

# Gut

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## Leading article

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### Microscopic colitis

Microscopic colitis may be defined as chronic inflammation of the colon that manifests itself as histological changes when the mucosa seems endoscopically and radiologically normal. The name is generally applied to a clinical syndrome of chronic watery diarrhoea for which no cause can be identified other than colonic inflammation. The first report of this came from St Bartholomew's Hospital, London, in 1982<sup>1</sup> but the concept is attributable to Fordtran's group in Dallas,<sup>2</sup> who had coined the term microscopic colitis in a study on chronic diarrhoea of unknown origin two years earlier.

There are relatively few published clinical and investigational studies on microscopic colitis, and its existence is still disputed. Groups from Baltimore<sup>3</sup> and Calgary<sup>4</sup>, however, have recently added their observations supporting the concept.

The three major case reports come from London,<sup>1</sup> Dallas,<sup>2,5</sup> and Baltimore<sup>3</sup> describing 31 patients, and all show a good measure of agreement. The patients are usually middle aged or elderly women and all have watery diarrhoea of lengthy duration as the predominant symptom. Nocturnal diarrhoea and incontinence are frequent. Weight loss is the only commonly reported constitutional symptom. Stool output is always high, and when quantitated, the daily volume is usually between 500 and 1500 ml.<sup>1,5</sup> Thus, the clinical features indicate an organic rather than a functional disorder, even though general health remains good. Laboratory tests are usually normal though occasionally there is a low grade anaemia, mild hypoalbuminaemia, or a raised erythrocyte sedimentation rate.<sup>1,3</sup>

The intensity of investigation has varied from series to series, but most patients have been adequately investigated. There has been no evidence of an infective agent, dietary factors, gut ischaemia, or hormonal causes. Stools contain no microscopic or occult blood. Pancreatic function is normal and the immune system is intact. Nutrient malabsorption is not a feature, though the diarrhoea is associated with salt and water malabsorption by the colon.<sup>5</sup> Surreptitious laxative or diuretic abuse has been arduously searched for but never found.

The most detailed investigations pertain to the six patients reported from Dallas.<sup>5</sup> Fasting reduced the mean daily stool output by about 50% in all but one patient, but there was no appreciable osmotic gap between the fasting and fed states. This is not a specific finding and similar results were obtained in five disease control patients with high volume diarrhoea in whom no diagnosis could be made, but in whom there was no evidence of microscopic colitis.<sup>5</sup> The same patients were subjected to colonic perfusion studies to assess unidirectional

and net water and electrolyte fluxes. Those with microscopic colitis had appreciable reduction of net water, sodium, and chloride absorption and bidirectional fluxes of sodium and chloride were also reduced when compared with control patients.

In the original report from London,<sup>1</sup> three of the six patients had abnormalities in jejunal biopsy specimens – subtotal villous atrophy in one, mild partial villous atrophy (coeliac disease in remission on gluten free diet) in another, and mild non-specific inflammation in a third. Ileal biopsy specimens were normal. In none of them, however, was there evidence of malabsorption, and jejunal perfusion studies showed normal handling of fluid and electrolytes. Jejunal morphology improved after treatment. In the Dallas patients,<sup>5</sup> two of six showed a reduction in jejunal and ileal salt and water absorption and one of these showed mild inflammation on jejunal biopsy specimen.

In the Baltimore study,<sup>3</sup> two of 18 patients had clinical evidence of malabsorption, with steatorrhoea and villous atrophy of some degree which did not respond to gluten withdrawal. These patients from Johns Hopkins were less extensively investigated, and faecal fat analysis and small bowel biopsies were not routinely performed. This undermines the validity of their assumption that the microscopic colitis was the cause of the watery diarrhoea. This apart, the disorder was remarkably similar to the more strictly defined cases reported in the other series.

There are two other single case reports<sup>6,7</sup> of patients with microscopic colitis and partial villous atrophy that did not improve on gluten free diet. The overall picture indicates that the association between microscopic colitis and abnormal small bowel morphology and function is a real one but its importance is obscure.

