

INFLAMMATORY BOWEL DISEASE IN THE ELDERLY

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Ulcerative colitis (UC) and Crohn's disease (CD) are collectively termed inflammatory bowel disease (IBD). Both are generally considered diseases that strike young adults. However, IBD makes its first presentation after age 60 in a significant number of cases (approximately 12% in UC and 16% in CD). With the proportion of elderly in the population rising, both the number of individuals carrying IBD into later life, and the number of individuals presenting with late-onset IBD, will increase. Making the diagnosis of IBD in older individuals can be a very difficult task because of the long list of diseases that may mimic or obscure IBD. The three main differential diagnoses of IBD in an older adult are infectious enterocolitis, ischemic colitis and diverticular disease. The principles of medical and surgical management of IBD in the elderly are essentially the same as in younger adults. However, clinicians must be vigilant in monitoring drug interactions and complications when treating older individuals with IBD. Patients with IBD are at increased risk of developing osteopenia and osteoporosis. Since the complications of cortical bone loss can drastically reduce quality of life, clinicians should pay special attention to preventing the development or worsening of osteoporosis in elderly patients with IBD.

Key words: Ulcerative colitis, Crohn's disease, aged

Inflammatory bowel disease (IBD) refers to ulcerative colitis (UC) and Crohn's Disease (CD). UC is a chronic and recurrent illness characterized by inflammation and ulceration of the mucosal layer of the colon beginning in the rectum and extending proximally. Rectal bleeding and diarrhea are the most common presenting symptoms. CD also has a chronic and recurrent course. However, this disease is characterized by focal, transmural inflammation occurring anywhere along the GI tract from mouth to anus (80% of patients have terminal ileum and ileocecal involvement¹). The transmural inflammation predisposes to complications such as inflammatory masses, strictures, abscesses and fistulae.

Presenting symptoms often vary according to location of the disease; however, crampy abdominal pain, diarrhea, perianal disease, weight loss and fever are common. In addition, individuals with UC and CD are predisposed to developing various asso-

ciated extraintestinal manifestations (Table 1).

IBD is considered a disease primarily of young adults; however, IBD can make its first presentation in the elderly. The term "late-onset" in the IBD literature usually refers to patients over the age of 60 or 65, although some series include individuals as young as 50. Individuals diagnosed with IBD at an earlier age carry the disease burden into later life.² As the proportion of elderly in Canada rises, the diagnosis and management of IBD in the elderly is increasingly important. Of particular concern is the ability to differentiate late-onset IBD from other more common gastrointestinal disorders, in order to facilitate prompt diagnosis and early medical management. This article reviews the epidemiology, presentation, differential diagnosis and management of IBD in the elderly.

EPIDEMIOLOGY

From the most recent Canadian population-based study, the incidence of CD is 14.3/100,000 and the prevalence is 198.5/100,000.³ The incidence of UC is 14.6/100,000 and the prevalence is 169.7/100,000.³ A review of the epidemiologic surveys by Grimm and Friedman⁴ showed that the proportion of patients who develop UC after the age of 60 is 12% (range 8%-20%), while the proportion of patients who develop CD after the age of 60 is 16%

Table 1. Extra-Intestinal Manifestations of IBD

| | |
|-----------|--|
| Cutaneous | erythema nodosum, pyoderma gangrenosum, erythema multiforme |
| Articular | ankylosing spondylitis, arthralgias, seronegative arthritis |
| Ocular | uveitis, iritis |
| Hepatic | fatty liver, granulomatous hepatitis |
| Biliary | cholelithiasis, primary sclerosing cholangitis, cholangiocarcinoma |
| Oral | aphthous ulcers and stomatitis |
| Urinary | calculi (both uric acid and oxalate) |
| Vascular | hypercoagulable state, spontaneous thromboses |

