CROHN'S DISEASE
A REVIEW

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Non-specific granuloma of the intestine, usually referred to as Crohn's Disease, is encountered now and again by every abdominal surgeon. In this country most have seen some cases, but few have seen many. The diagnosis must frequently be missed, and when made clinically or at operation many do not feel confident as to what should be done about it. Since the literature is large, it seemed that a review of the subject to the present date might be of help. No fresh cases are presented, as it is undesirable that this review should carry the bias of a small personal experience.

Nomenclature

The condition has been described under the names of non-specific (Ravdin, 1937), infective (Mock, 1931), or benign granuloma of the intestine, intestinal phlegmon or chronic cicatrizing enteritis (Harris, 1933), regional enteritis (Brown, 1934), sclerosing enteritis, regional enterocolitis (Devine, 1948), regional or terminal ileitis, or ileo-jejunitis (Crohn, 1941), according to its site. Shapiro (1939), in a review, favoured 'non-specific inflammatory granuloma.' It is recognized that jejunum, ileum and colon can be affected, and that the disease may be found in acute or chronic stages. The expression 'non-specific intestinal granuloma' is perhaps the least open to objection.

History

The first description is believed to have come from Charles Combe and William Saunders in a report to the Royal College of Physicians of London, on July 4th, 1806. 'A singular case of stricture and thickening of the ileum' was described as having three distinct contractions of the small intestine due to a benign granulomatous condition which resulted in death. Reference is again made by Combe and Saunders (1813) and John Abercrombie of Edinburgh gave a description in his book in 1828. In 1895, Senn differentiated between infective granuloma and cancer of the intestine, as did Braun (1901), while Moynihan (1907) reported six cases with intestinal masses simulating cancer; these were, however, all in the large gut, an unusual site.

Proust (1927) and again Braun (1909) referred to non-specific inflammatory tumours of the intestine, the latter reporting one case which might have been diverticulitis of the sigmoid, and two cases of caecal mass which resolved. Robson (1908) and Lejars (1908) also reported cases.

Dalziel (1913) described small as well as large gut involvement including a localized jejunitis in one case, and another in which the whole of the gut was involved. He called it 'chronic interstitial enteritis.' Tietze (1920) reviewed the condition but described no case suggesting typical 'regional ileitis.' Moschowitz and Wilensky (1923) reported four cases of benign intestinal granuloma and concluded it was of non-specific origin. One of their cases appears to have been a regional ileitis; however, all had involvement of the colon, one involving colon and small gut. Mock (1931) described granulomata attributable to various causes, but no case of typical regional ileitis.

Crohn, Ginzburg and Oppenheimer published their now famous article in 1932. This was a convincing description of 14 cases of 'regional (or terminal) ileitis,' a hypertrophic inflammatory process involving 8 in. to 12 in. of the terminal ileum and divisible during its course into four separate clinical types as follows:—

(1) With signs of acute intra-abdominal inflammation. (2) With symptoms of ulcerative enteritis. (3) The stenotic phase. (4) The phase of persistent fistulae. This description met with a widespread response and the interest thereby aroused has persisted. 1,127 cases were described in English publications between 1939-44, while 500 cases have been treated at the Mayo Clinic since 1932 (Lancet, 1948). Crohn himself had personally seen 115 cases by 1941, 75 being confirmed at operation (Bockus, 1944). Regional
ileitis is only one form of non-specific intestinal granuloma, as Crohn and his colleagues were among the first to realize subsequently.

Incidence

Cases have been reported from India, Africa, Sweden, Canada, Europe and the United Kingdom as well as the U.S.A. (Bockus, 1944). The disease appears to be rare in Latin America. Jews are especially susceptible (Jackman, 1937) and have it with thrice the usual expectancy, while negroes are almost immune. There is little difference in sex incidence and most patients are between the ages of 12 and 46; 75 per cent. occur between the ages of 20 and 40 (Bockus, 1944). No age group is immune, cases being reported in infancy (Erb, 1935) and in old age (Ravdin, 1937).

Pathology

The disease may occur as an acute inflammatory condition, which resolves or progresses to the chronic stage, or it may be chronic from the outset. Acute inflammation may be added to the chronic disease. The four clinical types described by Crohn et al. (1932) refer to the 'regional ileitis' form of the disease. In their original description they stated that the lesion did not pass below the ileo-caecal valve, a conclusion which was later corrected (Crohn, 1936). Colp (1934) reported the first case of large gut involvement following this statement, and in the same year Brown, Bargen and Weber (1934) described 18 cases of regional enteritis in five of which the caecum and ascending colon were also involved. In a typical case the process is most intense just proximal to the ileo-caecal valve (Harris, 1933). Two or more separated lengths of gut may be involved resulting in what are known as 'skip' areas. The jejunum may be diseased and even duodenal involvement has been recorded (Jackson, 1937 (b)), but is very rare. Barbour and Stokes (1936) record a case showing 13 separate inflamed lengths of small gut extending from 21 in. from the pylorus to 4½ in. from the ileo-caecal valve.

