

Revisión

Changes, functional disorders, and diseases in the gastrointestinal tract of elderly

M. Grassi¹, L. Petraccia¹, G. Mennuni¹, M. Fontana², A. Scarno¹, S. Sabetta¹ and A. Fraioli¹

¹Department Internal Medicine and Medical Disciplines. Unit of Internal Medicine E, Medical Therapy and Thermal Medicine - School of Specialization in Thermal Medicine. ²Department of Biochemical Sciences. Sapienza University of Rome. Rome. Italy.

Abstract

This article describes changes in the basic digestive functions (motility, secretion, intraluminal digestion, absorption) that occur during aging. Elderly individuals frequently have oropharyngeal muscle dysmotility and altered swallowing of food. Reductions in esophageal peristalsis and lower esophageal sphincter (LES) pressures are also more common in the aged and may cause gastroesophageal reflux.

Gastric motility and emptying and small bowel motility are generally normal in elderly subjects, although delayed motility and gastric emptying have been reported in some cases.

The propulsive motility of the colon is also decreased, and this alteration is associated with neurological and endocrine-paracrine changes in the colonic wall.

Decreased gastric secretions (acid, pepsin) and impairment of the mucous-bicarbonate barrier are frequently described in the elderly and may lead to gastric ulcer.

Exocrine pancreatic secretion is often decreased, as is the bile salt content of bile.

These changes represent the underlying mechanisms of symptomatic gastrointestinal dysfunctions in the elderly, such as dysphagia, gastroesophageal reflux disease, primary dyspepsia, irritable bowel syndrome, primary constipation, maldigestion, and reduced absorption of nutrients. Therapeutic management of these conditions is also described.

The authors also review the gastrointestinal diseases that are more common in the elderly, such as atrophic gastritis, gastric ulcer, colon diverticulosis, malignant tumors, gallstones, chronic hepatitis, liver cirrhosis, Hepato Cellular Carcinoma (HCC), and chronic pancreatitis.

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Correspondence: Antonio Fraioli.
Dipartimento di Medicina Interna e Specialità Mediche.
UOC Medicina Interna E, Terapia Medica e Medicina Termale.
Sapienza Università di Roma.
Azienda Policlinico Umberto I V.le del Policlinico 155.
00161 Rome. Italy.
E-mail: antonio.fraioli@uniroma1.it

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CAMBIOS, DOLENCIAS FUNCIONALES Y ENFERMEDADES EN EL SISTEMA GASTROINTESTINAL EN PERSONAS MAYORES

Resumen

Este artículo describe los cambios en las funciones digestivas básicas (motilidad, secreción, digestión intraluminal, absorción) que ocurren en el envejecimiento. Los individuos ancianos a menudo presentan una dismotilidad de la musculatura orofaríngea y una alteración de la deglución de los alimentos. Las reducciones en el peristaltismo esofágico y de las presiones del esfínter esofágico inferior (EEI) también son más frecuentes en las personas mayores y pueden causar un reflujo gastroesofágico.

La motilidad y el vaciamiento gástricos así como la motilidad intestinal son, por lo general, normales en los individuos ancianos, si bien se han notificado en algunos casos una motilidad y vaciamiento gástricos retardados.

La motilidad propulsora del colon también está disminuida y esta alteración se asocia con cambios neurológicos y endocrinos-paracrinos de la pared colónica.

En el anciano se describen frecuentemente disminución de las secreciones gástricas (ácido, pepsina) y alteración de la barrera mucosa-bicarbonato, lo cual puede favorecer la úlcera gástrica.

A menudo la secreción pancreática exocrina está disminuida, así como el contenido en sales biliares de la bilis.

Estos cambios representan mecanismos subyacentes de las disfunciones gastrointestinales sintomáticas del anciano tales como disfagia, enfermedad por reflujo gastroesofágico, dispepsia primaria, síndrome del intestino irritable, estreñimiento primario, maladigestión y disminución de la absorción de nutrientes. También se describe el manejo terapéutico de estos trastornos.

Los autores también revisan las enfermedades gastrointestinales que son más frecuentes en el anciano, tales como la gastritis atrófica, la úlcera gástrica, la diverticulosis colónica, los tumores malignos, los cálculos biliares, la hepatitis crónica, la cirrosis hepática, el carcinoma hepatocelular (CHC) y la pancreatitis crónica.

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Palabras clave: *Dolencias gastrointestinales. Enfermedades digestivas. Personas mayores.*

Abbreviations

LES: Lower esophageal sphincter.
HCC: Hepato cellular carcinoma.
UES: Upper esophageal sphincter.
NO: Nitric oxide.
NOS: Neuronal NO synthase.
ROS: Reactive oxygen species.
NSAIDs: Nonsteroidal anti-inflammatory drugs.
GERD: Gastroesophageal reflux disease.
CNS: Central nervous system.
PDS: Postprandial distress syndrome.
PUD: Peptic ulcer disease.
IBS: Irritable bowel syndrome.

Introduction

Modern-day gerontologists tend to regard aging as a biological phenomenon characterized by temporal continuity, heterogeneity at the somatic, cellular, and molecular levels, and the capability of being modulated.

The latter feature allows us to envision the elderly individual in a wide range of situations, ranging from disease that is more or less disabling through variable degrees of functional deficits to persistent productivity and creativity the so-called "successful elderly".

If we apply these concepts to the pathophysiology of the digestive system and to the classification of the digestive diseases of the elderly, we find subjects whose basic digestive functions remain more or less efficient; others with functional alterations of motility, secretion, and/or absorption, which not infrequently give rise to functional digestive diseases; and others with diseases that are more frequent and/or more severe in the elderly, sometimes due to disease that is primarily extragastrintestinal. Therefore, it is important to define the "normal" changes in digestive activity that occur as age advances, those that are part of the physiological phenomenon of aging and unrelated to specific diseases. General consensus holds that no digestive diseases or disorders are seen exclusively in elderly persons. However, the prevalence and incidence of functional disorders and diseases involving this system are clearly higher than those observed in younger subjects.

Motility

Oropharynx: In the oropharyngeal phase of swallowing, retention in the valleculae and the piriform sinuses increases, the driving force of the tongue diminishes, pharyngeal peristalsis is preserved, and the pressure and opening of the upper esophageal sphincter (UES) decrease;^{1,2,3} the efficiency of the pharyngo-UES contractile reflex also declines with age.^{4,5} On the whole, however, the persistence of effective glottal

closure protects the elderly subject from aspiration pneumonia.^{1,6,7}

Esophagus: The term presbyesophagus has been used to refer to the condition characterized by low-amplitude peristaltic waves, polyphasic waves in the esophageal body, incomplete upper sphincter relaxation, esophageal dilatation, delayed muscle relaxation after swallowing, reduced postdeglutition peristalsis secondary to esophageal distention, with incomplete clearance of low and high-viscosity liquids.^{8,9} Morphological studies have revealed loss of neurons in the esophagus.¹⁰ The reduced amplitude of the peristaltic waves decreases clearance of the esophageal contents and prolongs episodes of reflux.¹¹ In elderly individuals who are healthy, inverse correlations have been observed between age, esophageal sphincter pressures, and the amplitude and velocity of peristaltic waves in the esophagus.¹²

Numerous studies have shown that the amplitude of the peristaltic pressure wave decreases in the elderly, whereas wave duration and velocity are unchanged.^{8,13}

These changes result in dysphagia and gastroesophageal reflux, which are often provoked or aggravated by nondigestive disease.

Stomach: According to Madsen, gastric emptying and small-intestinal motility are not appreciably altered in the elderly,¹⁴ but other authors have described reductions involving liquid emptying,¹⁵ solid emptying,¹⁶ and peristaltic contractions.¹⁷ Some studies have found that postprandial gastric peristalsis is diminished in this age group and that gastric emptying after a high-fat meal is more markedly delayed, particularly in individuals with low physical activity levels.^{18,19}

These observations can be correlated with the reduced subpopulations of cholinergic neurons observed in aged rats.²⁰

These changes have clinical repercussions, and they would account for the increased incidence and prevalence of gastroesophageal reflux and functional dyspepsia in elderly individuals.

