# ILEOJEJUNITIS

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ILEOJEJUNITIS may be defined as the subvariety of regional enteritis in which the granulomatous process typical of that disease extends to involve the upper ileum and the lower or whole of the jejunum.

The original descriptions of regional ileitis concerned the form of ulcerous and hyperplastic inflammation in which the terminal loops of the small intestine, just proximal to the ileocecal valve, are implicated.[1, 2, 3] It was soon recognized that the pathologic process, while presenting its most typical aspect in the terminal ileum, was not restricted to that area; it could and did extend, in a limited number of cases, to the higher loops of small intestine and also, on occasion, transcended the valve to involve the cecum and colon.

It is appropriate to recognize that the clinical picture of upper ileojejunitis is somewhat different from terminal ileitis, bearing its own clinical, pathologic, and roentgenographic characteristics. While allowing it to remain within the category of regional enteritis, upper ileojejunitis has certain clearly recognizable and distinguishable settings.

To contrast the two forms, *terminal ileitis* is marked by a localized granulomatous mass; by numerous external and internal fistulae; by perirectal abscesses; by obstructive intestinal phenomena; and a low-grade febrile clinical course with slowly progressive inanition. The localized process is highly amenable to surgical intervention.

*Ileojejunitis* is the same ulcerative granulomatous disease extending orally for a variable distance to and including the jejunum, but without the mass, usually without fistulae or rectal complications, without obstructive phenomena. It is, in general, not favorable to surgical help. The course is low-grade, often less severe; a considerable degree of healing under conservative medical therapy is possible, though a complete anatomic restitution to integrity of the bowel is not conceivable.

*Etiology.*—To date, our experience with regional ileitis or enteritis approximates almost 200 cases. Out of this large number we are able to separate 17 examples of diffuse or high ileojejunitis. The latter serve as the basis for this report. It is immediately obvious that, in comparison with terminal ileitis, ileojejunitis is a less common form, occurring in proportion approximately one to ten of all granulomatous cases.

The age incidence in ileojejunitis is again one of youth, the average age at observation being 25½ years (terminal ileitis 27½ years), the range ex-

Submitted for publication July 26, 1940.

tending from a child of nine years to a maximum seen in a man of 70. Males predominate in the proportion of over two to one, 12 males to five females.

As regards the direct etiology of the disease, no further or new knowledge is available. The process is definitely not tuberculous, either by culture, histology, staining, or by animal inoculation.

In two instances we were able to recover a *Shigella dysenteriae* of the Flexner variety from the stool of the patients, proven by culture, reactions on sugar media, serum agglutinations, and absorptive phenomena carried out on the cultures.

Ileitis as a disease may be a clinical variety of dysentery, or at least at its initiation it may originate as a dysentery infection. If so, then the difficulties in discovering and recovering viable dysentery organisms from the stools of chronic cases is obvious to anyone familiar with the bacteriologic aspects of epidemic dysentery. In a recent endemic of typical dysentery in the personnel of the Training School for Nursing, of the Mt. Sinai Hospital, during the summer of 1939, over 250 cases were observed and studied. Positive dysentery cultures of the Newcastle strain were recovered in a large percentage of the cases (79.4 per cent), but only in the first one to three days of the onset; after that initial period, cultures of the stools were almost uniformly negative.

If ileitis is dysenteric in nature, then the difficulty of obtaining cultures in cases which have already run a course of from one to 14 years, before coming under observation, is self-evident. The ability to recover, in two of the 17 cases of ileojejunitis, viable Flexner organisms, is certainly striking. Again, one of the cases seen was a younger brother of one of the 14 original cases[1] of terminal ileitis. The brothers had lived together for some time, and the possibility of a transfer infection, through food handling and careless toilet hygiene must be considered. This latter instance is now one of five examples of ileitis in siblings, among whom, two, and in one instance, three members of the same family were affected.