The Acute Stage

A good description of the pathology of the acute phase is hard to find for the bowel is not resected at operation, and fortunately most patients recover, so that post-mortem material is rare. Accounts of pathology are frequently not explicit as to whether the condition was acute or acute-on-chronic; for instance Meyer and Rosi (1936) quote Jackman on the pathology of what appears to have been an acute case, but the presence of dense scar tissue suggests that there had been previous inflammation. As Homb (1946) states: 'Further details of the pathology and symptomatology of this (the acute) stage are seldom given and vague-ness seems to prevail . . .'. At operation there is found an appreciable quantity of clear or fibrinous (sterile) fluid, and the terminal ileum is swollen, spongy and reddened, with fibrin flakes on a serous coat which has lost its sheen. Erb and Farmer (1935) describe four cases with acute symptoms in children, in which the proximal large gut was also involved (which is unusual). They found enlarged Peyer's patches, congestion and oedema of the bowel, free fluid (sterile) and enlarged mesenteric glands in the three which were operated on. The fourth, aged 2½ years, died without operation. The post-mortem showed clear fluid with fibrin flakes, marked oedema of 20 cm. of ileum, also of the caecum and 8 cm. of the ascending colon. The appendix was normal, the mesenteric glands pale red and oedematous. On opening the specimen there was injection of the mucosa and the Peyer's patches were prominent with ulceration over them, part of the mucosa being replaced by slough. Gross oedema of the bowel wall had caused blockage of the lumen (unusual in the acute stage). Microscopically, there was lymphoid necrosis and swelling, mononuclear infiltration and very few polymorphs. The oedema was most marked in the sub-mucosal layer. Small haemorrhages were present. In acute jejunal involvement, the pathology found by Brynjulfsen (1948) is consistent with the above, though in his cases the mucosa was usually intact except for a few small ulcers. He also mentions thickening of the mesentery with small haemorrhages in it. Free perforation of the jejunum is described (Homb, 1946), but is rare.

The Chronic Stage

Most accounts of the pathology refer to the early chronic stage, or to its subsequent progression to stenosis or fistula formation. They are best considered together. Some idea of the relative frequency of site of involvement of the gut is given by Pemberton and Brown (1937) who report 39 cases seen from 1922-37, of which 24 were terminal ileitis, 6 terminal ileitis with involvement of caecum and ascending colon, 4 upper ileal disease and 2 multiple involvement with 'skip' areas. Shapiro (1939) reviewing 413 cases in the literature gives 261 terminal ileum, 80 terminal ileum and caecum, 20 terminal ileum, caecum and ascending colon, 47 other parts of the ileum and 16 jejunum. Other sites were less common. The terminal ileum is the commonest site of the disease, and from this, the centre of the intestine, the liability to attack decreases in both directions. Ileum is more liable to disease than jejunum and the duodenum is almost immune. Caecum and ascending colon are more liable than
transverse colon and primary involvement of the sigmoid is rare and of the rectum rarer still. The appendix is largely immune and any involvement is secondary, even when ileum and cæcum are both diseased. When the colon is involved, it is most commonly adjacent to ileal disease, i.e. in cæcum and ascending colon, and though the colon can be involved alone (Devine, 1948) the proximal colon is in any case the commonest site for large gut disease (Crohn, 1938). These writers also state, quoting 17 cases of 'regional colitis,' that the disease may start at any place in the colon and work downwards; it can also work upwards and usually involves the ileum as well. The sigmoid is apparently a natural barrier to downward spread though it too may become primarily involved (Epstein, 1947) as well as secondarily by the adherence to it of diseased ileum. Crohn and Rosenak (1936) presenting 60 cases of terminal ileitis, 9 of which had simultaneous involvement of the colon, refer to the latter as 'ulcerative colitis,' a term which is particularly unfortunate as cases of regional ileitis associated with 'ulcerative colitis' have been interpreted as a non-specific ulcerative colitis associated with granuloma of the ileum and not as an extension of the granuloma (Jellen, 1937). Moreover, many cases of non-specific intestinal granuloma are misdiagnosed as ulcerative colitis owing to the similarity of symptoms, and distinction between the two is most important.

**Macroscopic Appearances**

In the established chronic disease there is again clear or fibrinous fluid in the peritoneum (Mixter, 1935), the involved gut is thick and 'hose-like,' the serous coat dull, covered with exudate (Bockus, 1935) and possibly adherent. There may also be tubercle-like lesions of the serosa (Mixter, 1935). The process is well defined and shades off into apparently normal gut fairly abruptly, though ulcers may be present beyond gut which shows external evidence of disease (Jellen, 1937). The mesentery is swollen and boggy due to oedema (Meyer, 1935; Jones, 1935); later it is thick and fibrotic and may have a tendency to bleed (Jackson, 1937(b)). The mesenteric glands are enlarged and oedematous. In an excised specimen, the submucosa is the layer showing the greatest changes. This layer is markedly thickened by oedema, or fibrin or both; the mucosa is ulcerated over the Peyer's patches, chiefly at the mesenteric aspect of the bowel.

