5-1-1938

Regional enteritis

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REGIONAL ENTERITIS

SENIOR THESIS

CHARLES C. IMPEY

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PRESENTED TO THE

COLLEGE OF MEDICINE

UNIVERSITY OF NEBRASKA

OMAHA, 1938

Table of Contents

Definition and History

In 1932, Crohn(15) published an article setting forth what he believed to be a clinical and pathological entity, and at this time he chose to call the condition Regional(Terminal)Ileitis. In his paper he defines the condition as follows: "A disease of the terminal ileum, affecting young adults, characterized by a subacute or chronic necrotizing and cicatrizing inflammation, ulceration of the mucosa and excessive connective tissue through the wall, leading to stenosis and fistula formation." The pathological process is essentially that of granuloma formation and this, Virchow(60) defines as a tumor or neoplasm made up of granulation tissue. A specific granuloma is understood to be a chronic inflammatory tumor caused by a specific micro-organism(59). Golob(27), in turn, defines a granuloma as a circumscribed collection of epithelioid cells and leucocytes, resembling granulation tissue, surrounding a central point of irritation. He also states that Dr. Joseph McFarland, of the University of Pennsylvania,

has defined granuloma as a nodular induration resulting from inflammation, which cannot, however, "be acute or the whole would melt away by suppuration and result in an abscess."

Before Crohn's paper the condition, which he so aptly described, was thought to be rather rare and was frequently misdiagnosed. The condition has been described under a number of different headings as: "Crohn's Disease", "Chronic Ulcerative Enteritis", "Chronic Interstitial Enteritis", "Chronic Cicatrizing Enteritis", "Non-Specific Granuloma of the Intestine", and "Ileocolitis." This wide variety of terms tends to obscure the fact that the lesion is one and the same, that is, a chronic inflammatory process affecting, chiefly, the ileum and the adjacent bowel(51). Thus, it would seem that if the authors could agree on a definite name for the disease it would facilitate, to some degree, the study and teaching of the condition. As the disease process has been found in both the large and the small bowel, it would seem that enteritis would be justifiable. Likewise, as the condition tends to remain, to some extent,

fairly well localized, it might be termed as regional. Thus, it is believed that the most descriptive term would be Regional Enteritis.

The records show that similar lesions of the gastro-intestinal tract have been noted and recorded for some time. Although, W.J. Mayo(38), in 1888, reported cases in which typhlitis or perityphlitis gave rise to palpable tumors, little appeared in the literature until Wagner(61), in 1902, reported cases in which foreign bodies were the cause of inflammatory lesions having their origin in the intestine. Before the year 1895, most circumscribed, chronic lesions of the small intestine apparently were regarded as actual tumor growths; however, Senn(56) attempted to distinguish between infective granuloma and carcinoma. Moynihan(44), in 1907, reported six cases in which the original diagnosis of malignant disease of the large bowel had to be changed to that of granuloma of the intestine because of apparent resolution of the growth. Robson(54), in 1908, also noted cases which were at first diagnosed as malignancy yet, had become cured with little trace remaining. In 1913,

Dalziel(19) described cases which were evidentally granulomata and which involved the small as well as the large intestine. Moschcowitz and Wilensky(43) in 1922, were led to believe that these infective tumors of the intestine were of a non-specific origin. In 1931, Mock(42) concluded that these benign non-specific tumors of the intestine formed a definite clinical entity and that they should be treated as such. This leads us up to Crohn's paper.

Forbes(25) states that regional enteritis is by no means uncommon, as is shown by the many reports appearing from all parts of this country and from abroad. He also believes that a large number of cases have gone unrecognized in the past. While Barrington-Ward(5) states as follows: "It is our view that this is a new disease; we do not believe that a pathological condition of such a definite nature, and as unlike any of the known diseases of the intestine, can have remained for long unrecognized in this keen and critical surgical age. When operating on the first of the cases which form the basis of this paper, we were hardly aware of Crohn's descrip-

tion, and yet the pathological appearance, dis-
closed at operation, left us in no doubt that
here was something that was not tuberculosis,
malignant disease, or ulcerative colitis, and
something which for its cure required radical
treatment."

Etiology

The etiology of regional enteritis is at this time rather obscure. A large amount of work has been done and many facts have been established, and in order to clarify somewhat, these facts and suppositions will be discussed under predisposing causes and exciting causes. It must be remembered that all of these factors, therefore, will not hold true in all cases.

Predisposing Causes

Age Incidence - Meyer(40) says that regional enteritis may occur in individuals of all ages. Rockey(55) reports a case of thickening of the terminal ileum, apparently an acute regional enteritis, in a child five years of age; and Brown, Bargen and Weber(10) report a case in a man sixty-one years of age. It occurs most commonly, however, in young adults. The youngest in Meyer and Rosi's(40) series was seven years of age and the oldest was thirty-four years of age. Mixter (41), who observed eleven cases, found the youngest to be fourteen years of age and the oldest to be fifty-six years of age, and of his

eleven cases seven were in the twenties.

Koster(36) and his co-workers carefully fol-
lowed seventeen cases and of these seventeen the
age incidence was found to be as follows.

