ADVANCES AND PROSPECTS IN GASTROENTEROLOGY

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Contents

Summary

Gastroenterology constitutes one of the largest branches of internal medicine and is characterized by constant development, which results from two factors: 1) the progress in techniques and technologies, 2) the advances in basic medical sciences, including molecular biology, physiology, patho-morphology and genetics.

This chapter presents the current knowledge of various aspects of selected diseases of the digestive system. In the upper gastrointestinal tract, the attention is directed towards dyspepsia, gastro-esophageal reflux disease (GERD), *Helicobacter pylori* (HP) infection and its treatment, peptic ulcer disease, and toxicity of non-steroidal anti-inflammatory drugs (NSAID). The latter drugs are widely used agents, although their consumption is often associated with the development of serious gastrointestinal complications, such as acute ulcer bleeding. HP infection is also an established cause of peptic ulcer disease. In systematic reviews published up to 2006, the detailed analyses showed that these two factors act synergistically for the development of both peptic ulcer and ulcer bleeding.

The significance of acute infectious diarrhea, particularly in developing countries, is emphasized. Another enteropathy which now attracts much attention is celiac disease. Recent reports from various regional areas suggest that this disorder is a frequent condition affecting from 0.5% to 1% of the general population. Typically, celiac disease manifests itself as malabsorption syndrome. However, the disease often presents in an atypical manner and many cases remain undiagnosed carrying the risk for long term complications - osteoporosis, infertility or cancer.

In inflammatory bowel disease (IBD), the impact of new biologic therapies is described. The most frequent and most important diseases of the pancreas are reviewed. Of liver diseases, hepatitis B, hepatitis C and non-alcoholic fatty liver disease (NAFLD) are presented. These diseases may progress to cirrhosis or even carcinoma of the liver and constitute an important indication for liver transplantation.

A considerable space is devoted to neoplasm of the digestive system, including cancers of the esophagus, stomach, pancreas, large intestine and liver. These five most frequent gastrointestinal tract cancers throughout the world accounted for 3.2 million new cases and 2.6 million deaths in 2002. The two pillars in the prevention of these cancers are primary and secondary prevention measures. Primary prevention is based on popularization of a healthy life style, including diet, physical activity and reducing contact with carcinogenic agents – tobacco, alcohol, hepatitis virus B and C. Secondary prevention is based on early detection of neoplastic lesions. In the field of colorectal cancer, colonoscopy results in more polyps detected, down-staging of cancers identified and improved survival. Chemo-preventive interventions in colorectal neoplasia also have been documented by studies using acetylsalicylic acid and other NSAID. Emerging are data showing analogous findings for statins, although these deserve further investigation. Finally, the potential impact of genomics in gastroenterology and hepatology is discussed.

1. Introduction

Gastroenterology constitutes one of the largest branches of internal diseases. These

results from epidemiology: the incidence and prevalence of diseases of the gastrointestinal tract, the liver and the pancreas is the second highest following cardiovascular diseases. The digestive system is also the most frequent location of malignancies that are significant cause of deaths in males and females (Figure 1). In developing countries, viral, bacterial and parasitic infections of the gastrointestinal tract and the liver create a significant problem.

Gastroenterology is the field in clinical medicine characterized by constant, dynamic development, which mainly results from two factors:

1. the progress in techniques and technologies,
2. the development of basic sciences, particularly molecular biology, physiology, patho-morphology and genetics.
3. These factors, along with progress in gastroenterological diagnostics and therapy, will be presented below.