**Microscopical Appearances**

Bockus (1944) states that Hadfield (1939) gives the most complete histological description he has seen. This description is based on 20 cases of regional ileitis. The submucous thickening was the chief cause of the thickening of the bowel wall, and the thickening of the muscle layers was inconstant and variable. This thickening was often advanced with little ulceration present (though some ulceration was present in every case), suggesting that the submucosa is involved first and that ulceration follows. In the submucosa lymphoid hyperplasia was marked, and this together with obstructive lymphoedema accounted for the thickening. The germinal centres were replaced by proliferating endothelial cells, and the lymph nodules enlarged and irregular in shape. When about five times their normal size they retrogress. The glandular lesions show giant cell systems similar to those in the submucosa. They are indistinguishable from tuberculous lesions except that there is no caseation and no acid fat bacilli. Boeck's sarcoid is closely resembled in appearance, evolution and retrogression. The lymphoid tissue, then, appears to hold the primary lesion.

**The Advancing Disease**

In various other accounts the results of advancing disease are described. The bowel lumen is diminished by swelling and may even be blocked, and in this case the bowel above will be found distended. The mucosa is thickened and nearly always ulcerated, though not necessarily so. The ulcers lie in the long axis of the bowel (Meyer, 1935; Johnston, 1937), as would be expected, since they lie over the Peyer's patches, and they are chiefly on the mesenteric aspect (Harris, 1933). The ulcers may be confluent (Jellen, 1937) in which case the surface is likely to be granular and polyloid (Koster, 1936) or even replaced by dense scar tissue (Bockus, 1935). Ulcers may be found even beyond the main mass of the disease. The submucosa shows the changes described by Hadfield (supra). Giant cells are not always present (Koster, 1936) and polymorphs are scanty (Mixter, 1935), eosinophils, round cells and reticulum cells (Schwabacher, 1936), plasma cells, fibroblasts, fibrocytes and histiocytes may all be found. The muscle layers are thickened and infiltrated but to a considerably less extent than the submucosa. Fibrosis occurs as the disease advances. The serosa, mesentery and glands are described above. Abscesses may form and frequently invade the mesentery due either to the slow perforation of an ulcer lying opposite the mesenteric attachment, or to suppuration of the mesenteric glands (Devine, 1948). An abscess may be found in the pouch of Douglas (Arnheim, 1935). Local pus is white and not malodorous (Pollock, 1937). A chronic abscess may adhere to the wall of previously normal gut, perforate into it and thus form an internal fistula. Free perforation into the
peritoneal cavity is extremely rare, but has been reported (Halligan, 1937). Fistulous openings (Penner, 1938) may occur through the abdominal wall particularly through the scar of a previous appendicectomy. This sequence seems to be due not to the removal of the appendix followed by giving way of the stump, but to the perforation of an ulcer (Ginzburg, 1942) or the discharge of a previously formed abscess, a process which is obviously assisted if a drain is inserted (Bockus, 1944). Internal fistulae are commonest to the caecum and ascending colon, and to the sigmoid from an adjacent ileum. Abscesses which have formed in the pouch of Douglas have given rise to fistulae into the vagina, rectum, bladder and even the ureters according to Penner and Crohn (1938). They also state that the incidence of perianal fistulae was not noted at first, but then they found that eight out of 50 cases had this complication. These fistulae are of a different origin, and though occasionally one may come from the tracking down of an abscess in the pouch of Douglas, most of them are due to infection of the crypts of Morgagni by the concomitant diarrhoea, for any diarrhoea caused by inflammation of the gut may be complicated by fistula-in-ano. Non-infective diarrhoea, such as gastrogenous, neurogenic or allergic diarrhoea does not give rise to this complication. The above description of the pathology of the chronic stage covers the second (enteritic), third (stenotic) and fourth (fistulous) clinical stages of Crohn.

Etiology

Before reviewing the suggested possibilities it can be stated at once that there is as yet no agreement as to the cause of the condition, the majority preferring to regard it as a non-specific inflammation.

Tubercle. Several attempts have been made to incriminate the tubercle bacillus. The lesions are microscopically indistinguishable from tubercle, but there is no caseation and no acid fast bacilli (Hadfield, 1939). Repeated search for tubercle bacilli has failed (Mixter, 1935). An X-ray of the chest is in all cases normal (Bockus, 1944). The most recent attempt has been made by Merke (1947), who found that five of his nine cases showed evidence of tubercle elsewhere in the body, and in two further cases there was a history of tuberculosis in the patient’s household.

Dysentery. J. Felsen (1936) followed up 400 cases of acute bacillary dysentery in the New York area, and from these there ensued 29 cases of acute distal ileitis, 22 of chronic distal ileitis (18 confirmed at operation or post-mortem), 18 of chronic ileo-colitis (11 confirmed at operation or post-mortem) and 84 of chronic ulcerative colitis. He asserts that 10 per cent. of acute bacillary dysentery cases become chronic, and that intra-mural infection via the ulcers with enterococci and B. coli occurs. B. dysenteriae is sometimes found, as also is a positive agglutination test in the chronic cases. This work has not been confirmed (Manson-Bahr, 1946).

