Current Practice

Diagnosis of Crohn's Disease. A Continuing Source of Error

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While investigating a series of patients with Crohn's disease it became apparent that a considerable time had elapsed between the onset of symptoms and the establishment of the diagnosis. Since the disease may have protean manifestations, the differential diagnosis may prove difficult (Crohn and Yarnis, 1958; Pimparkar, 1964). Thus it is germane to assess the incidence of various presenting symptoms and signs, together with the initial diagnosis suggested in these patients, in an attempt to clarify the reason for the diagnostic errors.

Material and Method

The case notes of all patients indexed with the diagnosis of Crohn's disease at St. Bartholomew's Hospital during the 13-year period from 1955 to 1967 were reviewed. A total of 161 patients had the clinical, radiological, and/or pathological features of Crohn's disease.

Cases of acute ileitis were excluded. The patients underwent initial investigation in a number of different hospitals, so the results obtained have not been biased by selection of subjects from a single source. A further 28 patients indexed with the diagnosis of Crohn's disease had their diagnoses revised as a result of this study; these patients were also analysed to assess the incidence and nature of false-positive diagnoses.

Results

Delay in Establishing Diagnosis

There was great variation in the duration of symptoms before the diagnosis of Crohn's disease was established, the mean

TABLE I.—Time Interval Between Onset of Symptoms and Establishment of Diagnosis of Crohn's Disease (157 Cases)

Cases	Year:										
	<1	1-	2-	3-	4-	5-	6-	7-	8-	9-	10-11-31
No.	50	19	21	5	17	10	6	2	1	3	8
%	31	12	13	3	11	6	4	1	1	2	5

TABLE II.—Comparison of Age Incidence at Onset of Symptoms and at Time of Diagnosis of Crohn's Disease (161 Cases)

Age	Onset of Symptoms		Diagnosis	
	No.	%	No.	%
10-14	13	8	4	2
15-19	29	18	18	11
20-24	33	20	37	23
25-29	23	14	24	15
30-34	17	11	19	12
35-39	14	8	15	9
40-44	5	3	6	4
45-49	9	6	8	5
50-59	11	7	20	12
60-69	6	4	9	6
70-74	1	1	1	1

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delay being 4.3 years (Table I). Though one-third of the patients had been correctly diagnosed within one year of the onset of symptoms, one patient in seven was not diagnosed until at least 10 years had elapsed. Delay in diagnosis was particularly common in children and adolescents. The symptoms often developed before the age of 20, but diagnosis was rarely made in this age group and was usually established only after a series of misdiagnoses (Table II).

Clinical Features

Pain and diarrhoea were the most frequent presenting symptoms in this series. They occurred in 87 and 66% of patients respectively and were the dominant symptom in 37 and 30% respectively. These and other common presenting symptoms are listed in Table III. Only one patient was entirely asymptomatic and was diagnosed at caesarean section, but eight other patients had no symptoms attributable to the gastrointestinal tract and presented with complaints such as anaemia, weight loss, ankle oedema, and fever. Physical examination was often unhelpful, and in as many as 30% of patients physical signs could not be elicited. An abdominal mass was noted in only 24% and a perianal lesion in 23%. On rectal examination an abnormality was found in 35%, but non-specific findings such as tenderness were frequent. Vaginal examination showed an abnormality in 14 patients and occasionally extra-abdominal signs such as ankle oedema or finger-clubbing were found.

TABLE III.—Presenting Symptoms in 161 Cases of Crohn's Disease

Symptom	Overall Incidence	Dominant Symptom
Pain	139 (87%)	60 (37%)
Diarrhoea	106 (66%)	48 (30%)
Weight loss	88 (55%)	4 (2%)
Anorexia	60 (37%)	1 (1%)
Fever	59 (36%)	5 (3%)
Vomiting	56 (35%)	0
Lassitude	51 (32%)	0
Nausea	48 (30%)	0
Acute abdomen	41 (25%)	19 (12%)
Nutritional disturbance	39 (24%)	3 (2%)
Fistula	24 (15%)	7 (4%)
Miscellaneous	50 (31%)	14 (8%)

Initial Diagnosis

Only 6% of the patients were correctly diagnosed after the initial series of investigations (Table IV). The disease was most commonly misdiagnosed as a colonic lesion, appendicitis, or functional bowel disturbance, and in 9% a firm diagnosis could not be made.

