Epidemiology

Incidence of Crohn’s disease in Cardiff between 1934 and 1977

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SUMMARY The incidence of Crohn’s disease in Cardiff between 1934 and 1977 has been examined using hospital diagnostic indices and supplemented in recent years by personal records from clinicians. A total of 232 cases of Crohn’s disease were confirmed after all the notes had been reviewed. There has been a large increase from 0·18/cases/10^6 of the population per year in the 1930s to 4·8 cases/10^6/year in the 1970s. The major change in incidence is thought to be real rather than apparent and involves all forms of the disease in each age group. The recognition of Crohn’s disease of the colon in recent years appears to have played a minor part in the rise in incidence.

The city of Cardiff is particularly suited for a long-term retrospective study of Crohn’s disease. It has a relatively stable population and the medical records system, with a diagnostic index, has been carefully kept since 1926. Several recent studies in Nottingham (Miller et al., 1974), Clydesdale (Smith et al., 1975), Malmö (Brahme et al., 1975), and Basel (Fahrlander and Baerlocher, 1971) have shown that the incidence of this disease is increasing and Kyle (1971) in Aberdeen has attributed much of the increase to colonic disease in older women. Our study was undertaken to determine whether there was an increase in Cardiff and what part of this could be attributed to an increase in the diagnosis of Crohn’s colitis.

Methods

POPULATION AND AREA STUDIED
Cardiff is the largest city in Wales with a population that has grown steadily during the period of the study from 221,000 in 1934 to 280,000 in 1977. This population has been served by four general hospitals throughout the period and since 1926 patients’ records have been kept intact together with a diagnostic classification of all inpatients. Between 1926 and 1966 the diagnostic file was kept by medical clerks, but since 1967 a computer index has been used; information from these sources has been supplemented by personal diagnostic indices which belong to clinicians. Because of the intact record system it was possible to study epidemiological changes in the incidence of Crohn’s disease within a defined population since the time it was first described as a distinct entity (Crohn et al., 1932). Of the patients diagnosed with Crohn’s disease between the 1930s and 1960s most received treatment in hospital, but in recent years some have been managed entirely as outpatients (15 of 66 patients).

CRITERIA FOR CROHN’S DISEASE
Patients were considered to have Crohn’s disease and accepted into the study only if at least one of the following criteria was fulfilled: (1) histological confirmation of Crohn’s disease in either resected specimens or biopsy samples; (2) radiological evidence of Crohn’s disease with a suitable clinical history.

Cases of acute ‘terminal ileitis’ or unclassified ‘inflammatory bowel disease’ were not included in the study.

MEDICAL RECORDS AND PATIENT DATA
Between 1934 and 1977 264 patients with Crohn’s disease were identified. Two hundred and fifty-six of their medical records were obtained and examined; only 232 of these patients fulfilled either the histological or radiological criteria for Crohn’s disease as well as living in the city of Cardiff at the time of diagnosis. Patients were not included in the study if they had moved into the area, already with a diagnosis of Crohn’s disease.

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The following details were noted from the patient's file: their name, address, date of birth, sex, age at diagnosis, date of diagnosis, distribution of disease at the time of diagnosis, and the method by which the diagnosis was initially made. With this data it was possible to identify patients with multiple admissions to different hospitals in the city and to ensure that patients appeared only once in the analysis.

The distribution of the disease was recorded as ileocaecal, small bowel, colonic, anal, or a combination of these sites. The initial diagnosis was made at surgery with subsequent histological confirmation, by x-rays, by sigmoidoscopy or colonoscopy with histological confirmation from the biopsy or by post-mortem examination.

Details of the population structure of Cardiff throughout the period of the study, including analysis by age and sex, were obtained from census data and were used to calculate incidence figures.

Results

The annual incidence of newly diagnosed patients with Crohn's disease in Cardiff is shown in Fig. 1 which also gives mean values for each quinquennium. There has been a striking rise in incidence since the disease was first recognised in Cardiff in the mid 1930s, although from year to year the incidence figures vary considerably. The incidence increases for each five-year period, rising from 0·18/10^5/year during 1931-35 to 4·83/10^5/year during 1971-75 and exceeding 5/10^6 during 1961, 1971, 1973, and 1975 with a maximum value of 5·95 in 1973. The incidence figures have also been analysed according to sex and show a small preponderance of females throughout the study (1·1:1·4).