There is no consistent association with other disorders, although several patients have coexistent arthritis, thyroid disease, and putative autoimmune diseases.<sup>3</sup>

The diagnosis of microscopic colitis rests on histological examination of rectal and colonic biopsy specimens. The abnormality is pancolonic. In most reported case studies multiple colonoscopic as well as rectal biopsy specimens were available for review and all showed similar degrees of inflammation irrespective of site.<sup>1-5,8</sup> One of the major obstacles in the acceptance of microscopic colitis as an entity is the pathologist's ability to differentiate between the normal extent to which the colonic epithelium contains inflammatory cells and abnormal inflammation. The London<sup>1</sup> and Dallas<sup>5</sup> reports both used blind review of histological material from microscopic colitis patients in comparison with disease

control subjects and showed a clear demarcation. Multiple biopsy specimens certainly aid in discrimination. The essential features are as follows: mild, moderate, or severe infiltration of the lamina propria with a mixed but predominantly chronic inflammatory cell population and some surface epithelial flattening but minimal crypt distortion, cryptitis, and goblet cell depletion. The Baltimore group<sup>3,8</sup> has recently reported the importance of increased intra-epithelial lymphocytes and surface epithelial damage in microscopic colitis, features they consider particularly important in distinguishing this disorder from inflammatory bowel disease. They have suggested changing the name of the condition from 'microscopic' to 'lymphocytic' colitis. In my view this serves no function other than to fragment opinion and confuse.

The most important area of debate is whether microscopic and collagenous colitis<sup>9-14</sup> represent variants of the same condition. Most clinical and demographic characteristics are similar – both being associated with chronic watery diarrhoea in an elderly female population. This proposal was aired in 1986<sup>13</sup> by the principal authors of the Baltimore and Dallas studies, who had collaborated with a mutual review of histological sections. They concluded that most of the patients with microscopic colitis in Dallas would be diagnosed as 'collagenous colitis' in Baltimore and that the degree of inflammation in the collagenous colitis patients from Baltimore would entitle them to be classified as 'microscopic colitis' in Dallas. Institutions which recognise one condition tend to recognise the other, whether or not they lump together or separate the diseases, suggesting a readiness to attribute symptoms to a colonic abnormality which is not evident to the naked eye. Although I originally subscribed to the separatist school,<sup>1,10,12</sup> more recent (unpublished) observations persuade me that the transatlantic view<sup>13,14</sup> is correct. The two conditions may overlap with time, as has been reported by others.<sup>3,4</sup> However, in most cases the histological type of colitis remains true to form and polarised.

The aetiology and pathophysiology of both conditions are unknown. The abnormality may be the end result of several unrelated processes or insults. There is a ready analogy with small bowel mucosal inflammation associated with partial villous atrophy seen in coeliac disease, tropical sprue, and infantile infective enteritis or food protein allergies. Whatever the cause or causes, there is nothing to link the condition either clinically or histologically with inflammatory bowel disease. The association with coeliac disease (not always responding to gluten free diet) and other non-specific enteropathies remains an enigma.

Treatment of microscopic colitis has no scientific basis nor has it been subject to controlled clinical trials. Many patients respond well to conventional drug treatment used in inflammatory bowel disease. Treatment details are given in two studies.<sup>1,3</sup> Thirteen of 16 patients showed a noticeable improvement in stool frequency and output when treated with oral sulphasalazine, and a few responded to corticosteroids as well. A further six patients showed a slight improvement on non-specific or no treatment. Treatment of microscopic colitis seems more satisfactory than that of collagenous colitis.

In conclusion, microscopic colitis is a real syndrome associated with chronic watery diarrhoea. There are close similarities to collagenous colitis and in a few cases at least there is overlap between the two conditions. Whether the microscopic abnormalities cause the clinical symptoms is uncertain but circumstantial observations support this proposal.

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