# Antibiotics, Antidepressants Play Role in IBS Update

#### BY DAMIAN MCNAMARA Miami Bureau

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 diagno-

sis 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 the findings from a prospective, multicenter study that 4% of 454 people suspected of IBS actually had microscopic colitis.

"This is definitely new ... and poten-

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tially 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, then it is reasonable to consider taking random biopsies to exclude microscopic colitis," said Dr. Chey, professor of medicine at the University of Michigan, Ann Arbor.

The updated diagnosis recommenda-

Tetanus Toxoid, Reduced **Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed** 

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ACIOCCE: Brief Summary: Please see package insert for full prescribing information INDICATONS AND USAGE Adace<sup>®</sup> vaccine is indicated for active booster immunication for the prevention of tetanus, diphtheria and pertussis as a single dose in persons 11 through 64 years of age. The use of Adaced vaccine as a primary series, or to complete the primary series, has not been studied. Vaccination with Adaced vaccine may not protect all of vaccinated individuals. the primary senis, has not been studied. Vaccination with Adacel vaccine may not protect all of vaccinated individuals. CONTRAINDECTIONS A severe alleging reaction (e.g., anaphyckis) after a previous dose of Adacel vaccine or any other tetaruus toxid, diphtheria toxid or pertussis containing vaccine or any other component of this vaccine is a contraindication to vaccination with Adacel vaccine. Because of nucreatinity as to which component of the vaccine way be responsible, none of the components should be administered Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered (12) Encephalopathy within 7 days of a previous dose of a pertussi containing vaccine not attributable to another identifiable cause is a contraindication to vaccination with Adacel vaccine. (1-3)

anourer userunable cause is a contrainnocation to vaconation with Adacet vacone. (1-3) WARNINGS Persons who experienced Arthus-type hypersensitivity reactions (e.g., severe local reactions associated with systemic symptons) (4) following a prior of ose of tetarus toxoid usually have high serum tetarus antitoxin levels and should not be given emergency does of tetarus toxoid containing vaccines more frequently than every 10 years, even if the wound is neither clean nor minor. (12,5,6) if Guillain-Baré syndrome occurred within 6 weeks of receipt of prior vaccine containing tetarus toxoid, the decision to give Adacet vaccine or any vaccine containing tetarus toxoid should be based on careful consideration of the potential benefits and possible risks.(1-3) In the following situations, Adacet vaccine should generally be detered: Moderate or severe acute lines with or without fever, until the acute illness resolves. (1,2)
 In addescents, progressive neurologic disorder, including progressive encephalopathy, or uncontrolled epilepsy, until the condition
 has stabilized. (2)

In adults, unstable neurologic condition (e.g., cerebrovascular events and acute encephalopathic conditions), until the condition has resolved or is stabilized. (1)

resolved or is stabilized. (1) PRECAUTIONS General Before administration of Adacel vaccine, the patient's current health status and medical history should be reviewed in order to determine whether any contraindications exist and to assess the benefits and risks of vaccination. See CONTRAINDECTIONS and WARENINGS.) Eignephine Hydrochloride Solution (11:100) and other appropriate agents and equipment should be available for immediate use in case an anaphylactic or acute hypesensitivity reaction occurs. If Adacel vaccine is administered to immunocomponenticed persons, including persons receiving immunosuppressive therapy, the expected immune response may not be obtained.

Information for Vaccine Recipients and/or Parent or Guardian Betwaris receiving immunocuppressive diretary, the expected immuno information for Vaccine Recipients and/or Parent or Guardian Before administration of Adacel vaccine, health-care providers should inform the vaccine recipient and/or parent or guardian of the benefits and risks. The health-care provider should inform the vaccine recipient and/or parent or guardian about the potential for adverse reactions that have been temporally associated with Adacel vaccine or other vaccines containing similar components. The health-care provider should provide the Vaccine Information Statements (VISS) that are required by the National Childhood Vaccine Injury Act of 1966 to be given with each immunization. The vaccine recipient add/or parent or guardian should be informed that Sanof Paskeur Inc. maintains a pregnancy surveillance system to collect data on pregnancy outcomes and new providens usoften structure to report y succination with Adaced vaccine during pregnancy. They are pregnant or become aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or become aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or become aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or boxene aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or boxene aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or boxene aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or boxene aware they were pregnant at the time of Adacel vaccine during pregnancy. They are pregnant or boxene Adverse Event Reporting System by receptients and/or parents or guardian should be encoursed. The toliffeer number for VARES forms and information is 1-800-822-7367. Reporting forms may also be obtained at the VARES website at www.vares.his gov.