On the other hand, to date, as far as we know, none of the 250 nurses, involved in the hospital epidemic of 1939, have developed any sequelae or evidence of any chronic symptoms of the malady, either as chronic colitis or as ileitis.

*Pathology.*—The pathology of ileojejunitis varies only slightly from that of regional ileitis. It is a granulomatous and ulcerating, nonspecific inflammation, in which all of the coats of the intestinal wall, particularly the submucosa, undergo a granulomatous, proliferative change. The overlying mucosa undergoes a process of linear necrosis, paralleling the extension of the ulcerative process. Miliary-like tubercles consisting of lymphoid and epithelioid mononuclear cells are common and frequently enclose giant cells, probably of foreign-body nature.

Grossly, dense mass formation in ileojejunitis is unusual, nor does the process concentrate on any one area to produce a large granuloma with encroachment upon the lumen of intestine, as is seen in terminal ileitis. The

process is more diffuse, a large part of the small intestine is usually involved (except for the duodenum) by numerous "skip-areas," separated by large-spaced distances of free mucosa. The process does not reside in one place long enough to create obstruction to the lumen or to originate fistulous tracts; instead, the disease seems to disseminate its power, continually advancing upward by kangaroo-like jumps to involve higher intestinal segments (Chart 1). Enlarged mesenteric lymph nodes accompany the extension of the dis-

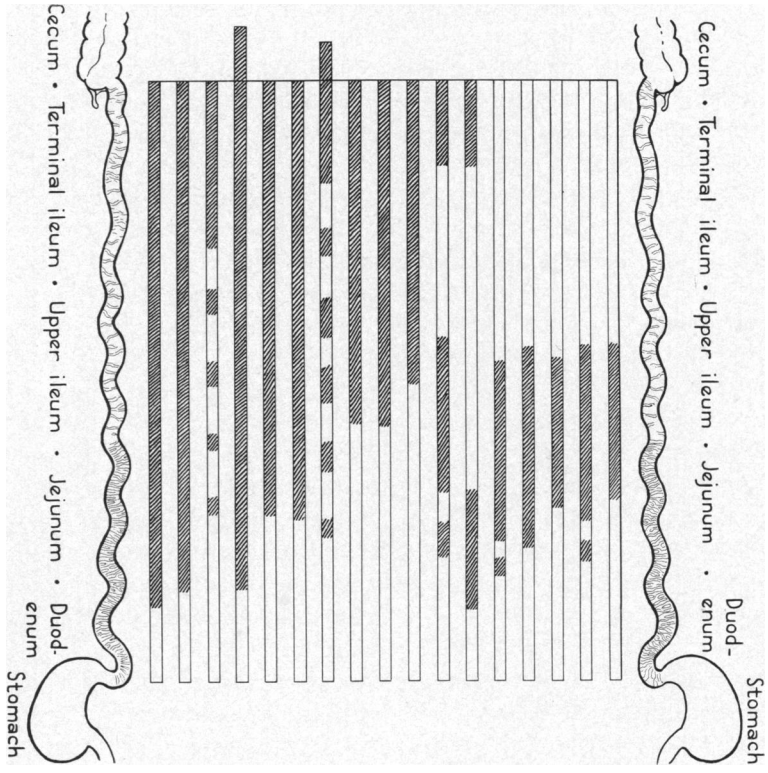


CHART 1.—Demonstrating, graphically, the anatomic distribution of the lesions in diffuse or high ileojejunitis. (Shaded areas denote the extent and location of the pathologic involvement.)

ease, though the nodes in the mesentery of the upper ileum and jejunum rarely achieve the massive and succulent proportions seen in the mesentery just proximal to the ileocecal valve. Whether the extension of the malady to new intestinal areas is achieved by mucosal transport or by invasion of the lymphatics is still controversial.

