Virchows Archiv (1994) 424:573–579

REVIEW ARTICLE

W. V. Bogomoletz

Collagenous, microscopic and lymphocytic colitis. An evolving concept

Received: 24 January 1994 / Accepted: 1 April 1994

Abstract Collagenous colitis and lymphocytic colitis (previously described as microscopic colitis) are two newly recognised forms of colitis. Both have generated much controversy and continue to do so; their aetiology and pathogenesis are unresolved and their association with a variety of immune-related disorders is intriguing. Response to available therapeutic modalities is often disappointing. The possible relationship or overlap between these two conditions remains a controversial issue. The aim of this review is essentially to present an overview of collagenous colitis and lymphocytic colitis and to propose an unifying concept with an adapted terminology.

Key words Microscopic colitis · Collagenous colitis Lymphocytic colitis

The golden years (1976–1985)

The expression "microscopic colitis" was first used by Read et al. [44] in a study of 27 patients investigated for severe chronic diarrhoea of undetermined origin. Eight of these patients had normal sigmoidoscopy and barium enema, but colorectal biopsies showed a mild increase in the number of inflammatory cells. Hence, the designation of microscopic colitis was applied to these eight patients. The authors did not consider such inflammatory change to be diagnostic of ulcerative colitis.

There was no mention in this paper of another entity which had been described four years earlier by Lindström [35]. He had coined the term "collagenous colitis" to describe a new and unusual form of colitis. The patient reported by this author had chronic watery diarrhoea and an endoscopically normal colorectal mucosa. However, rectal biopsies showed a thick collagen layer under the surface epithelium of the mucosa and an increased number of plasma cells in the lamina propria. Interestingly, in the same year that Lindström [35] published his now classical paper, there was an abstract published in Canada, which briefly recorded two patients with apparently similar clinical and histological findings [20]. Between 1980 and 1982, 14 additional cases of collagenous colitis, involving all segments of the colon, were reported from different countries; for review see [4]. The collagenous nature of the deposit was confirmed by histochemistry, electron microscopy and immunofluorescence. Most of the authors also noted a variable excess of inflammatory cells in the lamina propria and some damage to the surface epithelium.

In 1982, Elliott et al. [13] proposed the term "minimal change colitis" for a group of eight patients with symptoms suggestive of inflammatory bowel disease (Crohn's disease or ulcerative colitis), normal barium enema and normal sigmoidoscopy, but showing histological low grade colitis in rectal biopsies. Also in 1982, the second paper on the concept of microscopic colitis was published by Kingham et al. [29]. These authors reported six patients with severe watery diarrhoea, but no abnormality on barium radiology and endoscopy. Diagnosis could only be made by microscopic examination of colorectal biopsies which showed an excess of chronic inflammatory cells in the lamina propria. There was total involvement of the colon. The authors considered microscopic colitis to be a clinical entity different from minimal change colitis. Collagenous colitis was only mentioned in passing.

Hence, the stage was set for two newly described forms of colitis, collagenous colitis and microscopic colitis. Both occurred mostly in women, predominantly in their fifties or sixties, who presented with chronic watery diarrhoea and endoscopically normal colon. Histologically, both forms of colitis showed an excess of mucosal inflammatory cells, but only collagenous colitis was characterized by the presence of a subepithelial collagen deposit Both were apparently unrelated to inflammatory bowel disease. Between 1983 and 1985, 26 additional cases of collagenous colitis were reported from different geographical areas, with the notable exception of the Asian continent (this exception continues to prevail).

W.V. Bogomoletz (✉)
Laboratoire d'Anatomie Pathologique, Institut Jean Godinot, BP171, F-51056 Reims, France

These newly recorded cases included several patients in whom there coexisted some form of immune-related pathology, particularly degenerative osteo-articular diseases [16]. Another point of interest at this stage was that all the patients with collagenous colitis reported so far had no clinical or biopsy evidence of coeliac disease.

In 1985, two additional papers on microscopic colitis were published, corresponding to a total 13 patients [6, 17]. The diagnosis of microscopic colitis was essentially made on the basis of the histological criterion proposed by previous authors [29, 44]: an excess of chronic inflammatory cells in the lamina propria. Minimal crypt distortion was also noted. Bo-Linn et al. [6] furthermore stressed the presence of reactive changes of the surface epithelium. Whilst Bo-Linn et al. [6] did not mention collagenous colitis as a possible differential diagnosis, Fisher et al. [17] commented that their seven cases of microscopic colitis were histologically unrelated to collagenous colitis.