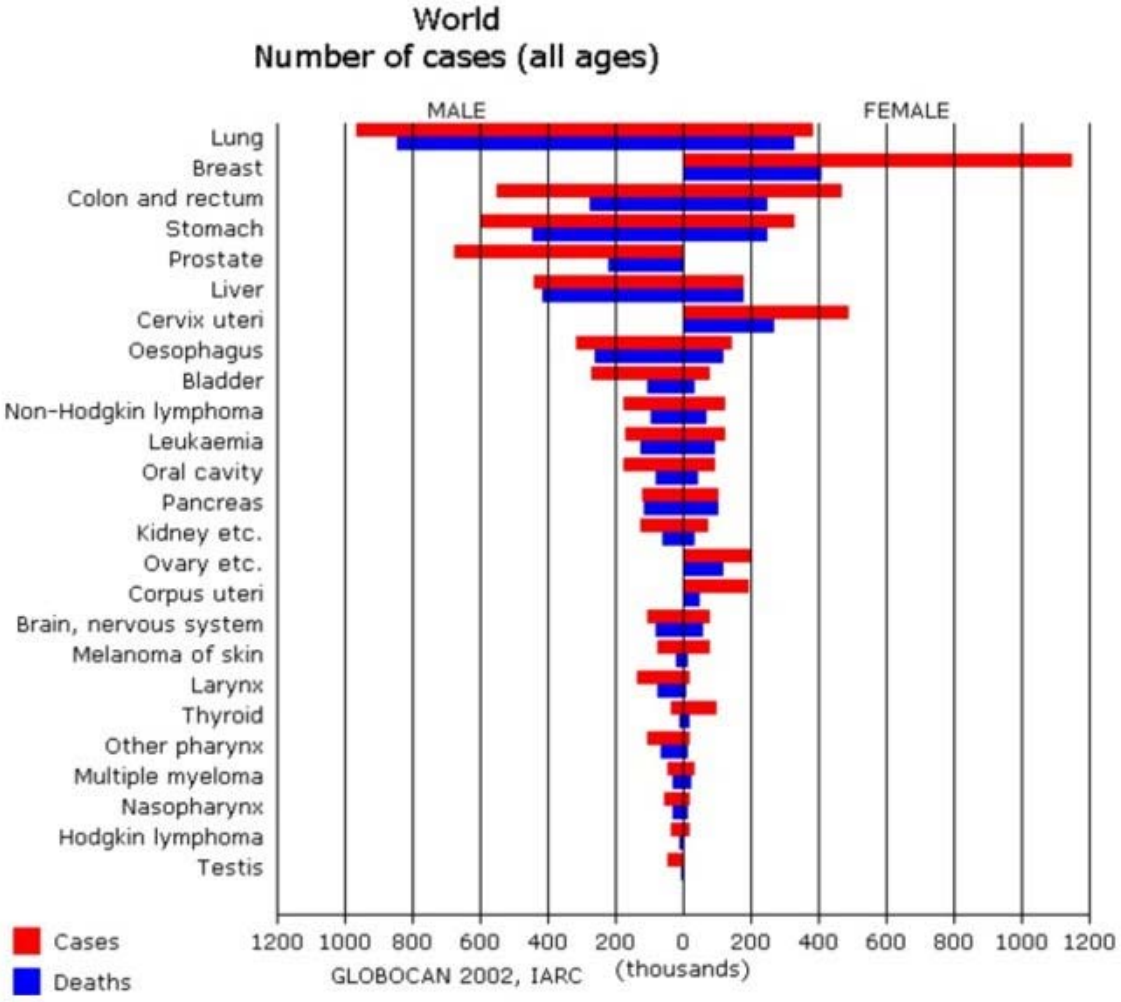

Figure 1. Incidence and mortality according to cancer site (source: GLOBOCAN 2002, IARC)

2. Diagnostic Tests in Gastroenterology

In addition to methods traditionally used in diagnostics of the gastrointestinal tract, such as radiological examinations, endoscopy and histopathology, newer techniques have been more widely used in recent years, including capsule endoscopy, positron-emission tomography or endoscopic ultrasound.

Capsule endoscopy, previously used solely for small bowel assessment, has developed a new indication to use. When the number of pictures made by the capsule had increased to 14 per second, diagnosing gastro-esophageal reflux disease, and detecting esophageal varices became feasible.

Positron-emission tomography (PET) is a non-invasive imaging technique using the decay of isotopes that emit positrons. This method, most commonly based on the metabolism of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) in tissues, is used mainly for the assessment of malignancies before and following oncological treatment.

Optical coherent tomography is a technique used along with endoscopy. The spatial resolution of this method is 10 μm, whereas penetration depth is 1.5 mm. This facilitates a microscopic assessment of tissues in vivo (during endoscopy), for instance to visualize transmural intestinal inflammation in Crohn's disease and to differentiate this disease from ulcerative colitis, which involves mucosa alone.

