Infections of the Gastrointestinal Tract,
2nd Edition
Blaser MJ, Smith PD, Ravdin JI et al, eds
Lippincott, Williams and Wilkins, 2002
ISBN: 0-7817-2847-9; $170.00

Infections of the Gastrointestinal Tract is a comprehensive multi-authored text of over 1300 pages covering luminal infection of the mostly adult gastrointestinal tract excluding the liver and biliary tract. The text is logically organized into ten different sections (a total of 81 chapters) with the first three sections covering epidemiology, physiology, and pathogenesis; the next two sections covering gastrointestinal syndromes in immunocompetent and immunocompromised hosts; and section six covering gastric infections, the bulk of which is on *H. pylori*. The remainder of the book is composed of detailed discussions of various infectious agents in section 7 followed by diagnosis, therapy, and prevention and control.

Infections of the Gastrointestinal Tract is an infectious diseases textbook rather than a gastroenterology text with emphasis on infectious diseases—not surprising given that most of the authors and editors are infectious diseases specialists rather than gastroenterologists.

Infections of the Gastrointestinal Tract is the only book a practicing gastroenterologist will ever need if he or she desires information on the bugs and drugs in the gut. For example, the chapter on Norwalk virus contained everything I ever wanted to know about the viral structure, genome (including a map of the capsid protein), and virulence of the organism. The chapter on Whipple's disease was similarly detailed and comprehensive enough to prepare a fellow lecture on the subject. On the other hand many chapters present a relatively cursory discussion of clinical symptoms, something which I suppose is not unreasonable since most the viral infections cause self-limited diarrhea. Still the brief paragraph on Norwalk agent didn't seem to paint a clear picture of the viral illness, something which many of my patients had seen on the six o'clock news and inquired about. In my opinion, the main deficiency of most of the chapters is the lack of clinical information about the infection relative to the detailed presentations on the laboratory findings of the infectious agents. Even the three chapters on *H. pylori,* although more inclusive about clinical presentation, seemed somewhat lacking. For example, the section on diagnosis did not mention the importance of prevalence on the accuracy of serology. Although the authors state that proton pump inhibitor therapy can cause false negative urea breath test and rapid urease test, no specific recommendations were given as to what to do with such patients. Finally most chapters only briefly mention the possible role of endoscopy in evaluating gastrointestinal infections. For example, the otherwise excellent chapter on *C. difficile* stated that endoscopy is rarely used for diagnosis; in my experience the reflexive reaction to inpatient diarrhea by most internists and surgeons is to order stool studies and a flexible sigmoidoscopy knowing that one can often get an endoscopy faster than a stool study. The chapters on *H. pylori* mentioned that multiple biopsies are often required for diagnosis but does not discuss where or how; for example in patients with recent antibiotic use, proton pump inhibitor use, and bleeding. In my opinion, *Infections of the Gastrointestinal Tract* is an excellent reference resource for most practicing gastroenterologists who have questions about infectious organisms, especially about the laboratory aspects, but those looking for a comprehensive clinical discussion about the infection syndromes could probably obtain the same information from any gastroenterology textbook.

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Hepatology: A Textbook of Liver Disease,
4th Edition
Zakim D and Boyer J, eds
W. B. Saunders, Philadelphia, PA, 2003
ISBN: 0-7216-9051-3; $325

No gastroenterology library is complete without at least one of the two standard hepatology texts. Of course, *Zakim and Boyer's Hepatology: A Textbook of Liver Disease* is one of them. Now in its fourth edition, this reference remains essential and timely. The editors have again assembled an array of authors with expertise that spans from the basic science of liver cell biology, biochemistry, and physiology to the clinical art and science of intrinsic and systemic diseases of the liver.

As with all texts, it is not possible to keep pace with the rapid expansion of science and medicine. However, I was impressed with the timeliness of this latest edition of *Hepatology.*

The two-volume set includes 61 chapters in 1761 pages, approximately 30 pages per chapter including references. This length allows for a comprehensive overview of each topic with detailed references for the reader who wishes more depth. The use of tables, charts, figures, and color plates adds considerably to the ease of using this reference.

