to the last question, Dr. Shay, we used both hypertonic and isotonic solutions and obtained practically identical effects with both solutions. They were obtained more readily with the hypertonic solutions and we did somewhat more work with them to make clearer our understanding of the mechanisms involved.

We believe that the presence of carbohydrates or fats in the upper intestine acts on some unknown substance in the mucosa to liberate another substance not previously present; this is absorbed in the blood stream and carried to the stomach to produce the inhibition.

This reaction seems to be specific, for the effect is only initia-

ted from the upper intestine and, apparently, only the stomach which is affected by the humoral factor. In the case of carbohydrates, we found that the lower ileal and colonic motility is not modified but the present investigation has not determined whether the same is true in regard to fats.

I am very happy to find that the results of Dr. Shay and also Dr. Thomas are so much in agreement with our investigations. I have talked with Dr. Thomas on previous occasions and found no disagreement. His investigation was involved chiefly with the nervous control, ours with the humoral control, and they seem to fit together very well.

CHRONIC INFLAMMATORY LESIONS OF THE SMALL INTESTINE (REGIONAL ENTERITIS)

PHILIP W. BROWN, M.D.*
J. ARNOLD BARGEN, M.D.*
Division of Medicine

and

HARRY M. WEBER, M.D.*

Section on Roentgenology

ROCHESTER, MINNESOTA

FOR many years, occasional instances of chronic inflammatory disease of the small intestine have been reported, yet the condition was not thought of as an entity until Crohn, Ginzburg and Oppenheimer published their excellent report in 1932. These observers considered that the disease manifested itself in the terminal portion of the ileum, but the more we see of these cases the more we are impressed by the fact that inflammatory, ulcerative disease in the jejunum, ileocecal coil or in regional areas in the colon pathologically is indistinguishable from that in the terminal portion of the ileum. The affection appears to be a clinical and not a pathologic entity; it may occur at any point in the intestine. This same conception had been advanced previously by Harris, Bell and Brunn and by Homans and Hass. The paper of the last mentioned investigators was discussed by Clute, Ladd, and Mixter, clinicians, who also inclined to the opinion that the ailment might occur at any point in the small intestine and that it was indistinguishable pathologically from "terminal ileitis".

The present report comprises eighteen patients who have been observed by us recently. From the pathologic standpoint a study of the record of similar cases might place many others in this group, but we have selected only these eighteen cases because the patients had come under our care since the time when we began to make a careful and intensive scrutiny for clinical and anatomic characteristics of the disease. The situation of the lesions was established at operation in seventeen cases and in the remaining case by roent-genologic observation. As a result of this information we shall endeavor to demonstrate that there is a significant relationship between the situation of the lesion and the clinical signs and symptoms.

CLINICAL AND PATHOLOGIC FEATURES

The ages of these patients ranged from nine to sixty-one years, two being nine years of age, one eighteen, seven between twenty and thirty, three between thirty and forty, four between forty and fifty and one sixty-one. Fourteen of the patients were men. It will be remembered that, in Crohn's series, the youngest patient was seventeen years of age and the oldest fifty-two and that there were twice as many

males as females. The somewhat similar age distribution in the two groups may be more than incidental.

Sites of lesions. May they not suggest some significant factor predisposing to the disease? In nine of the cases the ileum alone was involved, in three the jejunum alone was involved, in one the terminal portion of the ileum and a very small portion of cecum were involved and in five the terminal portion of the ileum, the cecum and part of the ascending colon were involved.

Gross description of lesions at operation. Descriptions of the lesions by the different surgeons at exploratory operation were remarkably similar. They noted an inflammatory process, rather sharply localized in area, but involving all layers of the intestinal wall; it was associated with hypertrophy and its similarity to a stiff rubber tube was commented upon (Fig. 1). Subserous tubercles were not observed. Enlarged lymph nodes along the mesentery usually were encountered. Detailed pathologic study failed to add significant data to the careful descriptions originally reported by Crohn, Ginzburg and Oppenheimer.

Preoperative histories of patients. Most of the patients had been ill for years, with symptoms running a rather constant and progressive course; several had been ill for ten years and some for more than twenty years. Only five had symptoms of less than a year's duration.

