

Antibiotics, Antidepressants Part of IBS Guidelines Update

BY DAMIAN McNAMARA
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ORLANDO — A recommendation for antibiotic therapy to combat bacterial overgrowth, a stronger recommendation for antidepressants to ease symptoms, and serum testing for celiac disease are forthcoming updates to the American College of Gastroenterology's irritable bowel syndrome guidelines.

New recommendations on the diagnosis of irritable bowel syndrome (IBS) are also expected in the updated guidelines, which the college plans to publish in January 2009, with an earlier release online.

The guidelines also will recommend the addition of microscopic colitis to the differential diagnosis of IBS. This addition is based on a prospective, multicenter study that found 4% of 454 people suspected of IBS actually had microscopic colitis.

"This is definitely new ... and potentially a very, very important message from this document," Dr. William D. Chey said during a media briefing at the annual meeting of the American College of Gastroenterology.

"If a patient has diarrhea-predominant IBS and undergoes colonoscopy, it is reasonable to consider taking random biopsies to exclude microscopic colitis," said Dr. Chey, who is professor of medicine at the University of Michigan, Ann Arbor.

Updated diagnosis recommendations will be reassuring for many clinicians, he said. "Doctors are uncomfortable with assigning a diagnosis of IBS. They are worried that they are missing something else" such as colon cancer, ulcerative colitis, or Crohn's disease.

"The reassuring bit of information that comes out of our analysis ... is that the likelihood of a person who has IBS symptoms and no warning signs having some other organic diagnosis such as colon cancer, inflammatory bowel disease, or thyroid disease is no greater than in the general population," he continued. "Although I understand why it's a concern, it is not an entirely rational concern."

Doctors in clinical practice often characterize people with only abdominal pain as having IBS, he added. "These recommendations, based on the best available evidence, apply to people with pain and altered bowel habits."

The link between pain and bowel disturbance is very close, Dr. Nicholas J. Talley said. "They have pain, they pass stool and get relief—that is IBS. It's absolutely obvious to me." Dr. Talley is chair of the department of internal medicine at the Mayo Clinic, Jacksonville, Fla.

Because of a greater risk of organic disease, patients who present with IBS symptoms plus other warning signs such as unexplained weight loss, GI bleeding, or a family history of colon cancer, inflammatory bowel disease, or celiac sprue require a more detailed evaluation, Dr. Chey said.

Another new recommendation is for use of a "nonabsorbable antibiotic" to re-

lieve IBS symptoms. The only approved antibiotic that remains in the gut to alter flora without systemic absorption is rifaximin (Xifaxan), now under investigation as a treatment for IBS. Rifaximin was found to be superior to placebo for improvement of IBS symptoms, especially bloating, in recent studies (*Ann. Pharmacother.* 2008;42:408-12; *Adv. Med. Sci.* 2007;52:139-42).

"What is uncertain is how long the symptom relief lasts and what you should

do if the symptoms recur," said Dr. Philip S. Schoenfeld, a gastroenterologist at the University of Michigan, who also spoke at the media briefing.

"There is evidence of benefit in the short term [with rifaximin]. It is critical that you know that," Dr. Talley commented. He predicted this recommendation will be controversial because IBS is chronic and antibiotics are typically prescribed acutely.

Dr. Schoenfeld said that physicians may

be concerned about increasing antibiotic resistance if the agents are given to thousands of IBS patients.

There is a greater focus on the use of antidepressants to treat IBS in the new guidelines.

"There is a stronger recommendation that tricyclic antidepressants, used in low doses before people go to sleep at night, are an effective medicine for irritable bowel syndrome," Dr. Schoenfeld said. The agents can reduce bloating and discomfort

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The Office of the Surgeon General's Call to Action Against Deep Vein Thrombosis and Pulmonary Embolism

The high incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE), collectively known as venous thromboembolism (VTE), has a devastating effect on patients and their families. The Surgeon General has announced a Call to Action to raise awareness about the risk factors and prevention of VTE.

*"DVT/PE are major national health problems that have a dramatic, negative impact on the lives of hundreds of thousands of Americans each year."*¹

Rear Admiral Steven K. Galson, MD, MPH, US Public Health Service, Acting Surgeon General

According to the Surgeon General's Call to Action, VTE is a major cause of morbidity and mortality among hospitalized patients.^{1,2} It is the third leading cause of cardiovascular death in the United States, following myocardial infarction and stroke.²

- There are up to 600,000 cases of DVT and PE annually, resulting in at least 100,000 deaths per year¹
- More annual deaths are attributed to VTE than breast cancer and AIDS combined³
- Many patients with VTE do not have any clinical signs or symptoms, with 25% of patients presenting with sudden death⁴

Even when accurately diagnosed, complications due to VTE can be long-standing and reduce quality of life, despite adequate treatment. The first step in reducing the incidence of DVT is to increase awareness among the public as well as health care providers about risk factors that may lead to DVT. By understanding patient risk factors, appropriate prophylaxis may be initiated.

