Monozygotic twins with ulcerative colitis

J. F. MAYBERRY
M.D., M.R.C.P.

M. J. DEW
M.D., M.R.C.P.

J. S. MORRIS
M.D., F.R.C.P.

Bridgend General Hospital, Quarella Road, Bridgend, Mid-Glamorgan

Summary
Monozygous twin sisters developed ulcerative colitis within 7 years of each other. Both had distal colitis confirmed by histology and radiology. Their maternal grandmother subsequently developed the disease. The long interval between the onset of the disease in the twins suggests a role for environmental factors in addition to genetic influences. Although about five hundred sets of twins with ulcerative colitis may be expected in Britain, this is the first set to be reported.

Introduction
The prevalence of ulcerative colitis in the general population is about 80/100 000 (Evans and Acheson, 1965). Familial occurrence of the disease is unusual and only 4% of patients have other affected relatives (Lewkonia and McConnell, 1976). To date, six sets of twins with ulcerative colitis have been reported, all with total colonic involvement. Few observations of their early life and possible aetiological factors have been recorded. The purpose of this report is to describe limited ulcerative colitis appearing at an interval of 7 years in monozygous female twins. Early life was in a similar environment and no obvious aetiological factors were identified. The relative importance of genetic and environmental factors are discussed.

Cases
Twin 1 was born in November 1950. During childhood she had measles, chickenpox and mumps, but otherwise remained well until at 21 years of age she developed diarrhoea with loose stools mixed with blood, mucus and pus. Sigmoidoscopy showed severe inflammatory changes and rectal biopsy revealed changes consistent with ulcerative colitis. A barium enema showed that the disease extended from the rectum to the splenic flexure. Subsequently her illness relapsed frequently but responded well to sulphasalazine and rectal steroids. Twin 2 also had measles, chickenpox and mumps during childhood. At 28 years of age she developed blood-stained diarrhoea and at sigmoidoscopy to 12 cm had severe proctitis with contact bleeding and pseudopolyps. Histological examination supported the diagnosis of ulcerative colitis. The barium enema revealed that the changes continued into the sigmoid and descending colon. Her disease followed a similar course with frequent relapses which responded to prednisolone enemas and oral sulphasalazine.

In each twin, barium meal and follow-through examination did not show changes suggesting Crohn's disease.

In 1980, the twins' 80-year-old grandmother presented to hospital with a 5-month history of blood-stained diarrhoea. Sigmoidoscopy showed a reddened mucosa and histological examination of a biopsy was compatible with ulcerative colitis. A barium enema demonstrated that the fine ulceration was confined to the rectum. She responded rapidly to treatment with prednisolone suppositories. Other relatives have no symptoms of inflammatory bowel disease. The twins' parents were not consanguineous.

Investigations
Monozygosity was established by HLA typing, blood group analysis and dermatoglyphics. Their tissue types were A2,3-BW44,27 and their blood groups were also identical:
A1 R/r (CDé/cdé), Mš/Mš, Pš, Lu (a−), K neg, Le (a−b+), Fy (a−)a.

Although the fingerprints of monozygous twins are not identical, their total finger ridge count is similar (Smith and Penrose, 1955). Twin 1 had a total finger ridge count of 146 and Twin 2 a count of 156. A difference of between 8 and 12 suggests that the twins are monozygous (P>0.74). The overall probability that the twins are monozygous was
Calculated from the HLA status, blood groups and total finger ridge count; 36 of every 125 twins born in England and Wales are monozygous (Propping and Kruger, 1976) and account was taken of this distribution in the calculation which indicated a 0.999 probability that the twins are monozygous.

Each twin was asked to complete independently a questionnaire about factors which may have contributed to the development of colitis. Both twins were bottle fed as infants; neither had severe episodes of diarrhoea necessitating hospital admission. Menstruation began when they were 12 years old and subsequently both sisters used the contraceptive pill. At the age of 19 years both left the parental home for further education at different colleges for training as teachers. They married at the ages of 21 and 22 respectively. Twin 1 remained nulliparous, while Twin 2 had a male child. Both twins found that colitis was worse in the winter and particularly precipitated by stress and alcohol. Twin 1 had atopic dermatitis, but neither had a history of hay fever, asthma or eczema.

