

Interdisciplinary Topics in Gerontology

Editors: P.R. Hof, C.V. Mobbs

Vol. 32

# Aging and the Gastrointestinal Tract

Editors

**A. Pilotto**

**P. Malfertheiner**

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## **Aging and the Gastrointestinal Tract**

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# Interdisciplinary Topics in Gerontology

## Vol. 32

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# Aging and the Gastrointestinal Tract

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## **Preface**

With the dramatic increase in the aging population, the study and care of gastrointestinal disorders in the elderly have become priority topics for both clinicians and researchers.

Little attention was focused on the gastrointestinal tract of the elderly until very recently. In the last few years, however, the medical literature has provided more studies on the changes that occur in gastrointestinal physiology as a function of advanced age, as well as on gastrointestinal diseases associated with aging.

The aim of this book is to assemble in one place the results of the more recent studies in geriatric gastroenterology and to review both basic research and clinical aspects of this field. The book explores selected subjects of wide interest. The geriatric approach to gastrointestinal disorders includes the epidemiology of gastrointestinal disorders in the elderly and the effect of aging on the pharmacokinetics of gastrointestinal drugs, as well as a comprehensive clinical assessment of older patients with gastrointestinal disorders. A comprehensive multidimensional assessment is particularly important in managing older patients with chronic and disabling illnesses, such as gastrointestinal disorders, since these patients are likely to have multiple interacting problems that interfere with their daily function and complicate their treatment. For example, an older patient who presents with a common gastrointestinal problem such as peptic ulcer or chronic diarrhea typically has a multitude of other age-related disorders that can complicate diagnostic and therapeutic options. These clinical situations are particularly suited to a comprehensive geriatric assessment approach.

The effect of aging upon the physiology of the gastrointestinal tract is a crucial area for geriatric gastroenterology. Since the elderly patient may present with particularly unique variables, such as altered visceral function, which can impact profoundly on the presentation, diagnosis and treatment of disease, a deeper understanding of these variables is critical in order to provide optimal diagnostic modalities and design specific treatment care plans for elderly individuals. A section of the book is devoted to closely examining the structural and functional effects of aging on the physiology of the esophagus and stomach, small intestine and colon, liver and pancreas, focusing on distinctive features as they relate to pathophysiology as well as diagnostic and treatment modalities that are particularly relevant to the elderly population.

A significant component of this book is devoted to identifying the physician's clinical approach to the elderly with gastroenterological problems. Recent advances in diagnostic tools and treatments of elderly patients with dysphagia and gastroesophageal reflux disease, as well as with nonsteroidal antiinflammatory drug-related or *Helicobacter pylori*-associated gastroduodenal diseases, are reported in updated chapters. Moreover, the physician's approach to the management of disorders of the small intestine, colon, pancreas and liver is discussed, highlighting the specific aspects of such disorders in old age. Colon cancer, the scourge of the aged as a cause of gastrointestinal-related deaths in the older patient, is discussed in depth.

Diagnostic testing becomes very important in the elderly since clinical features such as history and physical signs are frequently most difficult to interpret in older individuals. There is no evidence that the risk of performing invasive diagnostic tests such as endoscopy of the upper or lower gastrointestinal tract is greater in the elderly than in the young. Clearly both the course and the therapy of a disease may be altered in an older individual. Indeed, very frequently, clinical manifestations and the response to therapy may appear to differ because the older patient has several concomitant disorders that may distort the classic features of the primary gastrointestinal disease. Due to these multidimensional aspects of the elderly subject, the process of geriatric assessment often requires the involvement of a multidisciplinary team with experienced specialists as well as primary care physicians and/or community health workers focused on identifying functional problems and disabilities of older persons.

We hope that this book will be useful for general physicians, specialists in geriatrics and gastroenterology and all health care providers who are involved in planning the care and management of elderly people with gastrointestinal disorders.

*Alberto Pilotto*  
*Peter R. Holt*  
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## **Epidemiology of Gastrointestinal Disorders in the Elderly**

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### **Introduction**

With the marked increase in the population aged 65 years and over, the study and care of gastrointestinal disorders should be a high priority for both clinicians and researchers.