The years of progress and controversy (1986–1993)

In 1986, the first three cases of collagenous colitis, coexisting with small intestinal villous atrophy [24, 25] and the first autopsy case [49] were reported.

Also in 1986, a letter heralded the days of "lumpers" versus "splitters". Jessurun et al. [26] argued that microscopic colitis and collagenous colitis were "part and parcel of the same spectrum of disease". This opinion was further publicized by the same group of workers, in a succession of papers published in leading journals in the USA [2, 27]. The stance taken by the John Hopkins group was held on the basis that collagenous colitis and microscopic colitis shared a number of features. Clinically, both caused watery diarrhoea in patients with normal endoscopy and normal roentgenographic findings. The John Hopkins group further argued that, with the exception of the subepithelial collagen band, microscopic colitis ressembled collagenous colitis histologically, because both showed injury to the surface epithelium, particularly increased numbers of intraepithelial lymphocytes, and excess of chronic inflammatory cells in the lamina propria. Another argument of the John Hopkins group was that there were a few cases in the literature in which apparent progression from microscopic colitis to collagenous colitis had been noted [30, 40, 52].

The views held by the John Hopkins group on collagenous colitis and microscopic colitis were to have a major influence on further publications on this topic in North America [50]. Nevertheless, other North American pathologists considered collagenous colitis as a separate disease [42, 53]. Several investigators in Europe and Australia also regarded collagenous colitis as a specific entity [47, 56].

In 1989, the John Hopkins group renamed microscopic colitis "lymphocytic colitis", on the basis of a comparative study involving 77 cases of microscopic colitis, collagenous colitis, inflammatory bowel disease, other forms of acute colitis and histological normal controls [31]. In this study, the authors showed that the most distinctive histological feature of microscopic colitis was a marked excess of intraepithelial lymphocytes, particularly in the surface epithelium, hence their renaming of the disease. The John Hopkins group also stated that "... although lymphocytic colitis closely ressembles collagenous colitis, each entity is distinct on biopsy".

The renaming of microscopic colitis as lymphocytic colitis in 1989 introduced an additional element of confusion. This was shown by subsequent publications on this entity which were variously entitled lymphocytic (microscopic) colitis [21], microscopic (lymphocytic) colitis [5, 38], lymphocytic colitis [23, 36] or microscopic colitis [1, 28, 33, 50]. Fortunately, the term collagenous colitis remained unchanged.

In another paper, also published in 1989, the John Hopkins group reported that there were striking non-histological differences between lymphocytic colitis and collagenous colitis [21]. Namely, the patients showed a statistically different sex distribution and dissimilar histocompatibility groups. The authors concluded that "...lymphocytic and collagenous colitis may be related yet distinct disorders".

A third study of the John Hopkins group described five patients with lymphocytic colitis and co-existing coeliac disease, a situation which the group called "lymphocytic enterocolitis" [11].

The first case of collagenous colitis in a child was also recorded in 1989 [14].

Several interesting and useful contributions on collagenous colitis and lymphocytic colitis appeared between 1990 and 1993 [3, 10, 22, 23, 32, 33, 45, 46, 51, 59].

Histopathological features (recognizable and recognized)

Which are the specific histopathological features of collagenous colitis and lymphocytic colitis?

The diagnosis of collagenous colitis relies on the histological demonstration of an abnormal collagenous band-like deposit under the surface epithelium of the colorectal mucosa (Fig. 1). However, this diagnosis is fraught with problems of sampling and interpretation which are related to the very nature of the disease.

Firstly, the collagenous band-like deposition is an uneven and discontinuous process along the length of the colon, and it is found more frequently in the proximal colon than in the rectosigmoid [24, 27]. There are also variations in thickness of the collagenous band-like deposit at different levels of the colon. Hence, multiple biopsies from both proximal (right) and distal (left) colon should be available. Moreover, careful measurement of the actual thickness of the collagenous band-like deposit is important, using either a calibrated eye-piece graticule or a computer-assisted morphometric method. The collagenous band-like deposit should be at least 10 μm thick to be of diagnostic significance [5, 33, 51].