Lymphatic obstruction. The experiments of Reichert and Mathes (1936) are often quoted in support of the theory that lymphatic obstruction is responsible for the condition. These workers produced experimental lymphoedema with thickening of the bowel wall and stenosis by injecting the mesenteric lymphatics of dogs with sclerosing agents and at the same time injecting bacteria intravenously. In man the lesions may well give rise to lymphatic obstruction (Blackburn, 1939) and the intestinal organisms to secondary infection, but this assumption brings us no nearer to the etiological cause of the primary lesion. Bockus (1944) believes that enteric tubercle may itself give rise to lymphatic obstruction and secondary invasion by other organisms. He points out that the segmental involvement of the bowel supports the theory of a primary extra-luminal pathogenesis possibly dependent on segmental areas of lymphatic blockage.

Mesenteric adenitis. A. S. Jackson (1937 a) believes the condition to be allied to non-specific granuloma. The ileum may be the most frequently involved part of the gut on account of its greater abundance of lymphatic tissue and of bacterial absorption. Surgeons have noted diffuse inflammation of the terminal ileum in an acute mesenteric adenitis (Bockus, 1944).

Appendicitis. The appendix appears never to be primarily involved although it may be involved in the adjacent inflammation. However attempts have been made to incriminate it (Arch. Path., 1934), and the possibility of appendicitis causing lymphangitis has been pointed out. It seems strange that this organ which has a superabundance of lymphoid tissue should remain immune.

Boeck’s sarcoid. This is closely resembled by the lesions in the submucosa and glands (Hadfield, 1939), but there is no other evidence that it is the same process (Manson-Bahr, 1946), nor is there any sign of generalization of the disease (Homans, 1933).

Other possibilities. There is no evidence that the ancient scapegoat, the Sp. pallida, is the cause. The resemblance to linitis plastica has been noted. The virus of lymphogranuloma inguinale has been mentioned, but Frei’s test is consistently negative (Manson-Bahr, 1946). A chronic fibrosis of the gut may follow strangulation in a hernia (Johnston, 1937). Bargen (1935), in discussion, advocated.
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the possibility that his diplostreptococcus might be a factor, as in ulcerative colitis. Paulley (1948) suggests that colitis and Crohn's disease may represent variations in reaction to a similar form of chronic recurrent gut dysfunction. It is said that few phlegmatic persons get the disease (Bockus, 1943) and psychoneuroses have been noted frequently in these patients (Blackburn, 1939), but it should be observed that chronic ill health from any cause paves the way for neurosis.

Summary. Barbour and Stokes (1936) state: 'Chronic cicatrising enteritis is not the result of any single etiological factor. It is a particular clinical example of granuloma of the intestine of non-specific origin. It is believed that in every case an initial factor impairs the vitality of the gut wall and allows bacterial invasion from the lumen of the gut...'. They then quote Mock (1931), who classifies all the possible factors producing the local lessening of resistance which is followed by the formation of these granulomata, e.g., trauma from fish bones, foreign bodies such as ligatures and fruit pips, infections by bacteria, protozoa and metazoa, etc. It still appears, however, that there is a very definite pathological entity, a granulomatous process, which is responsible for the majority of cases where benign intestinal inflammatory masses are formed. There is good histological evidence that a non-specific but typical primary lesion is present in the lymphoid tissue of the submucosa. The agent causing the lesion is unknown but the same process evidently causes the similar lesions in the mesenteric lymph nodes, and an acute or chronic inflammatory reaction is set up giving rise to oedema and later to fibrosis. Ulceration of the mucosa over the involved lymphoid tissue allows gut organisms to invade the bowel wall. Abscesses may originate from bowel or glands and subsequently give rise to fistulae.

Clinical Findings

Non-specific intestinal granuloma can give rise to many and diverse clinical pictures so that it is necessary to separate them one from another to obtain a clear view of each. A sub-division has been adopted as follows:—

(a) Acute. Regional ileitis, jejuno-ileitis. (b) Chronic. Regional ileitis, jejuno-ileitis, regional colitis.

Symptoms

Acute regional ileitis. This has all the features of an acute inflammatory abdominal condition, and since the symptoms are most frequently referred to the right lower quadrant many of these patients are operated on for supposed acute appendicitis. The usual age incidence is 18 to 40 (Homb, 1946). Pyrexia is present, usually up to 100° F., but even reaching 104° F. in a severe case (Forbes, 1937) whilst the pulse is correspondingly increased. In two-thirds the onset is gradual and in one-third there is a previous history of pain (Homb, 1946). The patient may have been ill for several days (Erb, 1935) with right lower quadrant pain, accentuated by periodic 'cramps' felt at the same site or more diffusely (Jackson, 1937 (a); Homb, 1946). Nausea and vomiting are present (Ryan, 1937) and possibly headache.