Ulcerative colitis was the most frequent colonic lesion to be diagnosed, but in older patients the diagnosis was made less often and such patients were diagnosed as having carcinoma or diverticulitis.

TABLE IV.—Initial Diagnosis after Preliminary Investigation in 161 Cases of Crohn's Disease

Correct diagnosis ..	9 (6%)	
No diagnosis made ..	15 (9%)	
Colonic disorders ..	44 (27%)	<ul style="list-style-type: none"> Ulcerative colitis .. 31 (19%) Sigmoid diverticulitis .. 5 Carcinoma of colon .. 5 Carcinoma of caecum .. 3
Ileocaecal disorders ..	33 (20%)	<ul style="list-style-type: none"> Appendicitis ± mass .. 30 (19%) Portal pyelephlebitis .. 1 Meckel's diverticulitis .. 1 Mesenteric adenitis .. 1
Functional disorders ..	17 (11%)	<ul style="list-style-type: none"> Irritable bowel disorders .. 12 (7%) Psychogenic symptoms .. 4 Anorexia nervosa .. 1
Upper alimentary disorders ..	13 (8%)	<ul style="list-style-type: none"> Peptic ulcer .. 4 Gall stones .. 2 Gastroenteritis .. 3 Coeliac disease .. 2 Ilejeunal diverticulosis .. 1 Pancreatic insufficiency .. 1
Genitourinary disorders ..	12 (7%)	<ul style="list-style-type: none"> Ovarian cyst/tumour .. 4 Other gynaecological disease .. 4 Urinary infection .. 4
Tuberculosis ..	11 (7%)	
Febrile illnesses ..	4 (2%)	<ul style="list-style-type: none"> Pyrexia of unknown origin .. 2 Glandular fever .. 1 Behçet's syndrome .. 1
Intestinal obstruction ..	3 (2%)	
Oesophageal lesion ..	1 (1%)	

Appendicitis or its sequelae was the commonest ileocaecal condition to be diagnosed, but very occasionally mesenteric adenitis or Meckel's diverticulitis was mimicked. Tuberculosis was diagnosed in 7% of the patients, in whom the lesion was situated in either the ileocaecal or anorectal region; this diagnosis was made in only the first six years of the period under review.

Functional bowel disorders were usually thought to be due to the irritable bowel syndrome or to one of its synonyms. Frank psychiatric disturbance was rarely diagnosed and only one patient was thought to have anorexia nervosa.

Genitourinary disease was mimicked in 7%. One-third of these patients were women who were thought to have an ovarian tumour or cyst, and another third had other gynaecological conditions diagnosed, such as uterine fibroids or Bartholin's abscess. The remainder presented with symptoms of urinary infection.

Occasionally the symptoms suggested that disease was present in the upper alimentary tract, and conditions such as peptic ulcer, gall stones, gastroenteritis, or coeliac disease were diagnosed. A diagnosis of intestinal obstruction without any further definition of the cause was uncommon as a presenting feature of the disease.

Febrile illnesses formed only a small proportion of the diagnoses; two cases were labelled pyrexia of unknown origin and another was called glandular fever. No other specific infections were mimicked, but one patient with fever, arthralgia, and orogenital ulceration was diagnosed as having Behçet's syndrome.