Because it has been suggested that the rise in Crohn's disease may be due to increased recognition of Crohn's colitis, we have examined the figures with reference to the site of disease at the time of diagnosis (Fig. 2). Although colonic involvement has been recognised in Crohn's disease since the 1940s, the clinical entity has only been widely recognised in recent years. During the period between 1960 and 1970 there was an increase in all of the major groups of Crohn's disease including colonic disease. The most recent seven year period is not strictly comparable but shows an additional increase. The figures for all cases include 51 patients with mixed disease where several major sites were involved in the same patient.

Fig. 1 Yearly incidence of new cases of Crohn's disease in Cardiff (n = 232). ○—○ mean incidence over each five year period.

Fig. 2 The number of new cases presenting during each decade from 1931 to 1970 and during the seven year period 1971 to 1977; colon, small bowel, and anus refer to cases where the disease was initially limited to those sites.
Figure 3 shows the age specific incidence for 143 patients during the period 1931-70; these values take into account the age distribution of the population of Cardiff using the 1951 census figures for the period 1931-70 and 1974 for the period 1971-77. The disease appears in the late teens with a considerable variation in incidence thereafter. There is a suggestion that the illness presents less frequently in the early 60s with another peak in the 70s; the most recent figures are essentially similar to those from the early part of the study. Figure 4 shows the major groups of disease according to 'site' at different ages. In all age groups, ileocaecal disease is the most common and colonic disease contributes less than 20% of the total for all ages with the exception of patients in their 30s and 60s where the figures were 25% and 33% respectively.

There are several possible reasons which may account for the increase in Crohn's disease; one of these is a change in the mode of diagnosis with more accurate radiological assessment contributing more cases in recent years. Table 1 shows the initial method by which the diagnosis was confirmed early after patients presented. Surgery has always played an important part, although radiology, endoscopic examination, and biopsy have been relied upon for diagnosis more often since 1961. Many of the patients who did not initially have surgery have subsequently had resection of diseased bowel. Milder cases have probably been recognised more frequently in recent years.

The observed increase in Crohn's disease may
partly reflect inadequate data during the early part of the study. With this possibility in mind we have examined the records of patients who might have been included in other diagnostic categories between 1926 and 1950. These included patients diagnosed as typhoid fever, colitis, and tuberculosis of the bowel (Table 2). Two patients who presented in the early 1930s were initially diagnosed as colitis but were subsequently reclassified as Crohn's disease. Typhoid fever was based on bacteriological evidence throughout the period. After the notes of patients with small bowel tuberculosis had been reviewed, in only two cases who presented in 1933 and 1946 could Crohn's disease be considered possible; these have not been included with our incidence data. All of the eight case records which could not be found belonged to the middle part of the study (1944-65) and had these cases fulfilled the diagnostic and residential criteria they would have had a small effect on the incidence figures for that period.

We examined the possibility that figures for the last decade may have been inflated by the inclusion of mild cases who did not receive hospital admission. We examined the source of patients between 1967 and 1976; 92 were on the computer index, seven other inpatients failed to appear on the index, while another 15 patients had never been admitted to hospital. The computer also listed 11 other patients incorrectly with a diagnosis of Crohn's disease; the diagnosis in these patients had either been misread or could not be justified. The group of outpatients make a minor contribution to the overall picture and had such patients been diagnosed in an earlier phase of the study they would probably have been admitted to hospital.

Because of the suggestion that there may be a seasonal variation in Crohn's disease (Cave and Freedman, 1975) we examined the date of diagnosis, as we had difficulty in establishing the precise time for the onset of symptoms. There was no significant difference between diagnosis of the disease at different times of the year.

### Table 1

<table>
<thead>
<tr>
<th>Decade</th>
<th>Surgery</th>
<th>Radiology</th>
<th>Sigmoidoscopy or colonoscopy and biopsy</th>
<th>Clinical picture or post mortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1931-40</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1941-50</td>
<td>11</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1951-60</td>
<td>35</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1961-70</td>
<td>43</td>
<td>35</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>1971-77*</td>
<td>29</td>
<td>34</td>
<td>25</td>
<td>1</td>
</tr>
</tbody>
</table>

*1971-77 refers to only a seven-year period.

