Landmark Article

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Non-specific Granulomata of the Intestine*

(Inflammatory Tumors and Strictures of Bowel)

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DURING THE PAST FEW YEARS, we have encountered cases, apparently with increasing frequency, which clinically and radiologically gave the impression of being tumors or tuberculosis of the bowel. At operation, these cases were usually considered to be either hypertrophic tuberculosis or malignant disease. Microscopic examination of resected specimens, however, failed to substantiate these views. No evidence of specific disease, such as tuberculosis, syphilis, or actinomycosis, could be found. Amoebic disease of the bowel was excluded both from a study of the sections and the stool, as well as by the inefficacy of emetin therapy in suspected cases. Carcinoma, lymphosarcoma, and Hodgkin's disease could be definitely excluded. A few of these cases were quite evidently secondary to diverticulitis, but aside from these, a large heterogenous group remained, differing etiologically, but with certain common clinical and pathological findings. These cases, which showed various degrees of hypertrophic chronic inflammatory lesions in different stages of healing have long been known to the English as well as the Continental surgeons. In 1921 Tietze (1) published a thorough resume of the subject with a very complete bibliography. In 1923, Wilensky and Eli Moschkowitz (2) reported four cases which they had collected from various institutions, using the designation "Non-specific Granulomata of the Intestine," a name, which perhaps best conveys an idea of the underlying pathology. Mock (3) has recently reported a series of cases using the same designation. Clinically these cases manifest themselves either by the development of palpable masses or symptoms due to an ulcerative stricturing of the bowel. They may, therefore, with propriety, also be designated as non-specific inflammatory tumors and strictures of the bowel.

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It is well known that both the intestine and its peritoneal covering have tremendous powers of resistance to infection and a marked ability to resolve inflammatory lesions. Furthermore, the intestinal mucosa is possessed of marked regenerative power (4). Surgeons have time and time again recorded their amazement at the rapidity and completeness of the disappearance of huge inflammatory exudates and masses from the abdomen. Similarly, both clinically and experimentally we know that there may be extensive mucosal disease or injury without any resultant permanent scarring. In some instances, however, following an infection or injury, this "restitutio-ad-integram" does not occur. The persistence of some infectious agent or irritating factor, or the inability of the tissues to overcome them, results in a cycle of reparative and destructive processes which leads to the formation of either hypertrophic extra-intestinal masses or extensive intramural hypertrophic ulcerative stenotic lesions or combinations of both.

Histological study of the various types of lesions shows simply evidences of various stages and degrees of acute and chronic inflammation with lymphocytic, polymorphonuclear and plasma cell infiltration, with varying degrees of degenerative changes or fibroblastic proliferation. In some of the perintestinal lesions there is considerable hyalinization, and early calcification and even early bone formation have been encountered. The presence of giant cells is a common finding. We believe that these are accidental findings due to the presence of non-absorbable vegetable matter, minute quantities of which extravasated around the lesion in perforative cases or became entrapped in the healing of ulcerative lesions. Wilensky and Moschkowitz reported the presence of large cells in the section of one of their cases. By special stain, we have been able in a number of our cases to demonstrate cells or groups of cells with much cytoplasm and little nuclear material, which are in all probability, vegetable cells. These apparently became entrapped in healing ulcers and were apparently taken up by the lymphatics, for we have found them in the serous and subserous layers of the bowel, as well as the submucous. Being nonabsorbable, they become encapsulated by foreign body giant cells. In the serosa they give rise to little nodules which are very difficult to differentiate grossly from miliary tubercles. Such foreign body tubercles, incidentally, have been experi-

mentally produced by the introduction of emulsions containing vegetable matter into the peritoneal cavity (5). We consider them as accidental, rather than etiological factors, in the course of the disease. Their importance is two-fold; firstly, their irritant action may be a factor in producing the marked hyperplastic fibrosis seen in some cases; and secondly, they are probably responsible for the confusion of these non-specific lesions with tuberculosis.

The following is a study of fifty-two cases which have been observed and operated upon mainly on the surgical service of Dr. A. A. Berg during the last ten years. Only those cases where resection was performed or specimens obtained are considered. These sections were restudied with the invaluable aid of Dr. Paul Klemperer to help us in settling questionable points. These do not include cases of sigmoid diverticulitis or any lesions situated distal to the recto-sigmoid junction. Gastric cases and two cases of ulcerative jejunitis near the fossa of Treitze have also been excluded from this study. An accurate etiological or pathological classification is at present impossible. We submit the following classification therefore, fully conscious of its defects and overlappings, but pleading in its favor, a certain degree of clinical utility. It is our plan to discuss each group and to report in abstract some of the typical cases.

1. Extra- or peri-intestinal granulomata secondary to sealed-off perforations of the bowel.

2. Granulomata secondary to known vascular disturbances of the gut.

3. Localized hypertrophic ulcerative stenosis of the terminal ileum.

4. Localized hypertrophic colitis with or without low-grade generalized colitis.

5. Simple penetrating ulcers of the colon.

6. Lesions secondary to inflammation of the appendages of the bowel, such as appendicitis, diverticulitis, typhlitis.

I

Lesions in Which the Inflammation Reaction Is Mainly Extra- or Peri-intestinal and Which Are Secondary to Sealed-off Perforations of the Bowel

As a response to a slowly perforating lesion of the intestine that has become sealed off by omental, parietal, or visceral adhesions, large inflammatory masses, with very little or no pus formation may develop, which are intimately adherent to the serosa and sub-serosal tissues but do not actually involve the sub-mucosal and muscular layers of the gut. A classical example is the type of lesion resulting from perforation of the colon by such foreign bodies as fish bones. Usually this accident results in the formation of ordinary intra-abdominal abscesses. In some instances, however, probably due to the slow rate of perforation, the inflammatory reaction is mainly productive. As a result of the continued presence of the foreign body and the low-grade infection resulting from the penetration of the intestinal wall, a markedly hypertrophic inflammatory reaction takes place in the peri-colonic and sub-serous layers of tissue which both clinically and at the operating table may give the impression of being a colonic neoplasm. Three such cases operated upon under the clinical diagnosis of neoplasm were recognized for their true nature at the time of operation and the foreign bodies sought for and found. Perforative lesions, from whatever cause, may involve the omentum with the development of a large omental mass containing necrotic xanthematous tissue, firmer fibrotic masses, areas of calcification or discrete encapsulated miliary abscesses. The lesion in the wall of the gut may be minimal.

An exceedingly interesting group are those cases in which a pseudo-tumor of the abdominal wall itself develops as a result of a perforative lesion, becoming sealed off by the anterior parietes. In two such cases, foreign bodies (fish bone, toothpick) were found in the center of large firm tumor masses involving the rectus muscle and pro-peritoneal tissue. These tumors had been excised under the diagnosis of sarcoma of the abdominal wall. The deep side of these inflammatory abdominal wall tumors was densely adherent to the omentum but there was no evidence of adherent bowel. In two other cases, in which the same preoperative diagnosis of sarcoma was made, adherent gut was found on the deep side of the tumor mass; a perforation apparently having been sealed off by the parietal peritoneum. The "tumors" were found to be edematous, granulomatous lesions involving the parietal peritoneum and the pro-peritoneal cellular tissue.

Altogether, ten cases were encountered in this group, five of which were definitely due to foreign body. In three cases, the inflammatory mass was mainly in the serosal and subserosal layers of the flexures of the colon. In two instances, the mass was mainly omental; the original perforation being in the transverse colon in one instance and in the small gut in the other. In four cases, the main mass and granulomatous tissue lay in the abdominal parieties, and in one instance was chiefly peri-vesical. (The large group of cases with marked productive peri-cecal changes due to appendicitis and peri-sigmoidal inflammatory masses from sigmoid diverticulitis also belong in this group, and are much more common than any of the other types of lesions noted. They are so well known, however, that they have not been especially studied or included in the enumeration of this group.)

Clinically these cases are characterized by the development of a palpable mass without the appearance of symptoms due to obstruction or ulceration. Because of the lack of intramural involvement of the bowel the barium meal or enema usually shows no abnormalities. Occasionally, a persistent spasm of the bowel adjacent to the lesion may be encountered which gives the impression of a filling defect. At operation, these tumors are found not to encroach upon the intestinal lumen and intra-intestinal irregularities or ulcerations are absent. This point serves to differentiate even the very adherent and intimately connected peri-intestinal masses from neoplasm or inflammatory diseases which actually involve the bowel walls.

1. Case of large peri-intestinal inflammatory tumor originating in the small bowel

E. H., age forty-five, admitted to Mount Sinai Hospital in 1925. Two years ago a laparotomy had been performed in the lower abdomen. Did not know what operation had been performed. She was well until few months before admission when she began to experience localized abdominal tenderness,

some constipation and loss of weight. Physical examination revealed a large mass, the size of a grapefruit, to the left of the midline adherent to the scar of the old operation. No evidence of any hernia at this point. G. I. x-ray was negative. Colon enema negative.

At operation, tumor was resected with the adherent skin and fascia and muscle. On its deep surface it was intimately adherent to and apparently an integral portion of the wall of the small intestine. This portion of the bowel together with the tumor was resected.

Pathological report. — "Macroscopic specimen consists of a tumor mass, the size of a large grapefruit, adherent to the skin and by its deep surface to a small segment of small intestine. The skin and intestine appeared to be normal. The tumor itself, is of a mottled character, darker portions appearing like hemorrhagic inflammatory tissue. The lighter yellowish portions are evidently the seat of necrosis. Below the attachment to the skin is a small, hard piece of tissue which cannot be cut, and which may be either foreign body or possibly new bone formation. The portion of tumor not adherent to the gut is covered by a thin sheet of tissue probably compressed omentum. Grossly, it cannot definitely be determined whether tissue is inflammatory or neoplastic in nature. Microscopic examination: shows no evidence of neoplasm. There is considerable acute and chronic inflammation with areas of fibrous tissue, areas of necrosis, hyalinization, calcification and ossification."

The patient made an uneventful recovery. Six months postoperatively she was well. Has not been seen since.

2. Case of peri-colonic inflammatory tumor, mainly omental, simulating sarcoma of the bowel. Healed colonic perforation

D. S., age fifty-three, admitted to the Mount Sinai Hospital in 1922. Nine months before admission he had developed pain in the right lumbar region. After three months, the pain became most marked in the right lower quadrant where it had persisted to the time of admission. The pain was dull and boring, and radiated posteriorly. It was more or less continuous and bore no relation to either meals or bowel movements. There had been no change in the character of the alimentary habits. Physical examination revealed a palpable mass in the right lower quadrant opposite the umbilicus, the dorsal portion of which appears to be fixed. Wassermann was negative. X-ray showed spasticity of the transverse colon and an apparently persistent defect in the caput coli. Whether this defect was due to new growth or to spasm could not definitely be determined from the roentgenogram.

At operation a mass was found adherent to the parietal peritoneum. The peritoneum was opened below this point and separated. There did not appear to be any involvement of the inside of the bowel wall. The mass was thought to be sarcomatous and accordingly, resection of the transverse colon with the adherent tumor and omentum was performed.

Pathological examination. — Macroscopic specimen consists of resected transverse colon with a portion of mesentery and adherent omentum. At about the central portion of the specimen is a small mucosal scar extending through the wall and at this site thickened omentum is densely adherent. No definite perforation can be established. The omentum proper is markedly infiltrated and is the seat of numerous abscesses, varying from 1 to 3 cm. in diameter. Diagnosis: Inflammatory tumor of the omentum with multiple encapsulated abscesses.