*"The majority of DVT/PE events are related to specific, identifiable triggering events..."*¹

Partial list of risk factors associated with DVT and PE^{5,6}

- Restricted mobility
- Age >40 years
- ICU admission
- Obesity
- Surgery
- Varicose veins
- Prior history of VTE (DVT and/or PE)
- Chronic lung disease
- Inflammatory bowel disease
- Smoking

Table 1. Partial list of risk factors. Clinicians are advised to consider other risk factors or conditions that may predispose to DVT/PE.

*"Much is known today about how to prevent DVT/PE, and how to minimize the impact for those patients who suffer from these conditions. If this knowledge were applied consistently, the burden could be reduced substantially."*¹

Advancing DVT Awareness

According to the American Public Health Association Deep-Vein Thrombosis Omnibus Survey, 74% of adults had very little or no awareness of DVT.⁷ Even among those mindful of DVT, 57% did not know of any risk factors associated with DVT. Surprisingly, 95% of respondents said their physician had never discussed the importance of DVT with them.⁷

Both patients and physicians must educate themselves about the dangers of DVT. It is important for health care providers to routinely assess DVT risk in hospitalized patients as well as screen high-risk patients more thoroughly. All hospitalized patients are at risk of developing DVT. Patients not receiving prophylaxis and undergoing certain general, urologic, gynecologic, or surgical procedures have a 15% to 40% risk of developing DVT.⁵ For hospitalized acutely ill medical patients, the risk is 10% to 20%. Patients having hip or knee arthroplasty are at even higher risk, 40% to 60% without prophylaxis.⁵ Given the high prevalence of DVT in hospitalized patients, all patients should periodically be risk assessed for DVT.

*"Individuals, families, and their communities need to understand DVT and PE, the risk factors for these diseases, and how to reduce these risks."*¹

DVT Prophylaxis Reduces the Incidence of DVT, Which May Lead to PE

The use of anticoagulation therapy has been shown to significantly reduce the risk of VTE by as much as 52%⁸; however, implementation and lack of appropriate prophylaxis in at-risk medical patients continue to be problematic,⁹ despite evidence-based DVT/PE guidelines (Table 2).

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by altering brain-gut signaling about motility and distention. He added that constipation, a side effect of tricyclic antidepressants, is actually beneficial in this population.

The authors of the guidelines also found enough evidence to support SSRIs for symptom improvement. "I want to emphasize that this does not appear to be related to depression," Dr. Talley said. "This appears to be related to effects of these drugs either in the brain or the gut, but probably both places."

Some treatment recommendations in the guidelines are not expected to change, such as those for treatment with lopera-

midate (Imodium) or alosetron (Lotronex). The new recommendation for serologic



'Serologic screening for celiac disease should be pursued' in a subset of IBS patients.

DR. CHEY

ic celiac disease testing is for a subset of IBS patients. "We made a much stronger recommendation for testing for celiac dis-

ease in patients with diarrhea-predominant or mixed IBS," Dr. Chey said. "We actually came out and said serologic screening for celiac disease should be pursued."

Evidence of benefit from probiotics is also addressed. "Every one of my patients with IBS asked about probiotics," Dr. Talley said. "The guidelines will basically say that probiotics are efficacious, but the evidence supporting this is not as good as we would like." The large number of probiotic products with varying degrees of efficacy precluded a stronger recommendation.

"Probiotics seem to be relatively safe as well, based on the data we have," Dr. Tal-

ley said. "So I'm not uncomfortable with recommending a probiotic to my patients." He added that some people are nonresponders.

In addition, recent evidence that indicates peppermint oil improves IBS symptoms will be in the update.

Dr. Schoenfeld is a consultant to, and is on the advisory committee for, Salix Pharmaceuticals Ltd., which markets Xifaxan. Dr. Talley is also a consultant for Salix and a variety of other pharmaceutical companies, and receives financial support from several firms. Dr. Chey reported no relevant financial disclosures for his presentation. ■

PE resulting from DVT is the most common cause of preventable death among hospitalized patients.⁵ In the DVT FREE study funded by sanofi-aventis, which included 5451 patients with ultrasound-confirmed DVT, 71% did not receive any prophylaxis within 30 days of diagnosis.¹⁰ Moreover, nonsurgical patients were much less likely than surgical patients to receive appropriate DVT prophylaxis.¹⁰ The American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines recommend that, for every general hospital, a formal, active strategy that addresses the prevention of VTE be developed (Grade 1A).⁵

"Providing preventive treatment (or primary prophylaxis) to these individuals can dramatically reduce the likelihood of a blood clot or PE."¹¹

