# Colopathies of the old adults

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## Abstract

**The increase of life-time together with the improvement of the social, sanitary and medical cares lead to the apparition of a cohort of «very old» subjects. The prevalence of symptoms compatible with colopathies among the olders is impressive. The spectrum of large bowel disease in the elderly is essentially similar to that found at a younger age but the incidence of some diseases increases with age. This review presents the specificity of colopathies of the olders and focuses the following medical topics : irritable bowel disease (IBS), clostridium colitis, ischemic disease, iatrogenous disorders. The specificity of the "geriatric" patients should be integrated into diagnosis and clinical management.** (Acta gastroenterol. belg., **2006**, 69, **304-312**).

**Key words** : elderly, older, colopathy, irritable bowel disease, clostridium colitis, ischaemic disease, side effects

## Introduction

The prevalence of symptoms compatible with colopathies was estimated in a representative sample of elderly community residents, and the impact of these symptoms was determined on presentation for health care. An age- and sex-stratified random sample of non-institutionalized Olmsted County, Minnesota, residents aged 65-93 years were mailed a valid questionnaire ; 77% responded (n = 328). The age- and sex-adjusted prevalence (per 100 persons) of frequent abdominal pain was 24.3 [95% confidence interval (CI), 19.3-29.2]. Chronic constipation and chronic diarrhoea had prevalences of 24.1 (95% CI, 19.1-29.0) and 14.2 (95% CI, 10.1-18.2), respectively. Faecal incontinence more than once a week was reported in 3.7 per 100 (95% CI, 1.6-5.9). The prevalence of symptoms compatible with IBS (greater than or equal to 3 Manning criteria with frequent abdominal pain) was 10.9 per 100 (95% CI, 7.2-14.6). Among the subjects sampled who had abdominal pain, chronic constipation, and/or chronic diarrhoea (n = 152), only 23% had seen a physician for pain or disturbed defecation in the prior year, and this behaviour was poorly explained by the symptoms. It is concluded that complaints consistent with functional gastrointestinal disorders are common in the elderly, but symptoms are a poor predictor of presentation for medical care (1). The spectrum of large bowel disease in the elderly is essentially similar to that found at a younger age but the incidence of some diseases increases with age (e.g. neoplasia, vascular diseases).

The aims of this review are to present the specificity of colopathies of the olders. We intend to discuss the following medical conditions : irritable bowel Disease (IBS), clostridium colitis, ischemic disease, iatrogenous disorders (polypharmacy, NSAI). We shall not discuss topics such lactose intolerance and inflammatory bowel diseases. Although considered to be GI diseases of the young, coeliac disease and IBD (including ulcerative colitis and Crohn's disease), both of which can present with symptoms similar to those of IBS, have been shown to afflict many older persons as well. In fact, IBD may afflict people at any age, although the age-onset curve shows a bimodal distribution with a major peak in the second and third decades of life and a second smaller peak between ages 55 to 65 ; however, this later peak may include some cases of ischemic colitis (2). Celiac disease, which commonly presents as anaemia (3), has been shown through the use of screening methods (anti-endomysial antibody or transglutaminase) to be more common in all age groups than previously thought, and Crohn's disease and ulcerative colitis have a peak in incidence in persons over age 60 (4).

We do not intend to analysis in this review the specificity of the treatments of these conditions among the olders.

## Irritable bowel syndrome

### *Epidemiology*

Irritable bowel syndrome (IBS) is a common functional gastrointestinal (GI) disorder characterized by abdominal pain or discomfort and altered bowel function that affects up to 20% of the North American population ; women are twice as likely as men to be affected (5). IBS is clinically categorized into 3 subtypes – IBS with constipation (IBS-C), IBS with diarrhoea (IBSD), and IBS with alternating diarrhoea and constipation (IBS-A).