As would be expected, we found that ten of these patients previously had undergone operation. In seven cases a diagnosis of appendicitis had been made and appendicectomy had been performed and, in six cases, an abnormal condition of the ileum or colon had been noted; it had been considered to be tuberculosis, Hodgkin's disease or intestinal inflammation of unknown etiology. In one case, appendicectomy had been followed later by resection of that portion of the intestine which was producing obstruction. One patient had undergone splenectomy for an otherwise unexplained anemia: the anemia persisted and finally was found to be due to an ulcerating, indurated lesion in the lower portion of the ileum. The remaining patients in this group previously had undergone resection of the ileocecal portion of the intestinal tract but later the disease had progressed into the distal portion of the ileum.

^{*}Respectively, Division of Medicine and Section of Roentgenology, Mayo Clinic.

Clinical symptoms. The most constant complaint was that of pain. This was a predominant symptom in sixteen of the eighteen cases. In twelve cases, the pain was described simply as cramp-like; in others the terms "colicky", "knife-like", "gripping", "obstructive", "sickening", "to-and-fro colic" were used. Only two patients did not complain of pain.

In two of the cases in which the affection was confined to the jejunum, the pain was localized around and just above the umbilicus. The third patient in this group did not complain of pain but chiefly of a sense of nausea.

In the nine cases in which the lesion was confined to the ileum, the pain was situated in the right lower abdominal quadrant in four, below and to the left of the umbilicus in two, around the umbilicus, left to

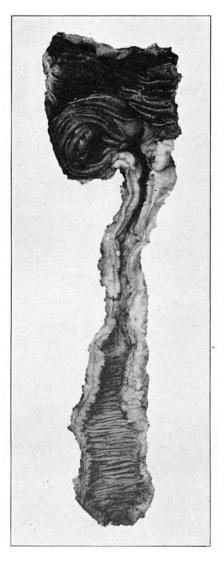


Fig. 1. The inflammatory process, rather sharply localized in area, but involving all layers of the intestinal wall may be noted.

right, in one, and radiating from gall bladder to the region of the appendix in one. One patient in this group did not complain of pain.

In the six cases in which there was involvement of cecum and ascending colon *with* the ileum, the pain was in the upper portion of the abdomen in three, in the right lower abdominal quadrant in two and across the lower portion of the abdomen in one.

Only six of the patients in the entire group complained chiefly of *diarrhoea*. Three of these had diarrhoea constantly and three intermittently. In four of these six cases, the disease involved the cecum and

the terminal portion of the ileum, in one the terminal portion of the ileum alone, and in one a large section of jejunum. In the patients who experienced diarrhoea, the pathologist described the lesions as "ulcerative". Deep longitudinal ulcers and subacute inflammatory lesions were present in four of these cases and hyperplastic and stenotic lesions in the other two. This information would suggest that the situation of the lesion, extent of involvement and the nature of the pathologic change had something to do with the absence or the presence of diarrhoea. It was not possible to determine enough about the diarrhoea for us to say whether or not, in the two cases in which stenotic lesions were present, the diarrhoea was of the obstructive type which is found with lesions of the rectosigmoid. In general, however, the stools were loose and watery, with much urgency and cramping, but without visible blood.

In nine cases, *vomiting* was an important symptom, so much so that the patients volunteered information about it and with several patients it was the most annoying symptom. The situation and character of the lesion seemed to be a factor in this. In all three cases of jejunal lesions this was a striking symptom. Three other patients in whom the disease was confined to the ileum, and three in whom the cecum alone was involved, complained of vomiting. The vomiting never was that of complete or impending obstruction, but was more intermittent; only partial loss of food and drink taken occurred.

Ten of the patients had fever. Fever was not recorded in the other eight cases nor was it ever known to be present. The fever came at intervals; in one instance with recurrent episodes up to 104° F. The usual range was 100° to 101° F., this alternating with periods of complete freedom from abnormal temperature.

Fourteen of the eighteen patients complained of *loss* of weight. One patient lost only 10 pounds (4.5 kg.) and a little girl lost 14 pounds (6.4 kg.); three patients lost 15 pounds (6.8 kg.) each, two lost 40 pounds (18.1 kg.), and one 45 pounds (20.4 kg.), The average loss of weight among the other patients was 25 pounds (11.3 kg.). This is a striking indication of the depleting nature of the ailment.

Pain relief. None of our patients had been able to find any constant method for the relief of pain. Four of them had realized that food would increase pain; three others would stop eating, and finally, after vomiting had occurred, they would be temporarily relieved. Forcing the bowel to move, either normally or by enemas, relieved three patients. Sedatives and rest in bed would help to ease the attack. Probably the outstanding observation was the patients' desire to stop food intake and then to empty the gastro-intestinal tract by vomiting or by movement of the bowels.