Over the years, geriatricians and gastroenterologists have speculated that the functioning of the gastrointestinal tract may decline with aging. It was thought that the efficiency of digestion and absorption declines with aging. Once this hypothesis was rigorously tested, however, it was found not to be true [1].

Gastrointestinal diseases are frequent in older patients and their presentation, complications and treatment may be different from those in younger patients. Oesophagus-stomach and colon-rectum disorders have higher prevalence rates than small intestine, liver and pancreas disorders, although few studies have been carried out in the general population [2].

The aim of this review is to summarize recent data and the current thinking of clinicians and researchers on the epidemiology of gastrointestinal disorders in the elderly.

### **Disorders of the Upper Gastrointestinal Tract**

The two most significant oral diseases in older people are root caries and periodontal disease. The World Health Organization has a global oral data bank that includes epidemiological studies from 1986 to 1996 on non-institutionalized

European adults aged 65–74 years. Results revealed that 12.8–69.6% of subjects were edentulous, the mean number of teeth ranged from 15.1 to 3.8 and the decayed, missing and filled teeth index ranged from 22.2 to 30.2. This wide range in scores suggests that oral health policies need to be developed and implemented, taking into consideration geographical and socio-economic differences in populations.

Dysphagia, i.e. the inability to swallow or difficulty in swallowing solid and/or liquid meals, increases with advancing years. European surveys suggested that up to 10% of people over 50 years of age experience some difficulty with swallowing [3], and a study of people in long-term care found that the prevalence of under-nutrition was close to 50% and was significantly associated with eating and swallowing problems [4]. The causes of dysphagia in older people are mostly associated with cerebrovascular and neurological diseases, including Parkinson's disease, motor neuronal disease, myasthenia gravis and Alzheimer's disease.

Dyspepsia, i.e. the presence of episodic or persistent pain or discomfort localized to the epigastrium or upper abdomen [5], is a very common syndrome. In the United States, about 25% of people report recurrent epigastric discomfort that occurs at least once a year. At least 10% of these persons seek medical care. Dyspepsia is the primary complaint of approximately 5% of all patients who visit their family physician [6]. An American survey of a randomly selected community sample of 1,120 people aged from 34 to 64 years identified a prevalence of upper abdominal pain within the preceding year of 25.8%; a subgroup of reflux-like dyspepsia was identified in 9.4%. One third of dyspeptics also had irritable bowel symptoms [7]. Community surveys in the United Kingdom [8] show that over one third of people reported dyspepsia within the previous 6 months, with the frequency appearing to fall with age (24% of women and 15% of men aged over 80). About half of the people with dyspepsia reported both heartburn and upper abdominal pain. Only one in four had consulted their general practitioner, with consultation rates increasing with age.

Gastroesophageal reflux disease (GERD) appears to be more common in the elderly than in younger persons, possible because of a reduction in the intra-abdominal length of the lower oesophageal sphincter and an increased incidence of hiatus hernia. The prevalence and incidence of GERD are not accurately known. Estimates vary depending upon whether studies have examined reported symptoms or used investigational methods. Study has been hampered by a lack of methodologically rigorous studies using validated survey instruments in truly random community samples, as well as the lack of a gold-standard disease definition. GERD defined as heartburn is extremely common; 44% of adult Americans surveyed by the Gallup Organization experienced it monthly. Recent work based on an age- and sex-stratified random sample of 2,200 residents of

Olmsted County, Minnesota, USA, aged 25–74 years incorporated a valid and reliable self-report questionnaire. The overall age- and sex-adjusted prevalence of any episode of heartburn in the preceding year was 42.4% [95% confidence interval (CI) 39.8–45.1%]. The proportion with frequent (weekly) heartburn was 17.8% (95% CI 15.8–19.9%). The prevalence of yearly and weekly acid regurgitation was 45% (95% CI 42.3–47.7%) and 6.3% (95% CI 5.0–7.6%), respectively. The overall prevalence of GERD (defined as either heartburn or acid regurgitation) in the preceding year was 58.7% (95% CI 56.1–61.3%), and for weekly episodes, it was 19.8% (95% CI 17.7–21.9%). There were no overall significant differences with respect to age or sex for GERD, although heartburn was inversely associated with age [9].