Traditionally, IBS has been considered a disorder of the nongeriatric (< 65 years) population. Patients usually experience symptoms in their teens and 20s and most commonly present to a clinician with symptoms between ages 30 and 50 (6). Although only about 10%

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of IBS patients are diagnosed after age 60, 3 studies indicate that between 10% and 20% of older persons in the general U.S. population have symptoms consistent with an IBS diagnosis (7). Reduced pain perception due to age has been offered as one explanation for the lower prevalence of IBS among older adults (6). However, despite a poorly defined prevalence, IBS clearly is an important problem for geriatricians to consider (6,7).

*Health impact*

In a study of 704 subjects from a randomly selected sample of 1,174 Olmsted County residents age 65 and older, patients with IBS (n = 73) had significantly lower health-related quality-of-life scores on all scales (physical, role, and social functioning ; mental health ; health perception ; and pain) of the Medical Outcomes Short Form General Health Survey (SF-36) when compared with age-matched controls (8).

*Diagnosis*

Because no specific markers can confirm the diagnosis of IBS, symptom based criteria have been developed to standardize this diagnosis (5). These criteria are primarily used in research studies for subject inclusion. Their usefulness in the clinical setting, particularly in the geriatric population, remains uncertain. The Manning (9) and the Rome (10) diagnostic criteria have been used and analyzed in multiple patient populations in the clinical setting (9-11). Both offer the highest probability of correctly establishing a diagnosis of IBS in persons younger than age 40 (11). It is important for the clinician to assess the presence of any factors that suggest increased risk for organic disease when assessing patient history, physical examination, and laboratory testing. These “red flags” include, but are not limited to, patients age 50 or older, anaemia, persistent fever, chronic severe diarrhoea, and family history of colon cancer or inflammatory bowel disease (IBD) (Table 1). By definition, therefore, all older patients presenting with symptoms of IBS have at least 1 red flag (age) and require further diagnostic testing, including, but not limited to, a colonoscopy (5).

*Differential diagnosis*

Several GI diseases affecting older adults are characterized by symptoms similar to those experienced with IBS. Because the prevalence of advanced neoplasia (high-grade dysplasia or colorectal cancer) continues to increase with age (12), the exclusion of this and other organic diseases when IBS-like symptoms are present becomes increasingly important as the patient population ages (6,7). For example, 90% of colorectal cancers occur in persons over age 50, with 23% to 40% of all colorectal cancers occurring in patients age 80 or older (6).

Older patients have an increased prevalence of other GI conditions, such as colonic diverticulosis (ranging from asymptomatic diverticulosis to diverticulitis), which some clinicians suggest may mimic intermittent IBS symptoms (6,13). Patients with IBS may also suffer from ischemic colitis – the incidence of ischemic colitis has been reported to be approximately 3 times higher in patients with IBS compared with that of the general population (14). Symptoms of ischemic colitis include rectal bleeding, which is not indicative of IBS and is considered a red flag in patients of any age (15) (Table 1).

Prevalence of pelvic outlet disorders increases in women as they age ; typical symptoms include a sense of incomplete evacuation and constipation, both of which are symptoms of IBS (6).

Chronic prostatic disease, a condition affecting older men, may cause intermittent loose stools, passage of mucus, lower abdominal pain, and a sense of incomplete evacuation (6). Patients with a history of radiotherapy for pelvic malignancy may develop radiation proctopathy, enteritis, or chronic ischemic injury to the GI tract. Symptoms of radiation proctopathy include rectal bleeding and pain, urgency, and evacuation difficulties (15).

Other diseases and conditions common in older patients that are associated with GI symptoms include thyroid disorders ; diabetes and other endocrinopathies ; achlorhydria ; ovarian cancer ; and small bowel bacterial overgrowth (6,7,16,17). The diagnoses need to be considered when evaluating an older patient with new-onset IBS-like symptoms. In addition to being at increased risk for diseases and conditions with symptoms that may mimic those of IBS, older persons take a disproportionate number of self-administered and prescribed medications for a variety of conditions ; these drugs may cause or exacerbate constipation or diarrhoea. Medication-induced constipation or diarrhoea should be considered in older patients with symptoms of IBS-C or IBS-D, respectively, especially those taking multiple medications.