In only two cases were fistulous tracts observed; in one, an ileorectal fistula, in another, an ileo-ileal fistula occurred. External fistulae to the abdominal wall were not observed, even though the recent scars of an exploratory celiotomy existed in five cases (in contrast to regional or terminal ileitis).

*Symptomatology.*—The onset is usually gradual (15 cases), the duration

of the symptoms, when first seen, being from six months to 14 years (average, three and one-half years). Only two cases presented an, apparently, acute onset: one, with gross hemorrhage, the other, with an acute febrile course. Both cases, when seen, were, however, already well-advanced in the chronic phases of the disease. Four patients had previously undergone an ineffectual appendicectomy.

The outstanding symptoms in all cases were: (1) A low-grade febrile course. (2) Abdominal pain, often amounting to severe cramps. (3) Diarrhea. (4) Gross hemorrhage. (5) Anorexia. (6) Marked loss of weight.

The temperature remained within normal range in six instances, and was elevated to 100° to 104° F. in the remaining 11 cases. The fever was irregular in nature, sustained often for several days or weeks, or alternating with periods of apyrexia.

Abdominal pain and cramps were universally present—diffuse, moderate at times, severe at others; ranging over the lower abdominal segments and periumbilical region. Paroxysms of severe cramp-like pain were common in both lower right and lower left iliac quadrants, usually followed by a diarrheal movement. With the passage of the fluid feces and gas, accompanied by an audible gurgling, the cramp was allayed. At times, the paroxysms called to mind low-grade intestinal obstruction, though none of the 17 cases ever came to operation because of suspected obstruction.

Diarrhea was universally present, two to four or six stools per 24 hours. This diarrhea is less severe than is seen in ulcerative colitis; the stools are mushy, or semisolid, and when more frequent, actually watery, containing mucus, but no pus, and only occasionally blood. At times, constipation alternated with diarrhea. It is of interest that the guaiac reaction in the feces was positive in ten cases, but persistently negative in five cases. Gross hemorrhage was present in three patients, in one, as the initial symptom.

Anorexia was a common manifestation, particularly in the febrile cases, and was associated in all instances with a marked loss of weight. The average weight loss amounted to 17½ pounds, the extremes ranging from four to 40 pounds. During the healing phases, after the initial stages of severity have passed, actual gains of 15 to 25 pounds of body weight have been observed.

Nutrition is usually poor, the skin dry, the mucous membrane pallid. An aphthous stomatitis was observed twice, and in one of these patients recurrent aphthous ulcers were accompanied by bleeding gums. Except for these manifestations of hypovitaminosis no striking clinical changes characteristic of vitamin deficiency were observed.

The degree of anemia was not marked; in one case, a low of 50 per cent was reached, but many patients preserved a hemoglobin ranging between 75 and 94 per cent. One patient had a macrocytic hyperchromic type of anemia, with a color index of 1.3. This individual had been treated as a case of sprue until a gastro-intestinal roentgenologic study showed the characteristic changes of ileojejunitis; interestingly enough, and in contrast with sprue,

the macrocytic anemia improved only slightly with daily injections of liver extract—a maximum reticulocyte response of only 7 per cent being attained. The remaining patients with anemias presented blood pictures of the microcytic hypochromic variety.

The leukocyte count in ileojejunitis was usually within normal limits, the highest (which was most unusual) being in one instance 12,900, and in another, 18,000 cells. The differential count was noteworthy of deviation from the norm in that a relative or absolute eosinophilia was present in five patients, the highest content being 14 per cent.

Oral glucose tolerance tests were performed on seven patients, and in five, flat curves consistent with poor absorption were obtained. The erythrocytic sedimentation rate exhibited varying degrees of acceleration in five patients (22 to 50 minutes—normal being 60 minutes or more). Sedimentation rates were increased in three of Snapper's[6] six cases of chronic ileitis. The total protein in the blood plasma was appreciably lowered (5.8 Gm.); in three cases, reaching a minimum of 4.0, 4.4 and 4.5 Gm. per 100 cc.; the albumin-globulin ratio was persistently disturbed, approaching a ratio of one, but never completely reversed. The urea, blood sugar, and phosphorus in the blood plasma were within normal ranges. The blood calcium was reduced in one patient; another patient showed an osteoporosis of the pelvis, thought to be due to loss of calcium in the stool. Improvement was noted following calcium therapy. Gastric analysis showed normal acidity titers in all cases except in one instance in which a true achylia was present.