Recommendations for VTE Prophylaxis in Select Hospitalized Patients⁵ (Adapted From 2008 ACCP Guidelines)

Prophylaxis of DVT in medical patients with restricted mobility during acute illness^{5,11,a}

- For acutely ill medical patients admitted to hospital with congestive heart failure (CHF) or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including active cancer, previous VTE, sepsis, or inflammatory bowel disease: ACCP recommends thromboprophylaxis with low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin (LDUH) (all Grade 1A)

Prophylaxis of DVT following abdominal surgery^{5,11,a}

- For higher-risk general surgery patients undergoing a major procedure for cancer: ACCP recommends thromboprophylaxis with LMWH or LDUH three times daily (each Grade 1A)
- For patients undergoing major general surgical procedures: ACCP recommends thromboprophylaxis continue until discharge from hospital (Grade 1A)

Prophylaxis of DVT following hip- or knee-replacement surgery^{5,11,a}

- For patients undergoing total hip replacement (THR) or total knee replacement (TKR): ACCP recommends routine thromboprophylaxis with LMWH (at the usual high-risk dose) or adjusted-dose vitamin K antagonist (VKA) (international normalized ratio [INR] target, 2.5; INR range, 2.0 to 3.0) for at least 10 days (all Grade 1A)
- For patients undergoing THR: ACCP recommends thromboprophylaxis be continued beyond 10 days and up to 35 days after surgery with LMWH (Grade 1A) or a VKA (Grade 1B)

Table 2. ACCP 2008 Guidelines: recommendations for VTE prophylaxis.

LOVENOX[®] (enoxaparin sodium injection) is indicated for the prophylaxis of DVT, which may lead to PE:

- In medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness
- In patients undergoing abdominal surgery who are at risk for thromboembolic complications
- In patients undergoing hip-replacement surgery, during and following hospitalization
- In patients undergoing knee-replacement surgery

Two Clinical Trials Showed LOVENOX[®] Provided Effective VTE Prophylaxis in Medically Ill Patients

MEDENOX (Prophylaxis in Medical Patients With Enoxaparin) was a multicenter, multinational, double-blind study that included 1102 acutely ill medical patients randomized to either LOVENOX[®] or placebo for 6 to 14 days during hospitalization.¹²

The incidence of DVT or PE was significantly lower in patients treated with LOVENOX[®] than placebo (5.5% vs 14.9%, respectively).¹² The use of LOVENOX[®] was associated with a 63% reduction in risk of VTE.¹²

There was no statistically significant difference in major bleeding events^{b,c} or thrombocytopenia comparing LOVENOX[®] with placebo.^{12,13}

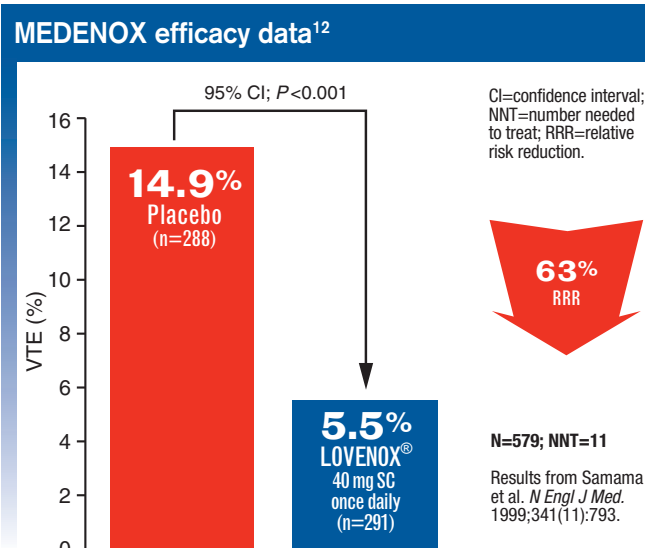


Figure 1. Short-term incidence and RRR of VTE in medical patients treated with LOVENOX[®] (40 mg) vs placebo. P values are for RRR.

^a Grades of recommendation – 2008 Guidelines: ACCP Evidence-Based Clinical Practice Guidelines (8th edition)—Grade 1A—strong recommendation based on high-quality evidence; Grade 1B—strong recommendation based on moderate-quality evidence; Grade 1C—strong recommendation based on low- or very low-quality evidence.¹¹

^b Based on the rate of major bleeding on LOVENOX[®] up to 24 hours after the last dose.¹³

^c Hemorrhage was classified as major if bleeding was overt and was associated with the need for transfusion of 2 or more units of packed red blood cells or whole blood, or with a decrease in the hemoglobin concentration of 2.0 g/dL or more from baseline, or if bleeding was retroperitoneal, intracranial, or fatal.¹²

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