Personally, I continue to use this text frequently for both clinical and research related questions. My only complaint is that I often lend my copy to students, residents, and fellows who enjoy it so much that they hesitate to return it promptly. A current edition of this text is truly essential for every gastroenterologist's library.

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The Clinician's Guide to Inflammatory Bowel Disease

Lichtenstein G, ed
Slack, Inc, 2003
ISBN: 1-55642-554-6; $44.95 (soft cover)

The Clinician's Guide to Inflammatory Bowel Disease is a multiple authored text that provides a good overview of the epidemiology of IBD, the changing course of the disease, and newer approaches to management and therapy. The title of the book describes it accurately. It is a quick reference resource for any clinician, especially for gastroenterology (GI) fellows. This book is organized in chapters in which the authors have addressed epidemiology, clinical features, complications and extraintestinal manifestations of IBD, and medical and surgical therapy for IBD. Additional chapters cover such topics as—Postoperative recurrence of Crohn's disease, Complications of the ileal pouch-anal anastomosis, Pregnancy and fertility with IBD, and Special considerations for pediatric and adolescent patients with IBD. Many authors are highly distinguished and recognized experts in the field of IBD.

This book is simple to read and is very "user-friendly." Each chapter provides a critical up-to-date overview with important references. Some of the information is repetitive: for example, there are chapters entitled "Medical therapy for Crohn's disease" and "Medical therapy for Ulcerative colitis" as well as a chapter titled, "Medical approach to the patient with IBD." These could have been consolidated into two chapters. The chapters in the book could have been arranged in a better sequence (e.g., the chapters on treatment could follow the chapter on evaluating patients with IBD; chapters on surgical therapy could have followed chapters on medical therapy). In some chapters though bibliography is provided, the references are not annotated in the text.

There is an occasional omission of important data like long term remission of Crohn's disease after (allograft) bone marrow transplantation. Different versions of Crohn's Disease Activity Index could have been effectively presented in detail (in a table format) in an easy to calculate form.

This book is an excellent resource and its cost is easily affordable by GI fellows who would get the maximum benefit by reading this book. Overall, I enjoyed reading the book and highly recommend this book as an important addition to any GI library.

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Chronic Anal Fissure

A literature review on MEDLINE Database was reported, including all treatments addressing the anomaly of a high anal pressure, associated with chronic anal fissure and addressing the concerns about the incidence of fecal incontinence after surgery, exploring the pharmacological means to treat chronic anal fissures. Several studies have investigated the effect of topical glycerol trinitrate ointment and healing ranged from 30 to 86 percent. Therapy was limited because of a high incidence of moderate to severe headaches in up to 84 percent of patients.

Comparable results were observed after injection of botulinum toxin into the anal sphincter (43 to 96 percent). Minor incontinence from flatus and soiling has been reported in up to 12 percent of patients. Further pharmacological approaches included treatment by way of calcium channel blockade and treatment with alpha-adrenoreceptor antagonists, still in a developmental stage.

It was concluded that topical glycerol trinitrate ointment and injection of botulinum toxin into the anal sphincter are advocated as the first line of treatment for chronic anal fissure. Lateral sphincterotomy should be offered to patients with relapse at therapeutic failure of pharmacologic treatment. (Utsig MJ, Kroesen AJ, Buhr HJ. "Concepts in Pathogenesis and Treatment of Chronic Anal Fissure: A Review of the Literature." *American Journal of Gastroenterology,* 2003; Vol. 98, pp. 968–974.)

Colchicine in Chronic Constipation

Sixteen patients, including 15 women and one man with a mean age of 47 years with chronic idiopathic constipation who were refractory to standard medical therapy, participated in the study. The patients randomly received either Colchicine 0.6 mg p.o. t.i.d. or an identical placebo for a total of 4 weeks in a double-blind-crossover fashion. Daily frequency of bowel movements and symptoms of daily nausea, abdominal pain and bloating were noted. Mean colonic transit was calculated at baseline at weeks 5 and 12.