3. Case of fish-bone perforation with peri-colonic mass

A. K. was admitted to the Mount Sinai Hospital in July, 1926, with a complaint of pain in the left upper quadrant of the abdomen of eight weeks' duration. The pain was localized, and did not radiate. It was more or less constant and had no definite relation to the intake of food. For the last three weeks, the bowels had moved only with the aid of cathartics. The patient also stated that the stools had become smaller in diameter. There was no melena, vomiting or diarrhea, nor were there any urinary symptoms. He had lost twenty pounds in weight since the onset of his illness. However, he appeared to be fairly well nourished and his hemoglobin was 95 per cent. In the left upper quadrant of the abdomen, and in the left flank, a slightly tender, large mass was palpable. X-ray and pyelogram of the urinary tract showed the kidney to be normal in size and in position. X-ray of the colon showed no filling defect. A pre-operative diagnosis of inflammatory tumor or carcinoma of the splenic flexure was made.

At operation, a large mass was found occupying the splenic flexure and upper portion of the descending colon. This was carefully separated into two component parts, one of which consisted of thickened, inflamed omentum; the other was a large smooth, firm peri-colonic mass. There was no evidence of any invasion of the colonic lumen. In the midst of this mass there was seen to be a depressed area, of what was apparently a healed fistulous communication with the gut. The omentum mass was then further explored and two fish bones were found lying in separate small abscess cavities. The abdomen was closed with rubber tube drainage and the patient made an uneventful recovery.

4. Case of fish-bone perforation with formation of inflammatory tumor of the abdominal wall

J. C., age sixty-five, was admitted to the Mount Sinai Hospital, April 30, 1925. For the past few months the patient had noted the development of a mass above and to the right of the umbilicus. There had been no pain associated with its development. It had never been reducible. Physical examination showed a hard, smooth, spherical mass about three inches in diameter, to the right and above the umbilicus. It was not tender and there were no signs of inflammation. There was no cough impulse. The preoperative diagnosis was that of a tumor of the abdominal wall.

An elliptical incision was made around the mass and the tissues found to be normal down to the rectus muscle. The posterior aspect of the rectus muscle, the posterior rectus sheath and peritoneum were involved in a mass of dense, grayish tissue. To effect its removal, the abdominal cavity had to be entered. The omentum was then found to be adherent to the mass, but was not apparently involved in the inflammatory process. There were no evidences of any adhesions of any of the abdominal viscera to the deep surface of the tumor. The tumor, when excised, was still considered to be a neoplasm, and the specimen was cut across for further inspection. In the depths of the mass a small collection of pus was found, and in its center was a fish bone, 2 to 3 cm. long. Culture showed staphylococcus albus and an anhemolytic streptococcus.

The pathological description follows: "The macroscopic specimen consists of tumor mass to which is attached a resected portion of omentum and some adherent muscle. The tumor mass measures about 7 to 8 cm. in diameter, is oval in

shape, firm in consistency and on section presents a small sinus tract, containing a foreign body about 3 cm. long (fish bone). Microscopic examination discloses a fibroma showing numerous inflammatory areas. A few multinuclear giant cells are present, in the tissue adjacent to the foreign body."

II

Lesions Secondary to Known Vascular Disturbances of the Bowel

The most striking example of this type of lesion that we have encountered is the stenotic involvement of the bowel, resulting when badly compromised but viable gut has been replaced following operation for strangulated hernia. In these cases there is permanent vascular injury affecting the intramural vessels of the bowel. Vascularization through anastomosis is sufficient to prevent a necrosis of the muscular and fibrous layers of the bowel. It is, however, insufficient to permit of the usual marked regenerative functioning of the intestinal mucosa. Ulcerative lesions involving the mucous membrane first result, followed by secondary infection and the production of gradual fibro-stenotic reactions which may result in extreme reduction of the caliber of the intestinal lumen. Five such cases have been encountered in this series, all in the form of a tubular stenosis, i.e., cases in which the entire segment of strangulated gut underwent fibrotic involution. In the literature, cases of narrow annular stricture corresponding to the site of constriction at the neck of the sac have been reported. In this series we observed one annular stricture in which a loop of gut had been caught under an encircling band of omentum. Small mesenteric tears have been reported as causing stenosis, both clinically and experimentally, in the same manner.

The symptoms are those of gradually increasing subacute intestinal obstruction, the ulcerative phase apparently passing by unnoted. The symptoms have appeared anywhere from two weeks to six months following strangulation. Short circuiting entero-anastomosis effected relief of symptoms in four cases; resection in one. One patient came to autopsy without operation.

In these cases we have definite evidence from the history and findings at the primary operation that there had been extensive vascular insult. How large a role this vascular mechanism plays in cases where the causal connection is not so clear-cut, it is difficult to say. The fact that such lesions as repeated and self-reducing intussusceptions or recurrent partial volvulus, especially at the ileo-cecal angle, may be responsible for certain chronic inflammatory lesions, must be borne in mind, although insusceptible of proof. It must be emphasized that the end stages of a lesion in which primary vascular insufficiency permitted necrosis and secondary infection of the bowel resemble almost identically those in which a primary infectious agent has produced secondary thrombotic and degenerative changes.

I. M. L., age forty-five, was admitted to the Mount Sinai Hospital in September, 1926. She had been operated on four years ago at another hospital for a left inguinal hernia, which had apparently recurred shortly afterwards. Eight hours before admission it had suddenly become large, painful and irreducible. She had vomited three times. Examination revealed an irreducible inguinal hernia about the size of a small grapefruit.

An immediate operation was performed, and a bilocular sac containing brownish, slightly foul-smelling fluid, was found. Two loops of intestine were found to be incarcerated, one of which showed considerable cyanosis with subserous hemorrhage. After a prolonged period of observation and irrigation with warm saline, the loop was considered viable and was replaced. The subsequent course was uneventful, and the patient was discharged well at the end of two weeks.

For four months following the operation the patient was apparently entirely free from symptoms. At that time she began to experience occasional attacks of colicky abdominal pain. There was no vomiting or constipation. Shortly afterwards, the patient was seen in the return clinic and visible peristalsis noted. A gastrointestinal x-ray was taken which showed unmistakable evidence of an incomplete small intestinal obstruction. Laparotomy was advised but refused. One month later, the patient was readmitted to the hospital in a moribund condition with signs of intestinal obstruction. Her condition was too poor to warrant operation. Respirations ceased soon after admission.

Autopsy showed the following: "Eighty cm. above the ileo-cecal junction, the intestine shows a narrowing 8 cm. long. The area is about one-third the diameter of the normal intestine. The ileum proximal is markedly dilated. In the region of the stricture the wall of the intestine is markedly thickened and the lumen markedly stenotic. The mucosa is cicatricial and there are polypoid excrescences of the preserved mucosa. Microscopically the wall of the ileum is seen to be several times normal in thickness. The mucosa is denuded of epithelium; the muscularis mucosa is fragmented. There is a marked inflammatory infiltration of submucosa and subserosa."

III

Hypertrophic Ulcerative Stenosis of the Terminal Ileum

In this group of cases the terminal ileum is the seat of the lesion, the changes being most marked at the ileo-cecal valve where it usually terminates abruptly on the ileal side of Bauhin's valve. Proximately, it diminishes in severity, signs of the disease being rarely found further than 10 to 15 inches from the cecum. We have no clue to its etiology but observation of various stages of the disease in different patients lead us to believe that the following are the steps in the development of the final process. The primary lesion, we believe, are a number of oval or lenticular shaped ulcerations located on the mesenteric side of the bowel. We have found this lesion on a number of occasions proximal to the main, hypertrophic mass and separated from it by normal looking mucosa. As the disease progresses, it is characterized. by two main features; firstly, a marked tendency to perforation and secondly, by an excessive proliferative reaction in the submucosa. The end stage of the process, the one most frequently encountered, is manifested by the conversion of the terminal ileum into a thickened hose-like tube. When opened, the normal transverse intestinal folds in the terminal portion of the bowel are seen to be partially destroyed and partially flattened and broken up into polypoid masses. A series of linear ulcerations along the mesenteric border is practically a constant finding. At times, especially near the cecum, the mucosa is almost completely atrophic and there may be papillary excrescences, especially along the margins of the ileo-cecal valve. The submucosa is enormously thickened and causes a marked diminution in the caliber of the lumen. Perforation frequently occurs in between the leaves of the mesentery and the enlarged glands and exu-

date gives rise to good-sized masses. The pus may track along the cellular tissue and form secondary communications with the cecum or colon. At times the perforation occurs into the peritoneal cavity with the formation of an intra-peritoneal abscess. Drainage of these abscesses results in the formation of intractable fistulae. Clinically, these patients have presented themselves with four different pictures.

1. Simulating acute appendicitis. — The first sign of the disease may be an attack impossible to differentiate clinically from appendicitis. At operation however it is at once noted that the terminal ileum is soggy, edematous and blotchy, and that there are numerous large succulent glands in the terminal mesentery. Resection has never been performed in this stage of the disease in this series, so that we have no idea of the underlying pathological changes present during this phase. A number of these patients gradually passed into the more chronic phases of the disease. One case is symptom-free two years after exploration, although x-ray shows definite narrowing in the terminal ileum.

Occasionally these patients are admitted with an abscess already present. Drainage may result in the formation of a chronic fistula starting immediately post-operatively, or there may be primary healing with secondary breaking down, occurring weeks or months later.

2. Symptoms of ulcerative enteritis. — There may be a low-grade diarrhea, loss of flesh and strength, mild colicky pains, and a development of a secondary anemia. This type is rather uncommon.

3. Symptoms of chronic incomplete small intestinal obstruction. — This is the most common manifestation of the disease. The patient may previously have passed through one of the phases described above, but frequently the obstructive symptoms appear without any previous history. Severe abdominal cramps, visible peristalsis, and borborygmus are the most common symptoms complained of. The duration of symptoms in this group varies from one to three years. At operation the typical hose-like ileum referred to above, frequently very densely adherent or communicating with the cecum, ascending colon or sigmoid is found. The occasional presence of small tubercle-like nodules may serve to render differentiation from tuberculosis more difficult. The nature of these foreign body tubercles has been discussed above.

A mass was palpable in every subacute and chronic case. Visible peristalsis was frequently noted. The barium enema as a rule shows no abnormality, as the disease ends at the ileo-cecal valve. As a result of pathological ileo-colic or ileo-sigmoidal communications, secondary changes may occur in the colon which are reflected in the barium enema and which may lead to a false conception as to the true nature of the pathological process. In two instances, definite narrowing has been demonstrated in the terminal ileum following the barium meal. In others, dilated loops of ileum and ileal stasis have been demonstrated. In most of these cases no attempt was made to administer a barium meal because of a fear of causing a complete obstruction.

4. Chronic intractable fistulae. — These have resulted following drainage of intra-abdominal abscesses, and have resisted closure by exposure and simple suture of the internal opening plus enterostomy. They have been cured either by short-circuiting operations with exclusion of the involved loop, or resection of the diseased segment plus entero-colostomy. The findings at operation are those described tinder the chronic form of the disease plus the presence of extensive adhesions.

There have been fourteen ileo-cecal resections in this group with one death. Of the remaining thirteen cases, one patient returned with an annular stricture a few inches proximal to the site of the original resection. The other cases have done well. We have only two proven cases where a previous short-circuiting operation with exclusion had been performed, both these cases later coming to resection. In one of these, an anastomosis had been performed elsewhere apparently through disease tissue with a resultant implantation of the disease on the colonic side of the anastomosis. Another patient, on whom an entero-colostomy with exclusion had been done, developed a new focus of the disease involving a segment of gut five or six feet proximal to the original area. There were four other patients who, we believe. fall into this group, in whom entero-colostomy exclusion proved curative. No specimens were, however, removed from these patients and they are not definitely included in this group.