Age Incidence	Number of Cases
1 to 10 years	1
11 to 20 years	2
21 to 30 years	8
31 to 40 years	5
49 years	1

In a careful review of the literature, Koster
found the following age incidence:

Age Incidence	Number of Cases
1st Decade	6
2nd Decade	10
3rd Decade	12
4th Decade	15
5th Decade	13
6th Decade	6
7th Decade	5

In Adams(1) series of fifteen cases, he
found the average age to be thirty-six.

Sex - The sex factor varies a great deal as
can be shown in the following chart.

Author	Number of Cases	Males	Females
Mixter(41)	11	8	3
Brown (10)	Ratio	2 to	1
Adams (1)	15	6	9
Koster(36)	62	33	29

Race - In reading through the literature, it
is found that an apparent majority of the cases
are to be found in the Jews. This may be due to
the fact that the condition was early recognized
by workers who were associated with Jewish hos-
pitals. Eight of the eleven of Mixter's cases
were found to be in Jews. Homans(32) also sug-
gests that there may be a racial factor, as he
found most of the cases to be in Jews.

Other Predisposing Causes - Here is where
we find a wide variety of causes. Ralph(51) be-
lieves that foreign bodies such as fish-bones,
unabsorbable suture material, food residues,
play an important part in etiology, that is, the
foreign body punctures the mucosa and allows sub-
mucosa to become inflammed. He bases such con-
clusions on the fact that many cases of granulo-
matous masses of the large intestine, from which
a foreign body, as a fish-bone or a pin has been

recovered. He writes, "The fate of a foreign body gaining access to the intestine wall through a break in the mucosa is variable. Rarely, we know, it may penetrate the gut wall and, escaping into the peritoneal cavity, occasion a virulent peritonitis. More often it will become immured in the wall, and resisting solution by the tissues, exert a permanent stimulus. From this chronic irritation a subacute inflammatory reaction occurs, with tracts of granulation tissue, the development of scattered abscesses in the indurated connective tissue, and sometimes fistula formation. On the other hand, it is conceivable that some foreign bodies, by reason of their minute size or chemical composition, eventually undergo solution by the tissues which temporarily harbor them. To say, then, without the most searching examination of a resected specimen, that no foreign body was present, would seem to beg the question of etiology!

A striking feature of many sections is the presence of giant cells of the foreign body type. These have been ascribed to the entrance of small particles of food residue through a mucosal de-

fect exciting a foreign body reaction. The con-
dition, believes Mock(42), is directly due to low
grade infection causing impaired circulation or
to an impaired circulation causing a low grade
inflammation. He also believes the stenosing
is due to early reparative process.

That a duodenal lesion(as an ulcer) with its
constantly irritating influence over the ileo-
cecal region may be conducive to a defensive re-
parative phenomenon developing into a palpable
mass sufficiently tense to produce symptoms of
obstruction, is the belief of Golob(27). That a
"silent" pyloric syndrome might give rise to a
pathological condition in the ileocecal region
facing the cecum and result in the formation of
a cecal granuloma is, in his opinion, an entire-
ly logical explanation of the modus operandi.

Mock(42) also states that the etiological
factors which predispose to infective granulomata
formation are:

1. Conditions existing within the gastro-
intestinal tract itself or its mesentery.- Cer-
tain types of sigmoid diverticulitis furnish the
best examples of the condition. The diverticulum

with a small opening on the mucosa, but with a
balloon-like protrusion on the peritoneal surface,
often contains a small amount of hard inspissated
feces. Erosion, low grade infection, necrosis,
round cell infiltration of the adjacent mesentery,
with this reaction extending upon, and around the
adjacent bowel, kinking or constricting the bowel,
and all of this accompanied by the peritoneal
and omental tissue reaction to inflammation soon
gives rise to a granulomatous mass about this
diverticulum that is almost impossible, grossly
to distinguish from a malignant tumor. The
inflammatory hyperplastic mass developing at the
site of a gastric ulcer, usually following a
small perforation, is another well known example.
It is a known fact that these are frequently mis-
taken for cancer. The differential diagnosis is
rendered more difficult because of the enlarged
glands. Ulcers existing anywhere in the intes-
tinal tract may act similarly. Polypi of the
intestine may undergo necrotic changes followed
by reparative inflammatory reactions and may de-
velop tumor-like masses sufficiently large as to
cause intestinal obstruction. These also are

frequently mistaken for cancer.

Foreign bodies within the intestines and even hard, inspissated feces in old people may likewise start this inflammatory reaction, resulting in a tumor-like formation.

A partial volvulus or partial obstruction from bands or adhesions may set up a low grade pericolic inflammation which does not cause such marked reaction in the gut itself, but which causes a hyperplastic reaction in the adjacent omentum until it is so thickened and enlarged that it resembles a good sized tumor.

Finally, constriction of the bowel and omentum in hernial sacs, both external and internal herniae, may result in an inflammatory hyperplasia until the whole is matted together in a tumor-like mass.

2. Extra peritoneal infections which gradually spread to and involve the gastro-intestinal tract. - A low grade infection in the retroperitoneal lymph glands may cause a necrotic mass, showing areas of reparative fibroelastic reaction, which gradually involves the parietal peritoneum or involves the colon at its splenic

flexure, causing the usual peritoneal and omental reaction to inflammation until a large, more or less necrotic, more or less solid tumor-like mass has formed in and about the colon, and this often results in an obstruction with a tumor which is very difficult to differentiate grossly from a malignant tumor.