False Diagnosis of Crohn's Disease

The main reason for the false diagnosis of Crohn's disease was inadequate or inconclusive radiography (Table V). Vague "inflammatory" changes were noted in the ileum in five patients, dilatation of the ileum in two, and a malabsorption pattern was present in another two patients. The remaining subject had a segmental area of dubious inflammation in the colon. Five patients had ulcerative colitis and four had ischaemic colitis. Both patients with haematomas in the wall of the small intestine had bleeding diatheses as a result of thrombocytopenia and anticoagulant therapy. The patients with polyarteritis nodosa, carcinoid tumour, colon spasm, and stercoral ulceration were all diagnosed on radiological features

which bore some resemblance to Crohn's disease. The patient with prestomal ileitis had an unusual inflammatory disease of the colon whose histological features were not diagnostic of either Crohn's disease or ulcerative colitis; after resection inflammation recurred in the terminal ileum and necessitated several revisions of the ileostomy. The patient with carcinoma of the caecum had a small area of granulomatous inflammation adjacent to the tumour. Another patient had involvement of the bowel wall in an inflammatory mass originating in the peritoneal cavity.

TABLE V.—Cases Originally Indexed as Crohn's Disease but Excluded from Survey

Reason for Exclusion	No. of Cases
Inconclusive radiographic features ..	10
Ulcerative colitis ..	5
Ischaemic colitis ..	4
Small bowel haematoma ..	2
Stercoral ulceration of colon ..	1
Colon spasm ..	1
Carcinoid tumour ..	1
Polyarteritis nodosa ..	1
Prestomal ileitis ..	1
Extrinsic inflammation of bowel ..	1
Carcinoma of caecum ..	1

Discussion

The low incidence of correct diagnoses is disquieting and is due to factors such as lack of awareness of the condition and failure to perform a barium follow-through examination when both the barium-meal and barium-enema radiographs are normal. Some of these misdiagnoses were swiftly corrected, since the incidence of correct diagnosis rose from 6% after preliminary investigation to 33% one year after the onset of symptoms (Table I). This improvement was often due to laparotomy, since 43 patients had had the diagnosis confirmed surgically within one year, but occasionally the diagnosis was made without recourse to surgery as a result of the persistence of symptoms or the development of new symptoms producing a more classical clinical picture.

Though Crohn's disease has a predilection for the terminal ileum (Crohn, Ginzburg, and Oppenheimer, 1932), it may involve any part of the alimentary tract (Shapiro, 1939; Crohn and Yunich, 1941; Comfort, Weber, Baggenstoss, and Kiely, 1950; Lockhart-Mummery and Morson, 1960; Dyer, Cook, and Kemp Harper, 1969; Dudeney, 1969), so the modes of clinical presentation are legion. A comprehensive list of the conditions which might theoretically cause problems in differential diagnosis is therefore clearly valueless, and this study has sought to emphasize those conditions which have been found to cause confusion in clinical practice.

The incidence of different symptoms in this series is comparable to that in other large series from the United Kingdom and the U.S.A. (Van Patter *et al.*, 1954; Crohn and Yarnis, 1958; Pimparkar, 1964; Atwell, Duthie, and Goligher, 1965; Schofield, 1965).

When diarrhoea was a major feature the differentiation from ulcerative colitis was important. Diagnostic problems were frequent when disease involved the colon (Lockhart-Mummery and Morson, 1960, 1964), but confusion also occurred when disease was confined to the small intestine; a point first noted by Crohn *et al.* (1932). Diarrhoea of acute or subacute onset may be labelled as gastroenteritis or dysentery and one of the present patients was initially admitted to a fever hospital for isolation. If steatorrhoea is present, various causes of malabsorption may be considered.

Though an abdominal mass was most likely to mimic an appendix mass, in the older age groups carcinoma was often the preferred diagnosis. A mass arising in the pelvis in a woman was sometimes attributed to the uterus or ovary.

It is often difficult to separate any abdominal disease from the irritable bowel syndrome, since the latter may coexist with

organic lesions. Similarly, it may be difficult to diagnose organic disease in the presence of psychiatric symptoms, which may even be related to failure of the medical attendants to diagnose and treat the underlying organic disease. Though Crohn's disease is known to mimic anorexia nervosa (Silverman, 1966; Gryboski, Katz, Sangree, and Herskovic, 1968), this occurred only once in the present series, possibly because there were not many adolescent girls included. Another 14-year-old girl initially presented with a fever which remitted after steroid therapy, but two years later she had a relapse of the disease which was clinically indistinguishable from anorexia nervosa.