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(range 7%-26%).⁴ The majority of IBD epidemiologic studies, but not all,⁵⁻⁷ have found a bimodal distribution in the age of onset. This bimodality was originally dismissed as an artifact because of misclassification of diseases that can mimic IBD, particularly ischemic colitis.⁸ However, since the description of ischemic colitis in 1963, epidemiologic studies have diligently excluded such cases and the bimodal distribution persists. The first mode consistently occurs in the 20's, whereas the second mode varies between the ages of 50 and 80.⁹⁻¹⁶ Various theories have been suggested to account for this phenomenon, including one suggesting two types of UC,¹⁷ but the reason for the age distribution remains uncertain. Many studies have also found incidence rates, in late-onset IBD, to vary according to gender. A pooling of data on late-onset CD revealed the female:male ratio to be 1.8:1.0.¹⁸ In contrast, the majority of studies have reported a higher incidence of late-onset UC in males compared to females.^{9,16,19,20}

PRESENTATION

Crohn's Disease

The presentation of CD in the elderly is generally similar to that of younger patients.²¹ As well, the laboratory abnormalities of anemia, leukocytosis, and hypoalbuminemia are equally present in late-onset CD.^{22,23} Extraintestinal manifestations also occur with similar frequency in both early and late-onset disease.^{23,24} However, researchers have observed several unique qualities in late-onset CD. Abdominal pain and cramps may occur less frequently in the elderly.²⁵ Others have noted an increased frequency of rectal bleeding in late-onset CD.²⁶ A predilection for colonic distribution of disease in the elderly may account for this finding.¹ Pooled data from 450 patients with late-onset CD showed the anatomical distribution of disease to be 59% colonic, 26% small intestinal and 15% ileo-colonic,¹⁸ whereas the observed distribution in younger patients is approximately 15% colonic, 30% small intestinal and 55% ileo-colonic.²⁷

Ulcerative Colitis

The presenting symptoms in late-onset UC, as in CD, generally do not differ greatly from those with earlier onset disease. Bloody diarrhea is the main feature of UC in both older and younger patients.²⁸

However, Zimmerman et al²⁹ observed that non-bloody diarrhea was significantly more common as a presenting symptom in late-onset UC. As well, liver enzyme abnormalities (slight elevations of AST, ALT, ALP and GGT) and anemia were observed more frequently.²⁹ The spectrum of extraintestinal manifestations can occur in late-onset UC, although cutaneous lesions and oral aphthous ulcers have been observed less frequently.³⁰ The extent of disease at the age of presentation is an area of controversy. Some studies report a tendency toward more distal left-sided colitis in the late-onset groups.^{24,29,31,32} However, a large population-based study found the extent of disease at presentation to be virtually identical in early and late-onset UC.³³ The initial presentation of UC in the elderly appears to be more severe (> 6 bowel movements per day, fever, tachycardia, anemia) than those presenting with UC at a younger age.³⁴ Consequently, the elderly are twice as likely to require hospitalization for an initial attack of UC.³⁵ Also, the duration of remission after the first episode has been observed to be shorter in late-onset UC²⁹ (Figures 1 and 2).

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosing IBD can be quite challenging. Indeed, there can be long delays from the onset of symptoms until the correct diagnosis is made.³⁶ In the elderly, the delay until a correct diagnosis is made can be even more pronounced than in younger adults presenting with similar symptoms.^{25,37} In addition, the physical signs in the elderly may be atypical due to altered sensory perception, particularly a blunted response to pain, polypharmacy or a coexisting systemic disease.³⁸ The approach to patients presenting with symptoms suggesting IBD are shown in Table 2. In order to reduce the delay in diagnosis in late-onset IBD, it is essential to exclude illnesses that cause similar symptoms, physical findings and laboratory abnormalities. The principal differential diagnoses of IBD in the elderly will be discussed here. A full discussion of all the possible disease entities is beyond the scope of this article. Table 3 contains a comprehensive list of the conditions that may mimic late-onset IBD.

The main diagnostic alternatives to late-onset IBD are infectious enterocolitis, ischemic colitis and diverticular disease.