Although IBS has long been considered a disorder of young and middle-aged patients, it also appears to be common among older adults and has a significant impact on their quality of life. Diagnosis is symptom-based, but can be confounded by the increased prevalence of organic diseases and co-morbid conditions in older patients. Diagnostic testing is warranted in all older patients to establish a confident diagnosis of IBS. Traditionally, management involved dietary and lifestyle changes. Several concomitant medications were often required to control the variety of symptoms experienced

Table 1. — **Irritable bowel syndromes : Red flags**

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| Age > 50 yrs old |
| Anaemia |
| Persistent fever |
| Chronic diarrhoea |
| Family history of colon cancer |

Table 2. — **Clinical presentations of Clostridium difficile**

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| Carrier state |
| Antibiotic-associated diarrhoea without colitis |
| Antibiotic-associated colitis without pseudomembrane formation |
| Pseudomembranous colitis |
| Atypical or rare presentations of C. difficile colitis |
| Fulminant colitis |
| Pseudomembranous colitis with protein-losing enteropathy |
| Relapsing infection |
| C. difficile infection in chronic inflammatory bowel disease |

by individual patients, adding to polypharmacy in the older patient population. Newer medications that directly target the intestinal pathology of this condition are leading to more effective IBS management in appropriate patient populations, but patients must be monitored carefully for severe adverse reactions.

## Clostridium colitis

Clostridium difficile is one of the most common hospital acquired (nosocomial) infections, and is a frequent cause of morbidity and mortality among elderly hospitalized patients. It colonizes the human intestinal tract only after the normal gut flora has been altered by antibiotic therapy and is the causative organism of antibiotic associated colitis. This topic review will discuss the clinical manifestations and diagnosis of C. difficile infection.

### *Clinical presentation*

C. difficile infection causes a spectrum of conditions in susceptible patients, ranging from the asymptomatic carrier state to severe fulminant disease with toxic megacolon (18) (Table 2). The typical presentation is acute watery diarrhoea with lower abdominal pain, low grade fever, and leukocytosis, starting during or shortly after antibiotic administration. Reactive arthritis is a rare complication of C. difficile infection (19).

### *The carrier state*

Approximately two-thirds of infected hospitalized patients remain asymptomatic (20) ; these individuals are sometimes referred to as faecal excretors. Although clinically silent, carriers are constantly shedding toxigenic organisms and provide a reservoir for continued contamination of the hospital environment. The carrier state may be due to the presence of serum IgG antibodies directed against toxin A, which protect against the development of diarrhoea and colitis. This was illustrated in a study that included 271 hospitalized patients with C. difficile infection who were followed prospectively (21). Patients who developed a systemic anamnestic response to toxin A (as evidenced by risking levels of serum IgG to toxin A) were much more likely to become asymptomatic carriers. In contrast, colonized patients with no or low antibody responses were more likely to develop diarrhoea. These data suggest that serum IgG antibodies directed against toxin A protect against the development of diarrhoea and colitis.

### *Antibiotic-associated diarrhoea without colitis*

Antibiotic-associated diarrhoea without colitis is a common presentation of C. difficile infection in hospitalized patients. It usually occurs during or shortly after a course of antibiotic therapy. The most frequently implicated antibiotics that predispose to C. difficile infection are penicillin, clindamycin, or cephalosporins, but virtually all antibiotics, including metronidazole, can predispose to colonization.

Diarrhoea is usually mild, with only three or four loose watery stools per day ; some patients also complain of cramps. Physical examination is generally normal with only minimal lower abdominal tenderness. Fever, leukocytosis, and dehydration are mild or absent. C. difficile toxins are present in stool but sigmoidoscopic examination is normal.

