

Updated Maastricht Guidelines Address *H. pylori* Testing, Therapy

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COPENHAGEN — The local prevalence of *Helicobacter pylori* and antibiotic-resistant *H. pylori* help determine who to test for gastric infection and how to treat them, according to the revised Maastricht guidelines.

The third edition of the influential Consensus Report of the European *H. pylori* Study Group was drafted last March by a panel of European experts; the new guidelines are called Maastricht 3.

The recommendations were detailed in a special session at the 13th United European Gastroenterology Week.

At press time a publication date had not been set.

The guidelines cover three issues: who to test and treat for *H. pylori*, how to test and treat, and how to prevent gastric cancer triggered by *H. pylori*.

Who to Test and Treat

Patients who should be tested for *H. pylori* include those starting long-term NSAIDs, patients with unexplained iron-deficiency anemia, and patients with immune thrombocytopenia.

Other indications include peptic ulcer disease, nonulcer dyspepsia, mucosa-associated lymphoid tissue (MALT) lymphoma, atrophic gastritis, a history of gastric cancer resection, first-degree relatives of patients with gastric cancer, and patients who, on consulting with a physician, want to be tested.

Test-and-treat is endorsed as a management strategy for dyspepsia because study results have shown that it is as effective as routine endoscopy while reducing use of endoscopy and of antisecretory medication, said Colm O'Morain, M.D., professor of medicine at Trinity College, Dublin, and a cochair of Maastricht 3.

In regions where infection rates by *H. pylori* are high (prevalence above 20%), test-and-treat is the preferred option, he added. In regions where the prevalence of infection is less than 20%, empiric treatment with antisecretory medication first is just as effective and may be more appropriate.

The guidelines also highlight the fact that eradication of *H. pylori* does not cause gastroesophageal reflux disease, but curing an infection and resolving an ulcer may unmask reflux that was not previously diagnosed.

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DR. O'MORAIN



Eradiation of *H. pylori* can also halt the extension of and may even cause regression of atrophic gastritis. But eradication will not affect the efficacy of

proton pump inhibitors. The guidelines say that *H. pylori* and NSAIDs are independent and synergistic causes of peptic ulcers. Eradicating *H. pylori* alone cannot prevent or stop bleeding caused by chronic NSAID use, but a patient starting a long-term course of an NSAID or aspirin should be tested for *H. pylori* and treated if positive, Dr. O'Morain said.

How to Test and Treat

Mainstays of testing are the urea breath test and stool antigen test, although serology tests also have a role, said Francis Mégraud, M.D., a professor of bacteriology at Pellegrin Hospital in Bordeaux, France, another conference cochair.

Both tests work best in patients not being treated with an antisecretory drug, and in those who do not have a bleeding ulcer, atrophic gastritis, or a MALT lymphoma. In patients who are taking an antisecretory drug or have one of these conditions, a serology test is best. But serology can be inferior because individual tests require validation, and it can be hard to distinguish between new and old infections.

In general, first-line treatment for *H.*

pylori eradication is a proton pump inhibitor, 500-mg clarithromycin b.i.d., and either amoxicillin or metronidazole. A 14-day regimen is more effective, but 7 days can be appropriate and cost effective when local studies prove that it's effective. A quadruple-drug regimen that also includes bismuth is an alternative first-line option. Resistance to clarithromycin is a growing problem. In some regions of southern Europe, 20% of isolates are resistant. There is a small advantage to using metronidazole instead of amoxicillin, but either is acceptable. Metronidazole is preferred in regions where the prevalence of metronidazole resistance is less than 40%.

The top second-line regimen is quadruple therapy that adds bismuth to the first-line trio of drugs. Another second-line option is a proton pump inhibitor plus metronidazole and amoxicillin. Although a quinolone, such as levofloxacin, can effectively eradicate many *H. pylori* infections, a quinolone is not a good first- or second-line choice because its use would lead to drug resistance, Dr. Mégraud said.

Patients should be retested to confirm eradication 4 weeks after starting treatment. A urea breath test is the top follow-up test, followed by stool antigen testing. If a patient remains infected despite treatment, the next antibiotic choice should be determined by susceptibility testing.