Tuberculin reactions (Mantoux and von Pirquet) were negative. Dysentery agglutinations for B. Flexner, Hiss, Shiga, Mt. Desert, and Sonne were negative in eight patients, and the blood Wassermann reaction was negative in all. Roentgenograms of the lungs in many cases were entirely negative.

*The Physical Examination.*—The physical examination of the patient, apart from malnutrition and pallor, evidenced tenderness over the entire abdomen, frequently more marked in the lower segments. A mass was never felt, nor were external abdominal wall fistulae observed. Visible peristalsis was not present. The edge of the spleen was occasionally palpable, soft and sharp.

The rectal examination was always negative, this again contrasting with terminal or regional ileitis in which a pelvic mass or induration is frequently palpable and corresponds to an involved localized granuloma with localized peritonitis and diffused fistulous tracts. Sigmoidoscopy was always negative.

*Roentgenologic Studies.*—The diagnosis of ileojejunitis, being marked by the lack of physical signs, rests mainly on roentgenographic evidence. The barium enema is usually the first procedure, for in every case of persistent diarrhea, the primary interest rests in recognizing or excluding an ulcerative colitis. A negative sigmoidoscopy does not exclude the possibility of a right-sided segmental colitis, the evidence of which is clearly demonstrable following a barium clysma.

In most cases of ileojejunitis the opaque enema is negative (15 out of 17

observations). In one instance a persistent cecal spasm, in another, definite spasm and deformity of outline in the transverse and descending colon gave warning of colonic participation in the process; this was confirmed at celiotomy.

The eventual diagnostic procedure was, and is, the barium meal, as performed with a reduced amount of barium (four ounces or less), and with frequent fluoroscopic observations and roentgenograms. When properly carried out, the roentgenographic demonstration of the disease is, and should be, a relatively simple task.

By roentgenologic studies following a barium meal, the degree and extent of ileal and jejunal involvement are definable with a good degree of accuracy. The lower jejunum and upper ileum were always seen to be involved; in five instances, the terminal ileum seemed to be exempt from the process. In two cases, six to seven inches of terminal ileitis was followed by a long free area, the distal half of the ileum and the lower jejunum being again the seat of an advanced pathologic process. Occasionally, clearly marked "skip-areas" were easily demonstrated in the roentgenograms.

Ten of the 17 cases have been subjected to exploratory celiotomy, in all of which the roentgenographic diagnosis of the disease, as well as the extent and degree of invasion, were amply and accurately confirmed.

*Differential Diagnosis.*—In terminal ileitis it is important to exclude primary and secondary tuberculosis and neoplasm, both of which are marked by extremely severe courses and are readily differentiated roentgenologically and by laboratory examinations.

With upper ileojejunitis, an entirely dissimilar problem comes into play. Here, benign new growths are uncommon, but Hodgkin's disease and sarcomatosis occur and are characterized by rapidly downhill course with hemorrhage and emaciation.

