

## Recommendations for the Management of Irritable Bowel Syndrome

In a supplement to the January issue of the *American Journal of Gastroenterology*, the American College of Gastroenterology published a new evidence-based systematic review on the management of irritable bowel syndrome (IBS). Some of the new graded therapeutic recommendations included the following:

- Although trials have shown that psyllium, fiber, certain antispasmodics, and peppermint oil are effective for treating IBS, the quality of the evidence is poor.
- Although some probiotics may be effective for reducing overall IBS symptoms, more data are required.
- Although antidiarrheals decrease the frequency of stools, they do not affect overall IBS symptoms.
- In IBS patients with diarrhea, 5-HT<sub>3</sub> antagonists have been shown to be effective, with good-quality evidence. However, careful patient selection is vital due to potentially serious side effects.
- In IBS patients with constipation, 5-HT<sub>4</sub> agonists have been shown to be modestly effective, with good-quality evidence, though there is a risk of cardiovascular events.
- In IBS patients of all subtypes, tricyclic antidepressants and selective serotonin reuptake inhibitors have been shown to be effective in trials of moderate quality (due to their small patient populations).

The following guidelines were among the recommendations for diagnostic IBS testing:

- Patients with typical IBS symptoms and no alarm features do not require routine diagnostic testing with complete blood count, serum chemistries, thyroid function studies, stool for ova and parasites, and abdominal imaging.
- Patients with diarrhea-predominant IBS and mixed-type IBS should undergo routine serologic screening for celiac sprue. If lactose maldigestion is a concern, despite changes in diet, lactose breath testing may be an option.
- Due to insufficient data, breath testing for small intestinal bacterial overgrowth in IBS patients is not currently recommended.
- In patients less than 50 years of age with typical IBS symptoms and no alarm features, routine colonic imaging is not recommended due to the low pretest likelihood of Crohn's disease, ulcerative colitis, and colonic neoplasia.

## Use of Antioxidants for Pain Relief in Chronic Pancreatitis

According to the January issue of *Gastroenterology*, researchers at the All India Institute of Medical Sciences in New Delhi, India, conducted a placebo-controlled, double-blind trial to assess the use of antioxidant supplementation on pain relief, oxidative stress, and antioxidant status in patients with chronic pancreatitis, as no effective medical therapy currently exists for these patients. The researchers randomized consecutive patients with chronic pancreatitis (age, 30.5±10.5 years, 86 male, 35 alcoholic, and 92 with idiopathic chronic pancreatitis) to antioxidants (n=71) or placebo (n=56) for 6 months. The primary outcome measure consisted of pain relief, with secondary measures of analgesic needs, hospitalization, and oxidative stress markers (thiobarbituric acid-reactive substances [TBARS]) and antioxidant status (ferric-reducing ability of plasma [FRAP]).

At the end of the trial, patients receiving antioxidants experienced a significant decrease in the number of days with pain each month compared to those receiving placebo (7.4±6.8 vs 3.2±4, respectively;  $P<.001$ ; 95% confidence interval [CI], 2.07–6.23). The decrease in the number of monthly analgesic tablets was also greater in patients receiving antioxidants (10.5±11.8 vs 4.4±5.8, respectively;  $P=.001$ ; 95% CI, 2.65–9.65). In addition, 32% of patients receiving antioxidants and 13% of patients receiving placebo were free from pain ( $P=.009$ ). The beneficial effect of antioxidants on pain relief was even noted early at 3 months. The decrease in TBARS and increase in FRAP were significantly greater in patients receiving antioxidants compared to those receiving placebo (TBARS: placebo 1.2±2.7 vs antioxidant 3.5±3.4 nmol/mL;  $P=.001$ ; 95% CI, 0.96–3.55; FRAP: placebo -5.6±154.9 vs antioxidant 97.8±134.9 μMFe<sup>2+</sup> liberated,  $P=.001$ , 95% CI, 44.98–161.7). The authors concluded that use of antioxidants was effective for pain relief and reduction of oxidative stress levels in chronic pancreatitis.