Small bowel: The majority of studies indicate that small intestinal motility does not change with normal aging.^{16,21,22}

Colon: In subjects over 80, the transit of fecal material through the colon is slowed as a result of the reduced number of neurons in the plexus, especially the myenteric plexus.^{23,24}

According to some authors, nitric oxide (NO) synthesis also decreases as a result of reduced levels of neuronal NO synthase (NOS) reflected by reduced numbers of cells displaying NOS immunoreactivity.²⁵ Other studies have revealed increased expression of opioid receptors in guinea pigs and the disappearance of constipation in elderly humans treated with opioid antagonists.²⁶ Finally, reduced release of acetylcholine has been observed in the myenteric plexus of aged rats, and this would explain the diminished rate and efficacy of peristalsis documented in these animals.²⁷ All of these findings help explain the higher frequency of

constipation in elderly subjects, although it is also related to a number of other dietary, behavioral, iatrogenic, and disease-associated factors, as we shall see in the pages that follow.

At the anorectal level, age-related changes include external sphincter thinning, thickening of the internal sphincter, reduced maximal squeeze pressures (in women but not men), reductions in resting anal canal pressures (similar in both sexes),^{28,29} and reduced pressure thresholds for relaxation of both sphincters. On the whole, these changes increase the probability of fecal and gas incontinence in the elderly.

Gastric secretions: Baseline and stimulated production of HCl are both reduced. However, this change does not appear to occur when the gastric mucosa is intact, i.e., in individuals without atrophic gastritis.^{30,31,32} In general, pepsin secretion seems to be within normal limits in older persons who are healthy and reduced in those with *Helicobacter pylori* infections.³³

Epidemiologic studies have revealed an increased prevalence of atrophic gastritis among the elderly with rates that range from 50% to 70%.³³

Haruma et al. found that gastric secretion was normal in subjects who were *H. pylori*-negative, but positivity was associated with reduced secretion secondary to atrophic gastritis and production of inflammatory cytokines that inhibits parietal-cell activity.^{34,35}

Atrophic gastritis leads to events that include reduced acid secretion, bacterial proliferation, malabsorption of nutrients and of vitamin B₁₂, and macrocytic anemia.³⁶ It also promotes the production of reactive oxygen species (ROS) that increase the risk of carcinogenesis.^{37,38} The atrophic gastritis associated with *Helicobacter* infection seems to reduce the production of ghrelin and stimulate leptin activity, effects that favor anorexia and undernutrition in the elderly.^{39,40,41}

There are decreases in the cytoprotective mucous-bicarbonate barrier and in cell proliferation in the gastric wall. The former change is caused by decreased concentrations of prostaglandins (PGs), PGE₂ in particular, which strongly influences the secretion of both mucus and bicarbonate.^{42,43} Proliferative activity in the cells of the gastric mucosa is also decreased as a result of the downregulated expression of growth factors and of growth-factor-related enzymes.^{44,45} Studies conducted in animals and in humans have revealed reduced gastric blood flow.^{46,47}

Collectively, these findings point to weakened gastric defenses that render the stomach more vulnerable to the damaging effects of nonsteroidal anti-inflammatory drugs (NSAIDs), which are used (and abused) frequently by elderly individuals.

Small bowel: The mucosa of the small bowel in rodents shows age-related loss of height involving both the villi and enterocytes, while studies in human have not revealed any changes in small intestine architecture.^{48,49} In aged rats, prolonged stress causes atrophy, impaired hydrolase activity, and reduced absorption.^{50,51} Conflicting findings have been reported on

nutrient absorption in humans. In one study, the absorption of fat was found to be normal in healthy elderly individuals, and there was no correlation between age and 72 h fecal fat excretion.⁵² According to other investigators, fat absorption is slowed in older subjects.⁵³

Pancreas: Age-related changes in pancreatic exocrine secretion include decreased flow rates and diminished production of bicarbonate and enzymes. These changes are generally not associated with clinical manifestations and do not require substitution therapy.⁵⁴ There is also a decrease in secretin-stimulated secretions.⁵⁵ Most studies have found relatively insignificant age-related differences in pancreatic function, although the volume of pancreatic secretions observed after stimulation and the volume of pancreatic enzymes are reportedly decreased in older subjects.^{56,57,58} One study revealed reduced absorption of radiolabeled fats in elderly individuals, which improved after the administration of pancreatic lipase.⁵⁹

Liver and bile: Elderly subjects exhibit increases in cholesterol secretion and decreased secretion of bile acids.⁶⁰ The prevalence and incidence of hypokinetic gallbladder disease and sphincter of Oddi dysfunction also increase.^{61,62}

Nutrient digestion and absorption: Endoluminal digestion of foods can be impaired secondary to hyposecretion of gastric acid and pepsin. Decreases in the secretion of pancreatic juice and bile salts also reduces and slows this process. As noted earlier, functional alterations involving peptic and HCL secretion can reduce the absorption of vitamins and minerals.⁶³ Glucose (D-xylose absorption test) and lipid absorption can be reduced by hyposecretion of bile and lipases, although this finding has not been observed in all studies.^{50,53} Excessive use of proton pump inhibitors can also promote bacterial proliferation in the small intestine and produce malabsorption and malnutrition.^{64,65}

The gastroenteric mucosa is characterized by active proliferation, and in normally fed aged rats this activity seems to be increased whereas apoptosis is less evident;^{66,67} lower caloric intakes are associated with an increase in apoptosis.⁶⁸

The proliferative and secretional responses to gastrin are also reduced, possibly reflecting the predominance of somatostatin-sensitive cells over those that are gastrin-sensitive.⁶⁹

Functional digestive disorders and diseases

Functional disorders of the digestive tract cause symptoms and distress with no evidence of organic disease. They include dysphagia, gastroesophageal reflux disease (GERD), primary dyspepsia, irritable bowel syndrome, and chronic primary constipation. These disorders are more frequent in the elderly, even in the absence of extradigestive diseases that favor their development.

Dysphagia: Is very common in elderly individuals, particularly those who are physically disabled and need assistance to eat.^{70,71,72} It can be caused by functional alterations that affect the act of swallowing (oropharyngeal dysphagia) or the transport of ingested food through the esophagus.⁷³ In elderly patients with this disorder, care must be taken to exclude local (pharyngo-esophageal or extragastrointestinal) causes and systemic disease, neuromuscular disorders in particular.⁷⁴ The former include oropharyngeal tumors, Zenker's diverticulum,⁷⁵ cervical osteophytes that impinge on the esophagus,⁷⁶ aortic cardiac compression,⁷⁷ thyroid hypertrophy, achalasia, diffuse esophageal spasm, drug-induced forms of esophageal dysmotility, esophageal neoplasms, organic stenosis of the esophagus, and iatrogenic esophageal lesions. The latter consist of CNS disease (above all stroke, Parkinson's disease, multiple sclerosis, and Alzheimer's disease),^{78,79,80} neuromuscular disorders (amyotrophic lateral sclerosis, dermatomyositis, myasthenia gravis),⁸¹ and systemic diseases like diabetes, atherosclerosis, and scleroderma.

Management of dysphagia in older subjects requires a multidisciplinary approach not only for diagnosing and treating the disorder: assistance must also be provided to ensure that the patient is adequately nourished.

Gastroesophageal reflux disease (GERD): The most common symptoms of GERD are digestive (belching, retrosternal burning and pain, acidity) and extradigestive (cough, hoarseness, laryngitis, asthma). This condition is quite common in elderly subjects. It is found in around 20% of all those seen in outpatient clinics.^{82,83} Gastroesophageal reflux disease is characterized by diminished, low-efficiency esophageal peristalsis with delayed transit of the food bolus, less effective mucosal clearance, incontinence of the lower esophageal sphincter, and delayed gastric emptying. Sometimes there is also shortening of the intra-abdominal segment of the lower esophageal sphincter (LES), an increased risk of hiatal hernia, reduced defense of the esophageal mucosa, and a higher frequency of duodenogastric reflux, which exposes the mucosa to the cytoaggressive effects of the bile salts.^{84,85,86} More recently, detrimental effects have been observed when the esophageal transit of alendronate (which is widely prescribed for older patients) is delayed in the presence of acid reflux.⁸⁷

In the elderly, GERD is generally manifested by dysphagia, vomiting, and breathing difficulties; less frequent symptoms include retrosternal burning and acid regurgitation.⁸⁸

Damage to the esophageal mucosa occurs frequently, with esophagitis, erosions (a frequent cause of bleeding), Barrett's esophagus, metaplasia, and carcinogenesis.