Preventing Gastric Cancer

Study results show that about 70% of noncardia adenocarcinoma is attributable to infection by *H. pylori*, said Peter Malfertheiner, M.D., director of the department of gastroenterology at Otto von Guericke University in Magdeburg, Germany, and the third cochair of Maastricht 3.

Eradiation of *H. pylori* prevents alterations in gastric chemistry and preneoplastic changes in the gastric mucosa. "In theory, *H. pylori* eradication should reduce the risk of gastric cancer," he said. "The optimal time to start treatment is before preneoplastic lesions appear, but it's never too late to eradicate," Dr. Malfertheiner said. ■

Advances in Ulcer Management Cut Hospitalizations

COPENHAGEN — Each of the two "major revolutions" in managing gastric ulcers that occurred during the past decade produced clear drops in hospitalization rates in the United States.

The 1995 onset of routine eradication of *Helicobacter pylori* infection and the 1999 introduction of selective cyclooxygenase-2 inhibitors were associated with sharp falls in the number of patients hospitalized for complicated gastric ulcers, duodenal ulcers, or peptic ulcer disease, Gurkupal Singh, M.D., said at the annual United European Gastroenterology Week.

He and his associates analyzed data collected by the National Inpatient Sample, a stratified, random sample of all community hospitals in the United States that represents about 85% of all hospitalizations.

Data were assessed for 1988-2003, a period of more than 490 million hospitalizations that involved 3.6 billion patient-years of observations. Almost 2.2 million of the hospitalizations were for a primary diagnosis of complicated gastric ulcer, duodenal ulcer, or peptic ulcer disease.

The period studied included striking increases in the use of NSAIDs, and in the use of proton pump inhibitors (PPIs), which play a key role in the regimens used to eradicate *H. pylori*. Prescriptions for NSAIDs rose from 68 million in 1990 to 113 million in 2001. Prescriptions for PPIs jumped from 4 million in 1992 to 74 million 9 years later. Prescription data were obtained from IMS Health, a company that collects information on the pharmaceutical industry.

The rate of hospitalization for complicated ulcer disorders per 100,000 NSAID prescriptions steadily dropped throughout the period 1992-2001, falling from 241.5/100,000 scripts in 1992 to 123.8/100,000 in 2001. But the overall downward trend was punctuated by two sharp drops in the hospitalization ratio.

In 1995, the ratio of ulcer hospitalizations to 100,000 NSAID prescriptions fell by 11%, probably reflecting the 1994 recommendation by a consensus conference to eradicate all diagnosed infections by *H. pylori*, said Dr. Singh, a physician who specialized in clinical outcomes research at Stanford (Calif.) University.

And in 1999 the ratio dropped by 22% compared with the prior year, likely a consequence of the introduction of selective COX-2 inhibitors in the United States in 1998, Dr. Singh said.

Chronic Cough Despite Acid Suppression: Surgery Indicated?

COPENHAGEN — Chronic cough during an acid-suppressive regimen identifies patients who could benefit from impedance pH monitoring and possible surgical management, based on a review of 50 patients.

"A positive symptom index for nonacid reflux directs the selection of patients who will benefit from antireflux surgery," Radu Tutuian, M.D., and associates wrote in a poster at the 13th United European Gastroenterology Week.

The investigators studied patients who

had a persistent cough despite taking a proton-pump inhibitor twice a day. Eighteen patients also took a dose of a histamine₂ receptor antagonist at night.

While their treatment continued, the patients were assessed by using combined, multichannel, intraluminal impedance and by pH monitoring.

The association between cough and reflux was judged positive if two criteria were met: a reflux episode preceded coughing by 5 minutes or less, which was called symptom index (SI) positive, and the

symptom association probability was greater than 95%.

The testing identified 13 patients as being SI positive and 14 as positive for symptom association probability, reported Dr. Tutuian, a gastroenterologist at the Medical University of South Carolina in Charleston.

The patients who were SI positive were more likely to be younger and male, compared with the other patients studied. The SI-positive group was 54% male, with an average age of 41 years, compared with

17% males and an average age of 51 years among the others.

Six of the 13 SI-positive patients underwent laparoscopic Nissen fundoplication. After 2-17 months of follow-up (with a mean of 9 months), all 6 patients were off antisecretory treatment and were asymptomatic.

Impedance pH monitoring while on treatment should be done in patients with persistent symptoms despite treatment with a proton-pump inhibitor, the researchers concluded. ■