## Long-term Chronic Hepatitis C Therapy With Low-dose Peginterferon

Led by Adrian M. Di Bisceglie, MD, of the St. Louis University School of Medicine in St. Louis, Missouri, researchers at various institutions conducted a randomized, controlled, multicenter trial of 1,050 patients with chronic hepatitis C and advanced fibrosis who had not

responded to prior treatment with peginterferon and ribavirin. The patients, who were randomly assigned to 90 µg of peginterferon alfa-2a each week (n=517) or no treatment (n=533) for 3.5 years, were stratified according to fibrosis stage (622 with noncirrhotic fibrosis and 428 with cirrhosis). The patients (the majority of which were men and had a mean age of 51 years) were followed every 3 months and underwent liver biopsy at 1.5 and 3.5 years after randomization. The primary endpoint of the study consisted of liver disease progression, as indicated by death, hepatocellular carcinoma, hepatic decompensation, or, for patients with bridging fibrosis at baseline, an increase in the Ishak fibrosis score of 2 or more points. The results of the study were published in a December issue of the *New England Journal of Medicine*.

The authors found that treatment significantly decreased serum aminotransferases levels, serum hepatitis C virus RNA levels, and histologic necroinflammatory scores ( $P<.001$ ); however, no significant difference was seen between patients who received treatment and those who received no treatment, in terms of any primary outcome (34.1% vs 33.8%, respectively; hazard ratio, 1.01; 95% CI, 0.81–1.27;  $P=.90$ ). In the treatment arm, 38.6% of the patients experienced at least one serious adverse event compared to 31.8% in the no-treatment arm ( $P=.07$ ). The authors concluded that patients with chronic hepatitis C and advanced fibrosis, with or without cirrhosis, who do not initially respond to prior treatment with peginterferon and ribavirin, are unlikely to respond to long-term maintenance treatment with peginterferon.

### Association of Colonoscopy and Colorectal Cancer Mortality

Researchers at several Canadian institutions conducted a population-based, case-control study to assess the association between colonoscopy and death from colorectal cancer (CRC). The patient population consisted of individuals in Ontario, Canada, from 52 to 90 years of age who were diagnosed with CRC from January 1996 to December 2001 and died of CRC by December 2003. For each of these case patients, 5 controls who lived in the same area and were of the same age, sex, and socioeconomic status were randomly selected. Administrative claims data were used to identify whether the patients had undergone any or complete colonoscopy (to the cecum) from January 1992 to an index date 6 months prior to the CRC diagnosis in each case patient and the same date in the controls. The researchers compared the two arms to determine whether death from CRC declined in patients who had undergone colonoscopy. The results of the study,

which lead author Nancy Baxter, MD, of the University of Toronto, described as surprising were published in a December issue of *Annals of Internal Medicine*.

The authors identified 10,292 case patients and 51,460 controls, of which 719 case patients (7.0%) and 5,031 controls (9.8%) had undergone colonoscopy. Compared to the control patients, case patients were less likely to have undergone attempted colonoscopy (adjusted conditional odds ratio [OR], 0.69; 95% CI, 0.63–0.74;  $P<.001$ ) or complete colonoscopy (adjusted conditional OR, 0.63; CI, 0.57–0.69;  $P<.001$ ). Complete colonoscopy was strongly associated with fewer deaths from left-sided CRC (adjusted conditional OR, 0.33; CI, 0.28–0.39) but not from right-sided CRC (adjusted conditional OR, 0.99; CI, 0.86–1.14). The authors noted that it was not possible to distinguish screening from diagnostic procedures and that the next step would be to determine why so many cancers, particularly those on the right side of the colon, were missed by colonoscopy and whether the findings could be improved.

#### In Brief

**A retrospective, exploratory analysis suggested that more patients with hepatocellular carcinoma could be candidates for liver transplantation if the current dual (yes/no) approach to candidacy, based upon the strict Milan criteria, were replaced with a more precise estimation of patient survival contouring individual tumor characteristics and use of the up-to-seven criteria** (hepatocellular carcinomas with seven as the sum of the size of the largest tumor [in cm] and the number of tumors). (*Lancet Oncol.* 2009;10:35-43.)

**A prospective study showed that rapid infusion of infliximab is safe and well tolerated, without any increase in infusion-related reactions.** Researchers also noted that when reactions do occur, they are usually mild and allow completion of therapy. (*Eur J Gastroenterol Hepatol.* 2009;21:71-75.)

**According to a multicenter, pragmatic randomized trial (with parallel preference groups) performed in the United Kingdom, laparoscopic fundoplication significantly increased measures of health status compared to long-term medical management** at least up to 12 months after surgery in patients with chronic gastroesophageal reflux disease. (*BMJ.* 2008;337:a2664.)