Confocal laser endoscopy (endo-microscopy) provides extraordinary diagnostic opportunities. German researchers previously showed that this method allows detection of intraepithelial neoplasia or colorectal cancer during colonoscopy. Now the same authors have published a case report on the in vivo visualization of the presence of the bacteria *Helicobacter pylori* on the surface of gastric epithelium and around its cells.

The importance of **endoscopic ultrasound** (EUS) in diagnosing diseases of the esophagus, stomach, bile tract and pancreas is increasing. This is reflected by the substantial amount of literature on this method. Its results change the preliminary diagnosis by 25% and diagnostic and therapeutic management in 50% patients.

3. Upper Gastrointestinal Diseases

3.1. Gastro-esophageal Reflux Disease (GERD)

Gastro-esophageal reflux disease is one of the commonest gastrointestinal diseases. It is caused by the reflux of gastric content to the esophagus, causing heartburn, which is a typical complaint. GERD is one of the causes of recurring retrosternal pain, which is named non-cardiac chest pain. This pain significantly affects quality of life and is often the subject of intensive diagnostic management. In 2005, two meta-analyses were published assessing the yield of proton pump inhibitor treatment (PPI) as a diagnostic test in this clinical situation. Both these studies showed that PPI treatment had good sensitivity (80%) and specificity (74%) in detecting GERD as the cause of chest pain.

Out of various methods of maintenance therapy for GERD, most evidence supports PPI used in doses that are half of the doses recommended by manufacturers. These drugs include omeprazole, pantoprazole, lanzoprazole, rabeprazole and esomeprazole. If PPI

are not tolerated, histamine receptors H_2 antagonists can be used, whose efficacy is lower but sufficient for maintenance therapy of mild GERD. Commonly recommended life style changes (avoiding alcohol, loose clothes, elevation of the upper body at sleep) are at best supportive. An alternative to continuous PPI treatment is the treatment "on demand", when GERD symptoms relapse.

Endoscopic therapies of GERD as an alternative to long term PPI treatment have evolved in the recent decade. They include: 1) the injection of substances that are neutral to tissues (Enteryx) in the lower esophageal sphincter region, 2) endoscopically applied "sutures" (EndoCinch system) that produce additional folds, preventing the reflux of gastric content to the esophagus and 3) thermal injury to the lower esophageal sphincter by means of radio frequency energy generator (Stretta procedure). The efficacy of these methods, however, particularly with regards to long term outcomes, has yet to be proven.

3.1.1. Complications of GERD

Serious complications of GERD include Barrett's esophagus and esophageal adenocarcinoma of the lower portion of the esophagus. Recent epidemiological studies have shown that important demographic and environmental factors promoting the development of these complications are white race, male sex and duodeno-gastro-oesophageal reflux. The risk factors of GERD include obesity and the use of drugs that decrease the pressure in the lower esophageal sphincter, while *H. pylori* infection is a protective factor. Barrett's esophagus, as a precancerous condition, necessitates surveillance; treatment is indicated when epithelial dysplasia appears. An international study assessing the efficacy of photodynamic therapy in Barrett's esophagus was published last year. This treatment used porfimer sodium and caused a complete elimination of the epithelium with high grade dysplasia in 77% of patients, and halved the risk of esophageal adenocarcinoma development compared to omeprazole. Another approach to eliminating dysplastic Barrett's epithelium is cryoablation using liquid nitrogen. Endoscopic and histopathology assessments confirmed a complete elimination of abnormal epithelium with this method in 78% cases.

3.2. Gastric Cancer

In 1983, Nobel Prize winners B. Marshall and R. Warren first proved that *H. pylori* infection is the cause of gastritis and peptic ulcer disease. In the following years, the hypothesis of *H. pylori*'s role in gastric cancer development was formed. In 2005, Japanese authors confirmed that the most important risk factor of this malignancy is atrophic gastritis caused by *H. pylori*. The authors evaluated the cancer risk using antibodies against *H. pylori* and pepsinogen I in a cohort of nearly 10,000 subjects followed-up and undergoing gastroscopy for 5 years. Another long-term study found beneficial effect of the eradication of *H. pylori* on the risk of gastric cancer in patients with peptic ulcer disease. After 3 years of follow-up, the cancer developed only in patients in whom the gastric ulcer had been previously diagnosed, and in none with a duodenal ulcer ($p=0.005$).