Colchicine increased the number of bowel movements and accelerated colonic transit, compared with baseline and placebo conditions. There were no significant differences between conditions on ratings with nausea and bloating. During Colchicine administration, mean abdominal pain was greater than the baseline or placebo conditions. However, the pain decreased significantly by the last week the patient was on that therapy.

It was concluded that Colchicine increases the frequency of bowel movements and hastens colonic transit in patients with chronic constipation. Colchicine may be an effective agent available to practitioners to treat a subset of patients with chronic constipation who are refractory to standard medical therapy. (Verne GN, Davis RH, Robinson MD, et al. "Treatment of Chronic Constipation With Colchicine: Randomized, Double-Blind, Placebo-Controlled Cross-Over Trial." *Gastroenterology,* 2003; Vol, 98, pp. 1112–1116.)

Aminotransferase Levels

Data on adults age 17 years and older were analyzed from the 3rd National Health and Nutrition Examination Survey from 1988 to 1994. Participants were classified as having elevated aminotransferase levels if either AST or ALT were elevated above normal, and were classified as explained if there was laboratory evidence of hepatitis B or C infection, iron overload or a history of alcohol consumption.

Analyses were weighted to provide national estimates, 15,676 records were reviewed. The prevalence of aminotransferase elevation in the United States was 7.9 percent, and more common in men (9.3 percent vs. 6.6 percent) in Mexican Americans and non-Hispanic blacks, compared to non-Hispanic whites. High alcohol consumption, hepatitis B or C infection and high transferrin saturation were found in only 31 percent of cases. Aminotransferase elevation was unexplained in the majority (69 percent). In both men and women, aminotransferase elevation was significantly associated with higher body mass index, waist circumference, triglycerides, fasting insulin and lower HDL and with type II diabetes and hypertension in women. It was concluded that aminotransferase elevation was common in the United States and the majority could not be unexplained by alcohol consumption, viral hepatitis or

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hemochromatosis. Unexplained aminotransferase elevation was strongly associated with adiposity and other features of a metabolic syndrome and thus may represent nonalcoholic fatty liver disease. (Clark JM, Brancati FL, Dodihl AM. "The Prevalence and Etiology of Elevated Aminotransferase Levels in the United States." *American Journal of Gastroenterology,* 2003; Vol, 98, pp. 960–967.)

Reliability of Commercially Available Assays For HCV RNA

To evaluate the impact of the international unit standard for measuring HCV RNA in the management of patients with chronic hepatitis C, three assays were reviewed, including Amplicor monitor PCR, the National Genetics Institute PCR assay and Branched Chain DNA. HCV RNA were measured at four points (baseline), three months after the start of therapy, at the end of treatment and six months after discontinuation of therapy in 106 consecutive patients who received Interferon and ribavirin for chronic hepatitis C. Of the 424 samples analyzed, 82 to 89 percent of values were within one log unit and 85 to 92 percent were within two log units by the various assays. This variability was not dependent upon HCV genotype. HCV RNA was undetectable in 1.4 to 6.8 percent of samples when virus was detected by another assay. The mean HCV RNA in these discordant samples was 1.47 to 6.3 logged i.u./mL. It was concluded that approximately 90 percent of serum values for HCV RNA were within one log unit by the international unit standard, regardless of which virologic assay was used. However, false positive and false negative results, as well as variations in HCV RNA levels of more than one to two log units can occur with any of the assays, and these results may have an impact upon the management of patients receiving Interferon therapy.

It is therefore unwise in clinical practice to base important treatment decisions upon a single HCV RNA determination. (Shiffman ML, Ferreira-Gonzalez A, Reddy KR, et al. "Comparison of Three Commercially Available Assays for HCV RNA, Using the International Unit Standard: Implications For Management of Patients With Chronic Hepatitis C Virus Infection in Clinical Practice." *American Journal of Gastroenterology,* 2003; Vol. 98, pp. 1159-1166.)