www.vaers.hts.gov.
Drug Interactions Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and
corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccins. ECE PRECAUTIONS,
General.) For information regarding simultaneous administration with other vaccines refer to the ADVERSE REACTIONS and
DOSAGE AND ADMINISTRATION sections.
Carcinogeneist, mutageneis, Impairment of Fertility. No studies have been performed with Adacel vaccine to evaluate
carcinogenicity, mutageneis, impairment of fertility.

DOSACE AND ADMINISTRATION sections. Carcinogenicity, mutagenic potential, or impairment of Fettility. Pregnany Category C Animal reproduction studies have not been conducted with Adacel vaccine. It is also not known whether Adacel vaccine can use fetal harm when administered to a pregnant woman or can affect reproduction capacity. Adacel vaccine. The effect of Adacel vaccine on emboy-fetal and pre-vaming development was evaluated in two developmental toxicity studies using pregnant rabbits. Animals were administered Adacel vaccine twice prior to gestation, during the period of organogenesis (gestation day 6) and later during repranyro ong estation day 29.0.5 ml/habtit/coscino 11 or 0-developmental toxicity studies using pregnant rabbits. Animals were administered Adacel vaccine twice prior to gestation, during the period of organogenesis (gestation day 6) and later during repranyro, ong estation day 29.0.5 ml/habtit/coscino 11 or 1-7-loil increase compared to the human doe of Adacel vaccine on a body weight basis), by inframuscular injection. No adverse effects on pregnancy, partition, lactation, emboy-fetal or pre-venang development. Were observed. There were no vaccine related fetal malformations or other evidence of teratogenesis noted in this study. (7) Nursing Mothers It is not known whether Adacel vaccine is given to a nursing woman. Pediatric Use Adacel vaccine is not indicated for individuals 65 years of age and older. No data era available regarding the safety and effectiveness of Adacel vaccine is not indicated for individuals 65 years of age and older. No datael are available regarding the safety and effectiveness of Adacel vaccine is not indicated for individuals 65 years of age and older. No data era vacine din ot include participants in the genatin population. ADVERSE BEACTIONS The safety of Adacel vaccine was evaluated in 4 clinical studies of Adacel vaccine. The principal steps study was a randomized, observerbilind, attwo comotoled trait hat monice parasity escentes that or c

evenus vai appear us ce reaers us vacune use anu un approximang raits or those events.
Serious Adverse Events in All Safety Studies Throughout the 6-month follow-up period in the principal safety study, serious adverse events were reported in 15% of Adaet vaccine recipients and 1.4% in Td vaccine recipients. Two serious adverse events in adults were neuropathic events that occurred within 28 days of Adaet vaccine recipients and 1.4% in Td vaccine recipients. Two serious adverse events in adults mere neuropathic events that occurred within 28 days of Adaet vaccine administration; one severe migraine with unitateral facial paralysis and one dagnosis of new compression in new and thet am. Smilli ar of over rates of serious adverse events were reported in the other trials and there were no additional neuropathic events reported. ited Adverse Events in the Principal Safety Study Most selected solicited adverse events (erythema, swelling, pain and fever) that