The main point in high ileojejunitis is to exclude nontropical sprue, and the intestinal manifestations of the deficiency diseases. Clinically, nontropical sprue is characterized by frequent, frothy stools, and by the finding of a severe anemia, frequently of the hyperchromic type. Fever is absent, the stools do not contain blood, and gross hemorrhage from the bowel is absent. The cases react well to liver extract, to careful and judicious dieting, and to hygienic measures. The roentgenographic picture of the small bowel in sprue is one of uneven distribution of the barium in the several loops of the jejunum and ileum, with delay in motility of the upper loops, and without changes in the terminal ileum.[7, 8]

It is necessary to differentiate ileojejunitis from the deficiency states and the disturbances of fat metabolism as described by Snell and Camp,[9] Kantor,[10] and by others. The small intestinal changes accompanying ulcerative colitis which have been described by Mackie and Pound,[11] are probably also deficiency states. The roentgenograms in both conditions are of a nature similar to that described in sprue, namely, mild puddling, delay and irregular outlines of the upper jejunum and ileal loops, absence of delay in the terminal ileum.

In true ileojejunitis of the granulomatous type, the whole small intestine including the lower and terminal ileum, is usually involved; but even when only isolated segments of upper ileum and jejunum are implicated, the roentgenographic appearance is quite characteristic. Prolonged delay and accumulations of barium in upper loops is unusual; the various involved segments are irregular and fuzzy in outline; areas of narrowing in the lumen (signifying involvement) alternating with areas of dilatation ("skip-areas") usually increase in severity as one travels distally and is most marked in the

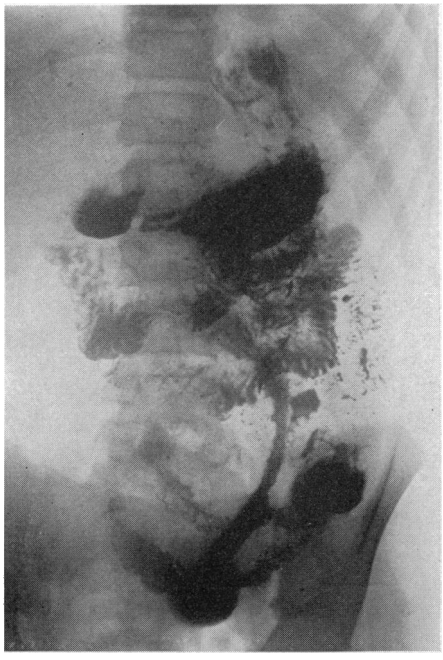

FIG. 1.—Roentgenogram showing the change in outline and in the mucosal pattern in the upper ileum and lower jejunum.

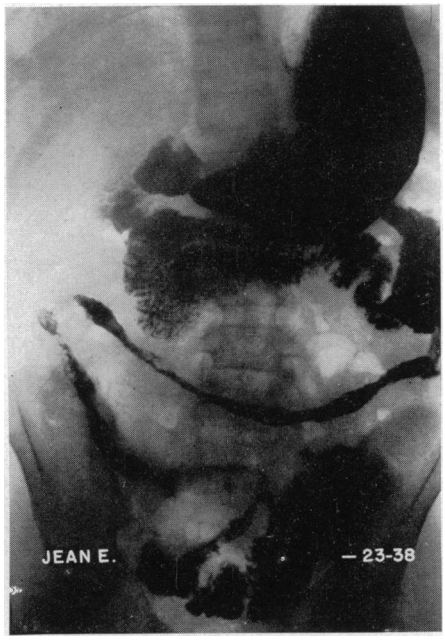


FIG. 2.—Roentgenogram showing the almost continuous "string-sign" involving the whole of the lower and upper ileum.

terminal loops of ileum where the pathognomonic "string-sign" just proximal to the ileocecal valve is frequently observed (Figs. 2 and 3).

*Course and Prognosis.*—The progress of a case of ileojejunitis depends, to a considerable degree, upon the severity and extent of the disease and the amount of involvement of the small bowel. In those instances in which the greatest part of the small intestine is continuously or intermittently continuously involved, surgical treatment is logically out of the question. To resect the whole implicated area, leaving only the jejunum and duodenum to assume the vital functions of chymification and absorption is to invite disaster. To attempt a high short-circuiting operation, of jejunum to colon, is tantamount to a total exclusion of the small intestine, and is again representative of poor surgical judgment. In those widely diffuse cases, medical treatment, whatever that implies, is the only resort, and is apparently, from a study of conservatively treated cases, most promising.

