Epidemiological aspects of Crohn's disease in Clydesdale 1961-1970


From the Stobhill General Hospital, Glasgow

SUMMARY A retrospective study of Crohn's disease has been carried out in Clydesdale covering the decade 1961-1970. Three hundred and fifty-seven patients had acceptable evidence of either acute ileitis or of chronic granulomatous bowel disease. Of those fulfilling the criteria for inclusion in the study of chronic disease, 95% had accurate pathological and/or operative documentation of the lesions. Overall, females outnumbered males by 1.6:1 but colonic disease alone tended to affect females, particularly those over the age of 50. The annual incidence of all forms of the chronic disease in both sexes has increased during the decade, but diagnosis of colonic disease alone increased two-fold in the latter half of the study.

Material and Methods

Since 1961, all Scottish hospital admissions have been coded under the International Classification of Disease (ICD) and entered on a computer at the Scottish Home and Health Department in Edinburgh. Reference to the computer allowed identification of cases coded as regional enteritis (Crohn's disease) over the 10-year period 1961 to the end of 1970, in 12 National Health Service hospitals serving Clydesdale. Epidemiological data were collected by retrospective analysis of the case records available in these hospitals.

Criteria

Much of the difficulty in comparing the results of studies of Crohn's disease from different centres has arisen from the lack of clarity in criteria used for the diagnosis of this disease (Law, 1969).

At the outset, two categories require definition.

ACUTE ILEITIS (ACUTE REGIONAL ENTERITIS)

An inflammatory condition of the terminal ileum, the patient presenting with a short clinical history, which is diagnosed by macroscopic appearances at emergency laparotomy, and is usually followed by spontaneous remission.

CHRONIC GRANULOMATOUS CROHN'S DISEASE (CROHN'S DISEASE)

The suggested criteria for this diagnosis include:
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(1) clinical features; (2) radiological signs—mucosal changes, stricture, or fistula formation; (3) at operation, the presence of induration of bowel, indicative of chronic transmural inflammatory disease; (4) histological features as described by Morson (1971): transmural inflammation with focal aggregation of lymphocytes, fissuring ulceration, and non-caseating epitheloid granulomata.

For this review, before accepting a diagnosis of Crohn’s disease, we have demanded the presence of at least two of these four criteria, one of which should preferably be operative findings or histology. Patients diagnosed on the basis of clinical features and radiology were excluded unless the radiological findings were confirmed by further examination and long-term medical follow up. Care was also taken to exclude any patient who was receiving treatment for pulmonary tuberculosis or who had a history of abdominal tuberculosis, as the occurrence of ileocaecal granulomata in such patients could not with certainty be attributed to Crohn’s disease.

Results

Seven hundred and eighteen patients had been indexed as cases of acute ileitis and Crohn’s disease during the decade. Examination of their case records and the application of the criteria above allowed us to accept only 357.

Acute Ileitis

Fifty-eight patients (32 male, 26 female), were classified as having an episode of acute ileitis in the period 1961-1970. Ninety percent of these patients had no further relapse. Four patients, however, developed established granulomatous disease within two years of the diagnosis of acute ileitis.

Chronic Granulomatous Disease

The diagnosis criteria employed in 303 patients are set out in table I, together with details of the excluded 361 cases.

In 120 of the excluded patients it was apparent that the initial clinical diagnosis of Crohn’s disease was incorrect in the light of investigation and treatment on further admissions. No mechanism had existed for altering the incorrect computer input from the initial diagnosis. At five of the hospitals confusion had been caused by wrongly coding other forms of inflammatory bowel disease as Crohn’s disease since, under earlier International Classifications of Disease, they had all shared a common grouping. This confusion was avoided by the eighth revision of the Classification in 1967. At one other hospital, 68 patients were miscoded as regional enteritis when the clinical diagnosis recorded was loosely labelled ‘enteritis’. From the remainder, there was inadequate evidence in 33 cases to substantiate a diagnosis of Crohn’s disease but sufficient to suggest that these were indeed possible cases.

In order to check errors by omission, a survey of the diagnostic coding of ulcerative colitis, diverticulitis, and ischaemic colitis was undertaken on one sample year. From 1274 case records examined, only one patient with established Crohn’s disease had been omitted due to being wrongly coded as diverticular disease.

Age and Sex Incidence

Overall, there were 117 males and 186 females, a sex ratio of 1:1.6. Table II indicates the distribution according to decade. While a peak incidence for both sexes is observed in the third decade, 93 (31%) patients were over the age of 50 at the onset of the disease.