Well orientated and thin sections are a prerequisite for confirming or dismissing a diagnosis of collagenous colitis. By "well-orientated sections" are meant sections in which at least three adjacent crypts are cut in their vertical plane. In such well-orientated sections, the normal subepithelial basement membrane can be identified as a thin, sharp and slightly refractile line. But, in tangential sections in which crypts are cut transversely or obliquely, the same normal basement membrane will show fuzzy edges and hence appears artefactually "thickened", misleading the pathologist in making a diagnosis of collagenous colitis. This is a common pitfall which is probably responsible for some degree of overdiagnosis of collagenous colitis in the literature. Indeed, if one critically reexamines illustrations claiming to demonstrate typical collagenous colitis in some published case reports, tangential sectioning is so obvious that the diagnosis becomes questionable [5].

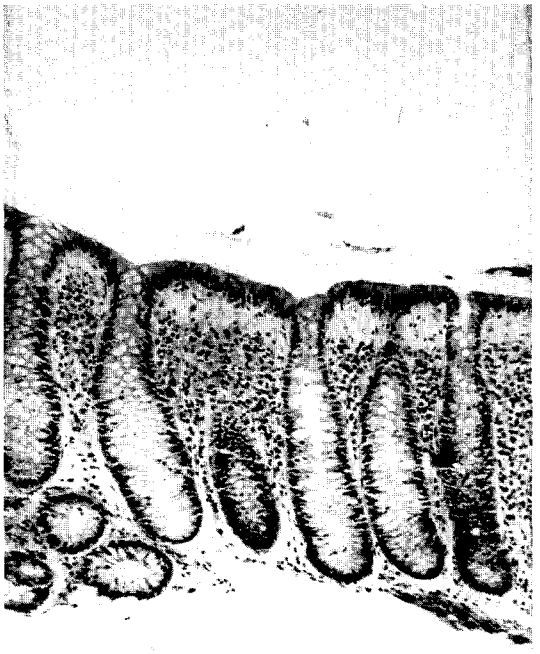

Fig. 1 Collagenous colitis with typical collagen band-like deposit under the surface epithelium. Mild excess of chronic inflammatory cells in the lamina propria. The crypts are regular and show no impairment of mucus secretion

The abnormal collagenous band-like deposit consists of predominantly of collagen types I and III [19].

In addition to the characteristic collagenous band-like deposit, other inflammatory changes, variable in intensity, are found in collagenous colitis. The cells of the surface epithelium often show vacuolisation and desquamation, but may also show an increased number of intraepithelial lymphocytes. The latter change is seldom as dramatic as observed in lymphocytic colitis. Moreover, in collagenous colitis, the lamina propria contains an excess of lymphocytes, plasma cells and mast cells. These inflammatory cells, when situated close to the surface and togeher with superficial capillaries may become "entrapped" within the collagenous band-like deposit. Eosinophils may also be increased, although marked mucosal eosinophilia is not a feature of collagenous colitis. Neutrophils are absent or scarce. In general, the crypts look remarkably normal, but very rarely they may show mild architectural distortion.

The histological hallmark of lymphocytic colitis is now accepted by most investigators as being a marked increase of intraepithelial lymphocytes (Fig. 2). This increase predominantly involves the surface epithelium, but can also be apparent in the crypt epithelium. To be of diagnostic significance, the increase must be 20 lymphocytes per 100 epithelial cells on average. This threshold compares to an average of about 4–5 lymphocytes per 100 epithelial cells in the normal colon, inflammatory bowel disease and infectious colitis [31]. Uniform sec-