Treatment consists in the use of proton pump inhibitors, prokinetic drugs, hydration with bicarbonated mineral waters along with the following dietary and behavioral measures: maintenance of an upright position after meals, sleeping with the chest elevated,

smaller low-fat meals, and avoidance of strong alcoholic drinks, carbonated beverages, and smoking.⁸⁹

Alpha-adrenergic antagonists, calcium channel blockers, nitrate vasodilators, and anticholinergic agents can also promote gastroesophageal reflux by altering lower esophageal sphincter continence and gastric emptying.

Functional dyspepsia (FD): This condition is defined as the presence of persistent or recurrent upper abdominal symptoms, including epigastric pain and/or burning, postprandial fullness, and early satiation.^{90,91} It is particularly common in elderly individuals, especially the variant known as the postprandial distress syndrome (PDS), which is similar to dysmotility-like dyspepsia.⁹⁰ Management includes prokinetic drug therapy, dietary management, and sometimes treatment of depression, which is often associated with the dyspepsia.^{92,93}

The causes of secondary forms of dyspepsia need to be identified and treated. They include drugs; organic disease of the digestive tract (particularly atrophic gastritis, peptic ulcer disease (PUD), tumors, gallstones) and extragastrointestinal disease (particularly vascular and neurological disorders); consumption of large, high-fat meals, strong alcoholic drinks, or carbonated beverages; smoking. Duodenogastric reflux is a frequent occurrence, and the presence of bile salts in the stomach can cause damage to the gastric mucosa (prokinetic drugs are useful in these cases).⁹⁰

Irritable bowel syndrome (IBS): The frequency of IBS in the elderly is similar to that in other age groups. The most common symptoms are abdominal pain or discomfort, that is relieved by defecation, changes in stool frequency and/or form, presence of mucus in the stools, and bloating or feelings of abdominal distension.⁹⁴ Organic disease has to be excluded in these cases. The prevalence of IBS is higher in women than in men and in adults and elderly subjects than in young. The overall prevalence is 10-20%, and IBS accounts for 20-50% of all gastroenterology consults.^{95,96,97} IBS is frequently associated with functional dyspepsia, colon diverticula, fibromyalgia, anxiety, and depression.⁹⁸ Treatment is based on dietary modifications, control of diarrhea (a frequent symptom of IBS) with drugs like loperamide, anticholinergic and antispasmodic drugs, control of constipation (another common symptom – see following paragraph) with laxatives, and antidepressants.⁹⁹

Chronic primary constipation: Manifested by persistent reductions in bowel movement frequency accompanied by sensations of difficult and seemingly incomplete evacuation,⁹⁴ chronic primary constipation is the most common functional disturbance encountered in older individuals. It may be associated with normal or reduced intestinal transit rates in the large intestine.¹⁰⁰

Like all functional digestive disorders, chronic primary constipation is diagnosed by a process of exclusion. In the presence of constipation, the first step is to

rule out organic disease. This includes digestive (especially neoplastic disease) and nondigestive causes.

The most frequent cause of constipation is delayed fecal transit in the colon secondary to reduced intestinal motility. In older individuals, this is more likely to be associated with chewing deficits, reduced gastric acid secretion, reduced fluid and fiber intake, and limited physical activity.^{101,102,103,104} A number of diseases can cause secondary constipation:¹⁰⁵

- Endocrine and metabolic diseases (especially diabetes and hypothyroidism).
- Myopathy (e.g., myotonic dystrophy, scleroderma, amyloidosis).
- Neurologic disease (especially cerebrovascular disease, multiple sclerosis, or Parkinson disease).
- Psychiatric disturbances (e.g., depression and anxiety).
- Organic colorectal disease: stenosis (caused by tumors, Crohn's disease, or other causes), hemorrhoids, fissures, rectal prolapse, etc.

Drug-related constipation is very important. It can be caused by anticholinergics, antidepressants, antihistamines, several antihypertensive drugs, opioids, hypnotics, and antacids.^{106,107} Treatment is based on ensuring adequate fluid intake, a diet rich in fiber (35-40 g/day), olive oil, physical activity, and laxatives.¹⁰⁸ The daily fiber intake should be at least 15 grams. Foods with high-fiber contents include whole-grain bread, bran, beans, filamentous vegetables, and fresh fruit.^{109,110} Laxatives include lubricants, such as vegetable and mineral oil, liquid paraffin, and docusate sodium, and hydrating agents (osmotics) like magnesium hydroxide, magnesium sulfate, magnesium citrate, and sodium biphosphate, which can cause potassium depletion, sodium and water retention, and diarrhea.¹¹¹ This latter group also includes sorbitol, lactulose, and polyethylene glycol (PEG). The first two can cause flatulence. PEG is metabolized by the microbial flora of the intestine and is therefore better tolerated.^{112,113} The so-called bulk laxatives (psyllium, agar, methylcellulose) are rarely used. They have been replaced by the use of high-fiber diets.

The stimulant laxatives (senna, bisacodyl, cascara) increase peristalsis in the colon and promote the secretion of water and electrolytes from the gut wall; they can sometimes cause cramps.¹⁰⁵ Their prolonged use can lead to electrolyte depletion and the condition known as *cathartic colon*, which is characterized by atonic dilatation with loss of haustra. Metoclopramide is of limited value.¹⁰⁵

More recently colchicine and misoprostol have been approved by the FDA to increase propulsive activity in the gut, and useful effects have been obtained with tegaserod, a 5HT-4 receptor agonist, and lubiprostone, a bicyclic fatty acid that softens the stool.^{114,115} The bathroom must be clean and accessible, and assistance must be available if needed. In addition, the seat of the toilet

should provide adequate support for the lower part of the body, and the weight-bearing area should be protected to avoid the development of decubitus ulcers.¹⁰⁵

Among the various treatments available for chronic primary constipation, it is important to recall the numerous mineral waters with laxative effects that are available in Italy. Sulfate and sodium sulfate waters are particularly useful in these cases.¹¹⁶

Fecal incontinence is defined as the accidental, involuntary passage of feces or gas. The prevalence of this disorder is 2%-7% in the elderly population in general, and over 45% among those who are institutionalized.¹¹⁷ Fecal continence depends on various factors including rectal compliance, anorectal sensitivity, sphincter function, and normal neuromuscular activity in the pelvic floor.¹¹⁸ Alterations that have been demonstrated in older individuals include decreased rectal elasticity, decreased tone of the external anal sphincter with respect to the volume of the fecal mass, and decreased resting and squeeze pressures in the internal anal sphincter.^{29,119,120}

The patient should be examined for local conditions (lesions of the anus and the pudendal nerves, hemorrhoids, fissures, rectoceles, previous surgery) and systemic disease (diabetes, cognitive deficits, neurological disease) that might favor the incontinence.^{121,122} Management includes patient teaching, elimination of local causes (inflammation, hemorrhoids, fissures, etc.), treatment of systemic disease that is causing or contributing to the incontinence, and treatment of diarrhea with loperamide, diphenoxylate, amitriptyline, or antibiotics that act in the intestinal lumen.^{123,124} The physician should pay close attention to sudden changes in the patient's bowel evacuation habits, the presence of occult or frank blood in the feces, and positive family histories, and prescribe appropriate testing when needed (rectocolonoscopy in particular).^{125,126}

Digestive diseases

The most common diseases of the stomach in elderly individuals are atrophic gastritis and peptic ulcer disease (PUD). The former is significantly associated with *H. pylori* infection and reduced acid secretion.³² As noted above, hyposecretion of gastric acid reduces the absorption of vitamin B12, iron, and calcium, and these deficits can lead to megaloblastic or iron-deficiency anemia and a higher frequency of osteoporosis.³⁶ Peptic ulcers in older patients are quite often caused by the use (or overuse) of NSAIDs.¹²⁷

The ulcerogenic activity of these drugs seems to be enhanced by the presence of *H. pylori*, so the eradication of infections should reduce the incidence of PUD.^{128,129,130} According to some reports, around 23% of elderly patients with PUD do not use NSAIDs and are not infected with *H. pylori*, which suggests that other factors play causative roles in the pathogenesis of PUD.^{131,132} H₂-receptor antagonists, cytoprotective

agents, and pump inhibitors are used to treat gastric ulcers that are not *H. pylori*-dependent.

