Current management of *Helicobacter pylori* infection

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Helicobacter pylori infection continues to be one of the hottest topics in gastroenterology, challenging the primary care physician daily with the clinical application of its new developments and frequency of involvement in differential diagnosis. This article offers the primary care physician a practical approach to the dyspeptic office patient that emphasizes the differential diagnosis of *H pylori*. Included is a strategy for rapid patient evaluation through key questions in the history, simple maneuvers in the physical examination, and a logical approach to testing and therapy based on the latest literature. The recommendations for all these office-based steps are designed to be efficient, cost-effective, and clinically relevant.

(Key words: *Helicobacter pylori* infection, gastroesophageal reflux, proton pump inhibitors)

H*elicobacter pylori* continues to be one of the hottest topics in gastroenterology, daily challenging the practicing gastroenterologist to digest the rapidly changing and sometimes contradictory medical literature, and then clinically apply that information in a practical fashion to patients in an office setting. This article presents for the primary care physician a step-by-step approach to the office patient with dyspepsia with special emphasis on *H pylori*. A time-efficient, cost-effective plan, beginning with the patient encounter, and progressing to the history, physical examination, decision process for testing, and approach to treatment is reviewed.

The setting is familiar: *It is a hectic day, you are a bit behind schedule, the waiting room is filling up, and you are beginning to feel the pressure to evaluate the patients properly, efficiently, and to offer the kind of care you know you are capable of. Per-*

haps you practice in an office setting where health maintenance organizations represent a significant part of your practice, making the efficient use of your time with patients all the more important.

Let us begin with a patient who comes to the physician's office with dyspepsia.

Definition of terms

The first element in any intelligent discussion is a mutual agreement on the definition of terms. Dyspepsia is defined as indigestion, impaired gastric function, or upset stomach characterized by epigastric pain, burning, nausea, or gaseous eructation. In other words, just about any upper gastrointestinal symptom may be placed under this heading. This seemingly all-encompassing term has been used for centuries in a scientific discipline that is supposed to at least attempt to be as precise as possible. Yet, dyspepsia remains, purposefully it seems, about as imprecise and all-encompassing as one can get. The method to this apparent madness lies in the nature of the clinical manifestations of gastrointestinal disease, when compared with disease symptoms in other body systems.

Perhaps the system that offers the greatest foil to the gastrointestinal tract is the heart. All physicians have been regaled with anecdotes relating the clinical diagnostic prowess of the learned physicians of yesteryear. With just stethoscope in

hand, and by virtue of being steeped in the finest nuances of cardiac auscultation, they could diagnose cardiac disease with at least as much accuracy as today's three-dimensional echocardiogram. No one ever made such claims concerning bowel sounds. The fact is that unlike other body systems, the gastrointestinal tract has a limited number of ways in which it can respond symptomatically. These common responses can indicate any of a large number of diagnoses. Hence, the inherent imprecise nature of gastrointestinal symptoms, and therefore, the conveniently all-encompassing terminology of dyspepsia.

Of course, there are the purists who think that dyspeptic patients can be categorized into at least two groups: the "functional" dyspeptic patient and the "organic" dyspeptic patient. The functional dyspeptic patient is distinguished by bloating and eructation, and these symptoms are thought to be consistent with a functional diagnosis such as irritable bowel syndrome. The organic dyspeptic patient is marked by a burning, searing pain, symptoms thought to be consistent with an organic endoscopically demonstrable disease such as peptic ulcer disease. For the majority of clinicians, however, there is just too much symptom overlap in live patients, and it is feared that this symptomatic and semantic hair splitting may lead front-line physicians down the wrong road of diagnosis and therapy.

A more generally accepted exception to the rule of all-encompassing dyspepsia is gastroesophageal reflux disease (GERD) symptoms. This diagnosis appears to stand out from common dyspepsia because of its radiation up the chest, typical "heartburn" description, and simple physical examination test, which will be described later.

Acquiring the history from the dyspeptic patient

When first faced with the dyspeptic patient, we intuitively apply the same basic approach as with all patients. A cacophony of visual, audible, and factual stimuli help us to immediately categorize patients into two groups: The "walking wounded" and the "worried well." The so-called walking wounded are those patients whose illness is potentially serious and who are in need of swift planning and care. The worried well are those patients who are thought to have a relatively easily handled medical problem. Every patient who enters your office with dyspepsia should be

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asked if he or she has any of the four "alarm symptoms," recalled by the simple-to-remember mnemonic: A, B, C, D (Figure):

■ **A, appetite**—Always inquire about its loss; the patient will describe the loss of desire to eat after only a few mouthfuls, associated with a feeling of "fullness," which is medically described as early satiety. A also reminds you of anemia, a critical laboratory finding.