Relation to Appendicitis

We do not believe that this group of cases has any relation to appendicitis. Approximately half of these patients had been subjected to previous appendectomies. In some of them, it had already been noted at the time of the primary operation, that distinct abnormalities were present in the terminal ileum. In those patients in whom the appendix was still present at the time of resection, no particular abnormalities were found in it, aside from a severe peri-appendicitis.

Relation to Tuberculosis

Careful study of these sections revealed no definite tubercles, no caseation, necrosis, nor could tubercle bacilli be demonstrated. In six instances, guinea pig inoculation, inoculation into rabbits and into chickens failed to show evidence of any variety of tuberculosis. Lowenstein cultures for tuberculosis were negative in three instances.

It might be argued that evidences of tuberculosis would be difficult to find in tissue which has undergone fibrosis. However, anatomical tubercles and the Koch bacillus could not be demonstrated even in the active ulcerative lesions found proximal to the main hypertrophic mass. Even in the tubercle-like structures occasionally seen on the serosa, definite evidence of Koch infection could not be found. During the past ten years there have been only five cases of localized hypertrophic tuberculosis resected at operation at the Mount Sinai Hospital. There have been a number of instances of multiple tuberculous foci in the intestines found at laparotomy. There have also been a number of cases with active or advanced pulmonary tuberculosis with x-ray evidence of involvement of the ileo-cecal region. In the latter instance, operation was never resorted to.

To sum up our impressions of localized hypertrophic tuberculosis, it has been our experience that most of the supposedly localized ileo-cecal tuberculosis proved on microscopic examination to be non-tuberculous, while on the other hand, most of the indubitably tuberculous lesions proved to be unsuitable for resection because of their multiplicity.

Case of hypertrophic stenosis of the terminal ileum, foreign body tubercles present

A. P., age thirty-six, was admitted to the Mount Sinai Hospital, July, 1930. Eight years ago an appendectomy had been performed, apparently for chronic appendicitis. The present illness was of two years' duration, first manifesting itself by weakness and loss of weight. Eighteen months before admission severe peri-umbilical pain had developed and had gradually increased in severity until it was almost continuous. She had suffered from moderate constipation until the last few weeks, when mild diarrhea movements, three to five per day, occurred. She was asthenic and had lost thirty pounds in two years. Physical examination revealed a mass, the size of an orange in the right lower quadrant, behind the old appendectomy scar. Hemoglobin was 50 per cent, Wassermann was negative. Stool showed no blood, ova or parasites. Barium enema showed dilatation of the entire colon with marked redundancy of the transverse colon. X-ray following barium meal showed some degree of ileal stasis. A preoperative diagnosis of either carcinoma or tuberculosis of the ileo-cecal region was made.

Operation revealed a large inflammatory mass involving the terminal ileum, cecum and ileo-cecal mesentery. There was a large mass of nodes along the right colic artery. Tubercle-like structures were found on the serosa of the terminal ileum. The post-operative diagnosis, following a resection of the terminal ileum, cecum and ascending colon was ileo-cecal tuberculosis.

Pathological description. — "Resected specimen consists of 12 cm. of ileum, cecum and ascending colon. Ileo-cecal junction is markedly thickened, forming a tumor the size of a tangerine. The mucosa of the ileum shows areas of ulceration as well as some areas of mucosal hyperplasia. Some of the ulcers appeared to be surrounded by tubercle-like structures. The ileo-cecal orifice was markedly narrowed and the wall of the valve infiltrated by dense connective tissue. The cecal wall also appeared hyperplastic but the main lesion seemed to stop at the valve. The serosa of the ileum and cecum presented a few discrete millet-sized tubercles."

Histological examination.—Marked thickening of all the layers of the gut due to fibrous proliferation with diffuse infiltration of large and small lymphocytes, monocytes, plasma cells and occasional polynuclear leucocytes. There are also areas of lymphoid hyperplasia. The mucosa shows ulceration. No tubercle bacilli seen. No anatomical tubercles seen. No evidence of caseation necrosis.

Numerous giant cells were seen and large cells and groups of cells with pale cytoplasm and small nuclei. These were considered vegetable cells with foreign body reaction.

Portions of the lesion were ground up and injected into rabbits, guinea pigs and chickens for tubercle bacilli identification. All were negative. Final pathological diagnosis: non-specific chronic and acute productive and ulcerative inflammation of the lower ileum.

8. Hypertrophic stenotic inflammation of terminal ileum with obstructive symptoms, spontaneous perforation into sigmoid. Preoperative diagnosis: Carcinoma of sigmoid

Male, D. H., age twenty-six, admitted to the Mount Sinai Hospital in October, 1928. For three years he had been suffering from severe abdominal colic and constipation. At times diarrhea had been present. There was no bloody stool. He had lost considerable weight, the exact amount was unknown. No anemia. Physical examination revealed moderate abdominal distention. Rectal examination showed a mass rather toward the left side of the pelvis which could be palpated bimanually and was interpreted as being a sigmoid mass, prolapsed into the cul-de-sac. Barium enema showed a stricture of a mid-sigmoid which, at that point was narrowed to the size of a quill. Preoperative diagnosis was carcinoma of the sigmoid.

Operation. — Terminal portion of ileum was found densely adherent to cecum and both were bound down to mid-sigmoid. Upon freeing the adhesions it was seen that there was an ileo-sigmoidal fistula. Aside from this site of perforation, the sigmoid appeared normal. It was realized that the main lesion was in the terminal ileum. The opening in the sigmoid was therefore closed in layers and a typical ileo-colectomy performed for the removal of the mass involving the ileum and cecum.

Pathological examination. — Resected specimen consists of 33 cm. of ileum and the cecum. The proximal 17 cm. of the specimen consist of normal but markedly dilated small gut. The distal half of the resected gut is considerably narrowed and its walls thickened. The narrowing of the lumen and the thickening of the wall increase toward the cecum. The thickening is due mainly to hyperplastic changes involving the submucosa and the mucosa. A series of superficial irregular ulcerations with reddish green base are seen throughout the stenosed portion of the ileum always at the mesenteric insertion. About $6\frac{1}{2}$ cm. from the cecum there is an irregular hemorrhagic area about $1\frac{1}{2}$ cm. in diameter with a centrally placed irregular perforation. About 1 cm. from the ileo-cecal junction is a large superficially ulcerated area from which pus escaped on pressure. Aside from these ulcerated areas the mucosa is edematous and has a cobble-stone appearance. The lymph nodes are hyperplastic.

Histological examination.—Marked mucosal ulceration with acute and chronic purulent inflammation. Diffuse thickening of all layers of the gut especially the submucosa due to edema granulation tissue and diffuse infiltration with large and small lymphocytes, plasma cells and occasional polynuclear leucocytes and occasional giant cells. No tubercles or tubercle bacilli seen. Final pathological diagnosis: Hyperplastic chronic ulcerative inflammation of ileum. Picture resembles hyperplastic tuberculosis of the ileo-cecal region but there is no evidence of tuberculosis in this instance.

9. Operation for acute appendicitis. Diseased terminal ileum noted at the time. Gradual development of obstructive symptoms. No relief from ileo-colostomy. Resection performed.

S. W., age thirty, operated at another institution on March 1, 1929, with a preoperative diagnosis of acute appendicitis. At operation, it was noted that the ileo-cecal junction and the terminal ileum were red and thickened and the serosa dull and opaque, and covered with plastic exudate. Many large mesenteric glands were seen. Gland was excised and reported as hyperplastic lymphadenitis. The appendix was reported as chronic atrophic appendicitis. He was readmitted to that institution in January, 1930, with a history of pain in the lower abdomen, repeated vomiting and obstipation for two days. A diagnosis of fibrosis of the terminal ileum causing intestinal obstruction was made and the patient was subjected to a

laparotomy. The terminal ileum was found narrowed and fixed by numerous adhesions. An ileo-transverse colostomy was performed without division and exclusion of the loop. The patient did not do well after operation and continued to have increasing abdominal colic and marked loss of weight.

When he was admitted to Mount Sinai Hospital in June, 1930, patient was emaciated and visible peristalsis was noted in the lower abdomen. Repeated studies with barium meal and enema failed to cast much light upon the condition in the abdomen. It was thought that the symptoms were due to entrapment of intestinal contents between the site of the ileo-colostomy and the stricture in the terminal ileum. With this diagnosis patient was subjected to a laparotomy which revealed an exceedingly complicated series of conditions. Near the site of the old ileo-colic anastomosis a small abscess was encountered, penetrating into the transverse mesocolon. Exploration revealed this to be due to a perforation of a piece of toothpick through the small intestine with considerable degree of stenosis and kinking at this point. As it was impossible to close the perforation about six inches of the small intestine were resected and an end-to-end anastomosis performed. Following this, further exploration revealed that the terminal ileum distal to the anastomosis and the transverse colon were the seat of chronic inflammatory disease. A rapid resection of the terminal ileum, cecum colon, ascending colon and transverse colon to a point distal to the old ileo-colic anastomosis was undertaken and a new ileo-colostomy performed. Patient did remarkably well after this procedure and was discharged greatly improved seven weeks later. Patient has been followed for the past year, has gained forty pounds in weight, and aside from a small sinus communicating with the closed end of the transverse colon, showed no symptoms.

Pathological findings. — The macroscopic specimen consists of a resected portion of the terminal ileum, ileo-cecal junction, cecum, and ascending colon, and a portion of the ileum which has been anastomosed with the transverse colon at previous ileo-colostomy. The terminal ileum is markedly dilated to a circumference of 10 cm. and contains several small serpiginous ulcerations. The ileo-cecal junction is markedly stenosed and barely admits a medium sized probe. The stenosis is due to a large proliferating polypoid mucosal mass overlying the junction and surrounded by numerous ulcerations. The ascending colon, from the ileo-cecal junction to the old ileocolostomy is normal. At this point the mucosa on both sides of the anastomosis is found hypertrophic with numerous ulcerations and small polyps. The lymph nodes in the mesentery are enlarged and hypertrophic. In addition, there is a separate portion of resected small intestine at the center of which there is a perforation in the vicinity of which the wall of the bowel shows marked thickening, fibrosis and annular narrowing. Microscopic examination shows ulceration of the mucosa of acute and chronic suppuration. The walls of the gut are infiltrated with numerous large and small lymphocytes and plasma cells. There are a few eosinophiles and polymorphonuclear leucocytes. There is extensive fibrosis involving all the coats, most marked in the submucosa and the muscularis. No evidence of tuberculosis or amebae disease.

Diagnosis. — Ileo-cecal stenosis due to polypoid ulcerative non-specific ileitis involving the terminal ileum and transverse colon.

10. Operation for supposed appendix abscess. Appendix not badly diseased. Development of fistula in right lower quadrant eight months later. Diseased terminal ileum at operation three years later, for intractable fistulae.

H. C., age twenty-eight, first admitted to the Mount Sinai Hospital in January, 1928. At that time he complained of colicky pains in the abdomen, unrelated to meals of three weeks' duration. The morning before admission, the pain became more severe and was referred to the lower abdomen, especially on the right side. There had been no vomiting, or chills. Temperature had not been taken.

On admission, temperature was 104. Blood count was 20,000 with 92 per cent polys. There was tenderness, rigidity and a mass in the right lower quadrant. Clinically the case was considered a case of appendix abscess. Laparotomy was performed and a large mass, the size of a large grapefruit was found in the iliac fossa. After packing off the intestinal contents, the mass was unraveled and found to consist of the cecum, appendix, terminal ileum and its mesentery and a loop of sigmoid. The appendix was lying in a bed in the mesentery of the terminal ileum, which was about two inches thick and oozing pus. The appendix was removed and rubber-dam drain led down to the necrotic tissue. Aside from a wound infection, patient did well and was discharged one month later. Pathological report of the appendix was acute and chronic inflammation.