Upper gastrointestinal tract erosions, ulcers, and bleeding can also be caused by steroids, antiplatelet drugs (above all aspirin), and anticoagulants, all of which are frequently prescribed for elderly patients. The NSAID that seems to be associated with the lowest risk of bleeding is ibuprofen, whereas the highest risk is related to the use of piroxicam and azapropazone.^{133,134,135} The increased frequency of bleeding in the elderly is caused by the reduced efficacy of the mucus-bicarbonate barrier and the widespread use of NSAIDs among older subjects. In 20% of all cases, the patients' physicians do not know that these drugs are being used, and in 40% their use is not necessary.^{136,137} Cytoprotective drugs (misoprostol or proton pump inhibitors) should always be prescribed with NSAID therapy. Calcium antagonists have also been implicated in upper gastrointestinal bleeding (due to their vasodilative and antiplatelet effects), but conflicting data have been reported on this issue.¹³⁸ Gastrointestinal bleeding in elderly patients is associated with mortality ranging from 5.45% to 11%. The duration of symptoms is generally brief, and epigastric pain is typically absent.

Some studies indicate that *H. pylori* infection increases the risk of hemorrhage, but others attribute a protective role to the bacteria, whose presence favors the synthesis of PGE₂ in the gastric mucosa.

Duodenal ulcers: The frequency of duodenal ulcers is increased in the elderly population because of the higher prevalence of *H. pylori* infection in this group and their increased use of NSAIDs.¹³⁹ Eradication of the infection can be achieved with combined antimicrobial therapy (amoxicillin + clarithromycin or clarithromycin + metronidazole) and a proton pump inhibitor.¹⁴⁰

Diarrhea: This is the second leading cause of mortality in the world, and in developed countries diarrhea is a prominent cause of mortality among the elderly.¹⁴¹ Regardless of the cause (infection, malabsorption, enzyme deficits, extraintestinal diseases, etc.), oral or parenteral rehydration are mandatory to prevent general hypotension and organ damage and failure.¹⁴² Stool examinations and culture must be performed. Depending on culture results and the clinical course of the disease, the diarrhea can be managed with oral antibiotic therapy, antispasmodics, antipropulsive drugs, and/or probiotics.¹⁴³

Diverticulosis and diverticulitis: The prevalence of diverticular disease is age-dependent with figures as high as 60-65% among individuals over the age of 65. Most (80-85%) of these subjects remain asymptomatic, and 15-20% develop symptomatic diverticular infection and inflammation.¹⁴⁴ Diverticulitis requires antibiotic therapy and, in complicated case, surgery.¹⁴⁵

Ulcerative colitis and Crohn disease: The prevalence of these inflammatory bowel diseases in elderly subjects is not significantly different from that observed in young or middle-aged populations.¹⁴⁶

Cancer of the digestive tract: The prevalence and incidence of esophageal cancer is increased in the elderly, due in part to the higher frequency in this age group of chronic esophagitis and prolonged histories of smoking and/or alcohol abuse.¹⁴⁷ The prevalence and incidence of gastric cancer is also increased, partly as a result of the higher frequency of gastric ulcer in these subjects and their prolonged exposure to causative factors (particularly *H. pylori*), which leads to atrophic gastritis and mucosal metaplasia.¹⁴⁸ As far as organic colon disease is concerned, it is important to recall the high prevalence and incidence among the elderly of colon cancer, polyps, adenomas (which are often the initial stages of cancer), and diverticulosis.^{149,150}

Biliary diseases: Cholelithiasis is more common in the elderly: the prevalence among subjects over 65 years of age is 14.5% for men and 25% for women.^{151,152,153}

This trend reflects the cumulative effects over time of lithogenic factors, the diffusion of the western lifestyle and dietary habits, age-related decreases in the bile acid pool, and the higher concentrations of biliary cholesterol described in certain ethnic groups.^{154,155} There have also been increases in the prevalence of postcholecystectomy syndromes and recurrent bile stones after cholecystectomy.

One problem might be the presence of conditions that are considered contraindications to cholecystectomy or that increase the risk for complications (respiratory insufficiency, severe cardiopathy).

In the presence of a single cholesterol calculus not exceeding 1.5 cm in diameter and normal intestinal absorption and hepatobiliary function, the patient can often be treated with hydrophilic bile acids (tauroursodeoxycholic acid, chenodeoxycholic acid).

After undergoing cholecystectomy, patients should be treated periodically with sulfate-bicarbonate and sodium-chloride mineral water, which stimulates bile flow and exerts a washing effect on the bile duct mucosa.^{156,157}

Liver diseases: There is naturally an increased prevalence among the elderly of chronic hepatitis (mainly HCV-related), cirrhosis, and HCC, which reflects the final phase of a long process involving the combined effects of liver-cell degeneration and necrosis, fibrosis, and regenerative processes within the hepatic parenchyma.¹⁵⁸ It should be stressed that use of interferon in these cases is associated with a higher risk of adverse effects—mainly hematologic and psychiatric (depression)—and an increased frequency of contraindications related to the high prevalence of thyroid disease in the elderly.¹⁵⁹

Pancreatic diseases: The frequency of acute and chronic pancreatitis is higher among older individuals due to the cumulative effects of exogenous toxins like alcohol as well as the increased prevalence and incidence of cholelithiasis.¹⁶⁰ The prevalence and incidence of pancreatic carcinoma is also higher in the elderly.¹⁶¹