Propanolol With or Without Isosorbide-5 Mononitrate in Prevention of Variceal Bleeding

A multicenter prospective, double-blind, randomized control trial evaluated whether combined drug therapy could be more effective than Propanolol alone in preventing variceal bleeding. 349 consecutive cirrhotic patients with gastroesophageal varices were randomized to receive Propanolol plus placebo or Propanolol plus Isosorbide-5 mononitrate. The only independent predictor of variceal bleeding was variceal size greater than 5 mm. However, among patients with varices greater than 5 mm, there were no significant differences than the incidence of variceal bleeding between the two groups. Survival was also similar. Adverse effects were significantly more frequent in the combined group, due to a greater incidence of headache. There were no significant differences in the incidence of new onset or worsening ascites or an impairment of renal function.

It was concluded that Propanolol effectively prevents variceal bleeding. Adding Isosorbide-5 mononitrate does not further decrease the low residual risk of bleeding in patients receiving Propanolol. However, the long-term use of this combination drug therapy is safe and may be an alternative in clinical conditions associated with a greater risk of bleeding. (Garcia-Pagan JC, Morillas R, Banares R, et al. and Spanish Variceal Bleeding Study Group. "Propanolol Plus Placebo Versus Propanolol Plus Isosorbide-5 Mononitrate in the Prevention of a First Variceal Bleed: A Double-Blind RCT." *Hepatology,* 2003; Vol. 37, pp. 1260-1266.)

NAFLD With Normal ALT Values

Fifty-one subjects with nonalcoholic fatty liver disease and normal ALT levels were identified and compared with 50 consecutive subjects with nonalcoholic fatty liver disease and elevated ALT. The major indications for liver biopsy in those with normal ALT were unexplained hepatomegaly and evaluation as a potential donor for living donor liver transplantation. The two groups were comparable.

Approximately 80 percent of patients in both groups had at least one feature of the metabolic syndrome as a major risk factor for NAFLD. The two groups were com-

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parable in respect to the grade of individual histologic parameters of NAFLD. A total of 12 subjects with normal ALT levels had bridging fibrosis and six had cirrhosis. Diabetes was the only factor independently associated with an increased risk of advanced fibrosis.

The mean steatosis and perisinusoidal fibrosis scores were lower in those with low normal versus high normal ALT. However, the prevalence of advanced fibrosis was similar. It was concluded that the entire histologic spectrum of NAFLD can be seen in individuals with normal ALT values, and that the histologic spectrum in these individuals is not significantly different from those with elevated ALT levels. A low normal ALT value does not guarantee freedom from underlying steatohepatitis with advanced fibrosis. (Mofrad P, Contos MJ, Haque M, et al. "Clinical and Histologic Spectrum of Nonalcoholic Fatty Liver Disease Associated With Normal ALT Values." *Hepatology,* 2003; Vol. 37, pp. 1286-1292.)

Capsule Endoscopy Vs. Enteroclysis

Forty patients were studied and reviewed from December 2001 to April 2002, all with normal upper and lower endoscopies and small bowel barium studies before wireless capsule endoscopy was performed. Two patients with chronic iron deficiency anemia had multiple small bowel ulcers and referred after capsule endoscopy for repeat small bowel barium studies by biphasic enteroclysis performed by experienced GI radiologists and the radiologists were aware of the capsule findings. Both studies were considered technically to be of perfect quality. Despite this, both studies were negative. All three patients improved. One patient with ileal ulcers and abdominal pain had an enteroclysis at another hospital before the wireless capsule endoscopy, which was reviewed and which study was considered of excellent quality and was considered normal.

It was concluded that wireless capsule endoscopy may be more sensitive for small bowel ulcers than the best enteroclysis available. (Liangphunakul S, Chadalawada V, Rex D, Maglinte V, Laptas T. "Wireless Capsule Endoscopy Detects Small Bowel Ulcers in Patients with Normal Results From State-of-the-Art Enteroclysis." *American Journal of Gastroenterology,* 2003; Vol. 98, pp. 1295-1298.)

Fecal Lactoferrin For IBD Vs. IBS

One hundred and four Crohn's disease patients and 80 ulcerative colitis patients, 31 irritable bowel syndrome patients and 56 healthy controls were recruited. Fresh stool samples were collected and assessed. Fecal lactoferrin concentration was determined, using a polyclonal antibody-based, enzyme-linked immunoassay. Fecal lactoferrin was 90 percent specific for identifying inflammation in patients with active inflammatory bowel disease. Elevated fecal lactoferrin was 100 percent specific in ruling out irritable bowel syndrome.