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occurred during Days 0-14 following one dose of Adacel vaccine or Td vaccine were reported at a similar frequency. Few participants (<1%) sought medical attention for these reactions. Pain at the injection site was the most common adverse reaction occurring in G3 to 78% of al vaccine compared to Td vaccine experients. Rates or moderate and severe pain and adverse this device in adolescent recipients of Adacel vaccine compared to Td vaccine groups. Among adults the rates of pain, after receipt of Adacel vaccine or Td vaccine, dd not significantly utility. Fever of 38°C and lighter was uncommon, although in the adolescent age group, it occurred significantly more frequently. Adacel vaccine end Td vaccine rol vaccine recipients. (2) Among diverse valides adverse vents headsher was the most frequently in Adacel vaccine recipients than Td vaccine recipients. (2) Among diverse valides adverse vents headsher was the most frequently in Adacel vaccine recipients than Td vaccine recipients. (2) Among diverse valides adverse vents headsher was the most frequently in Adacel vaccine recipients than the vaccine. Local and systemic solidet adverse vents headsher was the most frequently and vacuum adverse was adverse. Local and systemic solidet adverse vents headsher was the most frequently and vacuum adverse two rates of unsolidet adverse vents reported from day 14-29 port vaccination (with a mean duration of less than 3 days). The rate of unsolidet adverse vents from day 28 through 6' months. There were no spontaneous reports of whole-am swelling of the injected limb in this study, nor in the other three studies which contributed to the safety database for Adacel vaccine.

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REFRENCES 1. OC. Preventing tetranus, diphtheria and pertussis among adults: use of tetranus toxioli, reduced diphtheria toxoid and acellular pertussis vaccine. MWWR 2006;55(RR-17):1-36. 2. CC. Preventing tetranus, diphtheria and pertussis among addescents: use of tetranus toxiol, reduced diphtheria toxoid and acellular pertussis vaccines. MWWR 2006;55(RR-13):1-48. C. CC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MWWR 2006;55(RR-15):1-48. L. OC. Update: rule caccine side effects. Advesse reactions contraindications of the advisory Committee. ACID. WWWR 1990;40(RR-10):1-28. C. C. Update on adult immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP). MWWR 2006;57(RR-15):1-48. L. OC. Update: rule and other preventive measures. Recommendations of the immunization Practices. Advisory Committee (ACIP). MWWR 1991;40(RR-12):1-52. T. Data on file at 13 and Pasteur limited. 8. Stration Re: et al. editors. Adverse vents associated with childrod vaccine; evidence bearing on causality. Washington: National Academy Press; 1994, p. 67-117. 9. CDC. Current trends - Vaccine Adverse Event Reporting System VARSD). Unlisted. 8. Strational Academy Press; 1994, p. 67-117. 9. CDC. Current trends - Vaccine Adverse Event Reporting System VARSD Vacine Advisor Adverse vents. 3. TO, CDC. Current trends - vaccine Adverse Event Reporting System versionation records and for reporting of selected events after vaccination. MWWR 1988;37(13):197-200. 11. FDA. New reporting requirements for vaccine adverse events. FDA Drug Bull 1988;18(2):16-8.

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tions will be reassuring for many health care providers Dr. Chey continued. "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



What is uncertain is how long the symptom relief lasts and what you should do if the symptoms recur.'

DR. SCHOENFELD

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.

However, "These recommendations, based on the best available evidence, apply to people with pain and altered bowel habits," Dr. Chey said.

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 relieve 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 said. He predicted that 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 Continued on following page

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#### Continued from previous page

resistance if the agents are given to thousands of IBS patients.

In addition, there is a greater focus on the use of antidepressants to treat IBS in the new guidelines.

For example, "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 by altering brain-gut signaling about motility and distention. He added that constipation, a side effect of tricyclic

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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, including the use of loperamide (Imodium) or alosetron (Lotronex).

The new recommendation for serologic celiac disease testing is for a subset of IBS patients.

"We made a much stronger recommendation for testing for celiac disease 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," he stated. 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. Talley said. "So I'm not uncomfortable with recommending a probiotic to my patients."

He added, however, that some people are nonresponders.

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

Dr. Schoenfeld disclosed that he 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.



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