Given that the prevalence of hiatus hernia and oesophageal dysfunction increases with age [10], GERD may be thought to be more common in older people. A population-based random sample of 600 non-institutionalized Finnish subjects aged 65 years or over suggested an overall prevalence of at least monthly GERD (heartburn or regurgitation) of 53.5% in men and 66.2% in women [11].

Severe oesophagitis is much more common in patients beyond the age of 65 than in young people. The magnitude of the symptoms does not correlate well with the severity of mucosal disease, and so, very severe oesophagitis may be associated with a relative paucity of symptoms. Manifestations of GERD are thus more likely to be late-stage complications such as bleeding from a haemorrhagic oesophagitis, dysphagia from a peptic stricture or adenocarcinoma associated with Barrett's oesophagus. GERD-induced chest pain may mimic, or occur concomitantly with, cardiac disease.

Oesophageal carcinoma is a problem of advancing years, as most patients are over 65 years of age. Cancers of the middle and lower third of the oesophagus are most common. There is considerable geographic variation in this disease, suggesting that environmental factors are important. The highest annual incidence rates, exceeding 100 per 100,000, are reported in Iran, China and parts of Russia, whereas in Western Europe and among white Americans, rates are under 10 per 100,000. Several important risk factors for squamous cell carcinoma are recognized, including smoking, alcohol, chronic thermal injury, achalasia, nitrosamines, the Plummer-Vinson syndrome and diet. An estimated 0.2–2.0% of patients with Barrett's oesophagus eventually develop oesophageal adenocarcinoma. Because the prevalence of Barrett's oesophagus is higher in patients with GERD than without GERD, a possible causal relationship between GERD and oesophageal adenocarcinoma is suggested [12].

Drugs and the oesophagus is an important topic in older people since approximately half of adverse drug reactions affecting the oesophagus occur in patients aged over 65. Drugs damage the oesophagus either directly by local

contact, i.e. aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, alendronate, potassium and ferrous salts, or as a result of a reduction of the lower oesophageal sphincter pressure, i.e. dopaminergics, nitrates, theophylline, benzodiazepines and tricyclic antidepressants.

Recent studies have demonstrated that acid and peptic gastric secretion do not decline with age [13, 14]. In contrast, evidence indicates that aging is associated with a lower capacity of the gastric mucosae to resist damage, even in healthy persons. Indeed, many factors involved in cytoprotection, such as mucosal blood flow and gastric mucosal prostaglandin, glutathione, bicarbonate and mucus secretion, decline with age. These changes may account for the impaired barrier function of the gastric mucosa and the increased risk of peptic ulcer disease in the elderly, particularly in association with the use of NSAIDs. Aging is associated with a modest slowing of gastric emptying, which may predispose subjects to anorexia and weight loss by prolonging gastric distension and increasing meal-induced fullness and satiety.

Non-erosive gastritis is a histological entity that is common in the general population and is associated with advanced age. It is now accepted that *Helicobacter pylori* infection is the cause of approximately 80% of cases of non-erosive gastritis, which may progress to peptic ulcer disease. Gastritis is present in almost all patients with duodenal ulcer and nearly 80% of patients with gastric ulcer [15].

During the last 3 decades, the incidence of peptic ulcer and, concomitantly, its associated complications and mortality, has increased in the elderly. Complications occur in about 50% of patients aged over 70 years. The high mortality rate (up to 30%) may relate to the presence of co-morbidity [16].

*H. pylori* infection in patients with peptic ulcer aged over 65 years has been reported to range from 58 to 78%. However, in one study of elderly patients hospitalized for ulcer disease, the rate of diagnostic screening for *H. pylori* was less than 60%, and only 50–73% of patients who had a positive *H. pylori* test were treated with antibiotics [17].