Infectious enterocolitis is common in the elderly

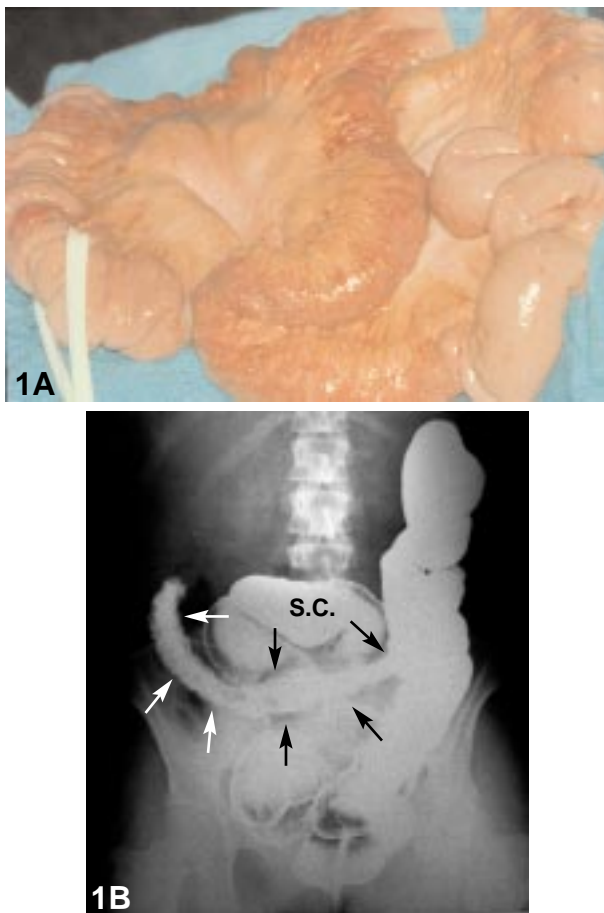


Figure 1. Crohn's Disease. A. View of CD enteritis at surgery, showing areas of narrowing, creeping subserosal fat, and enlarged mesenteric nodes. B. Barium enema shows CD involving transverse colon segmentally. There is a redundant normal sigmoid colon (S.C.).



Figure 2. Ulcerative Colitis. A. Air-contrast barium enema in an emaciated patient with frequent mucopurulent stools. Serrated border represents ulcerations (arrows). Loss of haustra, shortening and some narrowing of colon are typical of UC. B. Edematous, inflamed mucosa (pseudopolyps) between chronic ulcers.

and should be considered first in a patient with an acute diarrheal episode with or without hematochezia.⁴ A frequent cause is pseudomembranous colitis associated with the *Clostridium difficile* toxin.³⁹ This condition is often suspected after recent antibiotic use,²⁸ but nosocomial and long-term care facility outbreaks are common, thus making it an important consideration in the elderly.⁴⁰ The elderly are also at increased risk for developing *E. Coli* 0157:H7 colitis⁴ which may mimic IBD with symptoms of severe abdominal cramping and tenderness, bloody diarrhea, fever and leukocytosis. The risk of developing hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP) and even death, associated with *E. Coli* 0157:H7 infection, is higher in older individuals.²⁸

Ischemic colitis is another principal diagnostic alternative to late-onset IBD. Colonic ischemia must be considered in an elderly individual present-

ing with acute abdominal pain and bloody diarrhea.²¹ Features of ischemic colitis that may mimic IBD include segmental foci of inflammation with rectal sparing during the ischemic episode and the development of pseudopolyps, ulcers and strictures upon resolution of the ischemia.^{1,21} Ischemic colitis may occur in the absence of any predisposing condition. Clinical suspicion is raised with the presence of congestive heart failure, cardiac arrhythmias, atherosclerotic disease, embolic disease, vasculitis and diabetes mellitus.²⁸ Features that differentiate ischemic colitis from UC or Crohn's colitis include involvement of the classic "watershed areas" on barium enema (splenic flexure and the junction of the sigmoid and rectum),⁴¹ endoscopic visualization of the typical appearance of ischemia, and evidence of ischemia in other arterial beds.^{21,40}

Diverticular disease of the colon is the third principal diagnostic alternative to late-onset IBD.

Table 2. Approach to the Patient Suspected of Having IBD

| Ulcerative Colitis | Crohn's Disease |
|--|--|
| History and physical exam | History and physical exam |
| CBC (incl. serum iron, TIBC)* | CBC (incl. serum iron, TIBC, serum B12)* |
| Colonoscopy | Barium Enema or colonoscopy (if colitis is suspected) |
| Stool Culture for enteric pathogens (incl. Salmonella, Shigella, Campylobacter, Yersinia, E. Coli 0157:H7) | Small Bowel Follow Through |
| Stool Exam for C. difficile toxin, ova and parasites | Abdominal and Pelvic Ultrasound |
| | Stool Culture for enteric pathogens (incl. Salmonella, Shigella, Campylobacter, Yersinia, E. Coli 0157:H7) |
| | Stool Exam for C. difficile toxin, ova and parasites |

*Serum ferritin is an acute phase reactant and it is often misleadingly elevated in patients with IBD.