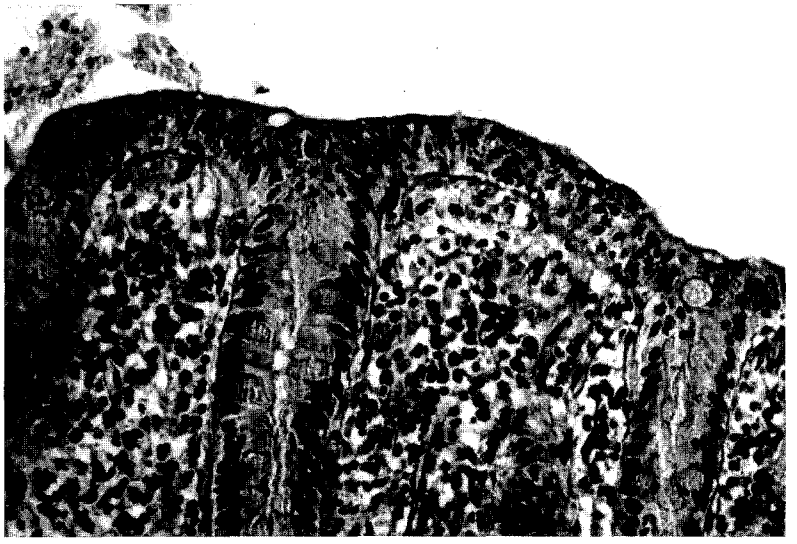

Fig. 2 Lymphocytic colitis showing characteristic increase of intraepithelial lymphocytes in the surface epithelium. The underlying normal basement membrane is thin and sharp. There is no abnormal collagenous deposit. Lamina propria contains a moderate of chronic inflammatory cells. Crypt architecture is normal

tion thickness is obviously important in the quantitation of intraepithelial lymphocyte counts for comparative assessment. The increased population of intraepithelial lymphocytes consists of cytotoxic-suppressor T cells which express HLM 1 antigen [5].

Besides the typical increase of intraepithelial lymphocytes, lymphocytic colitis usually shows other inflammatory changes. A diffuse infiltrate of lymphocytes, plasma cells and occasional eosinophils and neutrophils, albeit variable in amount, spreads throughout the lamina propria. Reactive changes of the surface epithelium as well as mild crypt alterations can also be seen.

In genuine lymphocytic colitis, no subepithelial collagen band-like deposit should be present.

Coexisting immune-related diseases

The presence of coexisting immune-related diseases has been reported in a number of patients with collagenous colitis and lymphocytic colitis. The difficulty is to assess objectively the frequency and the genuine or fortuitous character of such an association. A variety of immune-related diseases have been described. Examples of thyroiditis, chronic hepatitis, primary biliary cirrhosis, chronic gastritis, juvenile and maturity-onset diabetes, uveitis, idiopathic pulmonary fibrosis, scleroderma, etc. have been recorded. However, two forms of association are of particular interest: degenerative osteo-articular disease and coeliac disease.

Different varieties of degenerative osteo-articular disease, including seropositive rheumatoid arthritis, have been recorded in several patients with collagenous colitis [16, 22, 45] and lymphocytic colitis [21]. In the majority of these patients, degenerative osteo-articular disease preceded the onset of chronic diarrhoea and the biopsy diagnosis of collagenous colitis or lymphocytic colitis by some years.

Collagenous colitis combined with coeliac disease and some degree of villous atrophy has been described in about ten patients [9, 12, 24, 25, 47, 50]. However, the small number of patients with this combination is in marked contrast with over 200 reported cases of patients with collagenous colitis but without malabsorption and with biopsy-proven normal small gut.

More than a handful of cases of lymphocytic colitis coexisting with coeliac disease have been reported [11, 54, 57]. Nevertheless, there are also many recorded cases of lymphocytic colitis showing no evidence of combined clinical or histological involvement of the small bowel.

The terms "collagenous enterocolitis" [12] and "lymphocytic enterocolitis" [11] have been used by some authors for cases in which collagenous colitis or lymphocytic colitis coexisted with coeliac disease.

Aetiology and pathogenesis

The aetiology and pathogenesis of collagenous colitis and lymphocytic colitis are still unresolved.

For collagenous colitis, evidence indicates that the diarrhoea is secretory in type [43]. However, the cause and mechanism responsible for the formation of the subepithelial collagen band-like deposit remain obscure. It is generally assumed that the accumulation of collagen results from abnormal synthesis by the fibroblasts of the colonic pericryptal sheath [4, 25]. An inflammatory or toxic injury of undetermined nature could be the starting point. Several hypotheses as to the nature of this injury have been entertained: bile acid malabsorption [15], mast cell infiltration [37] and prostaglandin action [43]. Drug-induction has also been suggested, particularly the taking of non-steroidal anti-inflammatory drugs [45] and vascular tonics [3]. An immune-mediated mechanism could also be envisaged.