On examination, there is tenderness in the right lower quadrant, and though a mass may be present (Harris, 1933) it is uncommon at this stage. The white cell count may be raised (11-16,000) and can reach a high level (31,000). On opening the abdomen the condition described under pathology of the acute disease is found, but the true state of affairs may go unnoticed especially if a small muscle split incision is employed. The appendix may be removed and found to be mildly inflamed on the outside. Suspicion should then be aroused in the post-operative period, for convalescence may be stormy. The pyrexia continues with pain, cramps and vomiting, and the patient can become seriously ill. Fortunately, rapid subsidence is more frequent (Homb, 1946). Fistula formation is not unlikely to occur through the operation wound and to persist (Penner, 1938). Finally, after recovery, the patient may present the symptoms and signs of the chronic disease. Crohn et al. (1932) originally stated that half his patients with chronic regional ileitis had had their appendices removed, most of them, presumably, on account of the symptoms referred to the right lower abdomen; 13 of Brynjulfsen's (1948) 14 acute cases were opened for appendicitis.

Acute jejuno-ileitis. Homb (1946) describes eight cases with ages ranging from 24 to 63 years. The typical onset was acute with severe epigastric or generalized abdominal pain and repeated vomiting. There was pyrexia of 99°-100° F. with epigastric tenderness. Rigidity was uncommon. Meyer and Rosi (1936) noted a similarity to a gradual onset of small gut obstruction. Three of Homb's patients had melaena, and a further three had a positive benzidine test. White cells varied between 13,000 and 36,000. Five were operated on and sections of jejunum 20-100 cm. in length found to have the typical appearances of the acute disease. 'Skip' areas are described. Two patients died, one of whom had a free perforation of the gut into the peritoneum. Brynjulfsen (1938) describes 16 cases of 'acute phlegmonous jejunitis' seen over 12 years, and except for two children all were over the age of 30, six being over 70. The age therefore tends to be higher than in acute ileitis. Nausea and vomiting were invariably, and sometimes faecal. Eleven had
diarrhoea followed by constipation, and in five the stools were bloodstained. The picture was that of an acute gastro-intestinal upset with pallor, exhaustion, shivering and pyrexia. Tenderness was usually present in the left epigastrium with possibly some rigidity. A mass was present in only two. White cell count was 10,600-29,900. It is noted that a plain X-ray was suggestive of ileus, but less marked than the symptoms would suggest, and yet diarrhoea was usually present. Fourteen of these patients died, nine of them within five days of the onset.

Chronic regional ileitis. This is the typical 'Crohn's disease,' the uncomplicated and probably early chronic stage giving symptoms suggestive of ulcerative enteritis (second stage of Crohn). Abdominal pain is the chief symptom, usually in the right lower quadrant (Blackburn, 1939) but often accentuated by cramps and colic felt more diffusely (Jackson, 1937), centrally (Harris, 1933) in the epigastrium (New England Journal of Medicine, 1935) or lower abdomen. Symptoms have usually been present for some months or even years, e.g. four months to 20 years, with an average of four years (Pemberton, 1937). Lower abdominal pain may occur after food (Corrden, 1936). Vomiting is usually not marked (Meyer, 1935) but may occur with the cramps. Diarrhoea is prominent, occasionally with mucus. Blood and pus are usually absent (Jones, 1935; Bockus, 1945) but melaena can occur (Forbes, 1937). Occult blood is present in 60 per cent. (Bockus, 1944). The patient looks pale, may have lost weight and is perhaps having fever and sweats. On examination, a mass may be felt usually in the right lower quadrant, which is tender and usually fixed but may be movable (Bockus, 1935). Blood examination may be expected to show moderate anaemia, moderate leucocytosis and E.S.R. about 35 mm. (Blackburn, 1939). Eosinophilia is inconstant. When the third stage, that of stenosis, is reached, severe cramps and vomiting are likely to be present (Jackson, 1937 (b)), also 'gas pains' (Jones, 1935) and constipation (Forbes, 1937). Excess peristalsis (Schwabacher, 1936) may be visible (Harris, 1933) perhaps accompanied by distension. Finally in the fourth stage, that of fistula formation, discharge may occur from a previous appendicectomy scar (Jones, 1935; Penner, 1938) or elsewhere on the abdominal wall (Blackburn, 1939). The involved gut may communicate with the sigmoid (commonest), caecum, ascending or transverse colon. Vesical fistula is less common (Forbes, 1937; Garlock, 1946). Vagina, rectum and even the ureters have been involved (Penner, 1948). Fistula-in-ano due to crypt infection from diarrhoea may even be the initial picture. As early as 1935 Jones and Byrne record a case with a previous history of operation for fistula-in-ano. Jackman and Smith (1943) found that 36 of 114 patients with regional ileitis had anal abscess or fistula or a previous history of such. In eight cases fistula was the chief complaint, regional ileitis being discovered later.

Thus, as the Devine states (1948), the disease can present as an 'acute abdomen,' a chronic obstruction, subacute appendicitis, 'ulcerative colitis,' abdominal fistula, chronic abdominal pain or even as pyrexia of unknown origin. Bockus (1945) mentions also chronic abdominal abscess and anal fistula.

Chronic jejuno-ileitis. According to Crohn and Yunick (1941), when the chronic disease takes the form of jejuno-ileitis, which is the same process occurring higher up, frequently with 'skip' areas, the process is of low grade and often less severe, masses do not form, no obstruction occurs and there are usually no fistulae. Seventeen of their 200 cases were of jejuno-ileitis. Ginzburg and Garlock (1942) in 99 cases found 22 of jejuno-ileitis.