3. Trauma: (a) Surgical trauma or accidents. (b) Extraneous injuries. - That the importance of trauma in the formation of these obscure intra-abdominal tumor masses, so often mistaken for malignant tumors, has never been sufficiently stressed. No case of granuloma, the direct result of an accident, has ever been reported.

Under surgical traumas or extraneous accidents we have the following examples: (1) ligatures or sutures which constrict and act as a local interference to the blood supply, or sutures which act as a foreign body: (2) foreign material such as instruments, sponges, etc. left in the intra-abdominal cavity; and (3) trauma in general.

Exciting Causes

As regards the actual organism involved in the production of this disease there are many

organisms which in one way or another have been
connected with various cases. The tubercle
bacillus has been thought to be the exciting
organism because of the similar pathological
processes, however, Colbeck and co-workers(12)
have shown by many laboratory procedures that it
is not the cause.

The various workers have shown a variety of
organisms which have apparently been the exciting
causes of these cases. Mailer(37) reports two
cases in which the streptococcus viridan was
found, (1) from a blood culture following
simple laparotomy, (2) from the throat of a
patient who was explored and diagnosed as Crohn's
Disease. A case was presented by Bisgard(7) in
which dysentery bacillus was present in cultures
from urine obtained directly from the right kidney.
Identity was established by fermentation and ag-
glutination. However, streptococcus hemolyticus
was cultured from fluid free in the peritoneal
cavity and from a mesentery lymph node. Thus,
there is presumptive evidence that the dysen-
tery bacillus, present in the urine, had play-
ed a part in the process in the ileum and that

streptococcus hemolyticus, present also in the
urine and in the peritoneal lymph node and peri-
toneal cavity, had been a secondary, if not a
primary, invader of the bowel wall. In his case,
however, section of bowel was not made, hence,
diagnosis of regional enteritis was made from
clinical observation at the time of the opera-
tion.

"The extensive edema might indicate the
etiological factor to be a mutation or aner-
obic form of a hemolytic streptococcus. This is
substantiated by the incidence of fatal strept-
ococcus peritonitis that follow some resections",
states Pollock(48). Felsen(24), who has done a
large amount of work on chronic ulcerative col-
itis, believes that there is a definite relation-
ship between bacillary dysentery and regional
enteritis. In twenty-two patients having region-
al ent ritis, he was able to obtain agglutination
in all of the patient's serum for dysentery bacilli
of various strains.

Pathology

Macroscopic

The pathologic changes in the chronic forms
of regional enteritis have been thoroughly studied,
since these are the lesions most frequently seen
and resected at operation. The peritoneal cavity
usually contains a small amount of serous fluid(40).
The peritoneal surface of the ileum is injected and
may be covered in some places by a thin layer of
fibrin. The inflammatory process in the ileum either
stops abruptly at the ileocecal valve or continues
into the cecum, it extends orally for some distance
and gradually shades off into normal intestine.
Adhesions between loops of bowel may be firmly
held by well developed bands of fibrous tissues(12).
The mesentery of the involved bowel may be 2cm.
thick and usually contains hyperplastic lymph nodes.
Fistulae are often found between the terminal ileum
and the adjacent bowel, usually the sigmoid. Walled
off abscesses in the mesentery are not rare. Ex-
amination of resected specimens shows the wall of
the ileum thickened, as a result of inflammatory
hyperplasia of all the layers. This hyperplasia
is greatest near the ileocecal valve where the
wall may reach three to four times the normal

thickness. The mucosa is swollen, the intestinal folds thickened. Along the mesenteric border of the mucosa there are linear ulcerated areas a few millimeters in diameter. In the region of the ileocecal valve, there are areas of papillary and polypoid hyperplasia. The lumen of the ileum is usually constricted, and the narrowing most pronounced in the region of the ileocecal valve. The ulcerations along the mesenteric border in the ileal specimens show a tendency towards perforation. The earliest perforations are in the form of linear fistulae that begin in mucosal ulcers along the attachment of the mesentery and penetrate through the bowel wall and lead into a common cavity in the mesentery, which may form an abscess.

The cecum, when involved, becomes constricted at its distal end by a hyperplastic inflammatory process which appears to extend from the ileum and invade the cecal wall. The thickening of the cecal wall is greatest at the ileocecal valve and gradually diminishes distally into normal cecum and ascending colon. As a rule there is no ulceration of cecal mucosa. The musculature in the wall of the ileum above the length chiefly affected is gen-

erally hypertrophied. The mucous membrane in this region appears to be normal.

Pollock(48) says that internal fistulae are present in twenty percent of the cases. At first they are thin walled and penetrate into the mesentery of the terminal ileum. The adherence of loops of bowel permits perforation into the sigmoid, ascending colon or other loop of bowel. They form mesenteric abscesses containing white, thick and almost odorless pus. The old fistula is surrounded by an advancing wall of fibrous tissue so that perforation into the free peritoneal cavity is almost never seen. Querna(50) however, reports a case in which there was an acute perforation about two feet, orally, from the ileocecal valve, anti mesenteric, and which was followed by a fulminating peritonitis. The fistulae that point outward to the anterior abdomen wall are often mistaken for an appendiceal abscess. Gregory(28) believes it is due to the chronic nature of the process that adhesions and fistulae result.