As for lymphocytic colitis, the inflammatory lesions are probably responsible for the diarrhoea. However, the nature of the injury is still unknown. An infectious process is unlikely. As for collagenous colitis, bile acid malabsorption [41] and mast cell infiltration [1] have also been suggested at some stage. A definite diet-linked or drug-induced cause has not been identified [21]. Presently, the hypothesis of an immune-mediated disease is strongly favoured [21, 23], because of the high incidence of autoantibodies in patients with lymphocytic colitis, as well as the frequency of coexisting degenerative osteo-articular disease and coeliac disease.

Finally, it has been shown that collagenous colitis and lymphocytic colitis are unrelated to the conventional forms of inflammatory bowel disease, chronic ulcerative colitis and Crohn's disease [5, 31].

Natural history

The natural history of untreated collagenous colitis is variable, showing a waxing and waning course, and commonly consisting of alternating remissions and relapses of watery diarrhoea. The intensity and frequency of the remissions and relapses are apparently unrelated to the severity of the histological lesion of the disease. In effect, the collagenous band-like deposit, once formed, may persist, increase or decrease in thickness and extent or even disappear altogether. Patients with collagenous colitis generally suffer little morbidity other than the inconvenience of the chronic watery diarrhoea. But the situation can be different when there is a coexisting immune-related disease which could be severe and crippling.

The natural history of lymphocytic colitis is not known. The disease follows a prolonged course with chronic diarrhoea, the latter being continuous or intermittent as in collagenous colitis.

Rare cases of lymphocytic colitis with apparent progression to collagenous colitis have been reported [26, 30, 39, 52]. This is still a very difficult and controversial area.

Response to therapy

Patients with collagenous colitis have generally shown a poor response to symptomatic treatment of their diar-

rhoea with conventional antidiarrhoeal drugs (codeine phosphate, loperamide, adsorbing agents, opiates and antiseptics). Some patients have responded well clinically (in selected cases even with histological resolution of the lesion) to sulfasalazine, 5-aminosalicylic acid, oral corticosteroids, cortisone enemas, mepacrine and metrodinazole, alone or in combination. Unfortunately, the use of the same anti-inflammatory agents has been disappointing in other patients. At present, there is no accepted protocol which can effectively control the disease on a long-term basis and in all patients. Drug therapy remains empirical.

Conventional antidiarrhoeal treatment has generally been ineffective in most patients with lymphocytic colitis. Some patients have successfully responded to anti-inflammatory drugs, such as sulfasalazine or corticosteroids (taken orally or given by enema), as well as to antibiotics.

Other "collagenous" lesions of the gastrointestinal tract

Lindström [35] proposed the term collagenous colitis by analogy with collagenous sprue. Collagenous sprue was originally described as a special type of adult coeliac disease, characterised histologically by a flat jejunal mucosa and subepithelial collagenization of the lamina propria [55]. Clinically, patients with collagenous sprue showed a lack of response to gluten-free diet and consequently a poor prognosis. However, subsequent studies [8] indicated that subepithelial collagen deposition was not uncommon in mucosal biopsies showing complete or partial villous atrophy, particularly in adults with a long history of gluten sensitive enteropathy.

It is interesting to note that among the few reported cases of collagenous colitis combined with proven coeliac disease, at least two patients [12, 24] showed increase in mucosal collagen together with partial villous atrophy, a pattern corresponding to collagenous sprue.

On the basis of the few recorded cases of so-called collagenous enterocolitis [12] or lymphocytic enterocolitis [11], it may be tempting to consider a possible relationship between lymphocytic colitis and collagenous colitis in the colon as the mirror image of the link between coeliac disease and collagenous sprue in the small intestine. But this would be premature in our present state of knowledge.

Two unusual cases of collagenous gastritis have been reported [7, 48]. Histologically, biopsies showed an irregular collagenous deposit (30–60 μm thick) in the lamina propria of the gastric mucosa, and located between the foveolar pits. In both cases, the lesions extended into the proximal duodenum and hence the term "collagenous gastroduodenitis" used in both papers. The patients were both women, aged respectively 67 and 75 years, who presented with chronic diarrhoea. Gastroscopy and colonoscopy were normal. One patient also had concomitant collagenous colitis in colorectal biopsies [48]. We have had the opportunity to study a somewhat similar consultation case of collagenous gastritis in an elderly women (Dr. G. Bertrand, Angers: personal communication and published observation).