Chronic regional colitis. This is usually associated with regional ileitis and produces a very similar picture.

X-Ray Findings

Acute ileitis. 'The acute cases which subside spontaneously give no positive Rontgen findings during the acute phase other than irritability of the involved segment' (Smithy, 1943).

Acute jejuno-ileitis. One or more upper jejunal distended loops with fluid levels may be seen, and if barium is given it will be retained in the loops (Homb, 1946). The X-ray picture is that of high obstruction. Two points of distinction are that there are broad and elevated mucosal plicae opposite the gas, and that the patient usually has diarrhoea. A barium meal given after the acute phase is over shows changes of tonus, irregularity of the mucosa and delay, with air and fluid levels. One case was examined three months later and the X-ray appearances were normal (Brynjulfson, 1948).

Chronic regional ileitis. Barium enema. Where this is normal in the presence of symptoms of chronic enteritis, it is suggestive of Crohn's disease (Harris, 1933). A defect in the caput caeci may be shown (Meyer, 1935; Bockus, 1935; Mixter, 1935). Where the ileum is shown up there may be a filling defect (Jackson, 1937(a); Pollock, 1937). Barium meal. In the affected length of gut the usual mucosal markings are altered and may be obliterated. Polyploid mucosa may be detected. The ileum is rigid, the affected loop is fixed and there is no peristalsis. There may, however, be hypermotility and irritability and the
bowel then does not show up at all. Proximal delay with dilatation is sometimes seen (Pollock, 1937; Mixter, 1935; Meyer, 1935). Kantor (1934) describes (a) a filling defect proximal to the caecum; (b) an abnormal contour of the last filled loop of ileum; (c) proximal dilatation; (d) the 'string sign,' a term he borrowed from A. W. Crane denoting the appearance of the thin barium streak in the contracted length of gut. Fistulae may be outlined in later stages (Meyer, 1935) leading to the sigmoid or elsewhere (Pollock, 1937; Mixter, 1935).

**Chronic jejunoo-ileitis.** The findings are much the same as for terminal ileitis (Pollock, 1937). Crohn (1941) describes change of outline of mucosal pattern with delay of the barium, a blurred outline with both narrowed and dilated areas.

**Chronic regional colitis. Barium enema.** The diseased colon shows an irregular outline (Crohn, 1936) and filling defects not suggestive of carcinoma (Crohn, 1938). *Barium meal.* A very irritable right colon and caecum is shown. The absence of a normal barium shadow in the proximal colon in ileo-caecal tuberculosis (Stierlin's sign) is not characteristic of this condition alone (Pollock, 1937). Crohn and Rosenak (1936) refer to the appearance of 'ileitis and disseminated colitis,' also of 'typical ileitis and irregularity of the caecum, ascending and transverse colon suggesting ulcerative colitis'; this seems an ambiguous and unfortunate terminology.

**Differential Diagnosis**

**Acute ileitis.** This is most likely to be confused with acute appendicitis or other intra-peritoneal inflammation. The diagnosis may be made at operation or is perhaps missed even then. The presence of a quantity of free fluid and an apparently normal appendix should arouse suspicion. An inflamed and soggy ileum following local inflammation from appendicitis may be thought to be non-specific granuloma.

**Acute jejunoo-ileitis.** Acute or subacute upper small gut obstruction is suggested by the clinical condition (Homb, 1946). Distinctive points are the constitutional signs of inflammation, the presence of diarrhoea and an X-ray which shows upper small gut fluid levels with abnormal mucosal pattern. Brynjulfson (1948) describes the 'ileus-like' picture and the 'enteric' picture suggestive of typhoid, paratyphoid, dysentery or gastroenteritis. Massive haemorrhage may occur. Mesenteric vascular occlusion may be simulated.

**Chronic regional ileitis.** Abdominal cramps must be differentiated from other causes of colic and spasm, e.g. mesenteric adenitis. Diarrhoea is suggestive of chronic dysentery, ileal tubercle or colitis. Garlock (1946) states 'Non-bloody diarrhoea is one of the distinguishing clinical features from non-specific ulcerative colitis. This should be emphasized repeatedly.' A mass is to be distinguished from appendicitis, carcinoma, ileocaecal tubercle, actinomycosis (Rosenblate, 1936), lymphosarcoma, Hodgkin's disease, other granulomas and chronic perforating lesions (Johnston, 1937) and amoeboma. Later, all kinds of chronic obstruction may be simulated.

One of the first signs of disease may be a fistula-in-ano; vesical or vaginal fistulae are rarer. Chronic pelvic abscess may suggest pyosalpinx.

**Chronic jejuno-ileitis.** This gives a picture of chronic ill health and pallor with abdominal discomfort and tenderness, or even pyrexia of unknown origin (Devine, 1948).

**Chronic regional colitis.** An inflammatory mass forming in the colon may be due to diverticulitis (most common in the sigmoid), to underlying carcinoma, to amoebiasis or to inflammation round a small perforation, as from a fish bone (Devine, 1948).