Immunoglobulins (Ig) present in their sera were measured and were within the normal range; 5 ml of saliva were collected from each twin and the IgA and secretory component concentration measured and compared with normal controls and found to be similar.

Discussion

This paper reports the seventh pair of twins with ulcerative colitis, and the first in whom the disease is limited to the distal colon (Table 1). Monozygous twins have a prevalence of 360/100 000 population in England and Wales (Propping and Kruger, 1976) and consequently 140 monozygous twins could be expected to have colitis based on the prevalence figures from Oxford (Evans and Acheson, 1965). Dizygous twins have a prevalence of 890/100 000 and 350 dizygous twins could be expected to have the disease. Although it is probable that twins with only one member affected have not been reported, it is surprising that this is the first description of ulcerative colitis from England or Wales, where as many as 500 such cases may be expected.

The latency of 7 years reported in this paper contrasts with the simultaneous onset reported by some other workers (Table 1). Recent interest has focused on the role of neonatal and childhood factors, especially bottle feeding in the aetiology of inflammatory bowel disease (Whorwell et al., 1979).

It is interesting that the twins reported in this paper were bottle fed, for it has been suggested that this may sensitize individuals to cow's milk or perhaps alter the colonic bacterial flora and make the patient respond abnormally to Enterobacteriaceae (Whorwell et al., 1979). In contrast, work from Kansas (Engstrom et al., 1978) has suggested that families with a high incidence of inflammatory bowel disease may have an immunological abnormality with a deficiency in free secretory component for salivary IgA. In the present patients, serum immunoglobulins, salivary IgA and secretory component were normal, failing to confirm the postulated role of this abnormality in familial ulcerative colitis. However, ulcerative colitis has been associated with ankylosing spondylitis and, indirectly, HL antigen B 27, which was present in both twins.

Ulcerative colitis probably has a multifactorial pathogenesis. The present twin study and previous reports suggest that heredity is one of these factors. While an individual inherits a tendency to develop ulcerative colitis, a more complex interaction of genetic and environmental factors may determine the site and severity of disease. The authors have been unable to identify a specific immunological abnormality. Although stress seems to exacerbate the condition, specific environmental factors precipitating clinical disease have not been identified although they may operate in monozygotic twins who developed ulcerative colitis 7 years apart.

Table 1. Case reports of twins with ulcerative colitis. In one case the onset of disease was simultaneous with a maximum difference of 7 years in onset.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Monozygous/dizygous</th>
<th>Years between onset</th>
<th>Degree of colonic involvement</th>
<th>Other affected relatives</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>No comment</td>
<td>3</td>
<td>Total</td>
<td>None</td>
<td>Lyons &amp; Postlethwait (1948)</td>
</tr>
<tr>
<td>Male</td>
<td>Monozygous</td>
<td>Simultaneous</td>
<td>Total</td>
<td>Not stated</td>
<td>Webb (1950)</td>
</tr>
<tr>
<td>Female</td>
<td>Dizygous</td>
<td>Not stated</td>
<td>Total</td>
<td>Not stated</td>
<td>Bacon (1958)</td>
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<tr>
<td></td>
<td>Monozygous</td>
<td>4</td>
<td>Total</td>
<td>Non-twin sister</td>
<td>Sleight, Galpin &amp; Condon (1971)</td>
</tr>
<tr>
<td>Male</td>
<td>Monozygous</td>
<td>2</td>
<td>Total</td>
<td>None</td>
<td>Sanford (1971)</td>
</tr>
<tr>
<td>Female</td>
<td>Monozygous</td>
<td>4</td>
<td>Total</td>
<td>Mother and cousin</td>
<td>Fausa et al., (1972)</td>
</tr>
<tr>
<td>Female</td>
<td>Monozygous</td>
<td>7</td>
<td>Distal</td>
<td>Grandmother</td>
<td>This report</td>
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</table>
Clinical reports

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References
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J. F. Mayberry, M. J. Dew and J. S. Morris

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