Every year sees with new studies on *H. pylori* eradication methods for various upper

gastrointestinal conditions. In a Spanish study published in 2005, the triple therapy using the newest PPI esomeprazole was found to be as effective as treatment using omeprazole (around 80% eradication). Increasing the omeprazole dose (from 20 mg to 40 mg twice a day) and the duration of the treatment (from 7 to 10 days) appeared to have no influence on the eradication success rate.

3.3. Peptic Ulcers and Their Complications

H. pylori and nonsteroidal anti-inflammatory drugs (NSAID) are the main causes of peptic ulcers and their complications. In the Netherlands, 52% of patients with bleeding peptic gastric or duodenal ulcers were taking NSAID, and 43% were *H. pylori* positive. Recent evidence suggests that the current rate of bleeding idiopathic ulcers in different countries and continents is about 20%.

Endoscopic methods and pharmacologic treatment have been used in managing bleeding ulcers for several years. A meta-analysis comparing these methods in patients with an adherent clot at the base of ulcer was published in 2005. Endoscopic treatment involving the clot removal and (or) injection or coagulation of the visible vessel reduces the rebleeding rate when compared to H_2 receptor antagonists or PPI treatment.

The latest systematic review and meta-analysis confirm previous studies showing that either oral or intravenous PPI treatment reduces the risk of ulcer rebleeding. Moreover this treatment reduces the number of patients requiring surgery, but does not reduce the death rate of bleeding.

The risk of upper gastrointestinal bleeding is increased by anti-platelet treatment, such as acetylsalicylic acid, clopidogrel and ticlopidine. This risk can be reduced or eliminated by adding PPI. Researchers from Hong-Kong suggest that treatment with clopidogrel alone in patient with aspirin intolerance or a history of bleeding is not justified.

Nonsteroidal anti-inflammatory drugs include most toxic substances used for therapy. The most frequent and most dangerous complications affect the gastrointestinal tract (ulcers, bleeding, perforations). In 5% of patients hospitalized due to gastrointestinal complications from NSAID they cause death. One third of deaths are probably caused by treatment with small doses of acetylsalicylic acid alone. Capsule endoscopy studies revealed that a proportion of patients chronically taking NSAID have erosions, ulcers or other lesions in the small intestine.

This alarming data raises the question of whether it is possible to avoid at least some NSAID complications. Following the unexpected withdrawal from the market certain coxibs (selective cyclooxygenase-2 inhibitors), less toxic acetaminophen remained, and when classic NSAID treatment is necessary, the addition of PPI is recommended. PPI is mainly recommended in patients with a moderate risk of gastrointestinal NSAID adverse events (such as a history of peptic ulcer) and in patients suffering from dyspepsia on this treatment. NSAID or coxibs should not be used in patients at risk of serious ulcer complications (bleeding or perforation) or cardiovascular complications (coronary heart disease, previous myocardial infarction or a stroke).

3.4. Dyspepsia

Dyspepsia, defined as chronic or recurrent pain or discomfort in the epigastrium, is one of the commonest conditions. In Minnesota, USA, as much as 24% of those polled had experienced dyspeptic symptoms over the previous year. In patients with uninvestigated dyspepsia, one of three strategies of management is recommended: 1) upper gastrointestinal endoscopy, 2) a non-invasive test for *H. pylori* infection and eradication in positive patients, or 3) empiric treatment using PPI. Meta-analysis from 2005 has shown a small advantage of gastroscopy over the test-and-treat strategy for *H. pylori*. In the UK, this advantage is diminished by the extra 400 USD that the endoscopic procedure costs. Eradication as an initial treatment is indicated in young patients from countries characterized by a high prevalence of *H. pylori* infection. A recently published systematic review and meta-analysis confirm the benefits of this management. PPI are mainly used in countries where *H. pylori* prevalence is low and does not exceed 10%.