Patient was readmitted to the hospital in May, 1931. He had been well for eight months after the operation at which time the scar broke down in one place and for two months drained greyish, odorless fluid and then closed spontaneously. For the next one and one-half years, patient had no symptoms. Two weeks before the second admission he began to experience pain at the site of his scar, which gradually became more severe. On admission, patient's temperature was 103, and beneath the scar a fluctuant mass was present. Upon incision, about 1 ounce of thick, yellowish pus was evacuated. From this abscess cavity a tract led down toward the abdomen. Tube drainage was instituted. Patient drained feces for several days, and lipiodol injected into the wound seemed to run into the cecum. After about ten days the fecal discharge ceased and the wound began to granulate. Barium enema at this time revealed no abnormality in the cecum.

The patient was seen again in July, 1931, at which time, an exudate was still present in, the right lower quadrant. Conservative therapy was continued until November, when an exploratory laparotomy was undertaken. At operation, the terminal 2 feet of ileum were found to be greatly thickened, edematous, hyperplastic and in one of the loops was found, the inner opening of the fistulous tract. It was recognized that the fistula was not of appendicular or cecal origin but probably had at its base, a non-specific ileitis. Accordingly, resection of the $2\frac{1}{2}$ feet of terminal ileum, cecum and part of the ascending colon was undertaken and an ileo-transverse colostomy performed.

Pathological findings. — The specimen consists of 40 cm. of terminal ileum, 12 cm. of large bowel and attached skin. From the skin a fistulous tract leading to a point in the ileum, 4 cm. from the ileo-cecal junction. There are some enlarged, moderately firm glands in the ileo-cecal angle. Examination of the interior of the specimen shows cecum and colon to be normal. Beginning at the ileo-cecal valve and

extending proximately for 30 cm. there are marked mucosal alterations. The mucosa is markedly thickened, congested and thrown up with irregular folds. Rugae have lost their identity. The surface presents numerous hemorrhages, erosions and ulcerations interspersed with areas of mucosal hyperplasia. Lymph follicles are enlarged. The submucous layer is moderately thickened and fibrotic.

Microscopic examination. — Marked mucosal ulceration with acute-chronic purulent inflammation. Diffuse thickening of all layers of the gut, especially the submucosa, due to edema, granulation tissue and diffuse infiltration with large and small lymphocyte, plasma cells and occasional polynuclear leucocytes. No tubercles or tubercle bacilli seen.

Pathological diagnosis. — Hyperplastic chronic ulcerative inflammation of the ileum.

IV

Localized Hypertrophic Colitis

In addition to a purely localized definitely palpable inflammatory colonic mass, some of these cases at one time or another presented evidence of a low-grade general colitis, much milder in type than the ordinary severe, diffuse ulcerative form. In others, the disease remained localized. That ulcerative colitis may affect predominantly or almost exclusively certain segments of gut has been emphasized by Dr. Berg for years, and recently, Bargen has reported a series of cases illustrating the same point. In most of the present cases there were no roentgenological or sigmoidoscopic evidence of generalized colitis at the time of operation, and the symptoms were attributed entirely to the localized colonic disease. In a few of these cases, persistence of symptoms after resection led to renewed investigation, which in some instances showed evidences of mild colitis, which responded to medical therapy. In those cases where definite evidence of colitis involving other portions of the colon could be shown, coincident with the presence of a mass, it was sometimes possible to obtain a good result by a short-circuiting entero-colostomy. In only one case did definite symptoms appear first in a segment of gut other than in which the hypertrophic mass ultimately developed (case 11).

The cecum and ascending colon were the seat of the disease five times; the recto-sigmoid, three times; the mid-sigmoid, once; and the junction of the sigmoid and the descending colon, three times. In the right colon, the disease usually extended upward until a few inches from the hepatic flexure. The mucosa showed, at times, large irregular ulcerative areas up to 1/2 inch in diameter with areas of hypertrophic mucosa in between them. In other cases the ulcers were smaller and were overshadowed by the bullous polypoid mucosa. Papillomatous and polypoid changes were common in the mucosa. The submucosa was moderately thickened and edematous. The serosa was opaque, and there was marked thickening and hypertrophy of the subserosal fat both in the gut and meso-colon. Glands in the ileo-cecal angle were enlarged. Numerous adhesions to the omentum and surrounding loops of gut were found at operation.

In the sigmoid, the pathological changes were more of a fibrostenotic nature with narrower limits of involvement and relatively little ulceration and with more tendency to stricturing and papillary proliferation in the mucosa. Microscopically the picture was simply that of various stages of inflammatory disease. In addition to tuberculosis, careful search was made in these cases for amoebae. Evidences of neither were found.

Most of these patients had been sick for about six months when they appeared for operation. Abdominal pain, diarrhoea and bloody stools were the most common complaints in the right-sided lesions. When the sigmoid was involved, constipation and painful defecation were present. At times, the symptoms were mainly obstructive. A palpable mass was found either by abdominal examination or in the cul-de-sac by pelvic examination in every case. X-ray showed either an irregular filling defect or an area of narrowing in the involved segment. When the filling defect was unusually extensive, the presence of inflammatory rather than neoplastic disease was suggested. In two cases, radiological evidence of coexisting colitis, in addition to the presence of a local lesion, could be shown. By and large, however, radiological differentiation from neoplasm or tuberculosis was not possible with certainty. The sigmoidoscope is of value in diagnosis not only for removing specimens for microscopic examination but also for demonstrating multiple foci of disease.

At operation, the determination of the exact nature of the pathological changes is again very difficult. Most of these cases were resected under the operative diagnosis of carcinoma or tuberculosis. Ulceration on the inside of the bowel, projection of papillary growths into the lumen and the presence of annular infiltration mimic neoplasm very closely.

On the right side, ileo-colic resection was performed five times with no mortality; no other procedure being adopted for this form of the disease. One of these patients had a mild recurrence of symptoms which cleared up under dietetic treatment.

In the lesions involving the upper and mid-sigmoid, a Mikulicz operation was performed three times, and an exclusion anastomosis to the lower-most point of the pelvic colon once. In another case, where definite evidence of generalized colitis could be demonstrated, in addition to a recto-sigmoid mass, a cecostomy was performed. Marked subsidence in the size of the mass, and diminution in the severity of the symptoms followed. In two localized lesions at the recto-sigmoid junction, abdomino-perineal resection with restitution of continuity by an extra-peritoneal presacral anastomosis was performed according to the technique of Dr. A. A. Berg. The only alternative in these cases would have been a left inguinal colostomy which would probably have resulted in a stricture of the bowel below that site and prevented any attempt at closure of the inguinal anus without a secondary and more difficult resection of the involved area. There were no mortalities in this left-sided group.

11. A patient in whom the development of an inflammatory mass in the cecal region was preceded by a three-year history of intractable perianal inflammations. A period of recovery following resection of the inflammatory mass was followed in a few years by extension of the inflammatory condition to the adjacent distal segment of the colon.

I. F., age forty-four, admitted to the Mount Sinai Hospital for the first time in 1927 with a history of vague abdominal symptoms, and a history of recurrent peri-anal abscesses and fistulae. Examination at this time revealed a number of perianal ulcers and superficial fistulae. Sigmoidoscopy showed a congested mucous membrane covered with shreds of mucus. Stool was negative for blood. Ewald test meal showed an anacidity but neutral red appeared in the gastric contents fol-

lowing injection. Wassermann was negative. Physical examination revealed no other abnormalities.

Following this, there were a series of readmissions for intractable peri-anal ulcers and fistulae and fissures which proved recalcitrant to the ordinary operative measures. Tuberculosis was suspected but the excised specimen proved negative. Three years following his first admission, he was readmitted to the hospital with a history of peri-umbilical and right lower-quadrant pain of four months' duration. He had occasional periods of diarrhea, but in between his bowels were normal. On one occasion, he passed a moderate amount of bright red blood in his stool.

Physical examination showed a man, chronically ill, and moderately anemic (hemoglobin 68 per cent). In the right lower quadrant, a firm mass, about the size of a small grapefruit, was palpable. It was fairly fixed. Sigmoidoscopy revealed no abnormalities. Barium enema revealed a marked and constant irregularity and filling defect involving the cecum and ascending colon. The findings were considered suggestive of an intrinsic lesion, probably neoplasm.

Patient was operated upon under the preoperative diagnosis of either neoplasm or hypertrophic tuberculosis of the colon. At operation, a large mass, involving the cecum and the ascending colon was discovered to which there were numerous adhesions of omentum and transverse colon. An ileo-colic resection was performed.

Pathological report. — Macroscopic specimen consists of the resected portion of the cecum and ascending colon together with the appendix and small portion of the ileum. Cecum is very definitely thickened and narrowed by an inflammatory process beginning at the ileo-cecal junction and extending upward for 12 cm. This portion of the cecum shows a large, irregular ulcerative process, finely granular and red with numerous interspersed areas which have the appearance of hypertrophic granulations plus hypertrophic mucosa. Around the margins, of the ulcerated area, mucous membranes show a polypoid hypertrophy. Jutting out from this main area are numerous finger-like ulcerative areas surrounded by hypertrophic mucous membranes. The appendix is apparently involved in the inflammatory process. It is red and infiltrated and through its intestinal orifice there is a projection of polypoid mucosa. The distal 4 cm. of the ascending colon, in contrast to the remaining portion, is smooth, pale and atrophic. Numerous shotty lymph nodes are found in the meso-colon, appearing grossly hyperplastic. Cultures from the bowel show enterococci and colon bacilli. Guinea pig, rabbit and chicken inoculations for tuberculosis are negative.

Histological examination. — Showed acute and chronic inflammation. There are no evidences of tubercle or caseation necrosis.

Diagnosis. — Non-specific inflammatory disease of the cecum and the ascending colon.

Following operation, patient did well for about two years; he gained weight and his peri-anal ulcers healed. Recently he commenced to lose ground again. X-ray at the present time shows an apparent extension of the same type of inflammatory lesion previously present in the cecum, to the distal transverse colon.

12. Case of localized ulcerative colitis

I. L., age fifty-five, admitted to the Mount Sinai Hospital in 1924. The chief complaint was pain in the right lower quadrant and diarrhea of four months' duration. Pain in the right lower quadrant was dull and gnawing, frequently started after meals and continued for one-half to one hour. Bowels moved six to seven times a day. Occasionally they were tarry. Five weeks before admission, a mass became palpable in the right lower quadrant.

The appendix had been removed seventeen years previously.

Physical examination showed a man, chronically ill, apparently having lost considerable weight. The abdomen was slightly distended and in the right lower quadrant, a mass, the size of an orange, slightly tender, and slightly movable, could be palpated. Hemoglobin was 88 per cent. Wassermann was negative, stool contained small quantities of blood. X-ray showed a filling defect in the cecum and ascending colon. The rest of the colon appeared normal. Preoperative diagnosis of carcinoma of the cecum was made, and an ileo-colic resection performed.

Pathological examination. — Specimen consisted of about 10 cm. of cecum and 18 cm. of ascending colon. Colon and ileo-cecal angle were covered with a large amount of hyperplastic fat, almost obscuring the peritoneal covering. Where the peritoneum was visible, particularly over the ileum, there were small peritoneal nodules, suggestive of miliary tubercles or lymphoid infiltration in fatty deposits. On section, the ascending colon down to the cecum was the seat of an ulcerative colitis with polypoid infiltration. The very terminal portion of the ileum also showed evidence of superficial erosion.