In patients with these mild manifestations of infection, diarrhoea typically subsides when the initiating antibiotic is discontinued. It is important to appreciate, however, that most antibiotic-associated diarrhoea is unrelated to infection with C. difficile. The majority of patients who develop diarrhoea during antibiotic therapy do not have infectious diarrhoea but rather a type of osmotic diarrhoea. Osmotic diarrhoea during antibiotic therapy occurs when antibiotics reduce the ability of the intestinal microflora to break down unabsorbed carbohydrate (22).

Differentiation of this non-infectious form of antibiotic-associated diarrhoea from Clostridium difficile infection may be difficult, especially in patients who are also asymptomatic carriers : -approximately 50 percent of patients who are actively infected with C. difficile have leukocytes in their stool compared to none with osmotic diarrhoea ; fever and leukocytosis also favour infection over osmotic diarrhoea ; cessation of oral feedings causes the disappearance of osmotic diarrhoea but has no effect on C. difficile diarrhoea.

### *Antibiotic-associated colitis without pseudomembrane formation*

Colitis without pseudomembranes produces a more serious illness with systemic manifestations of malaise, abdominal pain, nausea, anorexia, and profuse watery diarrhoea of 5 to 15 watery bowel movements per day. Patients typically complain of left or right lower quadrant abdominal pain and cramps that are relieved by passage of diarrhoea. They are typically dehydrated and have a low-grade fever from 37.2 to 38.3ºC. Systemic leukocytosis is common. Sigmoidoscopic examination

may reveal a nonspecific diffuse or patchy erythematous colitis without pseudomembranes.

*Pseudomembranous colitis*

Pseudomembranous colitis is the full blown manifestation of C. difficile colitis. It is accompanied by the same symptoms seen in patients without pseudomembranes. However, sigmoidoscopic examination reveals classic pseudomembranes which appear as raised yellow or off-white plaques ranging up to 1 cm in diameter scattered over the colorectal mucosa. In some patients, however, sigmoidoscopy does not reveal pseudomembranes in the rectosigmoid area. In this setting, colonoscopy can detect pseudomembranes in the proximal colon in a significant percentage of patients (23). Abdominal CT scan in patients with pseudomembranous colitis reveals pronounced thickening of the colonic wall that may involve the entire colon.

*Atypical or rare presentations of C. difficile colitis*

Several variant forms of C. difficile infection exist, some of which are discussed in detail below. Some patients, for example, have a long latency between discontinuation of antibiotics and the onset of diarrhoea or other symptoms. Several patients in our practice have had documented infection up to one month after antibiotic exposure. There are also several forms of non-antibiotic related C. difficile colitis. One setting in which this can occur is after the administration of cancer chemotherapy agents in the hospital setting (24). C. difficile can infect the small bowel as well as the colon (25). Ileitis with high ileostomy output has been described in patients with prior proctocolectomy (26). Cases of extraintestinal involvement have also rarely been reported, including cellulitis, soft tissue infection, and reactive arthritis (25).

*Fulminant colitis*

Fulminant colitis is an uncommon complication of C. difficile infection, occurring in approximately 2 or 3 percent of patients. It can account for several serious complications, including perforation, prolonged ileus, megacolon, and death (27). Thus, an aggressive diagnostic and therapeutic approach is warranted in such cases. Patients with fulminant colitis may complain of severe lower or even diffuse abdominal pain, diarrhoea, and distension. Dehydration, hypotension, oliguria and azotemia are common in this setting. Some patients exhibit high fever, chills, and a marked leukocytosis. Diarrhoea is usually prominent, but may not occur in patients with ileus in who there is pooling of secretions in the dilated, atonic colon. A severe complication of C. difficile colitis is toxic megacolon, a clinical diagnosis based upon the finding of an enlarged dilated colon (> 7 cm in its greatest diameter) accompanied by severe systematic toxicity. Patients with megacolon may have dilatation of the small intestine on plain abdominal radiographs. Air-fluid levels may be present, mimicking an intestinal obstruction or ischemia, and “thumb printing” due to the presence of submucosal oedema may be seen. This finding is characterized by the presence of scalloping of the wall of the bowel due to oedema or haemorrhage ; it occurs in patients with ischemia, inflammation, or infection. Some patients with fulminant C. difficile infection may present with signs and symptoms of bowel perforation with severe point tenderness and rebound tenderness in the left or right lower quadrants. Most such patients also have abdominal rigidity, involuntary guarding, and reduced bowel sounds. Abdominal radiographs may reveal the presence of free abdominal air.