Microscopic

Ginzburg and Oppenheimer(26) studied fifty-two cases with resected specimens and they found

that the microscopic examination showed various
degrees and stages of acute and chronic inflammation
with production of much firbous tissue.

Colbeck(12),in the study of a case, reports the
pathological findings as follows. The five sections
from the affected portion of the ileum show that
the epithelium has been almost entirely lost over
the whole area and that the thickening is chiefly
due to large masses of very active granulation
tissue. The many small polypoid masses present in
the base of the ulcer are outgrowths of the well
vascularized granulation tissue forming the im-
mediate lining of the lumen. The inflammatory re-
action in the granulation tissue is much more ac-
tive in the inner layer of the ileal wall than in
the sub-peritoneal one where large areas of well
formed fibrous tissue are present. In its more
active areas the granulation contains many structures
histologically indistinguishable from tubercles.
Large multinuclear cells, with irregularly spread-
ing cytoplasm, are surrounded by zones of epithe-
lioid histiocytes and aggregations of lymphocytes.
Binney(6) believes that the giant cells are common
probably due to particles of vegetable matter en-

trapped in ulcers. These may form nodules which,
when present in the serous layer, are difficult
to distinguish from tubercles. These "vegetable
cells" may be responsible for hyperplastic fibrosis.
The arrangement of these tubercle-like structures
was very uniform. Sections stained by the Ziehl-
Neilson method fail to show the presence of any
acid fast bacilli. In addition to these tubercle-
like structures, the granulation tissue contains
very large numbers of histiocytes and eosinophilic
leucocytes, together with smaller numbers of plasma
cells.

Sections taken from the cecum below the af-
fected area show considerable edema of the sub-
mucous connective tissue, and a considerable in-
filtration of lymphocytes below and between the
epithelial cells of the mucosa. In the glands
taken from the retrocecal group there is some dil-
atation of the lymph sinuses and swelling of the
reticulo-endothelial cells. A few eosinophil leu-
cocytes are also present in the vicinity of the di-
lated sinuses.

Erb(22) reports many of the solitary lymph
follicles also showed necrotic centers with ulcer-

ation of the overlying epithelium, giving the
follicle a crater-like structure. Erdmann(23) says
an area containing mast cells and large groups of
lymphoid cells can be easily mistaken for cancer,
while the small round cells may so predominate the
picture as to make the tumor resemble sarcoma. The
blood vascular changes vary from newly formed chan-
nels to those presenting greatly thickened, well
formed walls with surrounding perivascular infil-
tration. The lymph channels in some instances show
marked dilatation.

Types

Clinically, Crohn and his associates distin-
guish four types of the disease. (1) Acute- showing
signs of intra-abdominal inflammation; (2) Symptoms
of ulcerative enteritis; (3) Stenotic phase with
symptoms of chronic obstruction of the small intestine;
(4) Fistulous stage with intractable and persistent
fistulae in the right lower quadrant..

1. Before operation these cases are almost
impossible to distinguish from acute appendicitis.
Colic-like pain and tenderness in the right lower
quadrant with fever to 101 to 102 degrees and mad-
erate leucocytosis are present. The onset of sym-
ptoms, however, appears to be more gradual than in
appendicitis. A mass in the right lower quadrant
may be present even without abscess formation.
At operation there is found a greatly thickened,
red, blotchy terminal ileum with marked edema of
the surrounding tissues and slight exudate of the
ileal wall. The mesentery is thickened and edema-
tous and contains numerous large glands. Clear
fluid is present in the abdomen. An abscess may
be encountered which is seen not to be of ap-
pendiceal origin, but because of the contiguous

inflammation the appendix may show some involvement
of its serosa and the pathologist may report "sub-
acute appendicitis" on the removed appendix. The
appendix, however, is not etiologically related to
this disease.

(2). Symptoms of Ulcerative Enteritis - There
is a history of diarrhea associated with colic-like
periumbilical pain and lower abdominal pain related
to defecation, there being three to five liquid
stools a day which may contain pus, mucus, or
visible blood. A constant low grade fever is pres-
ent and with the progress of the disease there is
marked loss of weight and a pronounced secondary
anemia. The course may continue for as long as
a year with increasing exhaustion or more frequently
the case gradually passes into the stenotic phases
of the disease. These cases are frequently treated
for colitis until they go on to obstruction.

(3). Stenotic Phase - This is the most common.
The symptoms are now those of a partial obstruction
of the small intestine. Violent cramps with attacks
of vomiting and constipation are present, visible
peristalsis and distension are common, a palpable
mass is usually present in the right lower quadrant.

The stenotic phase may occasionally occur as the first manifestation of this disease although minor symptoms may have been present for years.

(4). Fistulous Stage - Fistula formation is fairly constant in this disease. More commonly the connection is with the sigmoid, next in frequency the cecum and ascending colon and even the transverse colon. Practically diagnostic of the disease is a fistula in the abdominal wall persisting and appearing after operation for a supposed acute appendicitis and the removal of an innocent appendicitis. These fistulae seem to connect with the cecum, but are in reality communications between the necrotic terminal ileum and the abdominal wall. They differ from a simple appendiceal fistulae in that they never close spontaneously, resist simple surgical closure by excision and inversion of the stump and as already stated, connect with the terminal ileum instead of the cecum.