Histological sections showed simply various grades of acute and chronic non-specific inflammation. No evidence of tuberculosis or amebiasis could be found.

Following operation, patient developed a small fistula and continued to have diarrhea. This persisted for about six months when the diarrheal symptoms disappeared, and the fistula closed spontaneously. This patient has been observed in the Gastrointestinal Clinic of the Mount Sinai Hospital for the last seven years and has been noted to have occasional flare-ups of low-grade colitis, which at times could be seen to involve the lower sigmoid segment. His general condition is good.

13. Case of localized hypertrophic colitis. Fistula following previous appendectomy

A. S., age twenty-three, admitted to the Mount Sinai Hospital in 1929, complaining of severe cramps and diarrhea of three weeks' duration. The pain was increased after ingestion of food. Stool varied in consistency from liquid to mushy but contained no blood or pus.

Physical examination revealed a tender mass in the right lower quadrant. At this time the hemoglobin was 85 per cent and the white blood count was 23,000 with 81 per cent polys. Temperature varied between 100 and 101 degrees. Examination of the stool showed some pus; no parasites, ova, or amebae. Course of emetin had no effect. X-ray following barium enema showed a defect involving the cecum and ascending colon. Barium meal showed the same picture. Chest x-ray was negative.

Exploratory laparotomy revealed cecum and ascending colon to be rather thick and injected. No evidence of tuberculosis could be seen in the external covering of the bowel. No definite ulcerations were palpable inside the bowel. Appendix was removed and the patient was discharged.

Two months later he was readmitted with a loss of weight, continued diarrhea and persistent fistula in the right lower quadrant. Stools were negative for tubercle bacilli, actinomycosis and amebae. Another course of emetin was given without avail. One month later, as symptoms persisted, exploratory laparotomy was performed and ileo-colic resection plus an ileosigmoidostomy was performed.

Pathological description. — Macroscopic specimen consisted of cecum, ascending colon and a small portion of the terminal ileum. The mucosa of the colon showed marked edematous polypoid hyperplasia giving the mucosa a cobblestone appearance. Between the polypoid projections were occasional, irregular small ulcerations. There were a few papillary mucosal projections. Peri-intestinal lymph nodes appear hyperplastic. There does not seem to be much involvement of the deeper layers of the gut, except for an inflammatory edema.

Microscopic examination showed areas of ulceration in the mucosa with hemorrhagic and acute and chronic purulent inflammation. At other points the mucosa was hyperplastic. The submucosa showed mainly edema with round-cell infiltration. The muscularis was thickened and showed moderate fibrosis. There were no evidences of tubercle bacilli or anatomical tubercles. No amoebae seen on section.

Pathological diagnosis. — Non-specific ulcerative colitis and polyposis.

Patient made uneventful recovery and has remained well to date.

14. Localized hypertrophic sigmoiditis and peri-sigmoiditis with diarrhea and bloody stools

R. H., age 27, admitted to the Mount Sinai Hospital in September, 1922. Chief complaint was diarrhea of two years' duration. She had six to seven movements per day, and the stool frequently contained fresh blood. At times, there was severe cramp-like pain. She had lost 15 pounds in the past year. Red blood count was 3,500,000. Hemoglobin was 35 per cent. Stool showed fresh blood; no amebae, ova or parasites.

A mass was palpable in the left lower quadrant. Sigmoidoscopy showed an ulcerative infiltration 15 cm. from the anus, mainly on the anterior and right lateral wall. A specimen removed was reported as chronic inflammatory tissue. The fresh secretion was examined for amebae but none found. An appendicostomy was performed and the cecum was reported as being hard and indurated as though the seat of chronic inflammation. Patient was given a course of emetin and irrigation was performed through the cecostomy. Barium enema showed a narrowing of the sigmoid and a filling defect in the region of the descending colon and sigmoid. The rest of the colon appeared normal. Sigmoidoscopy again showed a granular infiltrating mass which the sigmoidoscopist considered carcinoma, but which was reported as inflammatory tissue. The mass in the left lower quadrant became larger and patient showed no signs of improvement.

At the second operation, a large mass, the size of a grapefruit, densely adherent to the latero-pelvic wall and surrounded by firm adhesions was found. Resection was performed.

Pathological examination. — Macroscopic specimen consisted of resected sigmoid about 20 cm. in length, showing a tremendous productive inflammatory process, infiltrating its wall, constricting the lumen and involving peri-sigmoid tissue. The mucous membranes showed a rather polypoid appearance with marked thickening of the sub-mucosa, apparently inflammatory in nature, and without ulceration or diverticula. In the center of the specimen where the inflammatory process was most marked there seemed to be a necrosis of the intestinal wall.

Microscopic examination showed acute and chronic inflammation. No signs. of neoplasm or tuberculosis. Pathological diagnosis: Chronic and acute sigmoiditis and perisigmoiditis.

15. Hypertrophic colitis (sigmoid) with gradually increasing obstructive signs

H. B., age 67, admitted to the Mount Sinai Hospital in May, 1926. Chief complaint was gradually, and markedly increasing constipation of a few months' duration. There had been occasional appearance of blood in the stool. One month before admission, barium enema showed a constriction with an incomplete but fairly tight obstruction at the junction of the descending colon and sigmoid, approximately at the level of the brim of the true pelvis. The appearance of the descending colon, judged by the barium in it after evacuation suggested colitis. At this time, a mass could be felt in the left lower quadrant. Since the x-ray had been taken patient had become gradually more obstipated, until upon admission he was passing only small quantities of gas.

Because of the increasing obstruction, it was felt advisable to resect or short-circuit the mass, regardless of its nature. At operation, a mass, 3 inches long, densely indurated, and very adherent to the parietes was found and a Mikulicz operation performed.

Pathological report. — Hypertrophic colitis. No signs of malignancy. No diverticula found.

The artificial anus was later closed, and when last heard from two years after operation, the patient was feeling well.

16. Localized inflammatory annular stricture with polypoid hypertrophy of mucous membrane just above recto-sigmoid junction

F. S., age 53, admitted to the Mount Sinai Hospital in June, 1925. She had been sick for a year, with increasing constipation and rectal bleeding. The severity of both symptoms had increased considerably, just before admission. On examination a mass could be felt in the left iliac region. X-ray showed a stricture at the recto-sigmoid junction. Proctoscopy showed no abnormality in the lower rectum, and a stricture was encountered at the recto-sigmoid junction.

Because of the increasing symptoms, it was decided to operate in spite of the fact that the exact nature of the lesion could not be definitely determined. It was felt that a colostomy would simply result in the production of a complete stricture if the lesion were benign. It was, therefore, decided to resect the involved lesion, which was done according to the technique of Dr. A. A. Berg by abdomino-sacral excision with restitution of continuity by end to end extra-peritoneal presacral anastomosis.

Pathological description. — Macroscopic specimen consists of resected portion of sigmoid 10 cm. in length containing an annular lesion 5 cm. in diameter, causing constriction at that site. There is a marked polypoid hypertrophy of the mucous membrane in this region. The muscular wall of the bowel above the lesion is thickened. The lymph nodes are slightly enlarged. Microscopic examination shows polypoid hyperpla-

sia of the mucosa, diffuse fibrosis and round cell infiltration of the rest of the wall of the sigmoid.

This patient was readmitted about six months later for dilatation of stricture developing at the site of the anastomosis. Following this procedure, patient has remained well to date.

V

Simple Penetrating Ulcers of the Colon

This term is applied to a group of cases which show one or more clean-cut penetrating ulcers which look almost like punched out peptic ulcers. It is apparently a purely local disease; the surrounding colon not appearing to be grossly diseased. In two cases, penetration had occurred through the colonic wall and had become sealed off by adhesions of omentum or epiploic appendices, with the formation of rather firm inflammatory masses, which gave the impression of being penetrating or perforating neoplasms. Both these lesions were situated in the ascending colon and, clinically, were operated upon with diagnoses of acute appendicitis. At operation they were mistaken for carcinoma of the colon and were resected as such.

Another patient, who probably belongs in this group is one who developed signs of incomplete obstruction in the transverse colon and who, at operation, was found-to have a narrow, inflammatory annular stricture. There were no evidences of disease of other portions of the colon, and the narrow, local, annular stricture can probably be best explained as a result of the healing of a penetrating ulcer.

Another manifestation of the same type of lesion was encountered at autopsy in a patient who had experienced severe repeated hemorrhages from the bowel, one of which finally proved fatal. Twelve cm. from the rectum a group of punched out ulcers was encountered. At the base of one of these was an arteriosclerotic vessel which had been eroded by the penetrating ulcer.

We have no exact idea as to the underlying etiology of these lesions. It is possible that they are due to injuries by ingested foreign bodies. There is also a possibility that they are of vascular origin due to blocking of a small vessel. Some point is lent to this latter view by our experience with a case encountered a few months ago. This latter patient was admitted to the hospital as a perforated duodenal ulcer with x-ray evidence of free air in the diaphragm. Exploration showed, however, that perforation had occurred in the lowermost ileum which contained four sharply punched-out perforations, about 1/2 cm. in diameter. These were sewn up and an ileostomy performed. The patient did well for a few days, then suddenly went into collapse, commenced to drain blood through the ileostomy tube, and died shortly thereafter. Autopsy showed a mesenteric thrombosis. The area of ileum where the perforation had occurred was normal except for the sharply punched-out ulcers. Our interpretation of this course of events was that the thrombus had originally been parietal and that small emboli had broken off, plugged some of the terminal arteries or arterioles and given rise to the rapidly perforating ulcers, and that later the parietal thrombus had become complete. These are the only facts which we can adduce, which at all throw any light on the etiology of this type of ulcers.

17. Penetrating ulcers and annular stricture

E. R., age 23, admitted to the Mount Sinai Hospital in December, 1928. For two months she had complained of increasing pain and constipation, borborygmus and occasional blood in the stools. She claimed to have experienced a similar attack one year ago, which lasted for a few weeks and then disappeared.

Physical examination revealed a sausage-shaped mass in the upper abdomen. There was occasional intestinal erection noted. The x-ray revealed an irregular narrowing of the transverse colon for a distance of two inches.

Laparotomy revealed a stenosing lesion of the colon, annular in nature, in the middle of the transverse colon. Resection with side to side anastomosis was performed.

Pathological examination. — Specimen consists of a portion of resected transverse colon 7 cm. in length, which was divided into two portions by a narrow linear stricture approximately 1 cm. wide which presents small nodular elevations in mucosa and a small polyp as well as several small irregular ulcerations. The gut proximal to this area is dilated to approximately twice the circumference of a normal bowel and the thickness of the wall approximately twice that of normal.

Microscopic examination showed acute and chronic inflammation. No evidence of malignancy or tuberculosis.

Pathological diagnosis. — Ulcerative stricture of the colon, non-specific in character.

VI

Inflammatory Masses Secondary to Appendages of the Bowel (Appendicitis, Typhlitis, Diverticulitis)

Probably the best known type of this variety of inflammatory mass is that which is secondary to sigmoid diverticulitis. These have been so much discussed in recent years that we feel there is no reason for including them in the present study. We wish, however, to emphasize in passing, that in addition to the large peri-sigmoidal inflammatory masses caused by perforation of a diverticulum or extension through it of infection from the lumen of the bowel there is another and less common type. In this, there is a gradually developing submucous infiltration of the sigmoid as well as an adherent peri-sigmoiditis, with the development of a considerable degree of intramural fibrosis and hyperplasia and a considerable degree of stenosis. This type is clinically and radiologically extremely difficult to differentiate from malignant stenosing lesions of the sigmoid and even at operation, differentiation may be impossible.