Diverticulosis in the elderly is extremely common, with 35 to 60% of those over age 60 affected.^{42,43} Complications of diverticulosis include diverticulitis, hemorrhage, fistula formation and obstruction.²⁸ The presenting symptoms of diverticulitis (fever, palpable mass, abdominal pain) may mimic those of CD, and misdiagnosis of diverticulitis in the setting of late-onset CD is frequent.^{44,45} Many series have reported high rates of concomitant diverticulosis in late-onset IBD,⁴⁶⁻⁴⁸ further complicating an already challenging clinical situation. The acute onset of diverticulitis compared with the more frequently indolent onset of CD can aid in differentiating the two diseases.⁴ In addition, the presence of perianal disease and atypical fistulae (perineal, rectovaginal, flank and thigh) favour the diagnosis of CD or CD with co-existing diverticulitis.^{4,49}

Table 3. Differential Diagnosis of Late-Onset IBD

| |
|--|
| Infectious Enterocolitis (Salmonella, Shigella, Campylobacter, Yersinia, Clostridium difficile, E. coli 0157:H7) |
| Ischemic colitis |
| Diverticular disease (incl. diverticulitis, chronic segmental colitis ⁶⁷) |
| Microscopic colitis (Collagenous ⁶⁸ and Lymphocytic colitis ⁶⁸) |
| Intestinal lymphoma ²¹ |
| Ileocecal carcinoma ²¹ |
| Radiation enterocolitis ²¹ |
| Carcinoid tumours ²¹ |
| Vasculitis ²¹ |
| Amyloidosis ²¹ |
| Drug-induced colitis (NSAIDs, gold compounds, 5-fluorouracil, methyldopa, penicillamine, isotretinoin, ticlopidine) ^{21,69} |

MANAGEMENT

Medical

The principles of treating UC and CD are broadly the same irrespective of age.⁵⁰ However, an awareness of co-morbid illnesses and polypharmacy are of paramount importance when treating IBD in later life. Mild flare-ups are generally treated with oral aminosalicylates (sulfasalazine or 5-ASA) or rectal preparations of corticosteroid and/or 5-ASA (Table 4). More severe flares are generally treated with oral or parenteral glucocorticoids and occasionally antibiotics (ciprofloxacin and metronidazole). Aminosalicylates are also used in maintaining remission.²¹ Immune system modulators such as 6-mercaptopurine (6-MP), azathioprine and infliximab are used when individuals become refractory to steroids, require long-term steroids or are intolerant of steroid side-effects. Use of these medications must be monitored carefully for serious side-effects, such as bone marrow suppression, diminished cellular immunity, and pancreatitis.¹

Sulfasalazine and 5-ASA compounds are as effective and equally tolerated in older individuals.^{1,28} However, sulfasalazine may interfere with the bioavailability of digoxin.⁵¹ 5-ASA is used in a suppository or enema form for more distal disease. Care must be taken when prescribing enema preparations of any kind in the elderly, as difficulties in self-administering and retaining the product can be encountered.²⁸ Prescribing suppositories first is worthwhile because they are better tolerated and equally as effective.

The use of glucocorticoids in the elderly warrants particular concern. Older individuals are more susceptible to complications caused by glucocorticoids, such as osteoporosis, hyperglycemia, hypertension, increased intraocular pressure and congestive heart failure.⁵² Glucocorticoid treatment must

