

New Monthly Newsletter Provides Physicians With Timely News on Inflammatory Bowel Disease Treatment

IBD Watch, a new one-page fax newsletter covering important developments in inflammatory bowel disease (IBD), was launched in September to provide physicians with the latest news on therapeutic trends related specifically to the management of ulcerative colitis and Crohn’s disease.

Distributed monthly via fax to 7,600 gastroenterologists and IBD specialists, IBD Watch offers brief summaries of recent peer-reviewed research published in the most widely-read gastroenterology journals. IBD Watch content is directed by a six-member editorial board chaired by Stephen Hanauer, M.D., co-director of the Inflammatory Bowel Disease Research Center, University of Chicago. Additional board members include Gary Lichtenstein, M.D, University of Pennsylvania; Daniel Present, M.D., New York’s Mount Sinai Medical Center; Sunandra Kane, M.D., University of Chicago; and Bruce Sands, M.D., Harvard Medical School.

“The average physician receives more than 40 medical journals a month,” said Dr. Hanauer. “IBD Watch is a wonderful tool for gastroenterologists and IBD specialists, providing them with the most up-to-date advances in the field without having to plough through all the key journals.”

Approximately one million Americans have either ulcerative colitis or Crohn’s disease, the other form of IBD, and most are diagnosed between the ages of 10 and 30. Depending on the type of IBD, any part of the digestive tract may be inflamed or ulcerated, causing abdominal pain, constipation, diarrhea and other debilitating symptoms.

IBD Watch encourages interaction with fellow physicians through the official web site, <http://www.ibdwatch.com>, where subscribers can e-mail clinical questions and comments to board members. Anyone interested in receiving IBD Watch can register via the fax form available on the web site. Archived issues and links to related sites will also be available.

The newsletter is sponsored exclusively by an educational grant from Salix Pharmaceuticals, Inc., makers of Colazal® (balsalazide disodium) 750 mg Capsules, a treatment for mild to moderately active ulcer-

ative colitis, and will be distributed by Market Development Group.

New Combination Treatment for Hepatitis C Reported More Beneficial Than Standard Combination Therapy

The September 25th issue of the *New England Journal of Medicine* published a report showing that a combination treatment with peginterferon alfa-2a (Pegasys)—a new long-acting interferon drug—and an antiviral medication is more beneficial than the standard combination therapy for people with the most-difficult-to-treat and most common strain of hepatitis C.

The large international study headed by researchers at the University of North Carolina at Chapel Hill is also the first published to show that treatment with the investigational drug peginterferon alfa-2a in combination with the oral antiviral medication, ribavirin, is linked to a lower rate of troublesome side effects—depression, flu-like symptoms (chills, headache, fever)—than the standard interferon (Rebetron) and ribavirin.

“Sixty-five percent of patients in the study were infected with hepatitis C genotype 1, the most prevalent genotype we see here in the United States, and typically the least responsive to therapy,” said study co-author Dr. Michael W. Fried, associate professor of medicine and director of clinical hepatology at the UNC School of Medicine. “With this research, we’ve found the most significant evidence to date suggesting these patients might benefit by taking peginterferon alfa-2a in combination with ribavirin.”

According to Fried, side effects of therapy can be very challenging for patients. “The study shows an approach that can offer patients superior efficacy without increases in some of the most common and difficult to tolerate adverse events associated with hepatitis C therapy.”

Of the six different strains, or genotypes, of hepatitis C, approximately 70 percent of people in North America are infected with genotype 1.

The study, funded by Hoffmann-La Roche, the maker of Pegasys, was conducted at 81 clinical sites in

(continued on page 56)

(continued from page 54)

18 countries. It involved over 1100 patients in one of three study arms: 453 were treated with peginterferon alfa-2a plus oral ribavirin; 224, with peginterferon alfa-2a plus placebo; and 444 with interferon alfa-2b plus ribavirin. Patients were treated for 48 weeks and then monitored for an additional 24 weeks.

A key variable measured by the study was sustained viral response, defined as undetectable serum hepatitis C RNA after the treatment-free follow-up period.

Overall patients treated with the peginterferon alfa-2a plus ribavirin combination achieved a 56 percent sustained response rate as compared to patients taking Rebetron (44 percent). Patients with genotype 1 had a sustained response rate of 46 percent, compared to patients on Rebetron (36 percent) and those on Pegasys plus placebo (21 percent).