The relation of the appendix to the development of certain hypertrophic masses in the ileo-cecal region is a moot point. In many cases an unresolved appendicitis is undoubtedly responsible for the formation of a hyperplastic fibrotic mass, the so-called “appendicitis fibroplastica,” but this does not account for all the lesions found in this region. In these cases, the appendix is found buried in the cecal wall or as in one case of this series, in the terminal ileum; and forms part and parcel of the inflammatory mass. The extension of the inflammation in these cases is simply by contiguity and as might be expected is mainly peri-cecal with involvement of the sub-serosal tissue. The submucous layer of the gut does not appear to be involved. Occasionally tiny abscesses between the appendix and the cecum will be uncovered when the former is mobilized. These are quite common, their true nature is usually appreciated and resection is rarely performed.

There is another, and much rarer type of lesion, however, which may he called chronic typhlitis, in which the appendix though thickened and indurated lies free and non-adherent.

Both it and the cecum show a marked submucous thickening, edema and fibrosis. The lesion does not extend up into the ascending colon or into the ileum except at the ileo-cecal valve, points which serve to differentiate it from the two other types of non-specific inflammatory disease encountered in this region, which have been discussed above. Large masses of firm glands are found in the ileocecal angle. Upon examination, the pathological alterations involving the appendix and cecum are seen to be continuous. If the route of spread were by direct extension, it would have to be through the contiguous submucous layers of the appendix and cecum. However, from the clinical standpoint, it is well known that inflammation of the appendix usually stops short of the extreme base even in the most virulent form of the disease. Dr. Klemperer, who was at one time greatly interested in the extent of the basal involvement in acute appendicitis, was able to substantiate our clinical observation from his pathological studies.

The question then arises as to whether the extension is into the cecum from some unusual form of acute appendicitis involving the base, or whether the ileo-cecal changes were primary, the appendix participating simply as a component portion of this segment of gut. We are inclined to believe that the type of chronic cecitis with extensive submucous-intramural involvement, but without evidences of mucosal ulceration is secondary to a partially resolved acute or chronic typhlitis.

There is no doubt about the existence of acute typhlitis as a clinical entity. On an active emergency service three or four such cases are encountered every year. Clinically and on physical examination they present the picture of acute appendicitis. Operation, however, reveals a succulent edematous, inflammatory lesion without much peritoneal injection or fibrin deposition. involving the cecum, the retro-peritoneal tissue, the appendix, and the ileocecal glands. The appendix does not appear to be more acutely involved than any of the adjacent tissues. In some of these cases, the appendix and a lymph gland from the ileo-cecal angle were removed. On pathological examination these revealed only acute inflammatory hyperplasia. In one subacute case, where ileocecal resection was performed, a small ulcer was still present in the cecum. The submucosal proliferative reaction was all out of proportion to the size of the ulcerative lesion. Most of these acute cases clear up, probably, either with or without operation. An especially severe case was recently encountered which came to post-mortem examination. The cecum was found greenish-black and gangrenous. There were numerous cecal ulcerations, two of which had gone on to perforation. The appendix was gangrenous. Jennings has recently called attention to this type of case.

In other cases, repeated attacks finally result in the formation of a chronic submucous and subserosal inflammatory infiltration. In these chronic cases, there are no ulcerative, polypoid or papillary changes in the mucosa; the glands are firm; the cecal wall thickened and indurated, and there are few adhesions present.

The symptom usually complained of is recurrent attacks of pain in the right lower quadrant without any history of blood in the stool, diarrhea or constipation. At times, the chief complaint is that of a mass. Radiologically, filling defects or irregularities in the cecum are present. The general condition is usually good, operation being mainly undertaken because of the presence of a mass. At operation, differentiation from tuberculosis may be difficult and most of the cases subjected to resection have been operated because of their similarity to that condition.

19. Peri-typhlitis. A case of so-called appendicitis fibro-plastica chronic productive peri-appendiceal inflammation leading to the formation of a large mass

L. K., age 18, was admitted to the Mount Sinai Hospital in October, 1929. For 2 1/2 months he had been suffering recurrent attacks of pain in the lower abdomen. Two days before admission, an especially severe attack had begun in the lower abdomen and had finally localized to the right side. There was nausea, but no vomiting. Examination showed tenderness and rigidity in the right lower quadrant. Preoperative diagnosis was acute appendicitis.

At operation the entire ileo-cecal region was found to be involved in a moderate sized, hard, stony mass which infiltrated the cecal wall. The ileo-cecal angle contained numerous glands of the same stony hardness. The appendix could not be visualized and seemed to be part of the large conglomerate mass. After considerable debate, an ileo-colic resection was performed.

Pathological examination. — Specimen consists of terminal ileum, cecum and part of the ascending colon. There is no intrinsic lesion of the mucosa of any of the resected bowel. In the ileo-cecal angle, surrounding the appendix and involving the terminal mesentery, is a chronic inflammatory mass of tissue including a large number of hyperplastic lymph nodes. The appendix, 7 cm. in length, appears to be chronically inflamed and stenosed, particularly in its distal two-thirds.

Microscopic examination showed a marked fibrosis of the appendix involving all the coats with a marked lymphocytic infiltration. The cecum simply showed chronic peri-typhlitis.

Diagnosis. — Chronic appendicitis and peri-typhlitis.

20. Case of chronic productive typhlitis resembling tuberculosis

A. B., age 35, admitted to Mount Sinai Hospital in March, 1930. One year ago patient had a severe attack of pain in the right lower quadrant which persisted for two weeks. She had no generalized abdominal pain at that time, no vomiting. She believes she had fever. Five days before admission she again developed pain in the right lower quadrant with rather marked severity, much more so than the occasional dull pain which she had been experiencing in the interval. She had no diarrhea or blood in the stool. There had been no increasing constipation or loss of weight. Physical examination revealed a mass, the size of an orange, in the right lower quadrant, rather firm, slightly irregular. The preoperative diagnosis was appendix abscess.

Exploring revealed a mass occupying the ileo-cecal region covered by thickened omentum. When the omentum was separated the appendix was found lying free and did not appear acutely inflamed. There was a marked infiltration of the ileo-cecal angle and cecum. It was thought that the lesion might be a hypertrophic tuberculosis and an ileo-cecal resection was performed.

Pathological description. — Specimen consists of terminal ileum, cecum and ascending colon. The region of the entrance of the ileum into the cecum appears firm, nodular and edematous. Upon opening the specimen the mucosa of the resected bowel appears grossly normal except for some edema of the ileo-cecal valve and the caput-coli. The mesentery

of the ileocecal junction appears firm, and infiltrated and on section seems to contain some succulent lymph nodes, surrounded by firm, hard, inflammatory tissue. The appendix was not adherent and appears moderately thickened. An inflammatory mass extends from the mesentery of the ileo-cecal junction and appears to involve the wall of the cecum. It is firm and irregular. On section of this area, the cecum appears to be markedly thickened, shows edema and infiltration of all the coats, especially the submucosa. Microscopic examination shows diffuse infiltration of the submucosa with round cells and with considerable edema. There is a moderate amount of fibrosis. There is a considerable thickening and edema of the serous coat as well as the mesentery. The appendix shows signs of chronic inflammation, fibrosis, but little inflammatory infiltration.

Diagnosis. — Chronic typhlitis, peri-typhlitis, chronic appendicitis.

21. Subacute, ulcerative and phlegmonous typhlitis

D. W., age 31. Was admitted to the Mount Sinai Hospital in March, 1930. He had been ill for two days with peri-umbilical pain and nausea. He had had two similar previous attacks, which were supposed to be due to appendicitis. Previous history was negative except for respiratory symptoms coming on during the winter. Examination showed slight tenderness and rigidity in the right lower quadrant; temperature was 101, and leucocyte count was 12,000 with 80 per cent polys. At times it was thought that a mass could be palpated in the right lower quadrant, but this could not be established with certainty. X-ray of the chest showed a chronic pulmonary phthisis.

At operation, which was undertaken with the preoperative diagnosis of appendicitis, the appendix was found to be normal, but there was a tumor in the cecum about the size of a pigeon's egg. An ileo-colic resection was performed.

Pathological examination. — Specimen consists of cecum, appendix 12 cm. of ileum, and a few cm. of the ascending colon. The ileum shows no gross lesion. The appendix shows some external signs of inflammation in the distal third. In the cecum, near the base of the appendix, but not involving it, there is an extensive ulcerative, necrotizing inflammation over an area about 3 cm. in diameter, with a gangrenous membrane about 2 cm. in diameter, and minute ulcerated areas covered with a yellowish sloughing base. The wall of the cecum is much thickened, the serosa inflamed. Regional lymph nodes are enlarged. Aside from this area, the cecum appears normal as does the ascending colon.

Microscopic examination. — The ulcerated area shows necrosis of mucous membranes with a diffuse purulent infiltration consisting of lymphocytes and polymorphonuclears through all the coats of the gut. There is considerable edema, small areas of hemorrhage extravasation. The ileum and ascending colon are normal. The appendix shows some slight increase in the submucosa, some injection of the serosa, but no signs of intrinsic inflammatory changes.

Diagnosis. — Ulcerative and phlegmonous inflammation of the cecum.

Summary

1. A study is reported, fifty-two cases exclusive of sigmoid diverticulitis manifesting themselves as tumors or strictures of the bowel.

2. Clinically, radiologically, and at operation these were usually regarded as malignancy or localized hypertrophic tuberculosis.

3. Microscopic examination of these resected specimens showed various stages and degrees of acute and chronic inflammation with the production of large quantities of fibroblastic and fibrous tissue.

4. No exact pathological or etiological classification is attempted. For clinical purposes they are divided into six groups, some of which are overlapping. 1. Peri-colonic or peri-intestinal granulomata due to sealed-off perforation. 2. Intestinal stenosis due to known vascular lesions of the bowel. 3. Localized hypertrophic ulcerative ileitis. 4. Localized hypertrophic colitis. 5. Local penetrating ulcers of the colon. 6. Granulomata secondary to inflammation of appendages, or diverticula of the bowel.

5. The various groups are discussed and illustrative cases briefly reported.

6. Localized hypertrophic tuberculosis of the bowel in patients without evidence of pulmonary tuberculosis, is less common at the Mount Sinai Hospital than the non-specific variety.

The authors are greatly indebted to Dr. A. A. Berg for so generously placing his extensive material at their disposal. To Dr. Paul Klemperer they wish to express their appreciation and thanks for his patience and kindness in aiding them in the study of the pathological phases embodied in this communication. To Drs. Harold Neuhof, Edwin Beer and Richard Lewisohn, Dr. I. C. Rubin and Dr. Maurice Rashbaum they are indebted for the use of individual cases.

Discussion

DR. GEORGE MORRIS PIERSOL: I can think of no one more fit to discuss the subject of Intestinal Tuberculosis than Dr. Lawrason Brown, who has had a tremendous experience with this condition. He was speaking, of course, of secondary intestinal tuberculosis. The importance of this subject to the clinician must be obvious when one considers, as Dr. Brown has already remarked, that it is the most common complication of pulmonary tuberculosis. Autopsies indicate, I believe, that over 50 per cent of cases of pulmonary tuberculosis exhibit some evidence of intestinal tuberculosis.

In the past the great difficulty has been that the diagnosis of intestinal tuberculosis was never arrived at sufficiently early to make it possible really to do anything for the condition. The reason for this was that the diagnostic methods available were inadequate and clinicians acquired the habit of looking for what were regarded as the classical signs of this condition which in reality were terminal or late manifestations. Such symptoms as pain or localized signs in the abdomen, and the appearance of blood and pus in the stools were looked upon as the criteria necessary to make the diagnoses of intestinal tuberculosis. Dr. Brown and his associates when they recognized the x-ray manifestations of intestinal tuberculosis made a noteworthy advance in the early diagnosis of this condition. Since this method of diagnosis has been generally adopted many cases have been recognized sufficiently early to do something for them. We must all acknowledge the debt which we owe to Dr. Brown and his associates for having pointed out this important aspect of the subject.