Table 4. Drugs Used in the Treatment of IBD

| Generic name | Trade names |
|-----------------------------|--|
| 5-Aminosalicylic acid | Asacol, Mesasal, Pentasa, Quintasa, Salofalk |
| 6-Mercaptopurine | Purinethol |
| Azathioprine | Imuran |
| Budesonide | Entocort |
| Ciprofloxacin hydrochloride | Cipro |
| Hydrocortisone foam | Cortifoam |
| Infliximab | Remicade |
| Metronidazole | Flagyl |
| Sulfasalazine | Salazopyrin |

be monitored with vigilance, because many older individuals will have pre-existing conditions that are susceptible to exacerbation (e.g. diabetes, hypertension, glaucoma, osteoporosis). In a study of steroid side-effects in elderly IBD patients, hypertension, hypokalemia and mental status changes were more likely to occur.⁵³ Despite these complications, glucocorticoid treatment is often required and short-term therapy is usually well-tolerated.⁴⁰ Steroid-induced osteoporosis is of particular concern, because older age alone is a risk factor.²¹ In addition, individuals with IBD, particularly CD, are at increased risk of developing osteopenia, osteoporosis and resulting fractures, presumably due to the inflammatory process itself.⁵⁴ Therefore, baseline or early bone density measurement in all patients upon diagnosis is recommended.²¹ Postmenopausal women with IBD are at the greatest risk for cortical bone loss,⁵⁵ so hormone replacement therapy along with calcium and vitamin D supplementation should be considered.⁵⁶ Similarly, supplementation with calcium and vitamin D should be used as prophylaxis during glucocorticoid treatment in all patients.⁵⁷ If glucocorticoids must be used for a prolonged period, prophylaxis with a bisphosphonate (eg. Actonel[®])⁵⁸ or transition to an immune modulating medication²¹ should also be considered. In the setting of left-sided or distal colitis, hydrocortisone foam is an excellent alternative to oral glucocorticoids. With only 40% of each dose absorbed, side-effects are minimal.

Studies of the immune modulators 6-MP and azathioprine have not shown any increased adverse effects in the elderly.^{59,60} However, older patients with gout who are being treated with allopurinol require close monitoring, because allopurinol inhibits the metabolism of 6-MP and azathioprine which may lead to higher drug levels and leukopenia.²¹ In addition, older patients on warfarin require closer monitoring of the INR when taking 6-MP or azathioprine, because these drugs have been shown to diminish the response to warfarin.²⁴ Metronidazole, an antibiotic used in the treatment of CD, also interferes with warfarin oxidation, thus requiring vigilant INR monitoring.¹⁸ Infliximab is a chimeric monoclonal antibody directed against TNF- α . It is one of the newest immune modulating medications in the treatment of IBD. Studies that have included older subjects have not shown any difference in efficacy or safety compared with younger subjects.⁶¹

Patients with long-standing UC or CD of the colon are at increased risk of developing colorectal carcinoma. The most important risk factors are the extent and duration of disease.⁶² Thus, individuals with early-onset colitis of both types are at increased risk of developing colorectal carcinoma as they get older. IBD patients with a family history of colon cancer may be at even greater risk.⁶³ Guidelines for screening UC patients suggest beginning surveillance colonoscopy after 8 years of pancolitis and after 12 years of left-sided colitis.²¹ Guidelines for Crohn's colitis are still in evolution. Data suggest that folic acid supplementation can reduce the risk of colorectal cancer,⁶⁴ so that individuals with UC who are at increased risk should receive 0.4-0.6 mg supplementation daily.

Surgical

When UC or CD become refractory to medical management, surgical resection becomes the next course of action. Surgery should not be thought of as a last resort. Sometimes it is the best choice for a particular problem; sometimes it is the only choice. Generally, with careful attention to concomitant illnesses, surgery in the elderly does not confer an increased risk of adverse outcomes.⁴⁰ When comparing an older and younger cohort of surgical CD patients, the older cohort had more cardiac and respiratory complications.⁶⁵ However, no differences in operative mortality or anastomotic leaks were found.⁶⁵ In UC patients and patients with extensive Crohn's colitis who require surgery, a near total proctocolectomy is performed. An ileal-pouch anal anastomosis is frequently offered to younger UC patients who require a proctocolectomy. However, this procedure is rarely offered to older individuals because of increased risk of fecal incontinence from decreased anal sphincter tone^{7,66} and the increased likelihood of developing post-surgical erectile dysfunction.⁶⁶ The preferred procedure in older individuals requiring surgery is a proctocolectomy with an end ileostomy.²⁸