■ **B, bleeding**—Inquire concerning melena, hematochezia, hematemesis, and of course, the Hemocult card. I have often said that the most important diagnostic limb on this specialist's body is my index finger. Rectal examinations are time consuming, embarrassing (for at least the patient and at times, some physicians), troublesome, and absolutely essential to the appropriate workup of the patient who is suspected of having gastrointestinal bleeding. If you opt not to do the Hemocult test in the office, consider sending three cards home with your patient to be returned to you by mail.

■ **C, cachexia, or weight loss**—Beware the patients who say that they are losing weight because they are on a diet. Think of all the people you know who are on diets and then consider how many of them are actually losing weight. From a medical point of view, weight loss should be considered an organic sign until proven otherwise.

■ **D, dysphagia alone or accompanying odynophagia**—This is considered one of the alarm signs.

How to proceed with the group of patients who answer these questions affirmatively will be discussed later.

Physical examination

We all recall our physical examination courses that emphasized the observation, auscultation, percussion, and palpation of the abdomen. Perhaps some of us may recall being taught the particularly useless auscultation of all four quadrants of the abdomen for 3 minutes to definitively establish the presence or absence of bowel sounds. Through our own clinical experience, we learned that the physical examination of the abdomen was, more often than not, quite unhelpful. Everyone would agree that a good physical examination of the abdomen is necessary. Are there any simple, reproducible maneuvers that can be performed during the physical examination that would help in the differential diagnosis of our dyspeptic patient? One

such maneuver is a GERD maneuver. This maneuver involves laying the patient down in the supine position and politely removing the pillow from under the patient's head. Place the tips of your fingers just under the patient's xyphoid process and press upward toward the esophagus. If the patient can feel fluid coming up the esophagus and into the throat, this is a positive GERD sign that has a high correlation with true clinical GERD. It is important to bear in mind that a negative GERD sign does not rule out the disease.

To test, or not to test, that is the question

If the patient with dyspepsia answers yes to any of the four alarm questions previously described, testing is a must. The choice of examinations is between an esophagogastroduodenoscopy (EGD), or an upper gastrointestinal x-ray series. Because of its superior sensitivity and specificity, as well as the capability of obtaining biopsy specimens, the standard of care in the vast majority of communities around the country would be an EGD. Further advantages of the EGD include the ability to better evaluate distal esophageal and gastric mucosal abnormalities, leading to more accurate and rapid diagnosis of Barrett's esophagus or *H pylori* infection. The recent drop in reimbursement for EGD has also made this procedure cost-effective.

Patients who answer no to the four alarm questions previously reviewed can be categorized in two groups: those younger than 45 years and those older than 45 years. The position paper of the American Gastrointestinal Association states that testing is indicated for patients in the group older than 45 years with dyspepsia.¹

Test and treat

For patients in the group younger than 45 years who answer no to the four alarm questions, the "test-and-treat" approach for *H pylori* infection has been proposed. The new test-and-treat approach contrasts with the original proposal for *H pylori* testing that stated that serum testing for *H pylori* infection is justified only for patients with proven peptic ulcer disease. The test-and-treat approach involves acquiring a serum antibody test for *H pylori* from dyspeptic patients who meet the following criteria:

- ☐ answer no to the four alarm questions, and/or
- ☐ are younger than 45 years, and/or
- ☐ do not have typical GERD.

The appropriate treatment of these patients will be reviewed later. Recall that the patients who are older than 45 years or who answer yes to the four alarm questions will most likely be tested with an EGD, which will be able to make the diagnosis of *H pylori* infection with great accuracy. In the forefront of supporters of the test-and-treat doctrine for *H pylori* infection have been the primary care physicians. There is support for such an approach. Note that the test-and-treat approach supports the testing for and eradication of *H pylori* infection with no concrete evidence of peptic ulcer disease.

There were some serious questions concerning the accuracy and reproducibility of results for the first generation of office-based *H pylori* tests. These difficulties appear to have been largely overcome in the newer second-generation office test kits, which are generally accepted to be more sensitive, specific, and reproducible.

New on the horizon are the stool *H pylori* tests, which are just now being marketed. Their specificity and sensitivity in preliminary studies appear good, but final judgment awaits more extensive clinical experience.