References

- Dejaeger E, Pelemans W, Ponette E, Joosten E. Mechanisms involved in postdeglutition retention in the elderly. *Dysphagia* 1997; 12 (2): 63-7.
- Shaker R, Ren J, Podvrsan B, Dodds WJ, Hogan WJ, Kern M, Hoffmann R, Hintz J. Effect of aging and bolus variables on pharyngeal and upper esophageal sphincter motor function. *Am J Physiol* 1993; 264 (3 Pt1): G427-32.
- Kern M, Bardan E, Arndorfer R, Hofmann C, Ren J, Shaker R. Comparison of upper esophageal sphincter opening in healthy asymptomatic young and elderly volunteers. *Ann Otol Rhinol Laryngol* 1999; 108 (10): 982-9.
- Shaker R, Ren J, Zamir Z, Sarna A, Liu J, Sui Z. Effect of aging, position, and temperature on the threshold volume triggering pharyngeal swallows. *Gastroenterology* 1994; 107 (2): 396-402.
- Ren J, Xie P, Lang IM, Bardan E, Sui Z, Shaker R. Deterioration of the pharyngo-UES contractile reflex in the elderly. *Laryngoscope* 2000; 110 (9): 1563-6.
- Ren J, Shaker R, Zamir Z, Dodds WJ, Hogan WJ, Hoffmann RG. Effect of age and bolus variables on the coordination of the glottis and upper esophageal sphincter during swallowing. *Am J Gastroenterol* 1993; 88 (5): 665-9.
- Davies AE, Kidd D, Stone SP, MacMahon J. Pharyngeal sensation and gag reflex in healthy subjects. *Lancet* 1995; 345 (8948): 487-8.
- Ferrioli E, Dantas RO, Oliveira RB, Braga FJ. The influence of aging on oesophageal motility after ingestion of liquids with different viscosities. *Eur Gastroenterol Hepatol* 1996; 8 (8): 793-8.
- Soergel KH, Zboralaska FF, Amberg JR. Presbyesophagus: esophageal motility in nonagenarians. *J Clin Invest* 1964; 43: 1472-9.
- Meciano Filho J, Carvalho VC, de Souza RR. Nerve cell loss in the myenteric plexus of the human esophagus in relation to age: a preliminary investigation. *Gerontology* 1995; 41 (1): 18-21.
- Ferrioli E, Oliveira RB, Matsuda NM, Braga FJ, Dantas RO. Aging, esophageal motility, and gastroesophageal reflux. *J Am Geriatr Soc* 1998; 46 (12): 1534-7.
- Grande L, Lacima G, Ros E, Pera M, Ascaso C, Visa J, Pera C. Deterioration of esophageal motility with age: a manometric study of 79 healthy subjects. *Am J Gastroenterol* 1999; 94 (7): 1795-801.
- Tack J, Vantrappen G. The aging esophagus. *Gut* 1997; 41 (4): 422-4.
- Madsen JL. Effects of gender, age, and body mass index on gastrointestinal transit times. *Dig Dis Sci* 1992; 37 (10): 1548-53.
- Kao CH, Lai TL, Wang SJ, Chen GH, Yeh SH. Influence of age on gastric emptying in healthy Chinese. *Clin Nucl Med* 1994; 19 (5): 401-4.
- Brogna A, Ferrara R, Buccheri AM, Lanteri E, Catalano F. Influence of aging on gastrointestinal transit time. An ultrasonographic and radiologic study. *Invest Radiol* 1999; 34 (5): 357-9.
- Huang CK, Chen GH, Nain HM, Wahn JR, Cheng YP, Chang CS, Liu JH, Ho KS. Use of real-time ultrasound for detection of gastric motility. *Zhonghua Yi Xue Za Zhi (Taipei)* 1995; 55 (2): 137-42.
- Shimamoto C, Hirata I, Hiraike Y. Evaluation of gastric motor activity in the elderly by electrogastronomy and the ¹³C-acetate breath test. *Gerontology* 2002; 48 (6): 381-6.
- Nakae Y, Onouchi H, Kagaya M, Kondo T. Effects of aging and gastric lipolysis on gastric emptying of lipid in liquid meal. *J Gastroenterol* 1999; 34 (4): 445-9.
- Phillips RJ, Kieffer RJ, Powley TL. Aging of the myenteric plexus: neuronal loss is specific to cholinergic neurons. *Auton Neurosci* 2003; 106 (2): 69-83.
- Husebye E, Engedal K. The patterns of motility are maintained in the human small intestine throughout the process of aging. *Scand J Gastroenterol* 1992; 27 (5): 397-404.
- Kagaya M, Iwata N, Toda Y, Nakae Y, Kondo T. Small bowel transit time and colonic fermentation in young and elderly women. *J Gastroenterol* 1997; 32 (4): 453-6.
- Madsen JL, Graff J. Effects of ageing on gastrointestinal motor function. *Age Ageing* 2004; 33 (2): 154-9.
- Gomes OA, de Souza RR, Liberti EA. A preliminary investigation of the effects of aging on the nerve cell number in the myenteric ganglia of the human colon. *Gerontology* 1997; 43 (4): 210-7.
- Takahashi T, Qoubaitary A, Owyang C, Wiley JW. Decreased expression of nitric oxide synthase in the colonic myenteric plexus of aged rats. *Brain Res* 2000; 883 (1): 15-21.
- Culpepper-Morgan JA, Holt PR, LaRoche D, Kreek MJ. Orally administered opioid antagonists reverse both μ - and κ -opioid agonist delay of gastrointestinal transit in the guinea pig. *Life Sci* 1995; 56 (14): 1187-1192.
- Roberts D, Gelperin D, Wiley JW. Evidence for age-associated reduction in acetylcholine release and smooth muscle response in the rat colon. *Am J Physiol* 1994; 267 (4 Pt1): G515-G522.
- McHugh SM, Diamant NE. Effect of age, gender, and parity on anal canal pressures. Contribution of impaired anal sphincter function to fecal incontinence. *Dig Dis Sci* 1987; 32 (7): 726-36.
- Rasmussen OO, Sorensen M, Tetzschner T, Christiansen J. Dynamic anal manometry: physiological variations and pathophysiological findings in fecal incontinence. *Gastroenterology* 1992; 103 (1): 103-13.
- Kekki M, Samloff IM, Ihama K, Siurala M. Age- and sex-related behaviour of gastric acid secretion at the population level. *Scand J Gastroenterol* 1982; 17 (6): 737-43.
- Katellaris PH, Seow F, Lin BPC, Napoli J, Ngu MC, Jones DB. Effect of age, Helicobacter pylori infection, and gastritis with atrophy on serum gastrin and gastric acid secretion in healthy men. *Gut* 1993; 34 (8): 1032-7.
- Feldman M, Cryer B, McArthur KE, Huet BA, Lee E. Effects of aging and gastritis on gastric acid and pepsin secretion in humans: a prospective study. *Gastroenterology* 1996; 110 (4): 1043-59.
- Pilotto A, Salles N. Helicobacter pylori infection in geriatrics. *Helicobacter* 2002; 7: 56-62.
- Haruma K, Kamada T, Kawaguchi H, Okamoto S, Yoshihara M, Sumii K, Inoue M, Kishimoto S, Kajiyama G, Miyoshi A. Effect of age and Helicobacter pylori infection on gastric acid secretion. *J Gastroenterol Hepatol* 2000; 15 (3): 277-83.
- Lee A, Veldhuyzen van Zanten S. The aging stomach or the stomachs of the ages. *Gut* 1997; 41(4): 575-6.
- Van Asselt DZ, van den Broek WJ, Lamers CB, Corstens FH, Hoefnagels WH. Free and protein-bound cobalamin absorption in healthy middle-aged and older subjects. *J Am Geriatr Soc* 1996; 44 (8): 949-53.
- Pignatelli B, Bancel B, Plummer M, Toyokuni S, Patricot LM, Ohshima H. Helicobacter pylori eradication attenuates oxidative stress in human gastric mucosa. *Am J Gastroenterol* 2001; 96 (6): 1758-66.
- Lenaz G, Bovina C, D'Aurelio M, Fato R, Formiggini G, Genova ML, Giuliano G, Merlo Pich M, Paolucci U, Parenti Castelli G, Ventura B. Role of mitochondria in oxidative stress and aging. *Ann NY Acad Sci* 2002; 959: 199-213.
- Bado A, Levasseur S, Attoub S, Kermorgant S, Laigneau JP, Bortoluzzi MN, Moizo L, Lehy T, Guerre-Millo M, Le Marchand-Brustel Y, Lewin MJ. The stomach is a source of leptin. *Nature* 1998; 394 (6695): 790-93.
- Azuma T, Suto H, Ito Y, Ohtani M, Dojo M, Kuriyama M, Kato T. Gastric leptin and Helicobacter pylori infection. *Gut* 2001; 49 (3): 324-29.
- Nwokolo CU, Freshwater DA, O'Hare P, Randeve HS. Plasma ghrelin following cure of Helicobacter pylori. *Gut* 2003; 52 (5): 637-40.
- Goto H, Surgiyama S, Ohara A, Hoshino H, Hamajima E, Kanamori S, Tsukamoto Y, Ozawa T. Age-associated decreases in prostaglandin contents in human gastric mucosa. *Biochem Biophys Res Commun* 1992; 186 (3): 1443-8.
- Cryer B, Redfern JS, Goldschmidt M, Lee E, Feldman M. Effect of aging on gastric and duodenal mucosal prostaglandin concentrations in humans. *Gastroenterology* 1992; 102 (4 Pt1): 1118-23.