### Table 2

<table>
<thead>
<tr>
<th>Year</th>
<th>Typhoid fever</th>
<th>Colitis</th>
<th>Small bowel tuberculosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1926-30</td>
<td>5</td>
<td>64</td>
<td>0</td>
</tr>
<tr>
<td>1931-35</td>
<td>5</td>
<td>36*</td>
<td>3</td>
</tr>
<tr>
<td>1936-40</td>
<td>4</td>
<td>57</td>
<td>1</td>
</tr>
<tr>
<td>1941-45</td>
<td>6</td>
<td>—</td>
<td>0</td>
</tr>
<tr>
<td>1946-50</td>
<td>—</td>
<td>—</td>
<td>4</td>
</tr>
</tbody>
</table>

Notes from patients with typhoid fever were examined between 1926 and 1945, ulcerative colitis between 1926 and 1940 and small bowel tuberculosis between 1926 and 1950, to identify possible cases of Crohn's disease.

*Two cases of colitis diagnosed during this period were subsequently reclassified as Crohn's disease by the clinicians.

### Discussion

There has been a striking increase in the incidence of Crohn's disease since it was first recognised in Cardiff in 1934. The low incidence figures early in the study may partly be due to poor recognition of the disease. However, severe cases with pain, diarrhoea, and weight loss often have a laparotomy and the pathological features would have been recognised. We questioned whether some of the early cases may have been classified with typhoid fever, intestinal tuberculosis, or colitis, but could identify only two patients who may have had Crohn's disease, but were classed as intestinal tuberculosis. Our findings support the view that Crohn's disease was rare in the 1930s and throughout the second world war; during the war years only one new patient was diagnosed. The marked rise in incidence which occurred after the second world war may be partly due to improved recognition of the condition with inclusion of less severe cases and patients with Crohn's disease limited to the colon who were previously classified as colitis. The role of surgery as a diagnostic procedure is perhaps some indication of severity and of the contribution made by 'milder' cases; the figures (Table 1) show a marked rise in patients where the diagnosis was confirmed by surgery early in the disease. In recent years radiology and endoscopy have been used more often as a basis for the diagnosis. The reclassification of colitis as Crohn's disease affecting the colon does not appear to have played a major part in the rise in incidence; there has been a marked rise in all forms of the disease, particularly ileocaecal. Our observations are given some support by annual mortality figures for England and Wales due to ulcerative colitis and Crohn's disease (Fig. 5). Since 1950, death from Crohn's disease has risen fairly steadily and, although there has been a fall in deaths from ulcerative colitis, the latter change is relatively small.

Such a steady rise in the incidence of the disease is
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**Fig. 5** Annual number of deaths from Crohn's disease and ulcerative colitis in England and Wales between 1950 and 1975. (Figures derived from the Registrar-General's Statistical Review of England and Wales (1950-1975).)

Table 3  Incidence of Crohn's disease in Britain, Europe, and Baltimore, USA

<table>
<thead>
<tr>
<th>Place</th>
<th>Authors</th>
<th>Time</th>
<th>Cases/10^5/yr (no.)</th>
<th>Cases (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxford</td>
<td>Evans and Acheson (1965)</td>
<td>1951-60</td>
<td>0.8</td>
<td>24</td>
</tr>
<tr>
<td>Gloucester</td>
<td>Tredarren et al. (1973)</td>
<td>1966-70</td>
<td>1.5</td>
<td>19</td>
</tr>
<tr>
<td>Aberdeen</td>
<td>Kyle (1971)</td>
<td>1955-61</td>
<td>1.7</td>
<td>166</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1962-68</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>Humphreys and Parks (1975)</td>
<td>1966-73</td>
<td>1.3</td>
<td>159</td>
</tr>
<tr>
<td>Nottingham</td>
<td>Miller et al. (1974)</td>
<td>1958-72</td>
<td>From 0.73 to 3.63</td>
<td>144</td>
</tr>
<tr>
<td>Clydesdale</td>
<td>Smith et al. (1975)</td>
<td>1961-70</td>
<td>From 1.0 to 1.6 (M)</td>
<td>303</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.4 to 2.2 (F)</td>
<td></td>
</tr>
<tr>
<td>Cardiff</td>
<td>Data with this paper</td>
<td>1934-75</td>
<td>From 0.18 to 4.8</td>
<td>212</td>
</tr>
<tr>
<td>Malmö, Sweden</td>
<td>Brahme et al. (1975)</td>
<td>1958-65</td>
<td>3.5</td>
<td>191</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1966-73</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Central Sweden</td>
<td>Norlén et al. (1970)</td>
<td>1956-61</td>
<td>1.7</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1962-67</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Copenhagen, Denmark</td>
<td>Høj et al. (1973)</td>
<td>1960-70</td>
<td>1.29</td>
<td>64</td>
</tr>
<tr>
<td>Norway</td>
<td>Gjone et al. (1966)</td>
<td>1956-63</td>
<td>0.26</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>Myren et al. (1971)</td>
<td>1964-69</td>
<td>1.03</td>
<td>233</td>
</tr>
<tr>
<td>Basle, Switzerland</td>
<td>Fahrlander and Baerlocher (1971)</td>
<td>1960-69</td>
<td>1.6</td>
<td>110</td>
</tr>
<tr>
<td>Baltimore, USA</td>
<td>Monk et al. (1967)</td>
<td>1960-63</td>
<td>1.8</td>
<td>99</td>
</tr>
</tbody>
</table>