Signs of the affection. Intestinal fistula occurred only twice in this group of cases, although Crohn observed it in several of his cases. One patient had been operated on for ruptured appendix, and following this, a fistula had persisted. At the time of his examination here, six months later, the fistula was found to be the result of marked ileitis of the terminal portion of the ileum accompanied by perforation. The other patient with fistula had undergone one-stage resection for inflammation of the terminal portion of the ileum and of the cecum. He had been well for nine years when a lower right abdominal abscess had developed which had terminated in a fecal fistula.

At the time of our examination, half of the patients had a mild to moderate secondary anemia. In one case, the concentration of hemoglobin was 20 per cent

(Dare) and enthrocytes numbered 2,700,000 per cubic millimeter of blood. This anemia later was explained by our discovering bleeding, ileal ulceration. However, it was noted that there seemed to be no relationship between the situation of the lesions and the incidence of anemia.

Leucocytosis of a moderate degree (10,000 per c.

mm. of blood) occurred in only six cases.

We were impressed by the paucity of physical findings. Of course, if the patient was seen during an acute or subacute attack, various degrees of abdominal distention and, perhaps, visible peristalsis might be observed. During the quiescent phase, however, it was difficult to be sure of the presence of anything abnormal on palpation of the abdomen or on digital

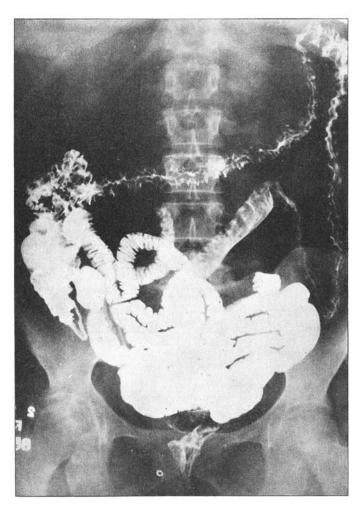


Fig. 2. Normal terminal portion of ileum, rendered visible by retrograde filling *via* the ileocecal orifice. The colon has been evacuated.

examination of the rectum. In one case, the fistula was obvious, since scars of a previous operation showed the site of trouble. Usually, however, apart from emaciation or, occasionally, anemia, very little was learned by physical examination. Next to the history, the chief aid to diagnosis was the roentgenologic findings.

ROENTGENOLOGIC STUDIES

The roentgenologic manifestations of inflammatory processes in the small intestine are practically the same as those exhibited by the large intestine when it is similarly involved. The general roentgenologic features depend upon the character, severity and extent of the pathologic changes present. These observations should be interpretable in terms of pathologic anatomy (Figs. 2 and 3).

From a roentgenologic point of view the significant pathologic changes taking place in the group of cases under consideration are: mural thickening with consequent narrowing of the lumen, stiffening and shortening of the involved portion and mucosal destruction. Associated with these anatomic changes is a more or less pronounced hypermotility.

These pathologic changes are quite readily revealed in the properly executed roentgenologic examination of the small intestine. Such examination demands close scrutiny of each individual segment by multiple, roentgenoscopic observations of the descending opaque meal and careful investigation of the terminal portion of the ileum after it has been distended by reflux of the opaque enema through the ileocecal orifice. Narrowing of the lumen and shortening of involved seg-

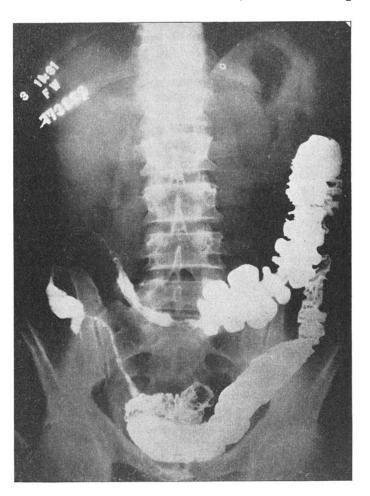


Fig. 3. Diffuse narrowing of terminal portion of ileum and right half of colon; the ulcerative ileocolitis proved to be non-tuberculous.

ments are readily observed if the hypermotility is not too pronounced. Greater and lesser degrees of mucosal destruction are manifested by changes in internal relief. In the interpretation of these, however, extreme caution must be observed, both because of the wide limits within which normal patterns may vary and because of the apparent rather than the real irregularities in mucosal relief patterns seen in hypermotile segments when no mucosal injury exists.