A retrospective analysis of the data showed that response to PEG interferon alpha-2a plus ribavirin is predictable. At week 12, 86 percent of patients treated with PEG interferon demonstrated an early viral response; of these, 65 percent attained a sustained viral response. However, 97 percent of patients who did not respond by week 12, failed to achieve a sustained response.

“This means that physicians can create an alternate treatment plan for patients who do not show any response by week 12,” said Fried. “And for those who do respond, it can be a motivation to continue to adhere to their treatment regimens.” Dr. Fried cautioned that these treatment decisions must be individualized for each patient.

The hepatitis C virus (HCV) is a life-threatening viral infection of the liver transmitted primarily through infected blood and blood products. Approximately 2.7 million Americans and 170 million people worldwide are chronically infected with HCV. HCV is often described as “silent” because people may be infected 10 to 30 years and not exhibit symptoms, yet still be carrying the virus. While many patients with HCV will not develop complications from their liver disease, chronic hepatitis C is still a leading cause of cirrhosis and liver cancer and is the major indication for liver transplants in this country.

The Center for Liver Diseases and Transplantation at the University of North Carolina at Chapel Hill pro-

vides highly specialized care for liver diseases for residents of North Carolina and surrounding regions. In addition to its commitment to patient care, the UNC liver program is dedicated to studying novel therapies for viral hepatitis, other chronic liver diseases, and transplantation.

NutraFlora® scFOS™ Recognized as Functional Fiber

GTC Nutrition LLC announced today that its NutraFlora® fructooligosaccharides product has been included in the functional fiber definition recently published by the National Academies of Science as part of their report on Dietary Reference Intakes.

“This new recognition of FOS as a fiber represents progress in an overall understanding in the science community of fructooligosaccharides and their many health benefits,” said Linda Chamberlain Douglas, PhD., R.D., Manager of Scientific Affairs for GTC Nutrition. “Although experts have always known that FOS acts as a prebiotic soluble fiber, the analytical methods used by the USDA and FDA historically have not detected dietary fiber in FOS, The National Academy of Science now recognizes the physiological effects of FOS as a fiber in addition to the fibers identified by laboratory analysis methods used in the past.”

The new fiber definition reads, “Functional fiber consists of isolated, nondigestible carbohydrates that have beneficial physiological effects in humans.” The NAS went on to recommend a daily intake of 38 grams of fiber a day for men and 25 grams a day for women.

Fructooligosaccharides are naturally occurring in plants. NutraFlora® scFOS™, the purest form of fructooligosaccharides available, is commercially produced through a natural enzymatic manufacturing process. NutraFlora® is used as a nutritional and functional ingredient in many food and beverage products around the world, including bars, meal replacement beverages, protein drinks and mixes, energy drinks, diet products, diabetic products, dairy, yogurt and soy products, confections, cereals, as well as in pet foods and animal feed.

For more information, please contact GTC Nutrition at 1-800-522-4682 or 303-216-2489.

FROM THE LITERATURE

Barrett's Esophagus in Asymptomatic Patients

Prospective screening for the presence of Barrett's esophagus was carried out in asymptomatic subjects older than 50 years of age, undergoing screening sigmoidoscopy for colorectal cancer. Exclusion criteria included symptoms of gastroesophageal reflux disease, use of medications for GERD, or previous endoscopy. Included as positives were long-segment Barrett's esophagus, short-segment Barrett's esophagus and microscopic specialized intestinal metaplasia of the esophagogastric junction. Of 408 potential study candidates, 110 were screened with a mean age of 61. Most of the patients were Caucasian. Intestinal metaplasia extending above the esophagogastric junction was detected in 27, or 25 percent. Eight, or 7 percent, had long-segment Barrett's esophagus and 19, or 7 percent, had short-segment Barrett's esophagus.

Patients with Barrett's esophagus were no more likely to be obese. Consumers of tobacco or alcohol

report a family history of GERD and show a toxic exposure or use of antacids more than once a month, compared to those without Barrett's esophagus.

It was reported that Barrett's esophagus was detected in 25 percent of asymptomatic male veterans older than 50 years of age, undergoing screening sigmoidoscopy for colorectal cancer. (Gerson LB, Shetler K, Triadafilopoulos G. "Prevalence of Barrett's Esophagus in Asymptomatic Individuals." *Gastroenterology*, 2002: Vol 123, pp. 461-467.)