### Table I

<table>
<thead>
<tr>
<th>303 Accepted as Crohn’s disease</th>
<th>303 Rejected</th>
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<tbody>
<tr>
<td>Clinical features and histology</td>
<td>141</td>
</tr>
<tr>
<td>Clinical features and operation</td>
<td>78</td>
</tr>
<tr>
<td>Clinical features, operation, and radiology</td>
<td>66</td>
</tr>
<tr>
<td>Clinical features and radiology</td>
<td>18</td>
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</table>

### Table II

**Age and sex distribution of 303 patients with Crohn’s disease treated 1961-1970**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age Distribution</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>All forms of Crohn’s disease</td>
<td>16</td>
<td>29</td>
<td>24</td>
<td>23</td>
<td>15</td>
<td>6</td>
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<td>—</td>
</tr>
<tr>
<td></td>
<td>Large bowel disease alone</td>
<td>1</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Females</td>
<td>All forms of Crohn’s disease</td>
<td>13</td>
<td>40</td>
<td>32</td>
<td>33</td>
<td>27</td>
<td>27</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Large bowel disease alone</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>11</td>
<td>10</td>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>

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SITE OF INVOLVEMENT
The patients have been classified into three groups according to the site or sites of primary involvement of bowel.

**Group I: small bowel (163 patients, 54%)**
The distribution of lesions in this group is indicated in table III. Of the 155 patients with ileal disease, 20 (13%) had proximal skip lesions.

<table>
<thead>
<tr>
<th>Site</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal ileum</td>
<td>147</td>
</tr>
<tr>
<td>Proximal ileum</td>
<td>8</td>
</tr>
<tr>
<td>Jejunum</td>
<td>5</td>
</tr>
<tr>
<td>Duodenum</td>
<td>3</td>
</tr>
</tbody>
</table>

Table III  Site of involvement (163 patients) in small bowel disease

**Group II: ileo-colitis (91 patients, 30%)**
Figure 1 shows the distribution of the areas of bowel involved. In 71 patients, involvement of a segment of distal ileum extended continuously into the caecum or more distally. In the other 19, the disease process appeared to involve separate sites in the small and large bowel.

**Group III: large bowel (49 patients, 16%)**
Involvement of the colon alone could occur as a localized stricture (12), segmental colitis (34), or diffuse proctocolitis (3). Figure 2 indicates, in a simplified manner, the numbers and sites of these forms of disease. Fewer patients had disease confined to the proximal colon and these 11 patients (average age 46.8 ± 4.5 years) tended to be younger than the 35 patients (average age 64.5 ± 1.8) in whom the distal colon alone was involved. Of the 49 patients, 38 (78%) were over the age of 50 at the time of presentation. Females outnumbered males by 8 to 1. All three patients with diffuse proctocolitis were teenagers.

ASSOCIATED DISEASE

**Peptic ulcer**
Seventeen patients had a history of previous peptic ulceration, five having undergone definitive ulcer surgery. Overall, this amounts to 7% of patients with small bowel disease (groups I, II).

**Ankylosing spondylitis**
Five patients developed sacro-ileitis or ankylosing...
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Fig 2  Site of involvement (49 patients) in large bowel disease.

Spondylitis while being treated for small bowel or ileo-colonic disease.

Annual Incidence

In fig 3, the annual incidence is shown for each year of the study. Thirty-eight patients diagnosed before 1961 are omitted, having been seen during the study period because of recurrence of the disease. A further five patients, residing outside the Clydesdale area (four Scots and one Persian), are omitted in the calculation of incidence figures.

Analysing the first quinquennium, 102 new cases of Crohn's disease were identified of which 12 (11%) involved the large intestine alone. In the second quinquennium, 35 of 158 new cases involved the large bowel alone (22%). This twofold increase in the diagnosis of large bowel disease does not wholly account for the increasing incidence, as cases with small bowel involvement also increased from 91 to 123, an increase of 33%.

During the study period, the population of the City of Glasgow fell by 14% from 1.053 millions in 1961 to 0.893 millions in 1971. This was almost balanced by an increase in the population of the surrounding area, such that the population of Clydesdale fell by only 3.5% from 1.7 millions in 1961 to 1.64 millions in 1971.

Annual incidence figures for males and females are, therefore, calculated separately over two five-year periods referring to national census figures for 1961 and 1971 (table IV). Examining the distribution as the annual risk per 100 000 of the population of each decade of life, it is apparent that the remarkable increases have been observed not only in females in

<table>
<thead>
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<th>Sex</th>
<th>Age Distribution</th>
<th>All Ages</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>10-19</td>
<td>20-29</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New cases 1961-1965</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Annual incidence/100 000</td>
<td>0.7</td>
<td>1.4</td>
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<tr>
<td>New cases 1966-1970</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Annual incidence/100 000</td>
<td>1.3</td>
<td>2.3</td>
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<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New cases 1961-1965</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Annual incidence/100 000</td>
<td>0.9</td>
<td>1.5</td>
</tr>
<tr>
<td>New cases 1966-1970</td>
<td>5</td>
<td>23</td>
</tr>
<tr>
<td>Annual incidence/100 000</td>
<td>0.7</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Table IV  Annual incidence of Crohn's disease for males and females by decade of life in 1961-1965 and 1966-1970

Fig 3  Annual incidence of Crohn's disease (1961-1970).
their third decade but also in both males and females over the age of 50.

Discussion

The increase in the annual incidence of Crohn's disease observed in the present study confirms the trend reported by Norlen et al (1970), Kyle (1971), and by Faerlander and Baerlocher (1971). The incidence is generally at a lower level than reported by these workers and this fact may partly be accounted for by the stricter criteria adopted for inclusion in this study.