DIFFERENTIAL DIAGNOSIS

These lesions of the small intestine simulate those of *tuberculosis* in many instances; in fact pathologists have emphasized that tuberculosis may mimic any pathologic process in any region of the body. All our cases but one were studied particularly for this possibility. Any gland or tissue removed at operation was

examined thoroughly. Tuberculosis was not demonstrated, although the presence of large, foreign body giant-cells occasionally raised some question. Roent-genograms of the thorax gave negative results in all eighteen cases. This lends weight to our impression that, in these days, primary ileocecal tuberculosis is rare. In the two cases in which the patients were children, skin tests for tuberculosis were negative.

Intussusception, disease of Meckel's diverticulum, appendicitis, carcinoma and, very rarely, actinomycosis or Hodgkin's disease may simulate regional enteritis. In any event, surgical exploration is necessary. To both surgeon and internist, the important point is the constant need to be aware of the possibility of regional enteritis.

In eight of our cases the *preoperative diagnosis* was "inflammatory lesion of the bowel". In eight other cases, an undetermined type of obstruction of the small intestine was diagnosed. In one case, carcinoma and, in the last case, cholecystitis, were the preoperative diagnoses.

TREATMENT

Treatment essentially is surgical. Usually resection of the diseased region is necessary. In the occasional case, specific medical measures may be of some value in addition to the usual supportive and dietetic recommendations.

In the seventeen cases in which an exploratory operation was performed at this Clinic, none of the patients died as an immediate result of the operation. Three patients succumbed six to seven months later; two had extensive jejunal lesions and the third was the patient who had had closure of the fecal fistula. In this patient, pulmonary abscesses developed afterward and caused his death.

The third patient of the group of three who had jejunal involvement is well two years after operation. The following is a summary of events:

Case 1—The patient was a man aged twenty-six. All his life he had suffered from distress in the middle portion of his abdomen and from vague indigestion. In the three years prior to his admission, (December, 1932), he had experienced several attacks, each lasting two or four weeks, of this abdominal, crampy pain; it had been associated with nausea and with vomiting; often he had vomited food eaten twelve hours previously. During attacks, he had lost 15 to 20 pounds (6.8 to 9.0 kg.). The barium meal revealed abnormal motility in the jejunal coils with slight dilatation,

On exploration about 200 cm. of marked thickening of the jejunum was found, "like a hose", which began at the proximal end and gradually tapered as it approached the ileum. The intestinal lumen was only a third or a fourth its normal calibre. Grayish patches were present below the serosa but tubercles were not seen. There was no glandular enlargement. A moderate amount of free fluid was found. Gastrojejunostomy was

performed.

Following operation, intermittent courses of non-specific streptococcus vaccine were administered. In February, 1934, the patient reported that his health was good and that he had very little abdominal distress.

Ileocolostomy was performed in three cases of disease of the terminal portion of the ileum and in one of ileocecal involvement. In reports received six months, and two, three and five years later, respectively, the patients stated that they were in good health. In these patients resection eventually may be necessary but it was not feasible at the first operation and, so long as these patients continue to do nicely, there is no need for it.

Two patients with involvement of 68 and 20 cm. of the ileum, respectively, underwent one-stage resection and anastomosis. Seven months and three years later, respectively, they reported that they were in good health. The following synopsis illustrates one of these cases: Case 2—A man, aged thirty, was admitted in May, 1932, with a four and a half year history of "intestinal colic". He had been subject to attacks of lower, right abdominal pain every two or three months; these had been associated with severe vomiting. Appendicectomy had been performed in 1930. With each attack of abdominal pain, he had lost 25 pounds (11.3 kg.) and his temperature had risen.

On admission, he stated that he had just recovered from an acute attack; without subjecting him to roentgenologic studies, operation was undertaken.

About 60 cm. of the upper portion of the ileum was tremendously distended and was covered with a thick exudate. The walls were greatly thickened and inflamed. Many enlarged mesenteric lymph-nodes were observed. Sixty-eight centimeters of ileum were resected and lateral entero-anastomosis established (Fig. 4).