Psychiatric Disorders With Hepatitis C Infection

All HCV-infected veteran patients who were hospitalized from 1992 to 1999 were identified in this study, searching inpatient and outpatient computerized files for predefined psychiatric, drug and/or alcohol use disorders. A case-control study was carried out among Vietnam veterans; controls without HCV were randomly

FROM THE LITERATURE

chosen from hospitalized patients. 33,824 HCV-infected patients, in whom 86.4 percent had at least one past or present psychiatric drug or alcohol use disorder were recorded. Only 31 percent had active disorders as defined by hospitalization to psychiatric or drug detoxification bed sections. 22,341 HCV-infected patients from the Vietnam period of service were compared with 43,267 patients without HCV as controls.

The cases were more likely to have depressive disorders, post-traumatic stress disorder, psychosis, bipolar disorders, anxiety disorders, alcohol and drug use disorders. It was concluded that several psychiatric drug and alcohol use disorders are commonly found among HCV-infected veterans, compared with those who are not infected. At least one-third of these patients have active disorders. A multidisciplinary approach to the management of HCV-infected patients is needed. (El-Serrag HB, Kunik M, Richardson P, Rabeneck L. "Psychiatric Disorders Among Veterans With Hepatitis C Infection," *Gastroenterology*, 2002; Vol. 123, pp. 476-482.)

Fracture Risk in Patients With Crohn's Disease

Medical records of all 238 Olmsted County, Minnesota residents diagnosed with Crohn's disease between 1940 and 1993 were reviewed for evidence of subsequent fractures, compared with a control group of county residents matched by age and sex. Sixty-three patients had 117 different fractures. The cumulative incidence of any fracture from the time of diagnosis onward was 36 percent at 20 years, versus 32 percent in controls,

Compared with controls, the overall risk factor for any fracture was 0.9, whereas the relative risk for an osteoporotic fracture was 1.4. The risk ratio for thoracolumbar vertebral fracture was 2.2. Age only was identified as a significant clinical predictor of fracture risk; specifically, use of corticosteroids in surgical resection

did not predict fracture among these unselected patients with Crohn's disease from the community,

It was concluded that in this population-based inception cohort of patients with Crohn's disease, the risk of fracture was not elevated relative to age and sex-matched controls. (Loftus EV, Crosson CS, Sandborn WJ, Tremaine WJ, et al. "Long Term Fracture Risk in Patients with Crohn's Disease: A Population-Based Study in Olmsted County, Minnesota." *Gastroenterology*, 2002; Vol. 123, pp. 468-476.)

Interferon Therapy on Life Expectancy in Hepatitis C

A retrospective cohort study design was used in the setting of seven university hospitals and one regional core hospital in Japan, including 2,889 patients with histologically proven chronic hepatitis C. 2,430 patients received Interferon therapy and 459 patients were untreated. For intervention, the median dose and duration of Interferon administration was 480,000,000 units and 137 days, respectively. Survival status was confirmed by medical records or direct questionnaires. The effect of Interferon therapy on survival was assessed by standardized mortality ratio, based on published mortality among the Japanese general population and by risk ratio calculated by proportional hazards regression.

Thirty of 459 untreated patients, 7 of 817 virologic sustained responders and 49 of 1613 nonresponders died in 5.4 years follow-up. 58 (67 percent) of 86 patient's deaths were due to liver disease (39 to hepatocellular carcinoma). Compared with the general population, overall mortality was high among untreated patients, but not among Interferon-treated patients. The risk of death for treated patients was reduced, compared with untreated

(continued on page 60)

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(continued from page 58)

patients, but specifically for liver-related death and improved further among sustained responders. The risk of liver unrelated deaths remained unchanged.

It was concluded that Interferon therapy improved the survival of chronic hepatitis C patients by preventing liver-related deaths. (Yoshida H, Arikawa Y, Sata M, et al. "Interferon Therapy Prolonged the Life Expectancy Among Chronic Hepatitis C Patients." *Gastroenterology*, 2002; Vol. 123, pp. 483-491.)

Diagnosing Cirrhosis in Hemochromatosis

Database of HFE genotype patients that were homozygous for C282Y mutation with laboratory data and liver biopsy performed to assess for cirrhosis and the absence of hepatitis C virus antibodies or hepatitis B surface antigen or a significant history of alcohol ingestion were reviewed, including ambulatory patients, including decompensated cirrhosis. 192 were eligible for analysis in the Canadian database. Variables significantly related to cirrhosis were evaluated by stepwise linear multivariate regression. A clinically applicable index for the noninvasive prediction of cirrhosis was devised and was then validated in similar patients in advance. Ferritin, blood platelets and AST levels were selected for the clinical index. A combination of ferritin levels of 1,000 mcg per liter or greater, platelet levels of 200 x 10³ per liter or less and AST levels above the upper limits of normal led to a correct diagnosis of cirrhosis in 77 percent of Canadian patients and in 90 percent of French patients.