SUMMARY

Approximately 15% of patients with IBD will have late-onset disease.²¹ As the medical and surgical management of IBD continues to improve and as the proportion of elderly in the population continues to rise, clinicians should expect to see a larger

number of elderly IBD patients. More recent studies suggest that the prognosis of late-onset IBD is slightly better than that of earlier onset IBD.^{22-24,34} However, arriving at the correct diagnosis in an older individual who presents symptoms of enteritis and/or colitis is often challenging. Clinicians must be aware of the broad differential diagnosis of late-onset IBD, particularly infectious colitis, ischemic colitis and diverticular disease, to avoid long delays in diagnosis and institution of treatment. The medical and surgical management of IBD in the elderly is the same regardless of age. Pharmacologic treatment in the elderly should be instituted with careful attention to co-morbid illnesses and issues of polypharmacy. Older individuals with IBD are at increased risk for osteoporosis because of several factors, and should be managed aggressively to prevent complications of bone loss.

REFERENCES

- Lashner BA, Kirsner JB. Inflammatory bowel disease in older people. *Clin Geriatr Med* 1991; 7: 287-99.
- Irvine EJ, Farrokhyar F, Swarbrick ET. A critical review of epidemiological studies in inflammatory bowel disease. *Scand J Gastroenterol* 2001; 36: 2-15.
- Bernstein CN, Blanchard JF, Rawsthorne P et al. Epidemiology of Crohn's disease and ulcerative colitis in a central Canadian province: A population based study. *Am J Epidemiol* 1999; 149: 916-24.
- Grimm IS, Friedman LS. Inflammatory bowel disease in the elderly. *Gastroenterol Clin North Am* 1990; 19: 361-89.
- Loftus EV Jr, Silverstein MD, Sandborn WJ et al. Crohn's disease in Olmstead county, Minnesota, 1940-1993: Incidence, prevalence and survival. *Gastroenterology* 1998; 114: 1161-8.
- Loftus EV Jr, Silverstein MD, Sandborn WJ et al. Ulcerative colitis in Olmstead county, Minnesota, 1940-1993: Incidence, prevalence and survival. *Gut* 2000; 46: 336-43.
- Pinchbeck BR, Kirdeikis J, Thomson ABR. Inflammatory bowel disease in northern Alberta: An epidemiologic study. *J Clin Gastroenterol* 1988; 10: 505-15.
- Shapiro PA, Peppercorn MA, Antonioli DA et al. Crohn's disease in the elderly. *Am J Gastroenterol* 1981; 76: 132-7.
- Ekbom A, Helmick CG, Zack M et al. The epidemiology of inflammatory bowel disease: A large population-based study in Sweden. *Gastroenterology* 1991; 100: 350-8.
- Kyle J. Crohn's disease in the northeastern and northern isles of Scotland: An epidemiological review. *Gastroenterology* 1992; 103: 392-9.
- Lapidus A, Bernell O, Heller G et al. Incidence of Crohn's disease in Stockholm county 1955-1989. *Gut* 1997; 41: 480-6.
- Rose JD, Roberts GM, Williams G et al. Cardiff Crohn's disease jubilee: The incidence over 50 years. *Gut* 1988; 29: 346-51.
- Bjornsson S. Inflammatory bowel disease in Iceland during a thirty-year period, 1950-1979. *Scand J Gastroenterol* 1989; 24 (Suppl 170): 47-55.
- Haug K, Schrupf E, Barstad S. Epidemiology of ulcerative colitis in western Norway. *Scand J Gastroenterol* 1988; 23: 517-22.
- Srivastava ED, Mayberry JF, Morris TJ et al. Incidence of ulcerative colitis in Cardiff over 20 years: 1968-87. *Gut* 1992; 33: 256-8.
- Riley R. Crohn's disease and ulcerative colitis: morbidity and mortality. *Health Rep* 1990; 2: 343-59.