4. Diseases of the Intestines

4.1. Acute Infectious Diarrhea (by Hanna Szajewska, M.D., *Department of Pediatric Gastroenterology and Nutrition, The Medical University of Warsaw, Warsaw, Poland*)

Enteropathogen	Acute watery diarrhea (usually resolves within 5–10 days)	Diarrhea with blood (dysentery)	Persistent diarrhea (>14 days)
Viruses			
Rotavirus	+	-	-
Enteric adenovirus (types 40, 41)	+	-	-
Calicivirus	+	-	-
Astrovirus	+	-	-
Cytomegalovirus	+	+	+
Bacteria			
Vibrio spp.	+	-	-
Enterotoxigenic *E coli* (ETEC)	+	-	-
Enteropathogenic *E coli*(EPEC)	+	-	+
Enteroaggregative *E coli* (EAggEC)	+	-	+
Enteroinavsive *E coli* (EIEC)	+	+	-
Enterohaemorraghic *E coli* (EHEC)	+	+	-
Shigella spp	+	+	+
Salmonella spp	+	+	+
Campylobacter spp	+	+	+
Yersinia spp	+	+	+
Clostridium difficile	+	+	+
Mycobacterium tuberculosis	-	+	+
Protozoa			
Giardia intestinalis	+	-	+
Cryptosporidium parvum	+	-	+
Microsporidia	+	-	+

Isospora belli	+	-	+
Cyclospora cayetanensis	+	-	+
Entamoeba histolytica	+	+	+
Balantidium coli	+	+	+
Helminths			
Strongyloides stercoralis	-	-	+
Schistosoma spp	-	+	+

Table 1. Etiologic agents of acute infections diarrhea
(based on: Casburn-Jones A. C., Farthing M. J., 2004)

Diarrhea is defined as a change in bowel movement for the individual person, characterized by an increase in the water content, volume (>200 g/24 h in adolescents and adults) and – usually – frequency of stools. Depending on the duration of the diarrhea, the illness may be considered *acute* (an episode of less than 10-14 days of duration) or *chronic* (longer than 14 days). Acute infectious diarrhea is one of the most common diseases, especially in children, and one of the leading causes of morbidity and mortality worldwide. The attack rate in developed countries ranges from 1.2 to 1.9 illnesses per person annually in the general population, and is higher in the first 2–3 years of life. The incidence is greater in developing countries, and in some tropical areas may reach even 6–10 episodes per child annually in children <3 years. In the vast majority of cases, acute infectious diarrhea is viral or bacterial, and less frequently parasitic (Table). Oral rehydration therapy with oral rehydration solutions (ORS) of lower osmolarity is the mainstay of treating acute diarrhea in patients of all ages, provided they are able to drink and that the dehydration is not severe. Fluids other than ORS are used for oral rehydration, including tea, cola drinks, fruit juices, or chicken broth. There is no evidence that fasting is beneficial. Thus, the optimal management of a mild to moderately dehydrated patient should consists of oral rehydration with an oral rehydration solution over 3-4 hours, and the reintroduction of normal feeding thereafter. For infants who are breast fed exclusively, the continuation of breastfeeding at all times results in decreased stool output, and is generally recommended. In a vast majority of patients, acute infectious diarrhea is self-limited and antibacterial drugs are generally unnecessary, even when a bacterial cause is suspected. WHO recommends the routine use of antibacterial agents only for shigellosis, suspected cases of cholera, symptomatic infection with invasive intestinal *Entamoeba histolytica*, and a laboratory-proven symptomatic infection with *Giardia intestinalis*. Although of unproven benefit, antimicrobial therapy is generally recommended for a suspected infection with enteroinvasive bacteria (i.e. *Salmonella gastroenteritis*) in patients with an increased risk of invasive disease, including infants younger than 6 months of age and persons with malignant neoplasms, hemoglobinopathies, HIV infection or other immunosuppressive illness or therapy, chronic gastrointestinal tract disease, or severe colitis. Nonspecific antidiarrheal agents (e.g., adsorbents such as kaolin-pectin), antimotility agents (e.g., loperamide), antisecretory drugs, and toxin binders (e.g., cholestyramine), are commonly used among older children and adults, but there is limited data regarding their efficacy. The beneficial effects of probiotics in acute diarrhea seem to be moderate, strain-dependent and dose-dependent, significant in watery diarrhea and viral gastroenteritis, but not existing in invasive, bacterial diarrhea, and more evident when treatment with probiotics is initiated early in the course of disease.