Frequently the finding of tubercle bacilli in the stools has been looked upon as evidence of intestinal tuberculosis. In this

connection it is important to remember that many times tuberculous individuals swallow their sputum so that the tubercle bacilli are found in the stools without intestinal tuberculosis being present. Therefore, the mere finding of the bacillus in the stool is not enough to make the diagnosis.

The cases Dr. Brown discussed were chiefly the usual ulcerative variety. He did not touch upon some of the sequelae which result in these cases. In the last paper, reference was made to certain sequelae found in some of the cases in whom proliferative changes occur in and around the bowel. They present great difficulty in diagnosis and are often mistaken for neoplasms and require surgical intervention. The type of case Dr. Brown discussed is, of course, not surgical. They only become so when, as the result of tuberculous ulcerations, stenoses develop and symptoms of varying degree of intestinal obstruction supervene. That, of course, is another aspect of intestinal tuberculosis that has to be borne in mind and which calls for a different type of therapy. I should like to ask Dr. Brown in conclusion how often they found tuberculous peritonitis in their cases of intestinal tuberculosis.

DR. FRANKLIN W. WHITE: I am sure the members of this Association realize the great service which Dr. Brown and his co-workers have given in studying this disease and in practically creating this diagnosis. If we look back a dozen years ago when his papers were first published, we find a condition which was very different from today. We find the best clinicians considering the early diagnosis of intestinal tuberculosis as practically impossible, and the evidence of later disease very uncertain. Now Dr. Brown comes here and shows us the figures of his positive diagnoses of 98 per cent accuracy in cases which have been checked up by autopsy and operation. Certainly something has happened in these twelve years, largely due to the work of Dr. Brown and his associates.

He has shown us the great frequency of intestinal tuberculosis in pulmonary cases with indigestion and abdominal symptoms and also the great rarity of intestinal tuberculosis in patients who have no tuberculosis elsewhere. How has this change in diagnosis come about? Not so much, it seems to me, by clinical study. We know that the early symptoms are much like the symptoms of pulmonary tuberculosis, slight, vague and indistinct at first. In our physical examination we do not find much in the abdomen in the early cases. We do not get much that is really helpful from the stools as far as my experience goes. Of course the proctoscope doesn't help us much because it doesn't get up high enough to see the things we are searching for. It seems to me the roentgen-ray has been our mainstay in bringing about this great change to better diagnosis. First, by finding the changes in function which come in the earlier stages of the disease, the spasm, the hypermotility, the vacant irritable areas in the bowels, and later in the more advanced cases by finding the actual deformity of the local lesion itself.

The question of whether to give a barium meal or a barium enema is not an important one, they both have their uses. I have been struck several times with the value of the double contrast enema by giving the ordinary barium enema and after letting the barium run out, inflating the bowel with air, thus bringing out the projection of masses in the wall into the lumen of the bowel. This brings them out much more clearly than the simple enema and takes only ten minutes more to do. Inflate the bowel under the fluoroscope and take an additional film and you have a picture which may show a great deal.

Of course Dr. Brown has not claimed that the x-ray picture was diagnostic in itself, but the presence of irritation and ulceration and the fact that it occurred in certain parts of the bowel, and that it also appeared in patients who had pulmonary tuberculosis makes a very strong combination which leads us to our diagnosis. Dr. Brown has emphasized the importance of finding constant defects, not merely in one examination which might be so misleading in the bowel, but on repeated examination. I was also struck with the changes which he was able to demonstrate by following the same patients over a period of time so that the progress of healing might be studied and followed very much as we do in gastric ulcer.

DR. H. BOCKUS: Mr. President and Members of the Society: This paper of Dr. Ginzburg and Dr. Crohn is of decided interest, not because these lesions that they are describing are at all common, but because of their rarity I think we are very apt to overlook them. As far as I know, this series of cases which they are reporting is the largest group of cases of this sort in the literature, although I ran across an article by H. E. Mock in *Surgery, Gynecology and Obstetrics*, written last year who reported a series of cases almost approximating that of Dr. Ginzburg and Dr. Crohn. They mentioned the same etiological factors which were discussed by the essayist here this morning. One of the particular things discussed in the paper mentioned is the fact that many of these cases of so-called inoperable carcinoma reported to have recovered are probably cases of non-specific granulomata. He stressed particularly the necessity for taking biopsy material even in the cases in which inoperable carcinoma seems to be present. I naturally have had very little experience with this condition and consequently, can't add anything particularly to the discussion from the practical standpoint, but there are several questions that I should like to ask.

I happen to have seen a patient within the past two weeks who possibly has a non-specific granuloma, but who certainly has a peri-sigmoiditis, with blood in the stools which followed almost immediately after deep x-ray and radiation therapy for carcinoma of the cervix. There is at present no indication of carcinoma in the pelvis. I am wondering whether in any of these cases Dr. Ginzburg or Dr. Crohn have noted the development of a granuloma following deep radiation or x-ray therapy.

Dr. Ginzburg mentioned the fact that amebic disease can cause this condition and very recently three cases of this sort were reported following a persistent isolated amebic ulcer and in all three of these cases it was only in the resected material in which the ameba could be found. So it is quite possible an amebiasis may account for some cases of non-specific infective granulomata. My experience comprises only two proven cases and interestingly enough, both of these cases occurred in luetic individuals. I don't mean to infer that these people had syphilomata; one was a case of old duodenal ulcer in which the gall bladder, pancreas and stomach were all bound up in a granulomatous mass which was not carcinomatous; the other case, a solitary ulcer of the ascending colon near the hepatic flexure, with a granulomatous mass associated with it.

I should like to say a word about the terminal ileitis, which I have never seen in my own practice. I went up to see the cases at Mount Sinai with Dr. Crohn and I have been thinking a good deal about it since that time. I don't know very much about anatomy, not being a surgeon, so I went out to Dr. Batson, professor of anatomy at the Graduate School, and saw some of his very excellent so-called extra-peritoneal dissections. He dis-

sects the peritoneum away from the fascia so he can throw all the peritoneal contents encapsulated within the peritoneum to one side and inspect the blood supply. He pointed out to me the fact that the ileo-colic artery, ascending branch, which supplies the cecum is more or less fixed in most specimens, but the terminal branch of the same artery which supplies the lower 6 to 12 inches of ileum is capable of a good deal of rotation. We were wondering whether in some individuals with undue ptosis the factor of disturbed circulation might be a contributing factor in the production of terminal ileitis by twisting the artery or by undue stasis in the vein (terminal branch). I should like to ask whether the habitus of these patients that have been described is of the visceroptotic type, the type in which ptosis and stretching of the mesentery is most marked.

DR. WALTER C. ALVAREZ: In view of the difficulties of early diagnosis of intestinal tuberculosis perhaps the logical thing to do would be to treat every patient with active pulmonary lesions as if he had trouble in the bowel and give him a smooth diet and plenty of vitamins from the start. Some of my friends who specialize in tuberculosis tell me that that is what they are doing, and that they are pleased with the results.

Some writers have stated that the physician can suspect the development of intestinal tuberculosis when the patient who was formerly optimistic becomes anxious and pessimistic. It is generally assumed that disease in the lungs does not produce the reactions on the brain that are produced by disease in the bowel. I haven't enough experience with these patients to say, whether or not this is true but I know any disturbance in the bowel that is associated with nausea is extremely disheartening.

There are good reasons for giving a smooth diet to these patients. If, in a dog, one takes a section of gut, reverses it end for end, and restores the lumen of the bowel with two anastomoses, the bowel looks exactly the way it looked before, with just as good a lumen. The difference is that the reversed loop will pass fluids but not solids. The dogs must be kept on a cellulose-free diet; otherwise they soon die of intestinal obstruction due to the accumulation of a mass of indigestible material immediately above the orad suture line. It is evident that before one can get solids through the digestive tract, one must have a normal downward gradient of forces. An irritant lesion of the bowel tends to reverse the gradient and this makes it hard for indigestible residues to go through.

The lesions that have been described by Dr. Crohn and Dr. Ginzburg interest me. I think I must have seen instances of this disease in the past; granulomas which I thought might be tuberculous but in which I could not find the characteristic histological structure. Unfortunately for the progress of our knowledge in some of these cases, the surgeon does a short-circuiting operation and the patient disappears. One must be careful not to tell these people that they have carcinoma. A prominent surgeon claims the credit for building a beautiful Christian Science Church. In a wealthy woman he found what he thought was an inoperable cancer of the bowel; he short-circuited it and sent her home with a hopeless prognosis. Later, when he had seen more of these lesions he understood why his patient didn't die.

I have long felt that there must be such a thing as terminal ileitis. I think it is a fairly common disease and some day I would like to disappear into a pathological "lab" to hunt for it myself. Ileitis would account for many of the cases of appendicitis in which the patient doesn't get well after one or more operations.

There is a reason why we should expect trouble in the terminal loop of ileum and this is because it is the one place in the bowel in which the gradient appears to be reversed. This, I think, accounts for the fact that all big gall stones that slough through into the bowel stop some 9 or 10 inches orad to the ileocecal sphincter. To explain it, authorities state that this is the narrowest part of the gut. This may or may not be true. For years I have been trying to plan an experiment which would show whether the gall stone stops where it does because this is the narrowest place or because it represents the place where the gradient is reversed. Finally a woman very obligingly performed the experiment that I wanted. She ate bran until she had to be operated on for the removal of a mass of it impacted right at the danger spot. The case was reported recently in the *Journal of the American Medical Association* (Davis, M. B., 97:24-25, July, 1931). This experiment indicates to me that it is not a narrowing of the gut but a reversal of the gradient that causes the trouble. We can see now why fish bones or any other indigestible remainders will tend to stagnate in this region.

DR. HARLOW BROOKS: Mr. Chairman and Members of the Society: I think the work which Dr. Gray has done is a very hopeful harbinger for the future. If the gastro-enterologists particularly will pay some more attention to the problems that we internists have and help us more effectively in the study of general disease it will add greatly to our mutual benefit. Then I have been very much interested in the work he has done because for eight years I was pathologist to a large tubercular service which comprised nearly 50 per cent of active cases of tuberculosis. I never saw a tubercular ulcer of the stomach although we found, even by our crude methods of that day, tubercle bacilli present in the mucus of the stomach swallowed from the sputum of the infected lung. The walls of the stomach have no immunity against tubercular infection. I know that because in subacute or even in active miliary tuberculosis the process starts in the peritoneal coat and through to the mucosa in quite frequent instances. All of you may confirm that by simply doing autopsies in miliary tuberculosis, particularly in the subacute type. On the other hand, in a very large number of active cases of tuberculosis which I saw in my medical youth, I never saw a tubercular ulcer originating from the mucosa of the stomach. I saw two instances which I thought might be of this nature, but when we examined these two ulcers histologically they were prepyloric ulcers and of the typical peptic ulcer type. We carefully examined the edges of these ulcers and I fully expected to be able to demonstrate the formation of tubercles, but that we were unable to do. In other words, there is no immunity against peptic ulcer in tuberculosis cases, but when a peptic ulcer occurs it does not, I think I may say with some assurance, become infected with tuberculosis when this ulcer is located this side of the pylorus. I think that this possibly has some bearing on the mucin or the protection which it affords to eroded surfaces of the mucous membrane.