The presentation as a pyrexia of unknown origin has been described before but is still worth emphasizing, especially in the younger patients (Crohn and Yarnis, 1947; Lee and Davies, 1961; Walker 1962). A specific diagnosis of glandular fever was made in one patient and we believe that such a mistake is not uncommon, since some patients have a febrile illness with lassitude and may show alterations of the white cell count and variable amounts of lymphadenopathy. Such a diagnosis, however, should not be upheld if the white blood cells are carefully examined and serological tests are performed. The association of orogenital ulceration resembling Behçet's syndrome with Crohn's disease has been discussed by Dyer *et al.* (1969).

There was a much lower incidence of intestinal obstruction in this series than in the cases reported by Atwell *et al.* (1965). Nevertheless, these authors had analysed the clinical presentation at the time of referral for surgery and this may have been different from the initial presentation. Acute abdominal symptoms in the present series were usually diagnosed as appendicitis.

The presence of pain in the upper abdomen may lead to the diagnosis of peptic ulcer or gall stones (Atwell *et al.*, 1965). Since both these conditions occur often in the general population, radiography may show such a lesion and, as a result, the presence of Crohn's disease may not be suspected. The recent finding that gall stones may occur as a result of Crohn's disease makes such a series of events even more likely even though the gall stones are usually asymptomatic (Heaton and Read, 1969).

Urinary symptoms often arise as a result of direct involvement of the urinary tract by Crohn's disease in adjacent segments of bowel. Since Crohn's disease often gives rise to abnormalities on renography and intravenous pyelography (Schofield, Staff, and Moore 1968; Present, Rabinowitz, Banks, and Janowitz, 1969), there is a danger that these investigations may result in a false localization of all symptoms to the urinary tract.

The problem is rather different when the patients whose diagnosis was changed on review are considered. More than one-third had radiographic signs which were inconclusive. An evaluation of the incidence and observer error in interpretation of the commonly accepted radiographic changes of Crohn's disease showed that only contraction and rigidity of the bowel wall were frequent and reliable signs in spot films and that many of the other signs could be detected in cases with various malabsorption syndromes (Dyer, Rutherford, Visick, and Dawson, 1970). Thus it is essential that the radiologist should repeat the examination in all cases of doubt before sentencing any patient with a diagnosis of a chronic relapsing disease.

It was also interesting to note that cases of ulcerative colitis may be called Crohn's disease, and with the current fashion

for diagnosing Crohn's disease of the colon in all atypical cases of colitis, this particular mistake may occur more often in the future. The syndrome of ischaemic colitis has recently been recognized, and the diagnosis may be suspected if there is an abrupt onset of symptoms together with a segmental colitis centred on the splenic flexure (Boley, Schwartz, Lash, and Sternhill, 1965; Marston, Pheils, Thomas, and Morson, 1966).

Small intestinal disorders which may resemble Crohn's disease are less common. Haemorrhage into the bowel wall results in a haemorrhagic rather than an inflamed appearance and the patients will usually have a bleeding tendency. The radiographic sign of "thumb-printing" is of uncertain significance and certainly is not pathognomonic of vascular lesions of the bowel, since it can be found in Crohn's disease (Dyer, Stanley, Fry, and Dawson, 1970).

Prestomal ileitis may run a course similar to that of Crohn's disease (Thayer and Spiro, 1962), and granulomata adjacent to carcinomata may suggest that the primary lesion in the bowel is granulomatous (Gregorie, Othersen, and Moore, 1962).

Collagen disorders may also have clinical and radiological features which resemble Crohn's disease (Pimparkar, 1964) and which may improve on steroid therapy. It is not yet known whether such bowel lesions are always part of the collagen disorder or whether Crohn's disease may coexist with collagen disease as the result of a common aetiological background (Kurlander and Kirsner, 1964).

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