How to treat

For the group of individuals in whom the *H pylori* test is positive, what is the regimen of choice? The initial question to be asked of every patient who is to be treated for *H pylori* infection is in regard to penicillin allergy. The importance of this inquiry cannot be overemphasized. I personally go as far as to document in my notes that a check of the data base reveals no evidence of penicillin allergy and a repeated questioning of the patient reveals no evidence of a penicillin allergy. In the patient without penicillin allergy, the recommended first-line treatment is a proton pump inhibitor—such as omeprazole (Prilosec), 20 mg twice a day, or lansoprazole (Prevacid), 30 mg twice a day—combined with clarithromycin (Biaxin), 500 mg twice a day, and amoxicillin, two 250-mg tablets twice a day, all to be taken for 2 weeks.

A combination of lansoprazole, clarithromycin, and amoxicillin (Prevpac) is neatly packaged in a clearly marked card that greatly simplifies the regimen for the patient and is thought to improve compliance.

For those who are penicillin allergic, a regimen of bismuth (Pepto-Bismol), one tablet, metronidazole (Flagyl), 250 mg, and tetracycline, 250 mg, all to be taken

Figure. Flow chart for workup of patient with dyspepsia emphasizing the role of *Helicobacter pylori* infection. GERD = gastroesophageal reflux disease.

four times a day, is recommended. This regimen (conveniently packaged as Helidac) should be combined with a histamine H₂-receptor blocker or proton pump inhibitor. An alternate regimen for penicillin-allergic patients involves a proton pump inhibitor, lansoprazole, 30 mg twice a day, or omeprazole, 20 mg twice a day, to be combined with clarithromycin, 500 mg twice a day, and metronidazole, 250 mg four times a day, for 10 to 14 days. There is some concern about *H pylori* resistance to metronidazole in connection with this regimen.

For all treatment regimens, the proton pump inhibitor should be continued at regular dose for at least 2 weeks after the combination antibiotic regimen has been completed.

Realistic predictions of treatment success

For the purposes of office-based treatment of *H pylori*, we can define treatment success as symptom relief. The first principle to remember is that treatment success is highly dependent on patient compliance, as well as the incidence of true peptic ulcer dis-

ease in this untested group. In uninvestigated dyspeptic patients, symptom relief can be anticipated in 20% to 30% of cases.

Persistence of dyspeptic symptoms despite appropriate *Helicobacter pylori* therapy

What should be done for the patient with continuing dyspeptic symptoms despite appropriate eradication therapy for *H pylori*? In this group of patients, it is reasonable to initiate a formal investigation that would probably include EGD. If retesting for *H pylori* is considered, then it

should be borne in mind that the serum antibody test is no longer dependable for patients who have been treated. The serum antibodies will remain positive for life. If an EGD cannot be performed, and testing for the continuing existence of *H pylori* is desired, then the carbon-14 breath test is probably the best choice.

Confirming eradication of *Helicobacter pylori* infection

Is it necessary to confirm that the *H pylori* infection has been eradicated? In the test-and-treat patient who has no complications and whose symptoms improve status posttherapy, it is not recommended that any further testing be performed because of the high eradication rate of the recommended regimens and the symptomatic improvement that lends support to the contention that the infection has been eradicated. In the patient who has a gastric ulcer, who was found to be *H pylori*-positive, and who was appropriately treated, the question of proving eradication of *H pylori* infection is academic. The gastroenterology literature reflects between a 1% and 5% incidence of malignancy in patients with gastric ulcer; therefore, a second EGD will be performed to confirm gastric ulcer healing. The second set of biopsies that are acquired to rule out malignancy will also be able to confirm or deny eradication of *H pylori* infection. In the patient with complicated peptic ulcer disease, confirmation of eradication is also recommended, either with a breath test or EGD.

Helicobacter pylori infection and GERD

The medical literature does not support a strong association between GERD and *H pylori* infection. In the symptomatic evaluation of dyspepsia, most authorities agree that in the differential diagnosis of dyspepsia, the classic case of heartburn can be singled out and treated empirically, without testing for *H pylori* infection.

Comment

A step-by-step approach to the patient with dyspepsia that is practical, efficient, and can be used by the primary care physician in daily practice begins with the history, with specific emphasis on the four alarm questions. By this approach, the primary care physician can immediately recognize the "walking wounded" for more advanced testing. The presented straightforward criteria based on age and symptoms allow for the appropriate workup of the remaining patients. A simple maneuver in the physical examination will help to distinguish those individuals who fit into the GERD category. This review includes the test-and-treat option for the appropriate patient setting and optimal therapeutic regimens for the penicillin-allergic and none-penicillin-allergic patients. It also presents options for continued workup of patients who fail to respond to treatment.

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