*Pseudomembranous colitis with protein-losing enteropathy*

A subset of patients with indolent or subacute infection develops hypoalbuminaemia, ascites, and peripheral oedema (28). Such patients usually do not have severe disease but give a history of intermittent or low grade diarrhoea for one to four weeks accompanied by low grade fever, abdominal pain, and anorexia. Hypoalbuminaemia is secondary to pancolitis which induces a severe leak of serum albumin through the damaged bowel wall. Loss of albumin into the feces is not fully compensated for by increased hepatic synthesis, resulting in rapid lowering of serum albumin, often to values of less than 2.0 g/dL (20 g/L). The protein-losing enteropathy responds to appropriate medical therapy of the infection.

*Relapsing infection*

Approximately 15 to 20 percent of patients treated for C. difficile infection relapse following discontinuation of metronidazole or vancomycin therapy (18). Relapse does not appear to be related to the persistence of resistant organisms, since antibiotic resistance in C. difficile has not yet been described. Reappearance of diarrhoea and other symptoms typically occurs within five days of stopping treatment with vancomycin or metronidazole. The majority of such patients are children or older adults, some of whom may become debilitated by repeated bouts of infection (29). Evidence suggests that impairment of the host immune response to infection may be a major contributing factor. One prospective study found that serum IgM concentrations directed against toxin A were higher through day 12 after the onset of diarrhoea in patients who had only a single episode of C. difficile infection compared to those with one or more relapses ; serum IgG concentrations were also higher at day 12 in these same patients (30).

*C. difficile infection in chronic inflammatory bowel disease*

Infection with C. difficile as well as other enteric pathogens may complicate the course of ulcerative colitis or Crohn’s disease (31,32). A retrospective study

evaluated the stool microbiology results of 237 relapses in 213 patients with inflammatory bowel disease (IBD) for enteric pathogens (33). An enteric infection was documented in 10 percent of relapses ; C. difficile accounted for half of the infections. Some patients have developed C. difficile at the onset of their first attack of IBD, a situation that can lead to considerable diagnostic confusion. Infectious diarrhoeas caused by Shigella, Salmonella, Campylobacter, and colonic parasites can also trigger an apparent flare of pre-existing IBD or, more rarely, can trigger the initial bout of IBD (33).

## Ischaemic disease

Intestinal (mesenteric) ischaemia is caused by a reduction in intestinal blood flow due to hypoperfusion, occlusion, or vasospasm of the mesenteric vasculature. The intestines have a rich collateral circulation but any area of the colon may be involved by mesenteric ischaemia. Mesenteric ischaemia can be classified into three types, based on the rapidity and extent of the disruption of the blood supply : acute mesenteric ischaemia, chronic mesenteric ischaemia and colonic ischaemia.

Acute mesenteric ischaemia refers to the sudden onset of intestinal hypoperfusion, usually presents with severe acute abdominal pain, does not usually present a diagnostic problem and will not be discussed here.

Chronic mesenteric ischaemia (intestinal angina) refers to episodic or constant intestinal hypoperfusion, resulting from a blood supply insufficient to satisfy the metabolic demands of post-pyramidal bowel activity.

Colonic ischaemia (ischaemic colitis) refers to colonic injury resulting from hypoperfusion. Consequent to inadequate tissue blood flow, the metabolic demands of the intestine outstrip oxygen delivery, producing a colonic injury.