Nine such cases which have been observed during the last five years have not had recourse to surgical treatment. Four have done very well, having gained strength and weight, in one instance, up to 50 pounds.

The remaining five conservatively treated cases, have gained some weight, anemia has diminished and the frequent bowel movements have decreased and been held under control. The treatment instituted has consisted of a strict nonroughage diet, very liberal vitamin therapy, the administration of iron and liver extract particularly by mouth, and the insistence on rest, sunshine and change of air. The fecal movements are controlled, where necessary, by very small doses of opium after alternate defecations. No specific form of therapy can be evolved in the absence of knowledge of the specific causative agency of the disease. Roentgenotherapy has proven useless, as have also occasional recent attempts at chemotherapy with the newer sulfanilamide compounds.

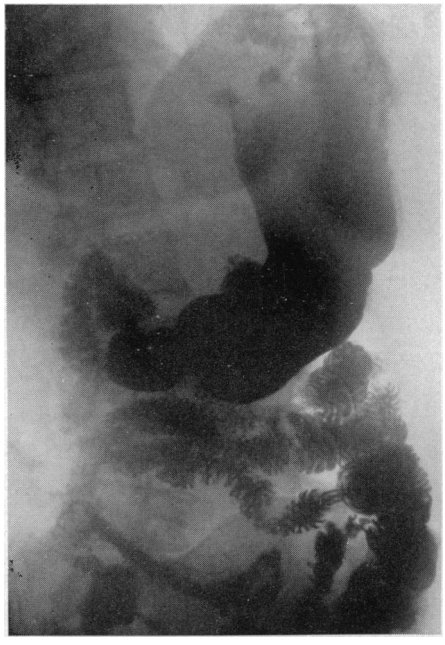

FIG. 3.—Roentgenogram showing the extent of the diffuse ileitis when first seen.

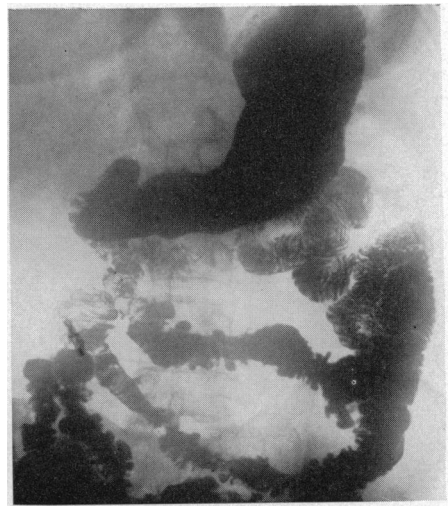

FIG. 4.—Roentgenogram of the same case as shown in Figure 3, three years later, after a gain of approximately 30 pounds. Note the partial restoration of the width of the intestinal lumen and mucosal pattern.

Clinical and symptomatic improvement takes hold gradually and seems to gain momentum as the years progress. In all the cases in which careful follow-up roentgenologic studies have been made, the observations continue to show the characteristic small bowel changes as originally seen at the first examinations (Figs. 3 and 4). This fact is most significant; two cases have been continually observed for five years; each case has gained from 30 to 50 pounds and is apparently quite well except for mild persistent diarrhea.

Where the disease begins before or at puberty a considerable retardation

of secondary sexual development takes place. One boy was 18 years old, weighed 81 pounds, had infantile testicular development, and was devoid of pubic or axillary hair. His voice was high-pitched and effeminate. (Case quoted by courtesy of Dr. John Sproul of Haverill, Mass.) The second boy, who has done very well on medical therapy, has permanently overcome his developmental sexual retardation, and with the subsidence of active symptoms has finally gained considerable weight, grown to normal stature, and has shown secondary sexual development.