44. Fligel SE, Relan NK, Dutta S, Tureaud J, Hatfield J, Majumdar AP. Aging diminishes gastric mucosal regeneration: relationship to tyrosine kinases. *Lab Invest* 1994; 70 (5): 764-74.
45. Relan NK, Fligel SE, Dutta S, Tureaud J, Chauhan DP, Majumdar AP. Induction of EGF-receptor tyrosine kinase during early reparative phase of gastric mucosa and effects of aging. *Lab Invest* 1995; 73 (5): 717-26.
46. Lee M. Age-related changes in gastric blood flow in rats. *Gerontology* 1996; 42 (5): 289-93.
47. Kawano S, Tanimura H, Sato N. Age related change in human gastric mucosal energy metabolism. *Scand J Gastroenterol* 1991; 26 (7): 701-6.
48. Höhn P, Gabbert H, Wagner R. Differentiation and aging of the rat intestinal mucosa. II. Morphological, enzyme histochemical and disc electrophoretic aspects of the aging of the small intestinal mucosa. *Mech Ageing Dev* 1978; 7 (3): 217-26.
49. Corazza GR, Frazzoni M, Gatto MR, Gasbarrini G. Ageing and small-bowel mucosa: a morphometric study. *Gerontology* 1986; 32 (1): 60-5.
50. Woudstra T, Thomson AB. Nutrient absorption and intestinal adaptation with ageing. *Best Pract Res Clin Gastroenterol* 2002; 16 (1): 1-15.
51. Salles N. Basic mechanisms of the aging gastrointestinal tract. *Dig Dis* 2007; 25 (2): 112-7.
52. Arora S, Kassarijan Z, Krasinski SD, Croffey B, Kaplan MM, Russell RM. Effect of age on tests of intestinal and hepatic function in healthy humans. *Gastroenterology* 1989; 96 (6): 1560-5.
53. Holt PR, Balint JA. Effects of aging on intestinal lipid absorption. *Am J Physiol* 1993; 264 (1 Pt 1): G1-6.
54. Laugier R, Bernard JP, Berthezene P, Dupuy P. Changes in pancreatic exocrine secretion with age: pancreatic exocrine secretion does decrease in the elderly. *Digestion* 1991; 50 (3-4): 202-11.
55. Stevens T, Conwell DL, Zuccaro G Jr, Van Lente F, Lopez R, Purich E, Fein S. A prospective crossover study comparing secretin-stimulated endoscopic and Dreiling tube pancreatic function testing in patients evaluated for chronic pancreatitis. *Gastrointest Endosc* 2008; 67 (3): 458-66.
56. Anand Bs, Vij Jc, Mac HS, Chowdhury V, Kumar A. Effect of aging on the pancreatic ducts: a study based on endoscopic retrograde pancreatography. *Gastrointest Endosc* 1989; 35 (3): 210-3.
57. Kreef L, Sandin B. Changes in pancreatic morphology associated with aging. *Gut* 1973; 14 (12): 962-70.
58. Gullo L, Ventrucci M, Naldoni P, Pezzilli R. Aging and exocrine pancreatic function. *J Am Geriatr Soc* 1986; 34 (11): 790-2.
59. Citi S, Salvani L. The intestinal absorption of ¹³¹I labelled olein triolein, of ⁵⁸Co vitamin B₁₂ and ⁵⁹Fe in the aged subjects. *G Gerontol* 1964; 12: 123-6.
60. Wang DQ. Aging per se is an independent risk factor for cholesterol gallstone formation in gallstone susceptible mice. *J Lipid Res* 2002; 43 (11): 1950-9.
61. Behar J, Corazziari E, Guelrud M et al. Functional Gallbladder and Sphincter of Oddi Disorders. *Gastroenterology* 2006; 130 (5): 1498-509.
62. Drossman DA, Li Z, Andruzzi E, Temple RD, Talley NJ, Thompson WG, Whitehead WE, Janssens J, Funch-Jensen P, Corazziari E et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. *Dig Dis Sci* 1993; 38 (9): 1569-80.
63. Holt PR. Intestinal malabsorption in the elderly. *Dig Dis* 2007; 25 (2): 144-5.
64. Parlesak A, Klein B, Schecher K, Bode JC, Bode C. Prevalence of small bowel bacterial overgrowth and its association with nutrition intake in nonhospitalized older adults. *J Am Geriatr Soc* 2003; 51 (6): 768-73.
65. Lewis SJ, Potts LF, Malhotra R, Mountford R. Small bowel bacterial overgrowth in subjects living in residential care homes. *Age Ageing* 1999; 28 (2): 181-5.
66. Atillasoy E, Holth PR. Gastrointestinal proliferation and aging. *J Gerontol* 1993; 48 (2): B43-9.
67. Xiao ZQ, Moragoda L, Jaszewski R, Hatfield JA, Fligel SE, Majumdar AP. Aging is associated with increased proliferation and decreased apoptosis in the colonic mucosa. *Mech Ageing Dev* 2001; 122 (15): 1849-64.
68. Holt PR, Moss SF, Heydari AR, Richardson A. Diet restriction increases apoptosis in the gut of aging rats. *J Gerontol A Biol Sci Med Sci* 1998; 53 (3): B168-72.
69. Majumdar AP. Regulation of gastrointestinal mucosal growth during aging. *J Physiol Pharmacol* 2003; 54 (Suppl. 4): 143-54.
70. Gupta SD, Petrus LV, Gibbins FJ, Dellipiani AW. Endoscopic evaluation of dysphagia in the elderly. *Age Ageing* 1987; 16 (3): 159-64.
71. Steele CM, Greenwood C, Ens I, Robertson C, Seidman-Carlson R. Mealtime difficulties in a home for the aged: not just dysphagia. *Dysphagia* 1997; 12 (1): 43-50.
72. Siebens H, Trupe E, Siebens A, Cook F, Anshen S, Hanauer R, Oster G. Correlates and consequences of eating dependency in institutionalized elderly. *J Am Geriatr Soc* 1986; 34 (3): 192-8.
73. Mendez L, Friedman LS, Castell DO. Swallowing disorders in the elderly. *Clin Geriatr Med* 1991; 7 (2): 215-30.
74. Buchholz DW. Neurogenic dysphagia: what is the cause when the cause is not obvious? *Dysphagia* 1994; 9 (4): 245-55.
75. Knuff TE, Benjamin SB, Castell DO. Pharyngoesophageal (Zenker's) diverticulum: a reappraisal. *Gastroenterology* 1982; 82 (4): 734-6.
76. Sudhakar CB, al Hakeem M, Quader MA, MacArthur JD, Shear P. Anterior cervical osteophytes: a rare cause of dysphagia. *Conn Med* 1997; 61 (6): 323-5.
77. Tosato F, Passaro U, Vasapollo L, Riccardelli F, Paolini A. Dysphagia associated with aorto-cardiac compression on the distal esophagus: a rare event but not exceptional in the elderly. *Minerva Chir* 1995; 50 (9): 773-7.
78. Negus E. Stroke-induced dysphagia in hospital: the nutritional perspective. *Br J Nurs* 1994; 3 (6): 263-9.
79. Ali GN, Wallace KL, Schwartz R, DeCarle DJ, Zagami AS, Cook IJ. Mechanisms of oral-pharyngeal dysphagia in patients with Parkinson's disease. *Gastroenterology* 1996; 110 (2): 383-92.
80. Bashford G, Bradd P. Drug-induced Parkinsonism associated with dysphagia and aspiration: a brief report. *J Geriatr Psychiatry Neurol* 1996; 9 (3): 133-5.
81. Kluin KJ, Bromberg MB, Feldman EL, Simmons Z. Dysphagia in elderly men with myasthenia gravis. *J Neurol Sci* 1996; 138 (1-2): 49-52.
82. Xie P, Ren J, Bardan E, Mittal RK, Sui Z, Shaker R. Frequency of gastroesophageal reflux events induced by pharyngeal water stimulation in young and elderly subjects. *Am J Physiol* 1997; 272 (2 Pt1): G233-7.
83. Mold JW, Reed LE, Davis AB, Allen ML, Decktor DL, Robinson M. Prevalence of gastroesophageal reflux in elderly patients in a primary care setting. *Am J Gastroenterol* 1991; 86 (8): 965-70.
84. Mittal RK, Lange RC, McCallum RW. Identification and mechanism of delayed esophageal acid clearance in subjects with hiatus hernia. *Gastroenterology* 1987; 92 (1): 130-5.
85. Kaul B, Petersen H, Myrvold HE, Grette K, Røysland P, Halvorsen T. Hiatus hernia in gastroesophageal reflux disease. *Scand J Gastroenterol* 1986; 21 (1): 31-4.
86. Tack J, Vantrappen G. The aging oesophagus. *Gut* 1997; 41 (4): 422-4.
87. Maconi G, Bianchi-Porro G. Multiple ulcerative esophagitis caused by alendronate. *Am J Gastroenterol* 1995; 90 (10): 1889-90.
88. Raiha I, Hietanen E, Sourander L. Symptoms of gastroesophageal reflux disease in elderly people. *Age Ageing* 1991; 20 (5): 365-70.
89. Collen MJ, Abdulian JD, Chen YK. Gastroesophageal reflux disease in the elderly: more severe disease that requires aggressive therapy. *Am J Gastroenterol* 1995; 90 (7): 1053-7.
90. Tack J, Talley NJ, Camilleri M, Holtmann G, Hu P, Malagelada JR, Stanghellini V. Functional Gastrointestinal Disorders. *Gastroenterology* 2006; 130 (5): 1466-79.