### *Chronic mesenteric ischaemia*

#### Clinical signs and symptoms

A review of 332 cases reported in the literature to 1997 (34) showed that 94% presented with abdominal pain, which was post-prandial in 88%. Most patients (78%) lost weight, while nausea or vomiting was present in 33%, diarrhoea was noted in 36% and constipation in 18%. The typical history is of a crampy pain in the upper abdomen that appears 10-15 minutes after eating. The pain steadily increases, plateaus and resolves during the next 1-2 hours. Patients become afraid to eat (sitophobia). Gastric involvement may present as multiple, small intractable ulcers and gastroparesis (35). Patients are usually in their 5th or 6th decade and there is a female predominance of 3:1 (36). Associated medical conditions include smoking (75%), peripheral vascular disease (55%), previous vascular surgery (52%), coronary artery disease (43%), hypertension (37%), chronic renal failure (20%) and diabetes (10%) (36). The examination of the abdomen is non-specific in most cases, although an epigastric bruit was present in 63% overall (34). Steatorrhoea and decreased D-xylose absorption, linked to non-specific abnormalities in small bowel biopsy samples, have been described (37).

#### Diagnosis

A high degree of clinical suspicion is required for the clinical triad of post-prandial upper abdominal pain, weight loss and an epigastric bruit. However, these findings together are often absent. Most diagnostic tests available demonstrate the anatomy of the blood vessels but not the functional significance of any stenosis. A definitive diagnosis requires symptom relief following a revascularisation procedure.

### *Colonic ischaemia*

Colonic ischaemia refers to a spectrum of disease ranging from reversible colopathy through transient colitis, gangrene and perforation, stricture formation and chronic colitis. Colonic ischaemia is estimated at 1 in 2000 acute hospital admissions [**3**], but is probably underdiagnosed (38). More than 90% of non-iatrogenic lesions occur in patients aged 70 or more. There had been only a small number of reports of treatment, but recently three studies with a combined total of 242 patients have been published (39-41). Korotinski *et al.* (42) grouped together these studies in order to better characterise the clinical picture, the diagnostic approach employed and the treatment.

#### Clinical presentation

The most important risk factors were hypertension in 139 (57.4%) patients, cardiovascular disease in 124 (51.2%), renal failure or nephropathy in 73 (30.2%) and diabetes mellitus in 45 (24.7%) patients. The mean age of the patients was 68.2 years and the gender distribution was similar : 123 (50.8%) were female and 119 (49.2%) were male.

Abdominal pain appeared in 77 of 113 (68.1%) patients and melaena or rectal bleeding was found in 124 (51.2%). Patients may have systemic signs : 20 of 129 (15.5%) had a temperature greater than 38.3°C and 22 of 129 (17.1%) had a systolic blood pressure less than 90 mmHg. The right colon was involved in 77 of 233 (33%), the transverse colon in 23 of 113 (20.4%), the splenic flexure in 33 of 129 (18.1%), the left colon in 110 of 233 (47.2%) and pancolitis in 30 of 233 (12.9%).

#### Diagnosis

The early diagnosis of colonic ischaemia depends on a high index of clinical suspicion and the use of repeat radiological or colonoscopic studies of the colon, which demonstrate either complete remission, segmental colitis or the presence of ulcers. Routine laboratory tests are unhelpful. For example, a leukocytosis was present in only 60 of 129 (46.5%) patients and a pH less than 7.34 in 15 of 129 (11.6%) patients (39). A stool culture

should be performed in order to check for infectious colitis including *Escherichia coli* O157:H7 (43).

Colonoscopy is the investigation of choice, enabling both direct visualisation of the mucosa and taking a biopsy (44). Few details were available regarding the diagnostic methods employed, but endoscopy was performed in a total of 166 (68.6%) patients, with no procedure-related complications.