DR. JULIUS FRIEDENWALD: Dr. Gray has presented a very important and interesting paper. Last year Dr. Morrison and I completed a study of the secondary gastric disturbances occurring in pulmonary tuberculosis which we, presented at the section on gastro-enterology of the Southern Medical Association. In the report we selected 100 cases of pulmonary tuberculosis of which fifty presented the initial and fifty the terminal types of dyspepsia. In the initial type the ages of the patients ranged from twenty to seventy years. Of these 76 per cent were females and 24 per cent males. In the instances of initial dyspepsia the gastric contents revealed hyperacidity in 42

per cent, normal acidity in 44 per cent and subacidity in 8 per cent and achylia in 8 per cent. The motor function of the stomach was normal in the early stages but became reduced with the progress of the affection. In the terminal dyspepsia the ages of the patients ranged from twenty-three to fifty-eight years, of which 82 per cent were female and 38 per cent male. In these cases the digestive disturbances were severe in 72 per cent, moderate in 24 per cent and mild in 4 per cent. According to our experience, as the mucous membrane becomes involved in an extensive secondary chronic gastritis the secretion of free hydrochloric acid is rapidly diminished and a true achylia is finally produced, and at the same time the motor function of the stomach becomes impaired. The gastric content at this stage reveals an absence of free hydrochloric acid and the presence of a considerable amount of mucus much in the form of swallowed clumps. In our series of cases of advanced pulmonary tuberculosis the gastric contents presented a normal acidity in 10 per cent, hyperacidity in 6 per cent, diminished acidity in 30 per cent and achylia in 54 per cent. There was, therefore, present in these cases a combined hypochlorhydria and achylia in 84 per cent. The stomach in the stage of terminal dyspepsia, therefore, ordinarily presents a high grade of motor and secretory insufficiency. These changes may occur due to the production of toxins as well as from the developing chronic gastritis. As a result there is a delayed gastric evacuation or atony. The acidity is usually reduced as well as the pepsin concentration, but the latter does not run parallel with the reduction of acidity. On the other hand, Rehfuss has pointed to the importance of visceral focal infections in resistant cases of pulmonary tuberculosis. He has been able to demonstrate in some instances infection of the bile of the gastric mucous membrane as well as of the intestinal tract with various organisms which he considers potent in causing a lessened pulmonary resistance. The secondary gastric disturbances due to pulmonary tuberculosis are, therefore, of unusual interest. This is due largely to the fact that in this disease, especially in its incipiency, the primary symptoms are frequently entirely gastric in character and consequently often overshadow the pulmonary signs. In the advanced forms, on the other hand, we are dealing with more or less severe types of chronic gastritis with marked secretory and motor changes which at this stage may result in symptoms so intense as to cause serious complications or may even overshadow those due to the primary affection.

Dr. Gray's paper is of great interest and his findings regarding the frequent presence of tubercle bacilli in the gastric contents, in the presence of lowered gastric acidity, is a valuable contribution.

Dr. Lawrason I. Brown (closing): Mr. President, tuberculous peritonitis is rare as a complication of pulmonary tuberculosis. We think that in some instances where there is a great deal of pain associated with intestinal tuberculosis that the cause of the pain may be due possibly to a localized peritonitis over the base of the ulcer. It is interesting to recall to Dr. Alvarez that when intestinal tuberculosis is most rare, pessimism is most common, i.e., in the early cases in the minimal cases. They very often start out by being exceedingly pessimistic and as the disease advances and hope is lost more and more and intestinal tuberculosis becomes more and more frequent, they become more and more optimistic.

Dr. Irving Gray (closing): We have reported this morning our findings of the studies that have been carried out for the past year.

The gastric chemistry apparently is not influenced by pulmonary tuberculosis except that there appears to be a decrease in gastric secretory power in the female group.

The intestinal complications of chronic pulmonary tuberculosis occur in many patients. There is certainly a fertile field for study relative to the prevention and treatment of tuberculous lesions of the small bowel. Undoubtedly, most of the cases of tuberculosis of the small intestine are secondary to pulmonary tuberculosis. The primary complex of tuberculosis may occasionally be found in the small bowel as pointed out by Walter Koch, of Berlin. On autopsy of the soldiers who came from South Africa, he (Koch) found after careful survey, there was no evidence of pulmonary tuberculosis in the lungs and that the primary complex with an active tuberculosis was present in the small bowel.

In the temperate zone one rarely meets with a case of intestinal tuberculosis in whom pulmonary tuberculosis is not present.

I know of a physician's wife who developed intestinal symptoms chiefly, diarrhea, with a fever between 101 and 102 degrees daily in the late afternoon. Tubercle bacilli were found in the stool and on animal inoculation, tuberculosis was established.

Studies are now being made to differentiate between the human and bovine type. Active intestinal tuberculosis will occasionally occur in humans who have no active pulmonary tuberculosis. The diagnosis depends entirely upon the findings of tubercle bacilli in the stool.

Dr. Burrill B. Crohn (closing): Dr. Ginzburg, Dr. Oppenheimer and I have been studying benign granulomata of the intestinal tract from the surgical and pathological standpoint for some time. I wish particularly to emphasize the condition which we have named terminal ileitis because that is a clinical condition to which my interest has been, for some time, directed.

Terminal ileitis presents a very definite clear-cut clinical entity. The patient presents himself apparently with symptoms of colitis. For several weeks, months, or sometimes for one or two years, one observes the complaint of diarrhea, the passage of some blood and mucus, a low grade temperature, a mild anemia. In each instance the primary diagnosis had been one of colitis. To my surprise the proctoscopic examination was regularly negative. A form of ulcerative colitis localized to the right colon or cecum suggested itself. Not only have we had experience with this localized form, but Bargen of the Mayo Clinic has described these localized areas of colitis where the transverse colon or ascending colon or splenic flexure are affected without involvement of the sigmoid or rectum. But the barium enema was again negative and we were forced to assume the existence of some lesion in the small intestinal tract to explain the condition.

In this manner we encountered a series of fourteen cases in which there existed a lesion which we did not recognize from the literature, a lesion involving eight, ten or twelve inches of the terminal ileum; a condition characterized anatomically and pathologically by tremendous thickening of the ileum, necrotizing ulcerating lesions of the mucous membrane, and the progress of this hyperplastic inflammatory condition to a stage of stenosis where the obstruction presents itself as a clinical manifestation. Sometimes the stenosing character of the lesion is apparently the first manifestation, and these cases present originally a high intestinal obstruction of a benign character. Another outstanding characteristic of this condition which we term "terminal ileitis" is the-tendency to form fistulae. Persistent abdominal fistulae are common in the experience of surgeons; medical men are not commonly called upon to analyze the for-

mation and rationale of such persistent fistulae. Those who work in large general hospitals will find that the internists are occasionally called to the surgical side to explain why a fistula persists after an appendix operation. Terminal ileitis has similarly a great tendency to form fistulae, which tracts run usually from the terminal ileum to the cecum, sometimes to the ascending colon, very frequently to the sigmoid, sometimes through the mesentery, and sometimes to the floor of the pelvis. Sooner or later a mass appears, usually at the right side of the lower abdomen and coincident with this mass the stenotic manifestations occur. Practically all of our cases have been operated upon by Dr. A. A. Berg; the cases are today all well except one, who died at the time of operation. The other fourteen cases are well; not only are well, but they remain perfectly well after the primary lesion has been removed or sidetracked.

We have been unable to find any etiological factor which can be proved to account for this disease. We took pains to eliminate tuberculosis, syphilis, and every other recognizable agency.

One may mistakenly think that we are demonstrating a very rare lesion. Now that we are aware of the clinical condition, we are seeing at Mount Sinai at least three, four or five cases a year. We had one case two months ago, and I have now a case which will be operated upon on our return. At a session of the New York Surgical Society about four weeks ago, one of the members of that association presented a case of granuloma of the terminal ileum; to my surprise he was showing this same condition. The chairman asked for general discussion; six surgeons of large experience with abdominal conditions discussed the subject. Several men recounted having seen a case six years ago or twelve years ago, upon which he had operated with good result. These were surgeons with wide experience; several of those surgeons in the course of a lifetime had seen such lesions, but had apparently not been able to recognize or identify the underlying pathological process.

(*Slide.*) Anatomically the terminal ileum is involved for 8, 10, or 12 inches. Dr. Ginzburg mentioned 24 inches because we have such an occasional case. The terminal part of the lesion ends abruptly at this point (indicating). The depth and greatest intensity of the lesion is along the line where the mesentery is attached to the small bowel. The thickening of the wall can be seen here, the tremendous thickening of the ileum, three, four, or five times the usual thickening.

(*Slide.*) This is another specimen of the lesion, first, the normal ileum, then the beginning diseased process and the terminal part of the ileum with its maximum involvement. The stilet shows one fistula formation, here another formation. The fistula burrowed through the mesentery and made an exit at the ascending colon. In one instance while doing a sigmoidoscopy, I saw a nipple-like projection on the mucosa of the sigmoid. I was actually seeing the end of a fistula which had burrowed from the terminal ileum into the sigmoid.

(*Slide.*) This is a photograph of one of the specimens exhibited; one notes the very abrupt ending of the lesion at the ileocecal valve with the tremendous thickening at the wall of the ileum, causing what will eventually be an obstruction.

The barium enema shows a narrowing of the proximal part of the transverse colon at this point; a tentative diagnosis of a carcinoma of the transverse colon was made. However, this was a case in which a fistula had burrowed through and into the transverse colon, simulating a malignant lesion. The case was operated upon as a supposed malignancy and the benign condition was discovered at this point.

(*Slide.*) This is the last slide, demonstrating barium meal by mouth, showing the strand-like terminal ileum. At this point one sees a small fistulous tract going up to the splenic flexure.

DR. GINZBURG (closing): I just wish to answer a few of the questions, first Dr. Bockus' question about the sigmoiditis following deep x-ray therapy. We have had no such personal experiences, but cases of that type have been reported in the literature. We know that deep x-ray therapy is very apt to cause sclerosis of the smaller vessels and I imagine the changes taking place in the sigmoid were secondary to vascular changes. Such ulcers have also been reported following deep therapy in the bladder.

As far as amebic granuloma is concerned, this report is based mainly on resected specimens and in none of them were ameba found either on section or by searching the stool. We did have a case of amebic granuloma which we thought was carcinoma of the recto-sigmoid. The removal of a specimen revealed its real nature.

As far as lues is concerned, I do not recollect any of our patients that had a positive Wassermann. I don't believe it has anything to do with the condition.

The point that Dr. Bockus brought out about the blood supply and the tendency to twist of the terminal ileum, had also entered our minds. In relation to the question of vascular changes to chronic granulomata, we said that repeated partial volvulous or intussusception may have something to do with these granulomata in the ileo-cecal region. Most of the cases as I remember them were of the slender visceroptotic type. However, we had a few patients quite the opposite, definitely stenic types.

On the question of appendicitis and terminal ileitis: At least half of the cases that finally came to operation had had their appendix removed at some earlier time. In some of those cases it was noted even at the first operation that there was something wrong with the terminal ileum. The surgeons had apparently thought, however, as they weren't quite sure what the nature of the lesion was, that they had better adopt a conservative course.

As far as tuberculosis is concerned, we have injected triturated material from the bowel wall into rabbits, guinea pigs and chickens in eight or ten instances and we have never been able to achieve any definite result. We have never been able to demonstrate tubercle bacilli in sections; never been able to demonstrate coagulation necrosis, never been able to demonstrate typical tubercles.

We have only two cases showing a definite x-ray finding with barium meal which Dr. Crohn showed. This is due mainly to the fact that a great many of these cases come in with signs of subacute obstruction and naturally one is rather loath to give them barium by mouth for fear of completing the incomplete obstruction.

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