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Bibliography

American Gastroenterogical Association medical position statement: evaluation of dyspepsia. (2005). *Gastroenterology* 129, 1753-1755. [This document presents the official recommendations of the American Gastroenterological Association on evaluation of dyspepsia]

Bernstein D. (2005). What's new in hepatitis C: current state of the field and future directions. http://www.medscape.com/viewprogram/4835 [Updated review of the pathophysiology, epidemiology and management of hepatitis C]

Casburn-Jones A.C., Farthing M.J. (2004). Management of infectious diarrhea. *Gut* 53, 296-305. [A well-balanced review article describing causes, diagnosis (with emphasis on specific investigations) and treatment of infectious diarrhea]

Chan A. T., Giovannucci E. L., Meyerhardt J. A., Schernhammer E. S., Curhan G. C., Fuchs C. S. (2005). Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer. *Journal of the American Medical Association* 294, 914-923. [Prospective cohort study of 82911 women showing that regular, long-term (>10 years) aspirin use reduces risk of colorectal cancer; maximal risk reduction was seen at doses greater than 14 tablets per week]

Cortez-Pinto H., Carneiro de Mora M., Day C. (2006). Non-alcoholic steatohepatitis: from cell biology to clinical practice. *Journal of Hepatology* 44, 197-208. [Extensive report from Monothematic Conference of the European Association for the Study of the Liver on pathology, molecular mechanisms of progression and management of non-alcoholic fatty liver disease]

DiMagno MJ, DiMagno EP. (2005). Chronic pancreatitis. *Current Opinion in Gastroenterology* 21(5), 544-554. [A review of new, important observations in chronic pancreatitis with emphasis on genetic, molecular and clinical aspects of the disease]

Kiesslich R., Goetz M., Burg J., Stolte M., Siegel E., Maeurer M. J., Thomas S., Strand D., Galle P. R., Neurath M. F. (2005). Diagnosing *Helicobacter pylori* in vivo by confocal laser endoscopy. *Gastroenterology* 128, 2119-2123. [A well-documented case report showing that confocal laser endoscopy (endomicroscopy) can identify in vivo the presence of *Helicobacter pylori* in the stomach]

Lazaridis K.N., Juran B.D. (2005). American Gastroenterological Association Future Trends Committee report: The application of genomic and proteomic technologies to digestive disease diagnosis and treatment and their likely impact on gastroenterology clinical practice. *Gastroenterology* 129, 1720-1752. [An excellent review of genomic and proteomic technologies that might be applied in diseases of the gastrointestinal tract and liver]

Leontiadis G. I., Sharma V. K., Howden C. W. (2005). Systematic review and meta-analysis of proton pump inhibotor therapy in peptic ulcer bleeding. *British Medical Journal* 330, 568-570. [The largest meta-analysis showing the benefit of using proton pump inhibitors in patients with peptic ulcer bleeding]

Nielsen O. H., Ainsworth M., Csillag C., Rask-Madsen J. (2006). Systematic review: coxibs, nonsteroidal anti-inflammatory drugs or no cyclooxygenase inhibitors in gastroenterogical high-risk patients? *Alimentary Pharmacology and Therapeutics* 23, 27-33. [This systematic review describes gastrointestinal and cardiovascular toxicity of nonsteroidal anti-inflammatory drugs, including coxibs – the selective inhibitors of cyclooxygenase 2]

Pancreatic Section, British Society of Gastroenterology; Pancreatic Society of Great Britain and Ireland; Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland; Royal College of Pathologists; Special Group for Gastro-Intestinal Radiology (2005). Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinomas. *Gut* 54 (suppl. 5), v1-16. [This article gives an excellent state of the art analysis of incidence and mortality rates, etiology, pathology and clinical features of pancreatic cancer. It also provides the guidelines for the current treatment of this disease]

