand our large percentage of failures following resection when the results are compared with those from other clinics practising resection. Our cases have all been carefully followed by the Depart-

ments of Surgery, Gastroenterology and Radiology. Under such close scrutiny, some who were clinically well were eventually found to present some evidence of recurrence. We can only assume that longer and more intensive follow-up surveys in series from other clinics will reveal a higher recurrence rate.

5. As a result of our experience with this condition, we believe that surgical intervention should be confined to those cases complicated by obstruction, abscess, fistulas, and those in which a most thorough medical regimen has failed.

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