Recent studies have shown that NSAID gastropathy and its life-threatening complications occur primarily in elderly patients [18]. Although increased NSAID use by elderly people is an obvious risk factor, epidemiological data suggest that aging itself is an independent risk factor for the development of NSAID gastropathy and its complications [19]. Patients who have had peptic ulcers or ulcer complications in the past are more likely to develop NSAID gastropathy. Other risk factors for upper gastrointestinal lesions are high dosages of NSAIDs and the concomitant use of more than one NSAID or corticosteroids, aspirin and warfarin [20]. In particular, an *H. pylori*-positive patient receiving aspirin or NSAID treatment should be carefully asked about any upper abdominal complaints she/he might have [21, 22].

Complications occur in about 50% of elderly patients with peptic ulcers. The most common complication is bleeding, which occurs in about 10–15% of ulcer patients of all ages, yet most frequently in elderly patients. About 10–20% of patients with bleeding ulcers do not have preceding symptoms. The mortality rate in elderly patients with bleeding ulcers is estimated to be 29–60%. Perforation occurs in about 5–10% of ulcer patients and is more frequent in duodenal ulcers. The risk is increased by the use of NSAIDs. Although most elderly patients with perforated ulcers report abdominal discomfort, about 16% have minimal pain [23].

Acute upper gastrointestinal haemorrhage constitutes a significant fraction of acute general medical admissions and an increasing proportion of these patients are elderly. Age is an independent risk factor for gastrointestinal bleeding, with the annual incidence of haematemesis or melaena in patients over 75 being 10 times that of those aged less than 44. The reasons for this are not clear, but almost certainly comprise a complex mix of risk factors, including the use of NSAIDs and the presence of significant co-morbidity resulting in a previous hospital admission [24].

The rate of benign gastric tumours increases with age. Hyperplastic polyps account for 75–90% of such growths and typically are small, solitary lesions that are not considered pre-malignant. They rarely produce symptoms and thus may be found incidentally during an evaluation of the upper gastrointestinal tract. In contrast, adenomatous polyps are true neoplasms and account for 10–25% of benign gastric tumours, which probably reflects their heterogeneity in size, age and histology.

Gastric cancer (primarily adenocarcinoma) is the second most common cancer worldwide. Its incidence has been declining in the United States, but it still causes approximately 6 deaths per 100,000, or 14,000 deaths annually [25]. Its incidence also increases with advancing age. Gastric cancer presents most frequently in the sixth decade of life, and men are affected twice as often as women. Implicated aetiological factors include habitual ingestion of smoked foods, foods with high salt contents, increased uses of nitrites, various vitamin deficiencies, carcinogens such as aflatoxin and the development of atrophic gastritis with achlorhydria.

## **Liver Disorders**

Several studies suggest that a significant proportion of patients with alcoholic liver disease not only present in old age but also are more likely to have severe disease at the time of diagnosis. In a British study, 28% of patients were diagnosed for the first time when over 60 years of age [26]. In France, a large

retrospective study found that 20% of patients were over the age of 70 years. In the United States, one study among white males showed that the seventh decade was the peak for presentation with cirrhosis. Prognosis is related to age. In one study, mortality among those less than 60 years old at presentation was 5% at 1 year and 24% at 3 years, whereas mortality among those presenting at over 70 years of age was 75% at 1 year and 90% at 3 years [27].

Adverse drug reactions are reported to occur more frequently in older than in younger people. Drug consumption rises with age, and it is therefore possible that much of the increased incidence of adverse drug reactions in later life is secondary to high drug consumption and polypharmacy. Primary biliary cirrhosis is found above all in middle-aged and older women. The average age at presentation is 55–60 years, but about 25% of patients present with this disease when over 65 years of age [28]. Its prevalence rate in women over 50 was found to be 1 in 1,500 in parts of Europe. In developed countries, primary hepatocarcinoma is predominantly a disease of older people, with more than 50% of patients being over 60 years of age and more than 40% over 70 years of age at presentation. It is usually associated with cirrhosis, regardless of the underlying cause, and it is probable that the length of time for which an individual has had cirrhosis is an important determinant factor [28].