probably due to one or more environmental factors affecting the population. The nature of such causative factors remains a matter for speculation and current suggestions include transmissible infective agents (Mitchell and Rees, 1970), viruses (Whorwell et al., 1977), poorly encapsulated mycobacteria (Burnham et al., 1978), and diet (Martini and Brandes, 1976; James, 1977; Mayberry et al., 1978).

There appears to be a small overall preponderance of the disease in women with a rate of 1:1.4. However, in the last seven years this difference has been lost with a slight preponderance occurring in males (1:1:1). Recent British studies also show a preponderance among females (Nottingham, 1:1.6 (Miller et al., 1974); Clydesdale 1:1.5 (Smith et al., 1975) and Northern Ireland 1:1.3 (Humphreys and Parks, 1975)), but in Norway (Myren et al., 1971) and Sweden (Norlén et al., 1970 and Brahme et al., 1975) the figures for males and females are almost equal. Although Kyle (1971) identified a substantial group of older women with colonic disease, our data, which have been adjusted because of the age structure of the population, does not show a similar increase of colonic disease in the elderly.

Table 3 summarises available data for the incidence of Crohn's disease in British communities with some comparative figures from Europe and Baltimore. The highest recorded figures come from Malmö with an incidence of 6/10^5/year between
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1966 and 1973. Our most recent data approached this figure (4.8/10^5/year in 1971 and 1975), and are next to the highest values in the literature. In Britain the earliest epidemiological study from Oxford, 1951-60 (Evans and Acheson, 1965) found an incidence of 0.8 cases of 10^5/year and a comparable figure from our data for that period is approximately twice this value. The Gloucester study (Tresadern et al., 1973), which covered the period 1966-70, was relatively small and included only 19 cases; the incidence was 1.5 cases/10^5/year compared with 3.62 cases/year in Cardiff for the same period. One of the largest series came from Northern Ireland (Humphreys and Parks, 1975) where 159 cases were identified between 1966 and 1973; the cases were obtained from all six counties and the data were retrospective. With all the limitations of such a study the incidence is perhaps not surprisingly low (1.3/year). A similar large study from Aberdeen and neighbouring counties (Kyle, 1971) recorded the disease between 1955 and 1968 and showed a small rise in incidence from 1.7/10^5 between 1955 and 1961 to 2.2/10^5 between 1962 and 1965. Miller et al. (1974), in a recent study which covered the period 1958 to 1972, identified 144 patients in the Nottingham district with an annual incidence which increased from 0.73/10^5 cases per year early in the study to 3.63/10^5 cases per year at the end. A study in the Clydesdale region (Smith et al., 1975) included more patients than in any other study and again showed an increase in the incidence between 1961 and 1970, but with figures that are substantially lower than ours (Table 3).

The overall picture from previous studies shows a rise in incidence, particularly during the last 20 years. A considerable variation in incidence in different studies may be real, or simply reflect more efficient retrieval of information. More complete data may be obtained with less difficulty in a stable, clearly defined population served by fewer hospitals. Cardiff is particularly suited for such a study.

Increased recognition of the disease with better use of radiology and endoscopic data probably contribute to the rise in incidence, but could not be responsible for the major change. The increase shows no tendency to form a plateau at the moment and is not due to Crohn’s disease affecting a particular site or age group. In the absence of any clear indication of the cause or of effective medical treatment to prevent recurrence and extension of disease, the medical, surgical, and social problems due to this condition are likely to increase considerably in the foreseeable future.

We gratefully acknowledge the cooperation from clinicians in Cardiff who made it possible for us to obtain the data; also to Michael Rhodes for help in retrieval of case notes.

References


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