Another peculiar feature of these fistulae is that they may develop months after the original drainage operation for a supposed appendiceal abscess. The original wound, meanwhile, has completely healed and the first sign of fistula formation is the ap-

pearance of the abscess in the wall which, in being opened is found to lead to the intestine.

Corr(14) believes that these types should merely be regarded as different phases of the same process. He regards the type which simulates appendicitis as the early phase, and that resembling ulcerative enteritis as the chronic phase. The stenotic type is a later phase of the chronic, and the fistula stage is thrown in under the heading of the fourth phase.

Sproull(58), in a study of the literature of one hundred and thirty-two cases, types the disease process as to its localization in the following chart.

Localization	Number of Cases
Terminal ileum alone	37
Terminal ileum and ileocecal valve	17
Terminal ileum and part of cecum	15
Terminal ileum, cecum, and part of ascending colon	13
Ileum alone(exact location not specified)	10
Cecum only	9
Cecum and ascending colon	5
Jejunum alone	5

Localization	Number of cases
Cecum and ileocecal valve, and ascending colon	4
Terminal ileum, ileocecal valve, cecum, and ascending colon	4
Terminal ileum, ileocecal valve, and part of cecum	3
Entire small and large intestine	2
Entire colon	1
Mid-ileum	1
Transverse colon only	1
Sigmoid only	1
Terminal jejunum and upper ileum (tuberculosis?)	1
Ascending colon	1
Cecum and ileocecal valve	1
Entire ileum exact three proximal feet and distal five inches	1
Total Cases	132

No proved cases of involvement of the duodenum have been found.

Symptoms

Pain - The most constant complaint is that of
pain. This pain may be cramp-like and is usually
intermittent and may be relieved to some extent by
a bowel movement or by vomiting. Dalziel(19), in
1913, in a study of five cases, writes, "The
symptoms in all the cases were similar; the character-
istic and most striking feature being most violent
colic, constant mucus from the bowel. The bowel
becoming exhausted, or the contents being forced
through the rigid portion, the patient would then
be at rest, quite comfortable and cheerful for a time.
In the case of the child even ten to twelve hours
might elapse between the attacks of pain, which
were truly distressing in their intensity. In the
young, one would naturally suspect intussusception,
except that the obstruction was not complete, while
the intensity of the pain put a chronic intussus-
ception out of the question. Above the affected
portion of the bowel peristalsis could be observed.
During a painful attack the inability to retain
food and the constant suffering leads to emaci-
ation, the temperature only occasionally rises,

and during the intervals of pain, the pulse is quiet."

Meyer and Rosi(40) also noted that the pain occured in paroxyms with relative freedom between the symptoms. This colic-like intermittent pain was present in three confirmed cases of regional enteritis and in these cases it resembled acute intestinal obstruction.

Diarrhea - Diarrhea was one of the most prominent symptoms in Crohn's series. The diarrhea may be constant or intermittent. It is usually seen in cases which involve the cecum along with the ileum, and it is also found when the lesion is ulcerative. Hence, diarrhea is dependent upon the situation of the lesion, extent of the involvement, and the nature of the pathologic change. In general stools are loose and watery, with much urgency and cramping, but usually without visible blood,(Brown,P.W.10). Even in the face of a marked diarrhea there is usually no tenesmus.

Vomiting - This is a striking symptom, and is of the intermittent variety. There is only a partial loss of food and drink, and it is seldom that of complete or impending obstruction. It is seen in those patients who have stenotic lesions.

Fever - The fever, when present, usually ranges
between 100 and 101 degrees. There may be intervals
when there is relative freedom from temperature. .

Loss of Weight - This may be a very prominent
symptom. Brown(10) found a loss of weight in four-
teen of eighteen patients. In this series the
average loss of weight was found to be twenty-
five pounds. In the very severe cases it may be
so marked as to resemble the emaciation of mal-
ignancy.

Fistula - Many of these patients may have
evidences of a fistula. This is more marked in
those who have had a previous appendectomy, so
much so that in Crohn's original series he mentions
the scar of a previous appendectomy as being one
of the prominent symptoms. Olson(46) says that
in the absence of tuberculosis or actinomycosis,
any fistulae which would resist a simple surgical
closure should be considered as a case of regional
enteritis.

Previous Operations - Pemberton(47) reports
the startling fact that twenty-six of thirty-nine
patients had undergone one and often more unsuc-
cessful operations for this disease and this is

evidence of its seriousness, as is the fact that
in the past the disease has remained unrecognized
even after the abdomen has been opened. Sixteen
patients in this series had undergone an appendicec-
tomy which had failed to relieve their symptoms.
Eight patients had fecal fistula which had followed
previous operations, such as drainage of an abscess,
or an effort to relieve obstruction in the term-
inal portion of the ileum by freeing the intestinal
loops. In one case the fistula had developed after
the ileum had been anastomosed to the ascending
colon. A diagnosis of tuberculosis was made in a
case in which the patient was subjected to a right
salpingo-oophorectomy after an appendicectomy had
been performed previously. In two other cases in
which an exploratory laparotomy had been performed,
the surgeon had made a diagnosis of tuberculosis and
had closed the abdomen. The symptoms had recurred
in four cases in which resection of the ileum or
colon had been performed. Two patients who had been
subjected to appendicectomy had been told they had
a disease of the ileum but they had not been ad-
vised about the proper treatment. A boy who had
undergone an appendicectomy had been told that he

had a disease of the ileum. One year after the ap-
pendicectomy had been performed, the boy had under-
gone an exploratory laparotomy. A diagnosis of
lymphosarcoma had been made but no attempt had been
made to remove the tumor. A fistula had developed
in a case in which appendicectomy and drainage had
been performed for either "cancer or actinomycosis."