## **Pancreatic Disorders**

Pancreatic disease is a common cause of morbidity and mortality in older persons. Acute gallstones, pancreatitis and pancreatic cancer are responsible for the great majority of pancreatic disease. As the numbers of elderly continue to increase, pancreatic disease will become even more common. Acute pancreatitis is responsible for 5–7% of cases of acute abdominal pain in older persons. The most important causes are ethanol consumption, gallstones and obesity. Drugs are another important cause of pancreatitis in elderly patients, among whom multiple-drug use is common. The mechanism of drug-induced pancreatitis is not well understood, as the association is often weak and rechallenge is usually contraindicated. Cardiovascular disease, common in older persons, may cause ischaemic injury to the pancreas. Pancreatic carcinoma can present as acute pancreatitis at any age, and it is the cause in 1–3% of cases of the latter condition. Despite this low frequency, there is a relatively high risk of pancreatic cancer in the elderly.

Alcohol is the most common cause of chronic pancreatitis and is responsible for 70–80% of cases. As alcohol consumption varies widely among nations, the incidence of chronic pancreatitis is also highly variable. Idiopathic causes of chronic pancreatitis are the second most common aetiology (20%).

Others include hypertriglyceridaemia, hyperparathyroidism, drug therapy, biliary stones, hereditary pancreatitis and obstruction or disruption of the main pancreatic duct. The aging process itself seems to be a risk factor for chronic pancreatitis in developed countries [29].

Carcinoma of the pancreas is the fifth leading cause of cancer death in the industrialized world. Age is a major risk factor, with three quarters of all pancreatic cancers occurring in patients over the age of 60. Other risk factors for pancreatic cancer include diabetes, cigarette smoking and chronic pancreatitis. Ninety percent of pancreatic tumours arise from the exocrine pancreas, while islet cell tumours, neuroendocrine tumours, sarcomas and primary lymphoma of the pancreas are rare. Ductal pancreatic adenocarcinomas, which are responsible for more than 90% of exocrine pancreatic tumours, are typically a disease of the elderly patient [29].

### **Gallbladder Disorders**

Gallstones are three times more common in women than in men and are more prevalent with increasing age. One in 5 women and 1 in 10 men above the age of 55 have gallstones. The prevalence of cholelithiasis increases with age, and by 70 years, around 30% of women and 19% of men have gallstones [30]. Most are asymptomatic, but some subjects will develop biliary pain and complications. An epidemiologic study carried out in Italian subjects over 60 years of age demonstrated that gallstones were present in 13.9% of the participants, while 12.8% had had a cholecystectomy; the overall prevalence of gallstone disease was 26.7% [31]. Risk factors for the development of cholesterol gallstones include female gender, pregnancy, the use of contraceptives, obesity and rapid weight loss.

Carcinoma of the gallbladder is a disease of old age, with the majority of patients being 70 years of age or over at presentation. Although this carcinoma is usually associated with gallstones, it is not clear whether the relationship is significant. The neoplasm is four times more common in women than in men [32].

### **Lower Gastrointestinal Tract**

Aging has minor effects on the structure of the small intestine, with some alteration in villus architecture and a reduction in the neuronal content of the mesenteric plexus. Aging does not result in major changes in small intestine motility, transit, permeability or absorption.

Bleeding from the small intestine is an important cause of morbidity and mortality in older persons, particularly caused by NSAID use and angiodysplasia.

Constipation is more common in elderly persons than in middle-aged persons. In the United States, the prevalence of constipation in people aged over 60 years of age ranges from 4 to 50%. The wide range in prevalence data is in part attributable to how constipation is defined in a given study. The most widely accepted definition is the passage of less than two bowel movements per week. Constipation is a symptom that can arise as a result of dietary factors, functional abnormalities, perceptual factors, neuromuscular disease, metabolic disease, obstructing lesions or iatrogenic causes. Constipation is one of the most common gastrointestinal complaints in the elderly, with up to 60% of elderly outpatients reporting laxative use. The overall prevalence of self-reported constipation is 24–37%, with women reporting constipation more often than men. In the institutionalized elderly, up to 50% self-report constipation and up to 74% use laxatives daily [33].