Colonoscopy may show haemorrhagic nodules, representing submucosal bleeding, or the presence of a single linear ulcer running longitudinally (colonic single-stripe sign) mainly in the left side of the colon in mild ischaemic colitis (45). Barium enema may show 'thumbprinting' (submucosal bleeding) and pseudotumours. Over distension of the colon at both barium enema and colonoscopy may cause high intraluminal pressure which could exacerbate ischaemic damage (44).

Abdominal CT typically shows a non-specific thickening of the colonic wall. Sequential investigations together with clinical follow-up are necessary both to confirm the diagnosis and determine the outcome of colonic ischaemia. The submucosal haemorrhages are replaced with ulcerations over 48 hours and subsequently resolve. Alternatively, there may develop segmental universal colitis suggestive of Crohn's disease (46).

Since colonic blood flow usually returns to normal by the time of clinical presentation, mesenteric angiography is not indicated and was only performed in 14 (5.8%) of the above 242 patients. In one series of 60 patients, diagnostic angiography was not performed at all (40).

The key points of the review of Korotinski *et al.* (42) are presented in table 3.

## Polypharmacy and iatrogeous problems

Polypharmacy is one of the characteristics of the geriatric patients and a leading cause of "iatrogenous" disorders. We would like to stress in this review on one iatrogenous conditions encountered among geriatric units : side effects associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs).

The gastroduodenal and small-bowel complications of nonsteroidal anti-inflammatory drugs (NSAIDs) are well recognized (48-50). However, toxic effects of NSAIDs on the colon (NSAID colopathy) are described much less frequently. NSAID-induced ulceration of the caecum was first described in 1966 in a patient with rheumatoid arthritis taking phenbutazone (51), but it is only in the last decade that a limited number of reports have emerged describing NSAID colopathy (52-58). This effect of NSAIDs is often forgotten in the differential of, for example, iron-deficiency anaemia, positive faecal occult blood tests, change in bowel habit, and crampy lower-abdominal pain, possibly leading to unnecessary diagnostic tests. With the introduction of enteric-coated and slow-release preparations, it is possible that NSAID colopathy may become more apparent and with it the added importance of recognizing this condition (53-56,58).

NSAID colopathy may present with iron-deficiency anaemia, faecal occult blood-positive stools, crampy abdominal pain, weight loss or alteration in bowel habit (56,59,60-62). Pain is thought possibly to suggest the presence of an NSAID-induced colonic stricture (53). On occasions, there may be no symptoms or signs of NSAID-induced colonic inflammation, and lesions may be identified at colonoscopy for other indications (62).

Most patients have a history of long-term NSAID use, often for joint disease. Colonoscopic examinations reveal web-like diaphragms, more broad-based strictures, ulceration or simply inflamed mucosa (63-65).

Barium studies often miss the diagnosis as the ulcers are usually shallow and the diaphragms thin (54). A high index of clinical suspicion aids appropriate investigation. In the first patient described in this report, diaphragms were found in the right colon. These were web-like as opposed to the longer strictures that have also been described in the colon secondary to NSAID use (66,67). The first case of diaphragm-like strictures in the colon in a patient on long-term NSAIDs was described as recently as 1989 (53,55). Less than 30 cases of diaphragm-like strictures of the colon in those on long-term NSAIDs have been reported to date (68,69). Large bowel diaphragms are thought by some to be pathognomonic of NSAID-induced damage (63), and the lesions consist of well-circumscribed ulcers and ulceration at the margins of thin septal-like diaphragms with normal intervening mucosa unrecognizable from the serosal surface of the colon. These changes are almost always seen in the right colon extending to the transverse colon (54,68,70,71). The diaphragm-like strictures are the same as those that occur in small-bowel NSAID disease (54,70). However, well-circumscribed focal ulcers randomly interspersed in the right colon (as in the other three patients described in this report) or occasionally elsewhere in the colon are often the endoscopic appearance in NSAID colopathy, without diaphragms or strictures.