Koster(36) and his co-workers carefully followed
seventeen cases and reported their findings in the
following chart.

Chart from Koster et al

	No. of Cases
Duration of Symptoms	
7 days or less	6
4 to 6 months	5
6 to 12 months	3
2,3, and 4½ years	3
Abdominal Pain	
Generalized	13
Localized in right lower quadrant	14
Diarrhea	1
Nausea	11
Vomiting (2 without nausea)	13
Previous attacks of abdominal cramps (prior to acute attacks that caused hospitalization)	10
Loss of weight (all advanced stage)	3
Previous operation(apparently complicated by fecal fistula 8 mo. before, 4 years before, 24 years before)	3
Tenderness	17
Spasticity(Right lower part of abdomen)	13
Distention	10
Rebound tenderness	13
Mass(palpable on both rectal and abdomen examination)	2
Visible peristalsis	2
Fecal fistula	2
Temperature	
Below 99 degreew	1
99 to 100 degrees	13
100 degrees or above	3
Pulse Rate	
80 or less	3
80 to 100	13
100 to 120	6
Respiratory rate - No elevation in any case	
White blood cell count and differential	
8,000 or less	2
8,000 to 10,000	1
10,000 to 12,000	2
12,000 to 14,000	2
14,000 to 16,000	2
16,000 to 18,000	3
18,000 to 20,000	3
20,000 or above	2

In most cases the symptoms were not marked
until the low grade inflammatory process had pro-
duced a sufficient degree of constriction in the
region of the ileocecal valve and in the large
intestine to induce partial intestinal obstruction
(Donchess,J.C.20). Hagen(29) says that the symp-
toms of constipation will also appear when the
lumen of the bowel becomes contracted and hinders
the progress of the digested food.

Bissel(8) reports a case in which there were
urinary symptoms in a male, age thirty-nine, who
had nocturia and frequency. In this case the
symptoms were due to the inflammatory mass dropping
behind the bladder and into the cul-de-sac, and in
physical examination this mass could be palpated
by rectal examination. In all such cases a rectal
examination should not be omitted, in so far as it
may be the key to the diagnosis.

X-ray Findings

In the diagnosis of regional enteritis perhaps
the most important single finding is to be gained
from the X-ray. In the correlation of the symptoms
with the X-ray findings it is sometimes possible to
make a positive diagnosis before laparotomy. It
is necessary to visualize the entire gastro-intes-
tinal tract; this may be accomplished by the use
of the barium meal and serial plates taken at
various intervals as the meal passes through. In
this respect both Connell(13) and Clute(11) sug-
gest that the films be taken every hour and pos-
sibly taken at various angles instead of the usual
six hour interval plates. In this way lesions in
the small bowel may show to better advantage.

Kantor(34) has done considerable work on the
X-ray findings in regional enteritis. He reports
them as follows:

1. Filling defect. There is a constant defect
in the filling of the terminal small intestine.
This is manifested in all observations and offers
a striking contrast to the familiar picture of the
final loop of the ileum as it rises out of the

pelvis to enter the ileocecal valve. The extent
of this ileac filling defect depends on the extent
of the stenotic process of the small intestine.

2. Proximal bowel. In half of the cases the
ileum proximal to the filling defect appeared ab-
normal in contour. The involved loops appeared
irregular in shape, or else the very last segment
of ileum showed a peculiar taper point. In some
cases this taper point became continuous with the
string sign to be described.

3. Obstructive Signs. Actual obstruction may
be present, however, as a general rule there is
usually only a slowing of the contents. The stasis
in the ileum will be revealed in the X-ray nine
hours or more after the opaque meal and also by
dilatation of the loops proximal to the filling
defect. Kinsella(35) reports that even in the early
stages of the disease there is a delay in the empty-
ing of the terminal coils of the ileum.

4. "String Sign" Perhaps the most striking
finding is the "string sign", a name borrowed from
A.W. Crane. This is a thin, slightly irregular
linear shadow suggesting a cotton string in ap-
pearance and extending more or less continuously

from the region of the last visualized loop of
ileum through the entire extent of the filling
defect and ending at the ileocecal valve. It re-
presents the attenuated barium filling of the great-
ly contracted intestinal lumen. Multiple or branched
"string signs" may be attributed to multiple areas
of involvement or to fistula formation. Meyer(39)
recommends the use of opaque media in following out
fistulous tracts which may open out on the abdominal
wall.