However, one should bear in mind that, with the exception and these instances of collagenous gastritis or gastroduodenitis, the vast majority of reported patients with collagenous colitis have had normal gastric and duodenal biopsies.

Where do we stand now?

Let us first sum up the more obvious similarities between collagenous colitis and lymphocytic colitis. Both occur predominantly in women in their fifties who present with chronic watery diarrhoea. In both, there are minor or no detectable radiological or endoscopic abnormality. In both, routine laboratory tests remain unaltered (microbiology has never yielded any responsible microorganism). Both may be associated with different immune-related diseases, particularly some form of osteoarticular degenerative pathology. When multiple colorectal biopsies are examined, but show distinctive inflammatory lesions of the mucosa.

If we now look at the main differences between collagenous colitis and lymphocytic colitis, the following features can be stressed. From the clinical viewpoint, the mean duration of the disease is longer and the female preponderance is higher in collagenous colitis. From the immunological viewpoint, autoantibodies are more frequently found in lymphocytic colitis, the latter showing a distinct HLA pattern when compared to collagenous colitis. From the histological viewpoint, the subepithelial collagenous "band-like" deposit is the hallmark of collagenous colitis, whereas a marked increase in intraepithelial lymphocytes is the major characteristic of lymphocytic colitis.

Unifying concept and adapted terminology

We recently proposed that collagenous colitis and lymphocytic colitis should now be considered, despite some clinical similarities, as two probably linked but different forms of colitis, under the blanket or umbrella term of microscopic colitis[18]. We would define microscopic colitis as any form of inflammation of colorectal mucosa, without radiological or endoscopic expression, but whose diagnosis is exclusively histological. The John Hopkins group has also made similar proposals [34]. Within this specific clinico-pathological context, other similar situations could be conveniently considered in future as also representing forms or types of microscopic colitis.

Dedication. Dedicated to Prof. H. Roels (N. Goormaghtigh Instituut voor Pathologische Anatomie, Gent, Belgium) on the occasion of his retirement.