Lennard-Jones (1968) and Law (1969) have commented on the importance of reporting only those cases with accurate histological or operative documentation of the chronic granulomatous lesion. Since many other conditions producing submucosal oedema may mimic the radiological signs and appearances recognized as being suggestive of Crohn's disease, it would be unwise to accept radiologically diagnosed cases in the absence of adequate follow up. In our group classified as 'radiological Crohn's disease', continuing follow up with medical treatment and further radiological studies leaves little room for doubt that they are indeed patients with chronic granulomatous disease.

It is unlikely that many patients in the area with Crohn's disease have been overlooked. The retrieval method in fact indicated that Crohn's disease was a condition which was clinically overdiagnosed rather than underdiagnosed. Admittedly, coding errors did occur but these were acts of commission due to the terms 'enteritis' and 'colitis' being considered as synonyms for Crohn's disease by coding staff at some hospitals. Errors of omission from coding Crohn's disease as other forms of colitis were shown to be insignificant in the sample check on the coding of inflammatory bowel disease.

A further theoretical method by which patients with Crohn's disease might have escaped the study requires explanation. As inpatients alone are recorded, any patient who was not admitted during the decade to a National Health Service hospital would not be included. It is rather unlikely that such a patient would satisfy the criteria for inclusion as adequate investigation and treatment are likely to require at least one inpatient stay.

Evidence for the existence of a clinical condition described as acute ileitis and separate from Crohn's disease is available (Kyle and Blair, 1965; Atwell, Duthie, and Goligher, 1965). Most authors accept a clinical history of less than one week's duration associated with clinical findings suggestive of acute appendicitis. The self-limiting nature of the illness is emphasized by the overall good prognosis with over 90% of patients having no recurrence of symptoms (Atwell et al, 1965; Gump, Lepore, and Barker, 1967). Clearly, inclusion of such cases in any study of chronic granulomatous disease would falsely improve the outcome of the latter condition. Sixteen percent of our overall number of 357 patients reviewed in the decade had evidence of acute ileitis, a figure which compares with the 20% of both Kyle (1965) and Atwell et al (1965). It remains possible that some cases of chronic Crohn's disease could present acutely and be mistakenly diagnosed as acute ileitis. Four of the present series of 58 patients, diagnosed initially as having acute ileitis, were shown to have Crohn's disease of the small bowel five months to two years later. The question remains open as to whether these may have represented an acute presentation of granulomatous disease.

The preponderance of females with all types of chronic Crohn's disease is a remarkable feature of the present study. Large series dealing with management from referral centres in Leeds (De Dombal, Burton, and Goligher, 1971), Birmingham (Burman, Thompson, Cooke, and Williams, 1971), and London (Ritchie and Lockhart-Mummery, 1973) have not shown such a difference, although the epidemiological studies of Kyle (1971) from a geographically separate part of Britain, and of Fäländer and Baerlocher (1971) from Basle, have produced sex ratios close to those of the present study. While the peak incidence was observed in the third and fourth decades for females and males respectively, 31% of Clydesdale patients were over the age of 50 at the time of presentation. This figure compares closely with both the Aberdeen and Basle series, where colonic disease was particularly frequent over the age of 50; in this series eight times more females over the age of 50 were affected by colonic disease alone than males. This marked preponderance of colonic disease might only have been apparent because of the limitation of this study to inpatients. It is possible, although unlikely, that males might have suffered a less marked form of left-sided colitis which responded to symptomatic therapy as outpatients.

With regard to the site of disease, it is well established that the distal ileum is most frequently involved. However, in many epidemiological studies information is lacking on the precise extent of involvement in ileocolitis and also in Crohn's colitis. The Clydesdale data on ileocolitis show marked similarity to the selected series of cases of ileocolitis reported by Marshak, Lindner, and Janowitz (1968). In particular, the relative frequency and sites of discontinuous involvement are almost identical. From the Basle study (Faerlander and Baerlocher, 1971) it is clear that Crohn's disease confined to the large bowel was recognized as a mainly left-sided
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The increasing incidence of Crohn's colitis may perhaps be explained by an increased awareness of a condition fully described in 1960 by Lockhart-Mummery and Morson. However, the incidence of Crohn's disease affecting the small bowel has also increased. On account of the criteria used for inclusion in this study, it could be argued that what really has been observed is an increased enthusiasm amongst physicians and surgeons to perform rectal biopsy or advise surgery (thus substantiating the diagnosis). Such an aggressive approach can be justified by the natural history of a chronic, progressive disease characterized by relapse and remission. This change in diagnostic fashion might have accounted for the observed increase, as patients discarded due to inadequate evidence were certainly more numerous in the earlier part of the decade. These discarded patients, however, appear to have remained in remission as study of their records did not reveal any further evidence to substantiate the provisional diagnosis. It is difficult to avoid the conclusion that the incidence of Crohn's disease in Clydesdale has undergone a real increase, following the trend observed in Aberdeen, Uppsala, and Basle. While both environmental and genetic factors may be operating, the suggestion of Fielding (1972) that the disease may result from an altered reaction to the tubercle bacillus deserves investigation. Studies of the incidence of abdominal tuberculosis would be of interest.

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