**Treatment**

**Acute ileitis.** If the correct diagnosis is made, conservative treatment is indicated, and a regime of rest and fluids only should be followed. In this stage, even a temporary obstruction is rare but should it occur the use of the Miller Abbot tube with parenteral fluids is indicated. A more frequent occurrence is for the patient to be operated on for appendicitis, or an undiagnosed abdominal inflammatory condition, and in the first instance a junior surgeon may well find himself contemplating a normal appendix through a McBurney incision. Clear or fibrinous free fluid will be present as well as the other appearances described under the pathology, but the usual search for a Meckel's diverticulum should bring to light the state of the ileum. There is complete agreement that resection should in no circumstances undertaken at this stage.

The acute inflammation usually resolves (Bockus, 1944; Pollock, 1937), and subsequent further intervention will probably be unnecessary, but in any case can be undertaken when the acute condition has subsided. An attempt at resection may result in severe haemorrhage owing to the hyperaemia (Mixter, 1935) and the enlarged glands are difficult to handle (Lahey, 1942). On first principles alone the performance of resection in the presence of such an extensive acute inflammation should be placed out of court. Peritonitis would be the probable sequel (Smithy, 1943).

Should the appendix be removed? The weight of opinion says 'No' (Ginzburg, 1942; Garlock, 1946; Cave, 1945). *Appendicectomy should not*
be done in the presence of an adjacent regional ileitis, and indeed it may result in the development of an abdominal wall fistula as was the case in each of our 12 cases of external abdominal wall fistula' (Marshall, 1943). Subsequent fistula is probably not due to 'blowing' of the appendix stump, but to perforation of one of the ulcers of the gut (Ginzburg, 1942). This possibility is increased by the pressure of drainage material (Mixter, 1935). The abdomen should therefore be closed without appendicectomy and without drainage. As might be expected from the above reasoning, the advice against appendicectomy is not unanimous (Bockus, 1944) and Smithy (1943) also does not believe that appendicectomy increases the risk of fistula.

After recovery from the acute attack it is essential that the patient be followed up by clinical and barium meal examination repeated as often as necessary until it is clear either that resolution has taken place or that the clinician is faced with the treatment of the chronic disease.

**Acute jejuno-ileitis.** This usually gives rise to upper small gut distension and vomiting which should be relieved by the passage of a Miller Abbott tube (Brynjulfson, 1948) and with fluids given parenterally in the hope that the acute condition will subside.

**Chronic regional ileitis.** There is, as yet, no effective medical treatment. In those cases where surgery does not appear necessary the medical regime does not differ materially from that adopted in ulcerative colitis. Arnold Starr (1948) summarizes present opinion on medical treatment as advocating 'High vitamin, high protein, high carbohydrate, low residue diet with liver, iron and calcium supplements and the judicious use of sedatives, antispasmodics and chemotherapy.' Psychotherapy is also thought by some to be of value.

All these patients should be observed both clinically and by barium meal examination at regular intervals so that it can be judged whether the disease is subsiding, is unchanged or is progressing. Patients with mild diarrhoea and suggestive X-rays who keep their weight should be observed and not operated on (Garlock, 1946). The further the disease has progressed, the more difficult is subsequent surgery likely to be, and an early decision as to its advisability is highly desirable.

Resection of localized disease has frequently been carried out (Harris, 1933; Crohn, 1936; Mixter, 1935; Meyer, 1936), and is favoured by many, even as a one-stage operation (Jackson, 1937(a); Pollock, 1937). In a one-stage resection there is a danger of peritonitis which is the commonest cause of death (Mixter, 1935) and an ileo-transverse anastomosis followed later by resection greatly reduces the risk. Severe haemorrhage during mobilization is a hazard, and 'skip' areas must not be missed. Anastomosis without subsequent resection may be curative (Jackson, 1937(b)), but Bockus (1944) states that short circuit in continuity without transection is valueless. Shapiro (1939) reports freedom from symptoms in the first year after simple short circuit as occurring in only 30.6 per cent. Ginzburg and Garlock (1942) lay great stress on the necessity for complete transection of the ileum well above the disease with closure of the distal end and implantation of the upper end into the transverse colon, they call it 'ileo-colostomy with exclusion,' and perform this, not as a first stage, but in the hope that it will be curative. Garlock and Crohn (1945) report 16 per cent. mortality and 19.5 per cent. recurrence in 55 primary resections; no mortality in 65 ileo-colostomies with exclusion, and 13.8 per cent. recurrence. In 25 instances resection was performed at a second stage and in every case complete healing was shown. Subsequent resection has therefore been discarded by these observers. Masses vanish and even fistulae close without it. Garlock (1946) reports a total of 100 cases of ileo-colostomy with exclusion and no mortality. Bockus (1944) however severely criticizes Ginzburg and Garlock's assumption that a patient is safe from recurrence after two years.