References

1. Baum CA, Bhatia P, Miner BP (1989) Increased colonic mucosal mast cells associated with severe watery diarrhea and microscopic colitis. Dig Dis Sci 34:1462–1465
2. Bayless TM, Giardello FM, Lazenby A, Yardley JH (1987) Collagenous colitis (editorial). Mayo Clin Proc 62:740–741
3. Beaugerie L, Luboinski J, Brousse N et al. (1994) Drug-induced lymphocytic colitis. Gut 35:426–428
4. Bogomoletz WV (1983) Collagenous colitis: a clinicopathological review. Surv Dig Dis 1:19–25
5. Bogomoletz WV, Fléjou JF (1991) Newly recognized forms of colitis: collagenous colitis, microscopic (lymphocytic) colitis and lymphoid idiopathic proctitis. Semin Diagn Pathol 8:178–189
6. Bo-Linn GW, Vendrell DD, Lee E, Fordtran JS (1985) An evaluation of the significance of microscopic colitis in patients with chronic diarrhea. J Clin Invest 75:1559–1569
7. Borchard F, Niederau C (1989) Kollagene gastroduodenitis. Dtsch Med Wochenschr 114:1345
8. Bossart R, Henry K, Booth CC, Dol WF (1975) Subepithelial collagen in intestinal malabsorption. Gut 16:18–22
9. Breen EG, Farren C, Conolly CE, McCarthy CF (1987) Collagenous colitis and coeliac disease. Gut 28:364
10. Carpenter HA, Tremaine WJ, Batts KP, Czaja AJ (1992) Sequential histologic evaluations in collagenous colitis. Correlations with disease behavior and sampling strategy. Dig Dis Sci 37:1903–1909
11. DeBois N, Lazenby AJ, Yardley JH, Hendrix TR, Bayless TM, Giardello FM (1989) Lymphocytic enterocolitis in patients with "refractory sprue". JAMA 262:935–937
12. Eckstein RP, Dowsett JF, Riley JW (1988) Collagenous enterocolitis: a case of collagenous colitis with involvement of the small intestine. Am J Gastroenterol 83:767–771
13. Elliott PR, Lennard-Jones JE, Bastram CI et al. (1982)Colonoscopic diagnosis of minimal change colitis in patients with a normal sigmoidoscopy and normal air-contrast barium enema. Lancet i:650–651
14. Esselinckx W, Brenard R, Colin JF, Melange M (1989) Juvenile scleroderma and collagenous colitis. J Rheumatol 16:834–836
15. Eusufzais S, Löfberg R, Veress B, Einarsson K, Angelin B (1992) Studies on bile acid metabolism in collagenous colitis: no evidence of bile acid malabsorption as determined by the SeHCAT test. Eur J Gastroenterol Hepatol 4:317–321
16. Farah DA, Mills PR, Lee FD, McLay A, Russell RI (1985) Collagenous colitis: possible response to sulfasalazine and local steroid therapy. Gastroenterology 88:792–797
17. Fisher D, Labayle D, Kemeny F (1985) La colite microscopique: une cause possible de diarrhée chronique? Gastroenterol Clin Biol 9:452
18. Fléjou JR, Bogomoletz WV (1993) Les colites microscopiques: colite collagène et colite lymphocytaire. Un concept unitaire? Gastroenterol Clin Biol 17:T28–T32 (suppl)
19. Fléjou JF, Grimaud JA, Molas G, Baviera E, Potet F (1984) Collagenous colitis. Ultrastructural and collagen immunotyping of four cases. Arch Pathol Lab Med 108:977–982
20. Freeman HJ, Weinstein WM, Shnitka TK, Wensel RH, Sartor VE (1976) Watery diarrhea syndrome associated with a lesion of the colonic basement membrane (BM) – lamina propria (LP) interface (abstract). Ann R Coll Phys Surg Can 9:45
21. Giardiello FM, Lazenby AJ, Bayless TM et al. (1989) Lymphocytic (microscopic) colitis. Clinicopathologic study of 18 patients and comparison to collagenous colitis. Dig Dis Sci 34:1730–1738
22. Giardiello FM, Hansen III FC, Lazenby AJ et al. (1990) Collagenous colitis in setting of nonsteroidal antiinflammatory drugs and antibiotics. Dig Dis Sci 35:257–260
23. Giardiello FM, Lazenby AJ, Yardley JH et al. (1992) Increased HLA A1 and diminished HLA A3 in lymphocytic colitis compared to controls and patients with collagenous colitis. Dig Dis Sci 37:496–499
24. Hamilton I, Sanders S, Hopwood D, Bouchier IAD (1986) Collagenous colitis associated with small intestinal villous atrophy. Gut 27:1394–1398
25. Hwang WS, Kelly JK, Shaffer EA, Hershflied NB (1986) Collagenous colitis: a disease of pericryptal fibroblast sheath? J Pathol 149:33–40
26. Jessurun J, Yardley J, Lee EL, Vendrell DD, Schiller LR, Fordtran JS (1986) Microscopic and collagenous colitis: different names for the same condition? (letter) Gastroenterology 91:1583–1584
27. Jessurun J, Yardley JH, Giardiello FM, Hamilton SR, Bayless TM (1987) Chronic colitis with thickening of the subepithelial collagen layer (collagenous colitis). Histopathologic findings in 15 patients. Hum Pathol 18:839–848
28. Kingham JGC (1991) Microscopic colitis. Gut 32:234–235
29. Kingham JG, Levison DA, Ball JA, Dawson AM (1982) Microscopic colitis – a cause of chronic watery diarrhoea. BMJ 285:1601–1604
30. Kingham JGC, Levison DA, Morson BC, Dawson AM (1986) Collagenous colitis. Gut 27:570–577
31. Lazenby AJ, Yardley JH, Giardello FM, Jessurun J, Bayless TM (1989) Lymphocytic ("microscopic") colitis: a comparative histopathologic study with particular reference to collagenous colitis. Hum Pathol 20:18–28
32. Lazenby AJ, Yardley JH, Giardiello FM, Bayless TM (1990) Pitfalls in the diagnosis of collagenous colitis. Experience with 75 cases from a registry of collagenous colitis at the John Hopkins Hospital. Hum Pathol 21:905–910
33. Lee E, Schiller LR, Vendrell D, Santa Ana CA, Fortran JS (1992) Subepithelial collagen table thickness in colon specimens from patients with microscopic colitis and collagenous colitis. Gastroenterology 103:1780–1796
34. Levison DA, Lazenby AJ, Yardley JH (1993) Microscopic colitis cases revisited. Gastroenterology 105:1594–1595
35. Lindström CG (1976) "Collagenous colitis" with watery diarrhea. A new entity? Pathol Eur 11:87–89
36. Mills LR, Schuman BM, Thompson WO (1993) Lymphocytic colitis. A definable clinical and histological diagnosis. Dig Dis Sci 38: 1147–1151
37. Molas G, Fléjou JF, Potet F (1990) Microscopic colitis, collagenous colitis and mast cells. Dig Dis Sci 35:920 (letter)
38. Ong G, Price AB (1990) Microscopic (lymphocytic) colitis; characteristic rectal biopsy features (abstract). J Pathol 160:170A
39. Ouyahya F, Michenet P, Gargot D, Breteau N, Buzacoux J, Legoux JL (1993) Colite lymphocytaire puis colite collagène associée à un lymphome T de type mycosis fongoïde. Gastroentérol Clin Biol 17:976–977
40. Palmer KR, Berry H, Wheeler PJ et al. (1986) Collagenous colitis – a relapsing and remitting disease. Gut 27:578–580
41. Rampton DS, Baithun SI (1987) Is microscopic colitis due to bile-salt malabsorption? Dis Colon Rectum 30:950–952
42. Rams H, Rogers AI, Gandur-Mnaymneh L (1987) Collagenous colitis. Ann Intern Med 106:108–113
43. Rask-Madsen J, Grove O, Hansen MGJ, Bukhave K, Henrik-Nielsen R (1983) Colonic transport of water and electrolytes in a patient with secretory diarrhea due to collagenous colitis. Dig Dis Sci 28:1141–1146
44. Read NW, Kejs GJ, Read MG, Santa Ana CA, Morawski SG, Fordtran JS (1980) Chronic diarrhea of unknown origin. Gastroenterology 78:264–271
45. Riddell RH, Tanaka M, Mazzoleni G (1992) Non-steroidal anti-inflammatory drugs as a possible cause of collagenous colitis: a case-control study. Gut 33:683–686
46. Stampfl DA, Friedman LS (1991) Collagenous colitis. Pathophysiologic considerations. Dig Dis Sci 36:705–711
47. Steadman C, Teague C, Kerlin P, Harris O, Hourigane K, Sampson J (1987) Collagenous colitis: clinical and histological spectrum in ten patients. J Gastroenterol Hepatol 2:459–466
48. Stolte M, Ritter M, Borchard F, Koch-Scherrer G (1990) Collagenous gastroduodenitis on collagenous colitis. Endoscopy 22:186–187