The changes in the colon are usually the result
of spasm secondary to the ileac involvement. The
situation in this regard is similar to the Stierlin
filling defect of the cecum in which the lesions
are present, not in the colon, but in the terminal
small intestine. The spasm in ileitis takes the
form of a contracture sometimes of the entire ceco-
colon, but most characteristically of the cecum
proper. There is often a marked spasm of the sphincter
of Busi as well as of the cecal tip, so that this
segment assumes a special bud-like or teat-like
appearance. In most cases of functional spasm of
the cecum or ceccocolon the changes are not con-
stant but intermittent. Furthermore, the opaque
enema usually suffices to fill out the involved

areas in normal fashion.

On the other hand, the colon may be actually involved by the disease process in the adjacent ileum, as by adhesion or fistula formation. In such instances a fixed deformity result, most commonly affecting the inner (mesial) aspect of the large intestine.

Kantor(34) records the X-ray findings in six cases of regional enteritis in the following chart.

Case	1	2	3	4	5	6
Ileum						
Filling defect	*	*	*	*	*	*
Irregularity of last						
filled loop	*	*	o	o	o	*
Stasis	*	o	o	o	o	*
"String Sign"	?	*	o	*	*	*
Colon						
Cecal Spasm	**	*	*	*	*	*
"Colitis"	*	*	*	*	*	*

*- indicates presence of sign

o- indicates absence of sign

?- indicates questionable

Cushway(18) believes that negative findings with the opaque meal by mouth or the barium enema in the presence of symptoms simulating ulcerative colitis or tuberculosis are suggestive of regional enteritis. Such negative findings with the opaque enema with clinical features suggestive of colitis and enteritis should suggest the advisability of making a careful serial roentgenological examination with the opaque meal. The internal studies of the small bowel after the administration of the opaque meal orally will show a definite delay in motility of the meal through the distal end of the small intestine. The milder degrees of stasis may be overlooked if the roentgenologist does not bear this condition in mind.

Differential Diagnosis

Cushway(18) states that regional enteritis must be differentiated from all conditions which produce a mass in the right ileac fossa with diarrhea, fever and the symptoms of a low grade or severe obstruction.

1. Hyperplastic tuberculosis of the ileum. Dr. Bargen(3), in discussing a case of regional enteritis, says that it is apparently more localized than the usual tuberculous enteritis. He believes that the two conditions are frequently indistinguishable grossly and that regional enteritis was previously called tuberculous enteritis. Tuberculous enteritis is probably rare as a primary process, thus, chest films are of value in differentiating. Ginzburg(26) found only six cases of localized hypertrophic ileocecal tuberculosis as against eighteen of the non-specific variety in the past ten years. He makes the note, however, that well defined active cases of pulmonary tuberculosis are not as a rule admitted to the Mount Sinai Hospital. Rockey(55) states that there were only nine cases of hyperplastic tuberculosis

of the terminal ileum reported in the literature up to 1933. Jellen(33) believes that so-called "primary" hyperplastic tuberculosis, in which the disease is limited to the intestine alone, and without evidence of tuberculosis elsewhere in the body, is very rare.

2. Ulcerative Colitis: usually colitis may be recognized by roentgenologic studies with the opaque enema. The spasm deformity of the portions of the colon involved and obliteration of haustra are quite characteristic of colitis. In regional enteritis changes are usually proximal to the ileo-cecal valve. A mass is rarely palpable in colitis.

3. Typhlitis or cecitis: usually causes more deformity and spasm of the cecum than is present in regional enteritis.

4. Lymphosarcoma: intestinal or mesenteric tuberculosis and Hodgkins disease may simulate regional enteritis because of the palpable mass and obstructive symptoms.

5. Actinomycosis of the ileocecal region with fistula formation to the external abdominal wall should be considered though rarely found in this region. Culture of the discharge on suitable media

will be of value in this condition.

6. The differential diagnosis between regional enteritis and malignancy of the terminal ileum, ileocecal valve or appendix may give considerable difficulty and may not be possible even at the operating table. It is usually only made by microscopic examination of tissue.

7. Intussusception: in the young it may be hard to differentiate between acute regional enteritis and insussusception. Probstein(49) reports a case of a five year old boy who had all of the symptoms of intussusception, there was a palpable tumor, visible peristalsis, intestinal hemorrhage and absence of temperature elevation. When the operation was performed the boy was found to have a regional enteritis.

Mulsow(45) stresses the difficulty of making a positive preoperative diagnosis of regional interitis believing it to be almost impossible. He mentions two cases, one in a woman, age forty-four, with a preoperative diagnosis of malignant disease in the region of the cecum, and one in a girl, age fifteen, with tuberculin positive skin, but negative chest X-rays with a preoperative diagnosis of tuber-

culosis of the cecum. Microscopic examination
ruled out both of the above diagnoses and established
that of non-specific enteritis.

Treatment

In the treatment of this condition most authors
now agree that surgery is the method of choice.
In general, management in all of these cases should
be similar, including the greatest possible rest
for the involved portion of bowel, with adequate
systemic treatment to control the infection. Thus,
complete resection, or short circuiting, together
with adequate medical care are the measures of
choice(4). The medical treatment of regional
enteritis is palliative and supportive only(21).