*Results and Nature of Surgical Intervention.*—Apart from exploratory operations, and the usually needless appendicectomy, a study of the attempts to approach this problem by radical surgical procedures is most interesting. Two cases had undergone wide and extensive resections of the lower bowel and cecum, including all of the ileum, and in one instance, much of the jejunum. The former case survived (Dr. A. A. Berg), and eventually gained 20 pounds in weight, but of late has lapsed, with the development of a diffuse colitis. The latter, and still more extensive resection, died of exhaustion and shock during his immediate postoperative course. Obviously, radical excision of the small intestine, in most of its entirety, is not to be recommended. In a third case, a high jejunocolostomy had been ill-advisedly performed elsewhere. An attempt to revise the operation and to stay the rapidly downhill course by taking down the anastomosis, resulted in a fatal peritonitis. In still another case, a man, age 71, with a course suggestive of neoplasm, a resection of 45 cm. of ileum was performed, though a more diffuse involvement was recognized at the time. This procedure also resulted fatally, and, at autopsy, the whole small bowel was seen to be almost continuously involved in the granulomatous ulcerative process. The operation was forced by the internists because of the obviously hopeless issue under conservative management.

These four cases (with only one survivor) demonstrate the futility of attempting to resect and excise so extensive a disease process.

Attempts at partial resection where the disease is not continuous, or where the distal ileum is exempt and only segmental high ileojejunitis exists, may possibly give more promising results. In two of the cases of restricted, high ileojejunitis, localized resections were performed involving in one case, 90 cm., in the other case, 75 cm. of upper ileum and lower jejunum. In the former case (case of Doctor Sproul), subsequent roentgenologic studies showed residual disease in the small bowel; at a subsequent celiotomy, it was obvious that the entire ileum and jejunum were markedly thickened, edematous, with roughened serosal surface, and a plastic peritoneal exudate. The colon appeared normal. Considerable later clinical improvement has taken place, but this betterment may well be attributed to the meticulous hygienic and conservative treatment instituted since the attempts at reconstructive surgery.

The second case of localized ileojejunal resection is too recent to allow

of any conclusion, although the patient is rapidly gaining weight, and is completely free of symptoms.

What shall or what can the surgeon do who opens the abdomen of a patient and finds a diffuse ileojejunitis involving not only in a severe degree the terminal ileum, but by continuous "skip-areas" the whole extent of the small bowel practically up to the duodenum? To close the abdomen without making some attempt at resection appeared in these remaining two cases as a surrender without an effort at some type of reconstructive surgery. In both instances, the downward preoperative clinical course and the progressive loss of weight and inanition marked the ineffectiveness of conservative attempts at therapy. In this extremity, both redoubtable and experienced surgeons decided upon the same procedure, namely, to resect the most advanced lesion in the ileocecal area (terminal ileum and ascending colon), with the performance of a transverse ileocolostomy. In both instances (Dr. A. A. Berg and Dr. J. W. Hinton) the obviously diseased upper ileum and jejunum were returned to the abdomen. Both patients made uneventful operative recoveries, and, remarkable to say, have apparently continued to show marked improvement (six and three months postoperative).

The improvement in these last two cases is real and cannot be doubted, though it is against all our experiences regarding the success or failure of surgery in regional ileitis. The 10–15 per cent of conceded recurrences following resection for regional ileitis are actually attributed to the fact that higher "skip-areas" have been overlooked at the time of operation. If that be the case, then any palliative and partial resections, such as these latter two, in which no attempt was made to include the higher diseased area, should have been total failures. One would expect to see a rapidly continued downhill course. Not so, however, for the postoperative course has been and continues to be most promising. How to explain such a deviation from the rule is most difficult.

Until medical science reveals how ileitis spreads, whether by mucosal transport or by lymphatic extension; until the cause of recurrences after resection shall have been adequately demonstrated, and the significance of "skip-areas" made clear, the explanation of clinical postoperative betterment in these two unusual cases will remain enigmatic.

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