Poynter J. N., Gruber S. B., Higgins P. D. R., Almog R., Bonner J. D., Rennert H. S., Low M., Greenson J. K., Rennert G. (2005). Statins and the risk of colorectal cancer. *New England Journal of Medicine* 352, 2184-2192. [A population-based, epidemiological, case-control study indicating that there is a strong inverse association between the risk of colorectal cancer and the long-term use of statins, a class of agents effective in the management of hypercholesterolemia]

Ransohoff D. F. (2005). Colon cancer screening in 2005: status and challenges. *Gastroenterology* 128, 1685-1695. [This review article presents various methods of screening for colorectal cancer and identifies current challenges in this area in the light of evidence, guidelines and practice]

Rutgeerts P., Sandborn W. J., Feagan B. G., Reinisch W., Olson A., Johanns J., Travers S., Rachmilewitz D., Hanauer S. B., Lichtenstein G. R., de Villiers W. S. J., Present D., Sands B. E., Colombel J. F. (2005). Infliximab for induction and maintenance therapy for ulcerative colitis. *New England Journal of Medicine* 353, 2462-2476. [Two randomized, double-blind, placebo-controlled studies demonstrating the efficacy of infliximab for induction and maintenance therapy in patients with ulcerative colitis]

Sherman M. (2005). Hepatocellular carcinoma: epidemiology, risk factors, and screening. *Seminars in Liver Diseases* 25, 143-154. [Epidemiology and risk factors for the development of hepatocellular carcinoma are described]

Silverberg M. S., Satsangi J., Ahmad T., Arnott I. D. R., Bernstein C. N., Brant S. R., Caprilli R., Colombel J-F., Gasche C., Geboes K., Jewell D. P., Karban A., Loftus E. V., Pena A. S., Riddell R. H., Sachar D. B., Schreiber S., Steinhart A. H., Targan S. R., Vermeire S., Warren B. F. (2005). Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal Word Congress of Gastroenterology. *Canadian Journal of Gastroenterology* 19 (suppl. A), 5A-36A. [An extensive report on clinical, molecular and serological classification of ulcerative colitis, Crohn's disease and indeterminate colitis]

Twelves C., Wong A., Nowacki M. P., Abt M., Burris III H., Carrato A., Cassidy J., Cervantes A., Fagerberg J., Georgoulias V., Husseini F., Jodrell D., Koralewski P., Kronning H., Maroun J., Marschner N., McKendrick J., Pawlicki M., Rosso R., Schuller J., Seitz J-F., Stabuc B., Tujakowski J., Van Hazel G., Zaluski J., Scheithauer W. (2005). Capecitabine as adjuvant treatment for stage III colon cancer. *New England Journal of Medicine* 352, 2696-2704. [This randomized trial in nearly 2000 patients showed that oral capecitabine can be an effective alternative to standard intravenous fluorouracil plus leucovorin in the adjuvant treatment of colon cancer]

Villatoro E., Larvin M., Bassi C. (2006). Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis (Cochrane Review). *The Cochrane Library, Issue 1, 2006*. [Systematic review performed to determine the effectiveness and safety of prophylactic antibiotics in acute pancreatitis complicated by pancreatic necrosis]

Watanabe H., Mitsushima T., Yamaji Y., Okamoto M., Wada R., Kokubo T., Doi H., Yoshida H., Kawabe T., Omata M. (2005). Predicting the development of gastric cancer from combining *Helicobacter pylori* antibodies and serum pepsinogen status: a prospective endoscopic cohort study. *Gut* 54, 764-768. [A prospective cohort study demonstrating that the most important risk factor for the development of gastric cancer is gastric atrophy caused by *Helicobacter pylori*]

World Health Organization. Hepatitis B. WHO fact Sheet 204 (revised October 2000). WHO Web site, 2000. http://who.int/inf-fs/en/fact204.html [Official publication of WHO on epidemiology and management of hepatitis B. The article contains recommendations concerning vaccination against hepatitis B virus]

Biographical Sketch

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