It was concluded that fecal lactoferrin is sensitive and specific for detecting inflammation in chronic inflammatory bowel disease. This noninvasive test may prove useful in screening for inflammation in patients presenting with abdominal pain and diarrhea. (Kane SV, Sandborn WJ, Rufo PA, et al. "Fecal Lactoferrin is a Sensitive and Specific Marker in Identifying Intestinal Inflammation." *American Journal of Gastroenterology,* 2003; Vol. 98, pp. 1309-1314.)

Pancreatitis in HIV Disease

Seventy-three HIV-infected patients with acute pancreatitis were identified retrospectively. Sixty-three had AIDS. The majority of the cases were medication-induced (46 percent), or idiopathic (26 percent). The incidence seemed to be declining in the late 1990 's. Eleven patients (15 percent) had a severe course as defined by death, admission to intensive care unit or local complications requiring surgery. Eighteen cases (24.6 percent), were considered severe by criteria established at the "International Symposium on Acute Pancreatitis," in Atlanta in 1992. APACHE II criteria best predicted outcome, with an overall accuracy of 75 percent.

It was concluded that HIV-infected patients have a clinical outcome similar to those of the general population, with the occurrence of pancreatitis. Clinical predictive scales are applicable and useful in this population. (Gan I, May G, Raboud J, Cilley J, Enns R. "Pancreatitis in HIV Infection: Predictors of Severity." *American Journal of Gastroenterology,* 2003; Vol. 98, p. 1278-1283.)

Murray H. Cohen, D.O., editor of "From the Literature" is a member of the Editorial Board of *Practical Gastroenterology.*

American Red Cross Plasma Services and OMRIX biopharmaceuticals, Inc. Announce U.S. Launch of CROSSSEAL™ Fibrin Sealant (Human)

American Red Cross Plasma Services and OMRIX biopharmaceuticals, Inc. have begun sales of CROSSEAL™, an all human protein, bovine component-free fibrin sealant approved for U.S. sales as an adjunct to hemostasis in liver surgery. Crosseal, like all fibrin sealants, is derived from human blood plasma and contains the coagulation factors necessary to stop bleeding in surgical settings.

One of Crosseal's many advantages is its quick and easy preparation. "Crosseal™ will significantly help surgeons and nursing staff save valuable time in the operating room," says Chris Lamb, Vice President and Chief Operating Officer, American Red Cross Plasma Services. "Because Crosseal™ requires no reconstitution, it can be ready to use with less than one minute preparation time."

Adds Robert Taub, President and Chief Executive Officer of OMRIX, "Crosseal™ not only achieves hemostasis quickly, but its transparent medium provides a clear tissue field for the surgeon. We believe Crosseal™ represents a significant advance in patient care."

During clinical trials, Crosseal™ stopped bleeding significantly faster than the conventional standard of care. Its efficient hemostatic sealing reduced post-hepatic surgery complications.

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Shipped frozen, Crosseal™ can be available in one minute when thawed and requires no reconstitution, special heating or stirring devices. It is stable for up to 24 hours at room temperature and, unopened, can be stored in a refrigerator for up to 30 days. It will be available in 1, 2 and 5-milliliter sizes.

The advantages of Crosseal™ can be summarized almost as quickly as Crosseal™ works: it achieves hemostasis quickly and safely; it is easy to prepare and easy to use with targeted delivery; lastly, it is more practical to use because there is less waste.

The American Red Cross Plasma Services markets a broad range of plasma derivatives including immune globulin intravenous (human), antihemophilic factor VIII (human), albumin (human) and now a fibrin sealant (human) to the U.S. market.

For more information on Crosseal™ or the American Red Cross, please call 1-877-ARC-BIOS (1-877-272-2467).

John Hopkins Researchers Find Potential New Treatment For Children With Chronic Hepatitis C

Researchers from the Johns Hopkins Children's Center and five other institutions have found that a drug recently approved for adults with chronic hepatitis C (CHC) also may be a safe and effective treatment for children with the disease. The study is believed to be the first to examine how the drug, peginterferon alfa-2a, affects the young.