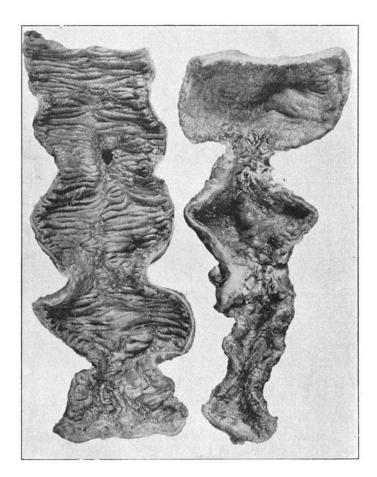


Fig. 4. Numerous confluent ulcers and stricturing, scarring, and thickening of the wall, may be noted.

A third patient also underwent one-stage operation. There was found terminal ileitis which extended into the cecum. Resection and end-to-end anastomosis were performed. This is the patient in whom an abscess with resultant fistula developed nine years later.

In the remaining six cases, entero-anastomosis was performed upon one patient and ileocolostomy on five. This operation was followed by a second-stage resection. For the patient with lower ileal involvement, a child aged nine years, resection was necessary three weeks after the first operation. Some months later a report was received that she was well. In the five cases of ileitis, and usually of some cecal extension, resection was performed two and a half to four months later, and until this had been done, the patients had been only moderately relieved. In fact, one patient was as miserable as ever until resection had been performed. In two cases, recent data are not available; in the other three, reports received one to three years after operation, indicated that the patients were in good health.

The following summary is characteristic of the cases in the above group:

Case 3—A woman, aged forty-two, was admitted in November, 1932, complaining of intermittent attacks, (lasting two or three days), of epigastric pain associated with vomiting. These had been present for over six years and finally had begun to occur about every two or three weeks. Fever, loss of weight and general depletion were observed. The barium meal revealed narrowing of the terminal portion of the ileum.

Ileocolostomy was performed for "an inflammatory lesion of the distal part of the ileum which extended into the cecum" (Fig. 5). The nation?'s convolescence was only fair and she

(Fig. 5). The patient's convalescence was only fair, and she was encouraged to try to regain her strength. However, by January, 1933, she could carry on no longer because of persistent pain and vomiting. At the second operation, 19 cm. of the lower portion of the ileum and part of the colon were resected. The pathologist reported the ileum as thickened and containing many deep, irregular and very inflamed ulcers with fairly normal mucosa between them (Fig. 2). The cecum and ascending colon evidenced only mild inflammation. Following the bowel resection, convalescence was prompt and the patient rather rapidly regained her health.

tients previously had been subjected to abdominal operation.

8. Entero-anastomosis alone has proved sufficient to relieve some patients, but resection of the diseased segment also usually has been necessary.

BIBLIOGRAPHY

- Crohn, B. B., Ginzburg, Leon, and Oppenheimer, G. D.: Regional lieitis; a pathologic and clinical entity. J. A. M. A., 99:1323-1329 (Oct. 15) 1932.
 Harris, F. I., Bell, G. H., and Brunn, Harold: Chronic cicatrizing enteritis: regional lieitis (Crohn). A new surgical entity. S., G. and O., 57:637-645 (Nov.) 1933.
 Homans, John, and Hass, G. M.: Regional lieitis; a clinical, not a pathological entity. New England Jour. Med., 209:1315-1324 (Dec. 28) 1933.

DISCUSSION:

DR. B. B. CROHN (New York City): Two years ago, opening the subject of ileitis, I spoke from knowledge of the first fourteen cases which we had experienced. Naturally, in describing a clinical entity, it is possible that the first cases did not completely cover all variations of type. For instance, the

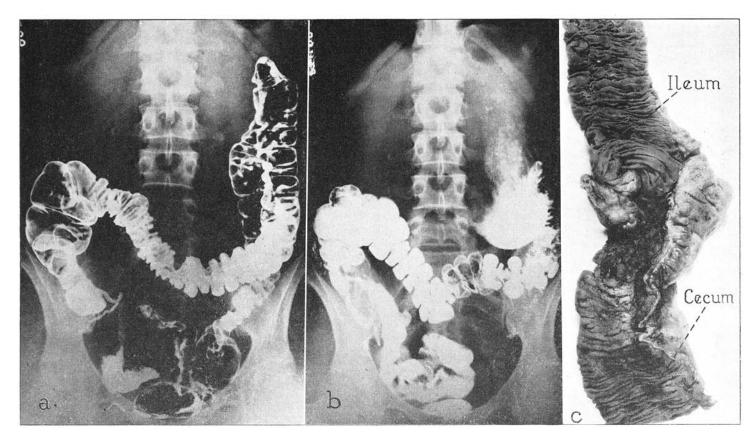


Fig. 5. a, "combined" roentgen method: deformity of cecum and terminal portion of ileum. The appendix is rendered visible. b, Opaque meal occupying terminal portion of ileum and proximal portion of colon. Deformity of terminal portion of ileum and cecum, without hypermotility. c, Thickened, inflamed ileum, with many deep, irregular ulcers.