- Burch PR, de Dombal FT, Watkinson G. Aetiology of ulcerative colitis. II. A new hypothesis. *Gut* 1969; 10: 277-84.
- Kadish SL, Brandt LJ. Inflammatory bowel disease in the elderly. In: 4th Edn, eds. *Inflammatory Bowel Disease ed. 4* (eds Kirsner JB, Shorter RG). Baltimore: Williams and Wilkins 1995.
- Langholz E, Munkholm P, Nielsen OH et al. Incidence and prevalence of ulcerative colitis in Copenhagen county from 1962 to 1987. *Scand J Gastroenterol* 1991; 26: 1247-56.
- Vucelic B, Korac B, Sentic M et al. Ulcerative colitis in Zagreb, Yugoslavia: incidence and prevalence 1980-1989. *Int J Epidemiol* 1991; 20: 1043-7.
- Robertson DJ, Grimm IS. Inflammatory bowel disease in the elderly. *Gastroenterol Clin North Am* 2001; 30: 409-26.
- Harper PC, McAuliffe TL, Beeken WL. Crohn's disease in the elderly. A statistical comparison with younger patients matched for sex and duration of disease. *Arch Intern Med* 1986; 146: 753-5.
- Stalniewicz R, Eliakim R, Diab R et al. Crohn's disease in the elderly. *J Clin Gastroenterol* 1989; 11: 411-5.
- Softley A, Myren J, Clamp SE et al. Inflammatory bowel disease in the elderly patient. *Scand J Gastroenterol* 1988; 23 (Suppl 144): 27-30.
- Wagtmans MJ, Verspaget HW, Lamers CB et al. Crohn's disease in the elderly: a comparison with young adults. *J Clin Gastroenterol* 1998; 27: 129-33.
- Walker MA, Pennington CR, Pringle R. Crohn's disease in the elderly. *Br Med J* 1985; 291: 1725-6.
- Mekhjian HS, Switz DM, Melnyk CS et al. Clinical features and natural history of Crohn's disease. *Gastroenterology* 1979; 77: 898-906.
- Fleischer DE, Grimm IS, Friedman LS. Inflammatory bowel disease in older patients. *Med Clin North Am* 1994; 78: 1303-19.
- Zimmerman J, Gavish D, Rachmilewitz D. Early and late onset ulcerative colitis: distinct clinical features. *J Clin Gastroenterol* 1985; 7: 492-8.
- Brandt LJ, Boley SJ, Mitsudo S. Clinical characteristics and natural history of colitis in the elderly. *Am J Gastroenterol* 1982; 77: 382-6.
- Riegler G, Tartaglione MT, Carratu R et al. Age-related clinical severity at diagnosis in 1705 patients with ulcerative colitis: a study by GISC (Italian Colon-Rectum Study Group). *Dig Dis Sci* 2000; 45: 462-5.
- Stonnington CM, Phillips SF, Melton LJ 3rd et al. Chronic ulcerative colitis: incidence and prevalence in a community. *Gut* 1987; 28: 402-9.
- Ekbom A, Helmick C, Zack M et al. Ulcerative colitis and colorectal cancer. A population-based study. *N Engl J Med* 1990; 323: 1228-33.
- Sinclair TS, Brunt PW, Mowat NA. Nonspecific proctocolitis in northeastern Scotland: a community study. *Gastroenterology* 1983; 85: 1-11.
- Jones HW, Hoare AM. Does ulcerative colitis behave differently in the elderly? *Age Ageing* 1988; 17: 410-4.
- Vermeire S, Peeters M, Rutgeerts P. Diagnostic approach to IBD. *Hepatogastroenterology* 2000; 47: 44-8.
- Foxworthy DM, Wilson JA. Crohn's disease in the elderly. Prolonged delay in diagnosis. *J Am Geriatr Soc* 1985; 33: 492-5.
- Holt PR. General perspectives on the aged gut. *Clin Geriatr Med* 1991; 7: 185-9.
- Jones EM, MacGowan AP. Back to basics in management of *Clostridium difficile* infections. *Lancet* 1998; 352: 505-6.
- Lindner AE. Inflammatory bowel disease in the elderly. *Clin Geriatr Med* 1999; 15: 487-97.
- Greenwald DA. Ischemic bowel disease in the elderly. *Gastroenterol Clin North Am* 2001; 30: 445-73.