Pemberton and Brown (1937) also favour ileo-colostomy with exclusion, and state that the disease invariably improves in the subsequent six months, but they use it as a first stage and do a resection three to four weeks later, or if the disease is advanced they leave it for six months. Donald and Brown (1942) state that short-circuiting gives success in only 25-50 per cent. of cases and consider it best to do a resection early, rather than wait for an exacerbation. They favour a two-stage operation. The mortality of resection is unpleasantly high, and Smithy (1943) gives it as 7-15 per cent. Mixter and Starr (1938) advocate wide resection of the mesentery and lymph nodes, and this appears to be the general opinion, but Ginzburg and Garlock (1942) state that wide resection so as to include the glands is not necessary, as it is probable that they do not cause retrograde spread of the disease, and they point out that extension has occurred even after the widest resection.

At the Lahey Clinic, the Lahey type of Mikulicz resection is advocated (Marshall, 1943) and this is done early. There was a 5.5 per cent. mortality in 55 cases; 37 patients were followed one to five years with only five recurrences. Bockus (1945) reports depressing results from resection, i.e. only 45 per cent. of good results in terminal ileitis. He
mentions the advantages of the Lahey technique. Where recurrence occurs above the site of an ileocolostomy with exclusion Colp (1947) advises transection above the recurrent disease, if not too high, and insertion of the top end into the sigmoid. He has not noted any trouble from the resulting blind ends. Bockus (1944) summarizes by suggesting that in a clean case resection should be done if a master surgeon is available. Ileo-colostomy with exclusion is reserved for ill patients and those complicated by abscess or fistula. It is the operation of choice for the less experienced. If an abscess is found this is drained (Mixer, 1935; Pollock, 1937) and ileo-colostomy performed if possible (Marshall, 1943) with resection later. Where fistula-in-ano is present, the ileitis must be treated and the fistula should close, if not, it must be laid open (Penner, 1938).

**Chronic jejuno-ileitis.** Surgical treatment on the above lines would often mean resection or exclusion of too much small gut, and many of these patients do well on medical treatment. Crohn and Yunick (1941) report nine cases observed for five years, four of which did well and five persisted with some symptoms.

**Chronic regional colitis.** Crohn and Berg (1938) advised ileo-sigmoidostomy with exclusion, and colectomy some months later in extensive disease. For localized disease a less extensive resection was adequate. They stress that operation is necessary whenever the disease shows signs of extension to the pelvic colon, as the basis of surgery is a healthy pelvic colon.

**Prognosis**

**Acute ileitis.** The prospects of survival from the acute stage are very good, and Homb (1946) found that symptoms and pyrexia subsided in a few days. Erb and Farmer (1935) report two deaths in four cases in children, but deaths in adults are uncommon, though convalescence may be stormy. After recovery from the acute attack the majority have no further trouble and radiological appearances usually return to normal (Meyer, 1936). Homb (1946) traced 28 patients between one and seven and a half years afterwards and generally found there was occasional mild discomfort in the first few months. Nine traced for over five years had no symptoms at all. Only two patients had to be re-opened within the subsequent two years. Brynjulfson (1948) re-examined 11 of 14 patients two to seven years after an acute attack, and only two showed evidence of disease. Lehmann (1939) reports similarly, and Cave (1945) and Pemberton (1937) even more favourably.

**Acute jejuno-ileitis.** This type has a wide range of intensity, and when very acute is extremely lethal; of Brynjulfson's (1948) 16 cases, 14 were fatal. Homb (1946) had two deaths in eight cases. Milder attacks are probably missed in diagnosis and thought to be a gastro-enteritis.

**Chronic regional ileitis.** There is a notable lack of adequate follow-up in the early reports, and even in 1939 Shapiro reviewing 413 cases admits insufficiency of five-year records. Bowel previously diseased has been observed at operation to be normal (Pessagno, 1937) and follow-up by X-ray often shows a return to normality (Smithy, 1943). The recurrence rates after various schemes of operative attack are given under the treatment (above). Bockus (1945) in 11 cases reports only 45 per cent. good results after resection and stresses that at least a five-year follow-up is essential. Starr (1948) had a patient who showed recurrence after 15 years. He states that only half of those having ileo-colostomy with exclusion will be relieved of the necessity for a second operation.

**Chronic jejuno-ileitis.** Crohn and Yunick (1941) state that this is of low grade and often less severe, without masses, without obstruction and usually without fistula.

**Chronic regional colitis.** Crohn and Berg (1938) observed three cases over a course of years by clinical examination and X-rays. All were seen to extend and required excision. Fistula formation is very uncommon. Distal recurrence was a not unlikely sequel to resection, especially if this was of limited extent (Crohn, 1936).

**Summary**

1. A review of the literature on non-specific intestinal granuloma (Crohn's disease) is presented.
2. Nomenclature, history, incidence, pathology and etiology are discussed.
3. The symptoms, signs, X-ray findings, diagnosis, treatment and prognosis are considered in relation to the various forms which the disease can take.

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CORRECTION

In the obituary notice of Sir William Hale-White, published in our issue of April last, it was stated that Sir William was the first Editor of the *Post Graduate Medical Journal*. This was an error, for which we apologize to our readers. Sir William was, as we said, the Founder of the *Journal*, but was never its Editor, the first to discharge this office being Dr. Adolphe Abrahams (now Sir Adolphe Abrahams), who was appointed in December, 1924.
Crohn's Disease: A Review

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