In the elderly, the risk of diarrhoea increases due to diminished physiological reserves, the burden of acute or chronic multisystem illness, under-nutrition, general debility and cognitive impairment. Diarrhoea is also relevant in the elderly as it is an important cause of morbidity and mortality. Older patients may not admit having chronic diarrhoea, particularly if they are also incontinent. Institutionalised elderly are particularly prone to gastrointestinal infections, but the manifestations may not be overt [34].

Faecal incontinence affects quality of life and causes caregiver strain. Among older people in the United Kingdom who live at home, the prevalence of faecal incontinence is estimated to be between 2 and 6%, while the prevalence among people who live in nursing homes is estimated to be between 4 and 30%. Sufferers are often reluctant to seek help because of embarrassment and a perceived lack of effective treatment. Consequently, underestimation of its prevalence is well recognized. Co-morbidities, such as stroke, dementia and limited physical ability, can contribute to an increased risk of faecal incontinence. Other aetiological factors include anorectal pathology, sphincter or pelvic floor damage, inflammatory bowel syndrome, irritable bowel syndrome, neurological diseases, faecal impaction with overflow, poor toilet facilities or inadequate care. Faecal incontinence occurs more frequently among women, and it is associated with symptoms of anxiety, depression and disability [35].

The risk of developing diverticula of the colon increases with age [36]. In Western countries, diverticular disease occurs in about 50% of persons greater than 65 years of age and in about 65% of those greater than 80 years of age. Diarrhoea can be a consequence of diverticulitis when acute or chronic inflammation due to a mechanical obstruction within the diverticula occurs [37]. Diverticulosis is the most common cause of massive lower gastrointestinal

bleeding in older persons [38]. Diverticular haemorrhage accounts for up to 25% of all complications in patients with diverticulosis. Overall, 3–5% of patients with diverticulosis will develop significant gastrointestinal bleeding, 70% of which occurs in the right colon and involves a single non-inflamed diverticulum. The presence of diverticular haemorrhage and diverticulitis are nearly mutually exclusive, with fewer than 5% having both processes simultaneously. The most common complication of diverticulosis is diverticulitis, which occurs in 10–20% of patients. It results from inflammation and increases the risk of subsequent perforation of a colonic diverticulum. Mild forms of diverticulitis usually present with gradually increasing symptoms from the lower left quadrant of the abdomen, whereas acute complicated disease is characterized by a dramatic onset of abdominal pain, followed by fever within a few hours [39].

Ischaemic colitis occurs almost exclusively in the elderly, as a result of the increased prevalence of atherosclerosis. When patients with iatrogenic causes, including surgical procedures and drugs, are excluded, more than 90% of patients are over 60 years of age. In the gastrointestinal tract, the colon is the part most frequently injured by ischaemia. This occurs in association with other pathologies characteristic in the elderly, including polycythaemia, diabetes mellitus, arteritis and digitalis preparations. Patients usually present with cramping, abdominal pain, faecal urgency and/or haematochezia.

Irritable bowel syndrome refers to a heterogeneous group of disorders in which the patient complains of abdominal pain and unstable bowel habits. Overall, 10–15% of the population of the United States has symptoms compatible with the diagnosis of irritable bowel syndrome, although only a minority seek medical attention [37].

Cancer of the colon or rectum is the most common malignancy of the gastrointestinal tract in older persons. It varies widely in frequency in different parts of the world, occurring much more commonly in North America, north-western Europe and New Zealand than in South America, south-western Asia, equatorial Africa and India. Colorectal cancer mortality is 44% higher for men than for women. The incidence rises sharply after the age of 50, with two thirds of all patients being over 50. The mean age at diagnosis is 62 years. Multiple epidemiologic studies have shown that rates of colorectal cancer are highest in countries with diets high in fat and calories but low in fibre. Up to half of colorectal cancer cases may be related to diet. Estimates suggest that 15–25% of colorectal cancer cases may be related to high fat intake and that 25–35% may be related to low intake of fruits and vegetables. An estimated 32% of colorectal cancer cases may be related to physical inactivity [25]. The importance of dietary factors has been shown in studies of immigrants. Japanese subjects who had immigrated to the United States acquired a higher incidence of colorectal

cancer with each subsequent generation, with the incidence in the third generation similar to that of native-born Americans [40].

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