42. Manousos ON, Truelove SC, Lumsden K. Prevalence of colonic diverticulosis in general population of Oxford area. *Br Med J* 1967; 3: 762-3.
43. Hughes LE. Postmortem survey of diverticular disease of the colon. II. The muscular abnormality of the sigmoid colon. *Gut* 1969; 10: 344-51.
44. Stampfl DA, Friedman LS. Collagenous colitis: pathophysiologic considerations. *Dig Dis Sci* 1991; 36: 705-11.
45. Tchirkow G, Lavery IC, Fazio VW. Crohn's disease in the elderly. *Dis Colon Rectum* 1983; 26: 177-81.
46. Fabricius PJ, Gyde SN, Shouler P et al. Crohn's disease in the elderly. *Gut* 1985; 26: 461-5.
47. Gupta S, Saverymuttu SH, Keshavarzian A et al. Is the pattern of inflammatory bowel disease different in the elderly? *Age Ageing* 1985; 14: 366-70.
48. Lee FI, Giaffer M. Crohn's disease of late onset in Blackpool. *Postgrad Med J* 1987; 63: 471-3.
49. Berman IR, Corman ML, Collier JA et al. Late onset Crohn's disease in patients with colonic diverticulitis. *Dis Colon Rectum* 1979; 22: 524-9.
50. Akerkar GA, Peppercorn MA. Inflammatory bowel disease in the elderly. Practical treatment guidelines. *Drugs Aging* 1997; 10: 199-208.
51. Holt PR. Gastrointestinal drugs in the elderly. *Am J Gastroenterol* 1986; 81: 403-11.
52. Thomas TP. The complications of systemic corticosteroid therapy in the elderly. A retrospective study. *Gerontology* 1984; 30: 60-5.
53. Akerkar GA, Peppercorn MA, Hamel MB et al. Corticosteroid-associated complications in elderly Crohn's disease patients. *Am J Gastroenterol* 1997; 92: 461-4.
54. Valentine JF, Sninsky CA. Prevention and treatment of osteoporosis in patients with inflammatory bowel disease. *Am J Gastroenterol* 1999; 94: 878-83.
55. Clements D, Motley RJ, Evans WD et al. Longitudinal study of cortical bone loss in patients with inflammatory bowel disease. *Scand J Gastroenterol* 1992; 27: 1055-60.
56. Clements D, Compston JE, Evans WD et al. Hormone replacement therapy prevents bone loss in patients with inflammatory bowel disease. *Gut* 1993; 34: 1543-6.
57. American College of Rheumatology Task Force: Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. American College of Rheumatology Task Force on Osteoporosis Guidelines. *Arthritis Rheum* 1996; 39: 1791-801.
58. Wallach S, Cohen S, Reid DM et al. Effects of risedronate treatment on bone density and vertebral fracture in patients on corticosteroid therapy. *Calcif Tissue Int* 2000; 67: 277-85.
59. O'Brien JJ, Bayless TM, Bayless JA. Use of azathioprine or 6-mercaptopurine in the treatment of Crohn's disease. *Gastroenterology* 1991; 101: 39-46.
60. Present DH, Meltzer SJ, Krumholz MP et al. 6-Mercaptopurine in the management of inflammatory bowel disease: short- and long-term toxicity. *Ann Intern Med* 1989; 111: 641-9.
61. Maini R, St Clair EW, Breedveld F et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. *Lancet* 1999; 354: 1932-9.
62. Sugita A, Sachar DB, Bodian C et al. Colorectal cancer in ulcerative colitis. Influence of anatomical extent and age at onset on colitis-cancer interval. *Gut* 1991; 32: 167-9.
63. Winawer SJ. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology* 1997; 112: 594-642.
64. Willett WC. Diet and cancer: one view at the start of the millennium. *Cancer Epidemiol Biomarkers Prev* 2001; 10: 3-8.
65. Norris B, Solomon MJ, Evers AA et al. Abdominal surgery in the older Crohn's population. *Aust N Z J Surg* 1999; 69: 199-204.
66. Mate-Jimenez J, Munoz S, Vicent D et al. Incidence and prevalence of ulcerative colitis and Crohn's disease in urban and rural areas of Spain from 1981 to 1988. *J Clin Gastroenterol* 1994; 18: 27-31.
67. Peppercorn MA. Drug-responsive chronic segmental colitis associated with diverticula: a clinical syndrome in the elderly. *Am J Gastroenterol* 1992; 87: 609-12.
68. Giardiello FM, Lazenby AJ. The atypical colitides. *Gastroenterol Clin North Am* 1999; 28: 479-90.
69. Grimm IS, Friedman LS. Colitis in the elderly. In: Bittar EE, Bittar N, eds. *Principles of Medical Biology*. Greenwich: JAI Press 1994.