49. Stueland DT, Gani KS, Magnin GE, Norfleet RG (1986) Collagenous colitis: report of a case with autopsy data. Wis Med J 85:26–27
50. Sylwestrowicz T, Kelly JK, Hwang WS, Shaffer EA (1989) Collagenous colitis and microscopic colitis: the watery diarrhea-colitis syndrome. Am J Gastroenterol 84:763–767
51. Tanaka M, Mazzoleni G, Riddell RH (1992) Distribution of collagenous colitis: utility of flexible sigmoidoscopy. Gut 33:65–70
52. Teglbjaerg PS, Thaysen EH, Jensen HM (1984) Development of collagenous colitis in sequential biopsy specimens. Gastroenterology 87:703–709
53. Wang KK, Perrault J, Carpenter HA, Schoeder KW, Tremaine WJ (1987) Collagenous colitis: a clinicopathological correlation. Mayo Clin Proc 62:665–671
54. Weger AR, Ellmnuter H, Hoffman-Weltlin Y, Oberhuber G (1991) Colonic lymphocytosis in patients with celiac sprue (letter). Hum Pathol 22:508
55. Weinstein WM, Saunders DR, Tytgat GN, Rubin CE (1970) Collagenou sprue – an unrecognized type of malabsorption. N Engl J Med 283:1297–1301
56. Widgren S, Jlidi R, Cox J (1988) Collagenous colitis: histologic, morphometric, immunohistochemical and ultrastructural studies. Report of 21 cases. Virchows Arch [A] 413:287–296
57. Wolber R, Owen D, Freeman H (1990) Colonic lymphocytosis in patients with celiac sprue. HumPathol 21:1092–1096