The hepatitis C virus (HCV), the leading cause of liver disease in the United States, is responsible for an estimated 10,000 to 12,000 deaths annually. It is spread primarily by contact with blood and blood products. Blood transfusions and the use of shared, unsterilized, or poorly sterilized needles and syringes have been the main causes of the spread of the virus in the U.S. among adults.

The findings could change the way doctors treat children with CHC, according to the study's lead author, Kathleen B. Schwarz, M.D., director of the Division of Gastroenterology and Nutrition at the Children's Center.

"At present, there is no FDA-approved treatment for children 18 years old and younger with the disease. Our results provide a basis for conducting a large-scale, randomized controlled trial to test this new form of interferon alone, or in combination with ribavirin, an antiviral medication, which is the current treatment of choice for adults with CHC," she said. "Such a study will be necessary before the Food and Drug Administration can approve the drug for children."

Some children with CHC have been treated with three shots a week of interferon to increase the amount of the naturally occurring infection fighter. Peginterferon alfa-2a is a new, longer acting version that, when taken weekly, maintains interferon levels in the blood for a longer period

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of time. The drug also has been shown more effective in adults with CHC than standard interferon.

In the multi-center study, 14 pediatric patients with CHC were given peginterferon alfa-2a once weekly for 48 weeks. No serious side effects were observed, and 43 percent of the children treated were free of the virus 24 weeks after the treatment ended.

"Thanks to screening programs for blood donors, transfusion-acquired HCV is now very rare. However, new pediatric cases continue to occur through maternal-fetal acquisition," said Schwarz. "There are approximately 150,000 children in the U.S. with CHC, and this new approach to treatment offers hope to both the children suffering from this infection and their worried families."

This study was sponsored by Hoffmann La Roche Inc., manufacturer of peginterferon alfa-2a (40KD) (Pegasys®). This study was presented during the Digestive Disease Week conference and sponsored by the American Association for the Study of Liver Diseases, American Gastroenterological Association, American Society for Gastrointestinal Endoscopy, and the Society for Surgery of the Alimentary Tract.

NSAIDs Cause Ulcers and Bleeding in the Small Intestine

New study shows prevalence and severity much higher than originally shown

Every day, 33 million Americans take OTC and prescription non-steroidal anti-inflammatory drugs (NSAIDs). While it has been widely known that NSAIDs can cause stomach problems, the prevalence and severity of small intestinal lesions has remained unclear. A new study shows that NSAID-related small intestinal ulcerations, lesions and bleeding, are as much as 40 percent higher than originally thought.

"Previously, researchers relied on autopsy studies showing that only a low number of NSAID users had non-specific small intestinal ulcerations," said David Graham, lead investigator on the study. "Through the use of video capsule endoscopy (VCE) we were finally able to prove that NSAID-related intestinal damage is many times more prevalent than originally thought."

Forty patients with various types of arthritis were enrolled in the study. Twenty took NSAIDS for more than three months, while 20 took acetaminophen alone or nothing at all. All fasted overnight and then underwent VCE. Two investigators, blind to therapy, reviewed each patient using definite erosions as the critical variable to predict NSAID-induced damage.

Results showed 71 percent of NSAID users had damage compared to 10 percent of non-users. Severe injury was seen in 25 percent of NSAID users compared to zero in the non-user group. Severe damage was associated with high-dose indomethacin, naproxen and ibuprofen use. Numbers show that small intestinal damage is found in the majority of chronic NSAID users.

These results open the way to studies comparing NSAID, identifying methods to prevent this damage, and attempting to equate damage with symptoms.

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A large proportion of PUUV-infected patients suffer from gastrointestinal symptoms of unclear origin. In this study we demonstrate that PUUV infection can occur via the alimentary tract.Methods: We investigated susceptibility of the human small intestinal epithelium for PUUV infection and analyzed the resistance of virions to gastric juice. As model for intestinal virus translocation we performed infection experiments with human intestinal Caco-2 monolayers.