Histologically, there is well-defined focal ulceration, and any diaphragms consist of normal mucosa with

Table 3. — **Ischaemic diseases : Key points**

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| Atherosclerosis can affect the mesenteric vasculature. |
| There are two main chronic presentations : chronic mesenteric ischaemia (intestinal angina) and ischaemic colitis. |
| Chronic mesenteric ischaemia presents as post-prandial abdominal pain and can be diagnosed non-invasively by CT angiography. |
| Ischaemic colitis is spontaneously reversible in many cases. |
| Treatment of these conditions is by revascularisation, which may be via surgery or angioplasty. |

localized submucosal fibrosis (72). The collagen bundles in diaphragms are aligned towards the apex of the stricture. The margins of diaphragms often show shallow ulceration and the inflammatory changes seem to be secondary and nonspecific (59). Two cases where patients with diagnosed NSAID colopathy were followed with colonoscopy while continuing NSAIDs showed that the disease may begin as ulcer formation at the crest of the haustra. Continuing NSAID therapy may induce fibrotic changes in the submucosa, leading to diaphragm formation over a 2-year period (59). NSAIDs may exert their deleterious effects on the large bowel through both local and systemic actions. In support of a direct toxic effect is the apparent dominance of right-sided lesions, as with each of the four cases in the report of Byrne *et al.* (73).

Use of slow-release and in particular enteric-coated preparations allows a substantial delivery of NSAID to the right colon, with the caecum acting as a faecal reservoir (54,55,59). Indeed, pill-coated fragments from NSAID preparations have been found in histiocytes in ulcer granulation tissue in the right colon (54). On the other hand, systemic absorption and effects on colonic cyclo-oxygenase isoforms may reduce the production of protective prostaglandins and promote inflammation. This is supported by ulceration of the small bowel in animals that have been given NSAIDs subcutaneously (74), and by the diaphragms in the right colon associated with use of indomethacin suppositories (75).

If there is a question of NSAID colopathy, then other causes that may give a similar endoscopic and/or histological appearance should be excluded. These include enteric infection, ischaemia and idiopathic inflammatory bowel disease (IBD) (54). It should be remembered that NSAIDs may also exacerbate pre-existing colonic disease. For example, patients with diverticular disease are more likely to have complications if taking NSAIDs (76). NSAIDs may increase the relapse rate in patients with IBD (77,78), and it has also been suggested that NSAID use may act as a trigger for development of collagenous colitis (79).

The management of NSAID colopathy involves discontinuation of the offending NSAID(s). Resolution of symptoms, usually within a few days, lends support to the diagnosis. The inflammatory changes also usually regress within a few days (54,59). The fibrosis associated with diaphragms and strictures is, however, irreversible. Endoscopic balloon dilation, or even surgery, may be necessary in some cases (80). It is interesting that the patient with large-bowel diaphragms described here improved markedly soon after discontinuing NSAIDs, as the diaphragms would have persisted. However, her symptoms may have been related more to the associated acute inflammatory changes. Long-term use of NSAIDs is common in elderly people, in particular for relief of degenerative joint disease. NSAID-induced colonic inflammatory changes as described in this series constitute a clinically significant disease. Increasing use of sustained-release preparations may increase the frequency of NSAID colopathy. Recognition of the symptoms and signs of NSAID-induced colopathy by careful history and recognizing the endoscopic and histological features should allow appropriate diagnosis, withdrawal of the offending NSAID, and avoidance of the necessity for further investigations, or even surgery, in the majority of patients. In those patients unable to stop NSAID use, co-prescription of misoprostol (a prostaglandin E1 derivative), sulfasalazine or metronidazole may possibly protect against mucosal damage or promote healing of ulceration and constitutes a compromise (67,81,82). Use of selective inhibitors of cyclo-oxygenase 2 may lead to less toxic effects on the colon, but conclusive data are awaited. The increasing number of reports of NSAID-related colonic problems suggests that NSAID colopathy may be underdiagnosed and should enter the differential diagnosis for symptoms and signs attributable to the colon.

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