91. Drossman DA, Corazziari E, Delvaux M, Spiller RC, Talley NJ, Thompson WG, Whitehead WE (Editors). Rome III: The Functional Gastrointestinal Disorders. 3rd Edition. McLean, VA: Degnon Associates, 2006; 1-1048.
92. Halder SL, Talley NJ. Treatment of functional dyspepsia. *Curr Treat Options Gastroenterol* 2005; 8 (4): 325-36.
93. Mertz H, Fass R, Kodner A, Yan-Go F, Fullerton S, Mayer EA. Effect of amitriptyline on symptoms, sleep, and visceral perception in patients with functional dyspepsia. *Am J Gastroenterol* 1998; 93 (2): 160-5.
94. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; 130 (5): 1480-91.
95. Saito YA, Schoenfeld P, Locke GRI. The epidemiology of irritable bowel syndrome in North America: a systemic review. *Am J Gastroenterol* 2002; 97: 1910-15.
96. Talley NJ, O'Keefe EA, Zinsmeister Art, et al. Prevalence of gastrointestinal symptoms in the elderly: a population based study. *Gastroenterology* 1992; 102: 895-901.
97. Ilnyckyj A, Graff LA, Blanchard JF, Bernstein CN. Therapeutic value of a gastroenterology consultation in irritable bowel syndrome. *Aliment Pharmacol Ther* 2003; 17 (7): 871-80.
98. Lea R, Whorwell PJ. New insights into the psychosocial aspects of irritable bowel syndrome. *Curr Gastroenterol Rep* 2003; 5 (4): 343-50.
99. Gunn MC, Cavin AA, Mansfield JC. Management of irritable bowel syndrome. *Postgrad Med J* 2003; 79 (929): 154-8.
100. Harari D, Gurwitz JK, Minaker KL. Constipation in the elderly. *J Am Geriatr Soc* 1993; 41 (10): 1130-40.
101. Wald A. Constipation in elderly patients: Pathogenesis and management. *Drugs Aging* 1993; 3 (3): 220-31.
102. Read NW, Celik AF, Katsinelos P. Constipation and incontinence in the elderly. *J Clin Gastroenterol* 1995; 20 (1): 61-70.
103. Lindeman RD, Romero LJ, Liang HC, Baumgartner RN, Koehler KM, Garry PJ. Do elderly persons need to be encouraged to drink more fluids? *J Gerontol A Biol Sci Med Sci* 2000; 55 (7): M361-5.
104. Liu F, Kondo T, Toda Y. Brief physical inactivity prolongs colonic transit time in elderly active men. *Int J Sports Med* 1993; 14 (8): 465-7.
105. Spinzi G.C. Bowel care in the elderly. *Dig Dis* 2007; 25 (2): 160-5.
106. Edwards IR, Coulter DM, Macintosh D. Intestinal effects of captopril. *BMJ* 1992; 304 (6823): 359-60.
107. Niwata S, Yamada Y, Ikegami N. Prevalence of inappropriate medication using Beers criteria in Japanese long-term care facilities. *BMC Geriatr* 2006; 6: 1.
108. Potter J, Wagg A. Management of bowel problems in older people: an update. *Clin Med* 2005; 5 (3): 289-95.
109. Hull C, Greco RS, Brooks DC. Alleviation of constipation in the elderly by dietary fiber supplementation. *J Am Geriatr Soc* 1980; 28 (9): 410-4.
110. Finlay M. The use of dietary fibre in a long-stay geriatric ward. *J Nutr Elder* 1988; 8 (1): 19-30.
111. Tramonte SM, Brand MB, Mulrow CD, Amato MG, O'Keefe ME, Ramirez G. The treatment of chronic constipation in adults. A systematic review. *J Gen Intern Med* 1997; 12 (1): 15-24.
112. Di Palma JA, DeRidder PH, Orlando RC, Kolts BE, Cleveland MB. A randomized, placebo-controlled, multicenter study of the safety and efficacy of a new polyethylene glycol laxative. *Am J Gastroenterol* 2000; 95 (2): 446-50.
113. Di Palma JA, Cleveland MV, McGowan J, Herrera JL. A randomized, multicenter comparison of polyethylene glycol laxative and tegaserod in treatment of patients with chronic constipation. *Am J Gastroenterol* 2007; 102 (9): 1964-71.
114. Kale-Pradhan PB, Wilhelm SM, Tegaserod for constipation-predominant irritable bowel syndrome *Pharmacotherapy* 2007; 27 (2): 267-77.
115. Barish CF, Drossmann P, Johanson JF, Ueno R. Efficacy and safety of Lubiprostone in patients with chronic constipation. *Dig Dis Sci* 2010; 55 (4): 1090-7. Epub 2009 Dec 11.
116. Del Duca T, Ricci M. Motilità del colon in rapporto alla somministrazione di alcune acque salso-solfato-alcaline. Studi roentgenocinetografici. *Clin Term* 1967; 20 (6): 321-38.
117. Dey An. Characteristics of elderly nursing home residents: data from the 1995 National Nursing Home Survey. *Adv Data* 1997; 289: 1-8.
118. De Lillo AR, Rose S. Functional bowel disorders in the geriatric patient: constipation, fecal impaction, and fecal incontinence. *Am J Gastroenterol* 2000; 95 (4): 901-5.
119. McHugh SM, Diamant NE. Effect of age, gender, and parity on anal canal pressures. Contribution of impaired anal sphincter function to fecal incontinence. *Dig Dis Sci* 1987; 32 (7): 726-36.
120. Goldstein MK, Brown EM, Holt P, Gallagher D, Winograd CH. Fecal incontinence in an elderly man. Stanford University geriatrics case conference. *J Am Geriatr Soc* 1989; 37 (10): 991-1002.
121. Keating JP, Stewart PJ, Eyers AA, Warner D, Bokey EL. Are special investigations of value in the management of patients with fecal incontinence? *Dis Colon Rectum* 1997; 40 (8): 896-901.
122. Feldman M, Schiller LR. Disorders of gastrointestinal motility associated with diabetes mellitus. *Ann Intern Med* 1983; 98 (3): 378-84.
123. Scarlet Y. Medical management of fecal incontinence. *Gastroenterology* 2004; 126 (Suppl. 1): S55-63.
124. MacLeod JH. Management of anal incontinence by biofeedback. *Gastroenterology* 1987; 93 (2): 291-4.
125. Locke GR 3rd, Pemberton JH, Phillips SF. American Gastroenterological Association Medical Position Statement: guidelines on constipation. *Gastroenterology*. 2000; 119 (6): 1761-6.
126. Rao SS, Ozturk R, Laine L. Clinical utility of diagnostic tests for constipation in adults: a systematic review. *Am J Gastroenterol* 2005; 100 (7): 1605-15.
127. Somerville K, Faulkner G, Langman M. Non-steroidal anti-inflammatory drugs and bleeding peptic ulcer. *Lancet* 1986; 1 (8479): 462-4.
128. Pilotto A, Leandro G, Di Mario F, Franceschi M, Bozzola L, Valerio G. Role of Helicobacter pylori infection on upper gastrointestinal bleeding in the elderly: a case-control study. *Dig Dis Sci* 1997; 42 (3): 586-91.
129. Cullen DJ, Hawkey GM, Greenwood DC, Humphreys H, Shepherd V, Logan RF, Hawkey CJ. Peptic ulcer bleeding in the elderly: relative roles of Helicobacter pylori and non-steroidal anti-inflammatory drugs. *Gut* 1997; 41 (4): 459-62.
130. Pilotto A, Franceschi M, Leandro G, Di Mario F, Valerio G. The effect of Helicobacter pylori infection on NSAID-related gastroduodenal damage in the elderly. *Eur J Gastroenterol Hepatol* 1997; 9 (10): 951-6.
131. Wyatt JL, Shallcross TM, Crabtree JE, Heatley RV. Helicobacter pylori, gastritis, and peptic ulceration in the elderly. *J Clin Pathol* 1992; 45 (12): 1070-4.
132. Kempainen H, Raiha I, Sourander L. Clinical presentation of peptic ulcer in the elderly. *Gerontology* 1997; 43 (5): 283-8.
133. García Rodríguez LA, Cattaruzzi C, Troncon MG, Agostinis L. Risk of hospitalization for upper gastrointestinal tract bleeding associated with ketorolac, other nonsteroidal anti-inflammatory drugs, calcium antagonists, and other antihypertensive drugs. *Arch Intern Med* 1998; 158 (1): 33-9.
134. Langman MJS, Weil J, Wainwright P, Lawson DH, Rawlins MD, Logan RF, Murphy M, Vessey MP, Colin-Jones DG. Risk of bleeding peptic ulcer associated with individual non-steroidal anti-inflammatory drugs. *Lancet* 1994; 343 (8905): 1075-8.
135. García Rodríguez LA, Jick H. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. *Lancet* 1994; 343 (8900): 769-72.
136. Nobili A, Tettamanti M, Frattura L, Spagnoli A, Ferraro L, Marrazzo E, Ostino G, Comelli M. Drug use by the elderly in Italy. *Ann Pharmacother* 1997; 31 (4): 416-22.