It was concluded that in C282Y homozygous patients, a combination of easily measured laboratory variables (ferritin, platelets and AST) can be used to make the diagnosis of cirrhosis in 81 percent of the cases, reducing the need for liver biopsy. (Beaton M, Guyader D, Deugnier Y, et al. "Noninvasive Prediction of Cirrhosis in C282Y-Linked Hemochromatosis." *Hepatology*, 2002; Vol. 36, pp. 673-678.)

Steatosis and Chronic Hepatitis C

Two hundred and ninety-seven consecutive patients with HCV were studied, including those with alcohol consumption. Demographics and serologic tests were corre-

lated with degrees of steatosis and fibrosis. On liver biopsy, the specimens were also examined for evidence of significant alcohol or nonalcoholic steatohepatitis. In univariate analysis, steatosis correlated with type II diabetes mellitus and the body mass index, but not with the intensity of alcoholic intake. Genotype 3A infection was an independent predictor of steatosis.

When patients with risk factors for NASH were excluded, genotype 3A infection was the only independent predictor of steatosis. Steatosis and inflammation scores on liver biopsy were the only independent predictors of fibrosis. Significant alcohol or NASH injury was found in only 6 percent of biopsy specimens.

It was concluded that steatosis and HCV infection is associated with risk factors for NASH, particularly obesity, rather than alcohol consumption. (Monto A, Alonzo J, Watson J, Grunfeld C, Wright TL. "Steatosis and Chronic Hepatitis C: Relative Contributions of Obesity, Diabetes Mellitus and Alcohol." *Hepatology*, 2002; Vol. 36, pp. 729-736.)

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

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BOOK REVIEWS

Gastrointestinal Disease; An Endoscopic Approach

DiMarino AJ, Jr and Benjamin SB, editors

Slack Incorporated, 2002

ISBN: 1-55642-511-2, \$ 289.00

This text, now in its second edition, is divided into seven sections; Considerations in Gastrointestinal Endoscopy, Diseases of the Esophagus, Diseases of the Stomach, Diseases of the Small Intestine, Diseases of the Colon, Diseases of the Pancreas and Biliary Tree, and Development of Endoscopic Technologies. It is shorter than other general GI texts, partly because it focuses on endoscopic gastroenterology and less on nonendoscopic diseases such as hepatitis.

The first section attracted my interest because it stressed the basics in endoscopy, including excellent chapters on the structure and functions of a video endoscope, informed consent, patient preparation, credentialing and scope cleaning and antibacterial prophylaxis.

The last section is also a fascinating discussion including chapters on uses of light other than white light, endosurgery, remote endoscopy, and how to develop endoscopic research.

There is a very nice section on the esophagus including a chapter on anatomic variants. I did not notice a discussion about the congenitally narrow esophagus or eosinophilic esophagitis, both emerging conditions important to endoscopists. I did also note that Chapter 11 and Chapter 12 have differing opinions about the muscle anatomy of the esophagus (I prefer the opinions in chapter 12).

One of the outstanding features of this text is the liberal use of black and white images, color photographs, and diagrams. These, including color photographs, are scattered throughout the text. This gives this book an immense advantage over other texts. (Other texts have the color photos in separate sections making them more difficult to use). However I wish there was more liberal use of arrows and labeling in most chapters. The chapter on Development of the Pancreas and Biliary Tract has beautiful and well-labeled images and diagrams. On the other hand I was disappointed in the photographs in the chapter about complications of Peptic Ulcer Disease. Some are uninterpretable.

Included with this text is a compact disk. I am not terribly sophisticated with a computer but after a couple of tries was able to access the figures and manipulate them in Acrobat Reader. Many are excellent photos to add to one's teaching file, such as Power Point presentations.

This is an excellent book for anyone who is interested in endoscopy. It would be particularly valuable for fellows and any endoscopy suite. My only disappointment is in the binding of my edition. While reading the text I noted that the covers became separated from the binding. I hope that does not happen with every copy.

George Meyer, M.D.
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George W. Meyer, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*

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