SUMMARY AND CONCLUSIONS

1. Eighteen patients with regional, inflammatory disease of the jejunum, ileum or the ileocecal region have been described.

2. Pathologically, the lesions were similar in all segments of the intestine.

3. The chronic inflammatory nature of the lesion emphasizes the importance of excluding tuberculosis as an etiologic factor.

4. Clinically, the symptoms are suggestive of the situation of the disease.

The outstanding symptoms include pain, vomiting, diarrhoea, fever and loss of weight.

The striking incidence in males is again emphasized (fourteen males, four females).

Difficulty in diagnosing these lesions is emphasized by the fact that over half of our group of paileitis was entirely restricted to the terminal portion of that segment of the intestine; eight to ten inches were involved, with no exceptions. Similarly, our first cases all had fistulae.

Within a year we were beginning to see higher lesions of the ileum, involving the upper ileum, and occasionally what we termed "skip areas" with free intervals of mucosa in the upper segments of the intestine.

A year ago, Harris, of San Francisco, published two cases with involvement of the jejunum. I was at first inclined to deny that jejunitis and ileitis were the same disease; since that time, we have had three instances of involvement of the upper ileum and jejunum, so that we are anxious to add to our origi-nal description of the disease, the fact that the whole ileum and jejunum may participate in the process.

In all instances, with but one exception, the terminal ileum was involved, not only involved, but appeared to be the oldest seat or the point of origin of the disease, the degree of extension of the disease, the degree of extension of the disease, the degree of extension of the disease. sion upward varying with individual cases.

In only one instance in thirty-eight cases was the colon involved; that was one of involvement by continuity from the ileum into the cecum.

Dr. Brown brings up the question of diffuse involvement of the colon with ileitis. In the following slide

(Slide). Radiography of upper jejunal involvement demonstrated by injecting barium through a duodenal tube into the upper intestine; the entire ileum and lower jejunum were involved; resection resulted in recovery.

The second case of ileitis with jejunal involvement unfortu-

The second case of ileitis with jejunal involvement unfortunately was fatal, as the patient could not survive the extensive

resection.

I should like to demonstrate the fact that a disease exists in which the terminal ileum is inflamed, and with it, a segment or segments of the colon. Those segments of the colon are seen at operation, are fiery red, covered with an exudate, but are separated by large areas of the colon free of disease. The terminal was involved in all four of this type of case seen. This clinical syndrome is differentiated from severe colitis with ileal involvement, insofar as there is, in this syndrome, a very slight diarrhoea (two to three stools daily), there is high temperature, much prostration, and abdominal tenderness; our cases have all recovered.

A colitis which is so severe as to show an inflamed, shaggy colon with peritoneal involvement and ileal engagement, may represent a terminal stage of a severe colitis with probably 20 to 30 stools a day, and may be regarded practically as a hopeless case. Spontaneous recovery may seem out of the question.

We, therefore, recognize ileitis, ulcerative colitis with ileal involvement, and now a third clinical entity consisting of a mixed form in which the terminal ileum and segments of the colon are involved. The clinical features and the clinical course of this third type of case differ materially, and can be recognized radiographically and by their clinical manifestations.

(Slide). Diffuse involvement of jejunum and ileum: The patient was regarded as a psychoneurotic and treated as such; the diarrhoea was regarded as of nervous origin. The history extended over many years. In fact, the clinical history in the cases of ileitis extended, not infrequently, over 10, 15 and 20 years.

The disease is a low-grade disease, with mild diarrhoea, low temperature and small loss of weight. Intestinal obstruction may be the first prominent feature.