137. Tamblin R, Berkson L, Dauphinee WD, Gayton D, Grad R, Huang A, Isaac L, McLeod P, Snell L. Unnecessary prescribing of NSAIDs and the management of NSAID-related gastropathy in medical practice. *Ann Intern Med* 1997; 127 (6): 429-38.
138. Pahor M, Guralnik JM, Furberg CD, Carbonin P, Havlik R. Risk of gastrointestinal haemorrhage with calcium antagonists in hypertensive persons over 67 years old. *Lancet* 1996; 347 (9008): 1061-5.
139. Johnston RD, Shinghal S, Bowling TE. Upper gastrointestinal disease in the elderly patient. *Rev Clin Gerontol* 2005; 15: 175-85.
140. Pilotto A, Franceschi M, Leandro G, Bozzola L, Fortunato A, Rassa M, Meli S, Soffiati G, Scagnelli M, Di Mario F, Valerio G. Efficacy of 7 day lansoprazole-based triple therapy for *Helicobacter pylori* infection in elderly patients. *J Gastroenterol Hepatol* 1999; 14 (5): 468-75.
141. Hoffmann JC, Zeitz M. Small bowel disease in the elderly: diarrhoea and malabsorption. *Best Pract Res Clin Gastroenterol* 2002; 16 (1): 17-36.
142. Holt PR. Diarrhea and malabsorption in the elderly. *Gastroenterol Clin North Am* 2001; 30 (2): 427-44.
143. Bures J, Cyrany J, Kohoutova D, Förstl M, Rejchrt S, Kvetina J, Vorisek V, Kopacova M. Small intestinal bacterial overgrowth syndrome. *World J Gastroenterol* 2010; 16 (24): 2978-90.
144. Comparato G, Pilotto A, Franzè A, Franceschi M, Di Mario F. Diverticular disease in the elderly. *Dig Dis* 2007; 25 (2): 151-9.
145. Kang JY, Melville D, Maxwell JD Epidemiology and management of diverticular disease of the colon. *Drugs Aging* 2004; 21 (4): 211-28.
146. Heresbach D, Alexandre JL, Bretagne JF, Cruchant E, Dabadie A, Dartois-Hoguin M, Girardot PM, Jouanolle H, Kerneis J, Le Verger JC, Louvain V, Pennognon L, Richecoeur M, Politis J, Robaszkiwicz M, Seyrig JA, Tron I; ABERMAD Crohn's disease in the over-60 age group: a population based study. *Eur J Gastroenterol Hepatol* 2004; 16 (7): 657-64.
147. Park K, Brewster D. Epidemiology. In Gilbert FJ, Park KGM, Thompson AM. Scottish audit of gastric and oesophageal cancer. Report 1997-2000. Edinburgh, 2002.
148. Inoshita N, Yanagisawa A, Arai T, Kitagawa T, Hirokawa K, Kato Y. Pathological characteristics of gastric carcinomas in the very old. *Jpn J Cancer Res* 1998; 89 (10): 1087-92.
149. Wilson JA. Colon cancer screening in the elderly: when do we stop? *Trans Am Clin Climatol Assoc* 2010; 121: 94-103.
150. Lux G, Langer M, Stabenow-Lohbauer U, Orth KH, Bozkurt T, Meyer MJ. Diverticulosis and diverticulitis in the elderly. *Fortschr Med* 1998; 116 (9): 26-8, 30, 32-4.
151. Barbara L, Sama C, Morselli Labate AM. A population study on the prevalence of gallstones disease: the Sirmione study. *Hepatology* 1987; 7: 913-7.
152. Rome Group for the Epidemiology and Prevention of Cholelithiasis (GREPCO). The epidemiology of gallstone disease in Rome, Italy. Part I. Prevalence data in men. *Hepatology* 1988; 8: 904-6.
153. Rome Group for the Epidemiology and Prevention of Cholelithiasis (GREPCO). Prevalence of gallstone disease in an Italian adult female population. *Am J Epidemiol* 1984; 119: 796-805.
154. Einarsson K, Nilsell K, Leijd B, Angelin B. Influence of age on secretion of cholesterol and synthesis of bile acids by the liver. *N Engl J Med* 1985; 313 (5): 277-82.
155. Valdivieso V, Palma R, Wunkhaus R, Antezana C, Severín C, Contreras A. Effect of aging on biliary lipid composition and bile acid metabolism in normal Chilean women. *Gastroenterology* 1978; 74 (5 Pt1): 871-4.
156. Grossi F, Fontana M, Conti R, Mastroianni S, Lazzari S, Messini F, Piccarreta U, Grassi M. Motility of the gastric antrum and the gallbladder following oral administration of sulphate-bicarbonate mineral water. *Clin Ter* 1996; 147 (6): 321-6.
157. Fraioli A, Serio A, Mennuni G, Ricci P, Scalabrino A. Studio sull'efficacia delle acque minerali salso-solfato-alcina (Regina) e cloruro-sodica ipotonica (Tettuccio) di Montecatini sulla dinamica motoria della colecisti. *Clin Term* 1992; 45: 9-17.
158. Popper H. Aging and the liver. *Prog Liver Dis* 1986; 8: 659-83.
159. Kitani K. Hepatic drug metabolism in the elderly. *Hepatology* 1986; 6 (2): 316-9.
160. Spanier BW, Dijkgraaf MG, Bruno MJ. Epidemiology, aetiology and outcome of acute and chronic pancreatitis: An update. *Best Pract Res Clin Gastroenterol* 2008; 22 (1): 45-63.
161. Konner J, O'Reilly E. Pancreatic cancer: epidemiology, genetics, and approaches to screening. *Oncology (Williston Park)* 2002; 16 (12): 1615-22, 1631-2; discussion 1632-3, 1637-8.