However, Homans(32) does not believe radical
surgery should be done because the disease is of an
infectious nature. This idea is supported, to
some extent, by the results of Rockey's work, in
which he found the clinical picture to be essenti-
ally that of regional enteritis, in four children
between the ages of five and nineteen years. At
operation in all, the ileum was described as thick-
ened and tube-like for the distal six to eight
inches. In these cases the appendix, which was
essentially normal, was removed and all had an un-

eventful recovery. Probstein and Gruenfeld(49)
also report three cases which responded without re-
section. Meyer and Rosi(40) also believe that
spontaneous recovery may occur. And they also
give three cases which, following the removal of
the appendix, had check up X-rays and two of these
showed spontaneous recovery. The other one sub-
sequently came to surgery for resection.

Clute(11) suggests that in those patients with
severe obstructive symptoms, a preliminary trans-
verse ileocolostomy may be the procedure of choice.
Later a resection may be done if the symptoms persist.

Mixter(41) believes that in view of the pro-
gressive character of the lesion treatment is de-
finitely surgical, but the hazards of operation
should be emphasized. Operative maneuvers may
activate a latent infection and cause a fatal peri-
tonitis or septicemia. Drainage should be avoided
when possible as it frequently leads to fistulae.
Resection of the involved segment in one or mul-
tiple stages is the ideal procedure. Technically
the operation is difficult due to the severe hemor-
rhage caused by mobilization of the bowel, the

extreme thickening of the mesentery and at times the presence of complicating fistulae. The cecum is removed with the terminal ileum, as the ileocecal valve is usually involved, and an end-to-side or side-to-side anastomosis established with the ascending colon. An ileostomy to relieve the suture line is often advantageous.

Adams(1) believes the method of choice is resection and he presents nine cases which had resection with no deaths. He believes that a short circuiting operation is dangerous because it leaves the diseased bowel as a source of infection, chronic perforation, abscess formation, fistulae and a constant manace to the health of the patient.

Holm(31), who did experimental work on five dags, and adds to this the clinical observations from two cases, concludes:

(1) The side tracked ileal loop of the lateral ileo-ileostomy or ileocolostomy for complete benign obstruction of the terminal ileum is likely to become greatly elongated, dilated, and ulcerated. An enterocolitis with mucosal degeneration, and degenerative lesions of the liver and kidneys will

probably develop(due to peritonitis).

(2) Whenever possible, the side tracked ileum should be resected at the time the lateral anastomosis is done.

(3) If resection is inadvisable because of the condition of the patient, the lateral anastomosis should be done as near the obstruction as possible, and should be regarded only as a first stage operation, to be followed by a resection of the side tracted loop of ileuma at a more favorable time.

(4) As an alternative procedure it is suggested that the ileum might be divided as close to the obstructive lesion as possible and be followed by an end to side anastomosis, which eliminates a blind end.

Meyer and Rosi(39) state that in thsoe patients where the regional enteritis is complicated by a fecal fistula, excision of the diseased ileum with the fistulous tract is necessary to obtain a cure. Failing this, the fistula will recur. Crohn(15) reports a case in which eight laparotomies were performed for closure of a fecal fistula, which followed the drainage of an abdominal abscess that developed after an appendectomy.

In any condition that a large inoperable mass
is found when exploring the abdomen, a biopsy should
be made in order to determine the nature of the con-
dition. If this had been done previously many so-
called malignancies with cures might have been
avoided.

In the treatment of the condition it must be re-
membered that there is usually an associated anemia.
This should be corrected by preoperative blood trans-
fusion in those patients where the condition is
severe. In some it may be corrected to a large ex-
tent by bed-rest, proper diet, and iron and liver
therapy.

As regards the prognosis in regional enteritis,
it is rather early to make any definite statements
because of the wide variety of treatments used. In
general the prognosis is dependent upon the acute-
ness of the case, the severity of the symptoms, and
the extent of the disease process. These factors
may be well recognized in those cases which were
described earlier and which resolved following a
simple appendicectomy or merely opening and clos-
ing the abdomen. On the other hand, the more severe
cases will resist such simple treatment and may

be the cause of much anxiety and tax the ingenuity
of the surgeon. This is well illustrated in a case
of Shearer and Jackson(57) in which a localized
terminal ileitis has recurred twice following re-
section of the diseased portion of the bowel after
intervals of three and one-half years and nine years
respectively. Also, in two cases in Ravdin's(53)
series, the disease process was so large and exten-
sive that a resection was not possible. He at-
tempted to treat the lesions with deep X-ray ther-
apy but his results were not promising.

In regards to those cases with an acute onset
and with a history of less than four months duration,
Crohn(17) says that they are not infrequent but are
beside the rule. In seven such cases of his, two
died without surgery and one died following resection,
The other five cases survived resection in the pres-
ence of the acute lesion and all have remained well.

Summary

1. That there is a definite clinical and pathologic entity which has been given a wide variety of names. R⊔gional Enteritis is suggested as a descriptive term.

2. While the etiology is rather obscure apparently it is of about equal sex distribution with the twenties and thirties the most common ages. The condition is possibly present more commonly in the Jewish race.

3. The most common type found is that of the stenotic where symptoms of partial obstruction are present.

4. In study of microscopic sections a number should be looked over in order to identify the process.

5. The terminal ileum is that section of the bowel most commonly involved, however, the disease prosess is not limited to this area.

6. There are rather characteristic X-ray findings in the disease and positive diagnosis is usually based upon these findings.

7. The most accepted treatment is resection of the diseased bowel.

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