DR. IRVING GRAY (Brooklyn): In a study of the gastrointestinal tract at autopsy during the past two years at the
Sea View Hospital, Staten Island, special investigation of the
small bowel was made. These individuals all died of pulmonary
tuberculosis. In addition to the lesions commonly seen in tuberculosis of the small intestine, occasional areas were noted which
grossly resembled non-specific inflammatory disease as described
by Dr. Crohn and mentioned by Dr. Brown. I should like to
ask Dr. Brown if in his studies of the histology whether or
not there was any similarity to tuberculosis. In these inflammatory lesions of the small intestine, it is possible that a primary tuberculosis complex, although exceedingly infrequent in
this region, may heal and be responsible for subsequent changes.
The underlying infectious process may possibly be due to
changes initiated by tubercle bacillus.

DR. PHILIP W. BROWN (in closing the discussion): I feel quite as Dr. Crohn does, that lesions of the colon, the true ulcerative colitis lesions, are not thought of in this group, but in the cases we have called the "ileocecal cases", inflammation has been found in the lower segment of the terminal ileum, extending into the cecum and ascending colon. At the first operation the surgeon has thought it might be tuberculous and has performed the short-circuiting operation; when the bowel was resected he has found that the terminal ileum has been involved, with the peculiar rubber-hose thickening and inflammation, but the inflammation has entirely disappeared in the ascending colon and cecum.

It seems as if the process begins to sweep on down the intestinal tract. I think that that perhaps may justify these cases in that group; maybe not.

From the standpoint of tuberculosis, that is an ailment about which one is most suspicious. In all these cases the chest X-rays were negative for tuberculosis; in the two children the skin tests were negative for tuberculosis, and the careful pathological scrutiny in every way possible substantiated Dr. Crohn's and his colleagues' feeling that these were not tuberculosis.

Primarily intestinal tuberculosis, while not impossible, of course, is certainly much less common these days than it was ten or fifteen years ago, but in spite of this, the point that is going to be the most difficult is to prove that these subjects are not tuberculous. However, I don't believe that any of this group which we are considering as the "regional enteritis", is tuberculous.

THE ROLE OF THE GASTROINTESTINAL TRACT IN CONDITIONING DEFICIENCY DISEASE

(AN ABSTRACT)†

THE SIGNIFICANCE OF DIGESTION AND ABSORPTION IN PERNICIOUS ANEMIA, PELLAGRA, "ALCOHOLIC" AND OTHER FORMS OF POLYNEURITIS*

Bu

MAURICE B. STRAUSS, M.D. BOSTON, MASSACHUSETTS

FIFTY-FOUR years ago, Fenwick wrote: I volume of the blood depends on the quantity of nutriment dissolved and absorbed by the digestive tract." It is with the latter half of this statement that this paper is concerned. Specifically, the concept reviewed is that "deficiency disease" in man may and frequently does develop because of some disturbance of the gastrointestinal tract in spite of an apparently adequate diet. The more immediate development of this thesis is due to the fundamental work of Castle, who first clearly demonstrated that an asymptomatic abnormality of gastric secretion might condition a dietary deficiency state irrespective of the adequacy of the diet. From his work, and that of many others, it now appears that pernicious anemia may result from any one of three mechanisms or from any combination of them: (1) the lack of a digestive juice in the stomach, (2) the absence of a substance associated with

MASSACRUSEUS.
†Printed by arrangement of "The Journal of the American Medical Association" in which the complete paper originally appeared.

vitamin B₂ (G) in the diet, or (3) the failure of absorption from the intestinal tract of the product of interaction of the stomach and dietary factors.

Pellagra as commonly seen in endemic form, is probably due essentially to the lack of vitamin B₂ (G) in the diet. In the North, however, with rare exceptions, pellagra is seen in individuals who have organic lesions or abnormalities of the gastrointestinal tract or who are habitual alcoholics. The effects on the gastrointestinal tract of overindulgence in alcohol are so well known that they need not be entered upon here. It seems not unlikely, therefore, that "alcoholic pellagra" results from the combination of these gastrointestinal disturbances, particularly anorexia, vomiting and diarrhoea, and the moderately faulty diet which many alcoholics take. Fifty-nine cases of pellagra have been reported secondary to the following gastrointestinal tract lesions: esophageal stricture, peptic ulcer, cancer of the stomach, gastric syphilis, gastroenterostomy, jejunostomy, jejunal stenosis, ileal stenosis, cancer of the ileum, dilatation of the colon, ulcerative colitis, amoebic dysentery, cloaca,

^{*}From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard). Boston City Hospital and the Departments of Medicine and Tropical Medicine, Harvard Medical School, Boston, Massachusetts.