lymphoma, although this condition is much less common. Many low-grade gastric B-cell lymphomas are dependent on *H. pylori* for continuing growth and proliferation, and these tumors may regress either fully or partially after *H. pylori* eradication. However, they require careful short- and long-term monitoring, and some necessitate additional treatment with chemotherapeutic agents.

Functional Dyspepsia Many patients have upper gastrointestinal symptoms but have normal results on upper gastrointestinal endoscopy (so-called functional or nonulcer dyspepsia; Chap. 348). Because *H. pylori* is common, some of these patients will be colonized with the organism. *H. pylori* eradication leads to symptom resolution a little more commonly (from 0 to 7% in different studies) than does placebo treatment. Whether such patients have peptic ulcers in remission at the time of endoscopy or whether a small subgroup of patients with "true" functional dyspepsia respond to *H. pylori* treatment is unclear.

Protection Against Peptic Esophageal Disease, Including Esophageal Adenocarcinoma Much interest has focused on a protective role for *H. pylori* against GERD (Chap. 347), Barrett's esophagus (Chap. 347), and adenocarcinoma of the esophagus and gastric cardia (Chap. 109). The main lines of evidence for this role are (1) that there is a temporal relationship between a falling prevalence of gastric *H. pylori* colonization and a rising incidence of these conditions; (2) that, in most studies, the prevalence of *H. pylori* colonization (especially with proinflammatory *cagA*$^+$ strains) is significantly lower among patients with these esophageal diseases than among control participants; and (3) that, in prospective nested studies (see above), the presence of *H. pylori* is inversely related to these cancers. The mechanism underlying this protective effect is likely *H. pylori*–induced hypochlorhydria. Because, at the individual level, GERD symptoms may decrease, worsen, or remain unchanged after *H. pylori* treatment, concerns about GERD should not affect decisions about whether to treat *H. pylori* when an indication exists.

Other Pathologies *H. pylori* has an increasingly recognized role in other gastric pathologies. It may be one initial precipitant of autoimmune gastritis and pernicious anemia and also may predispose some patients to iron deficiency through occult blood loss and/or hypochlorhydria and reduced iron absorption. In addition, several extragastrointestinal pathologies have been linked with *H. pylori* colonization, although evidence of causality is less strong. Studies of *H. pylori* treatment in idiopathic thrombocytopenic purpura have consistently described improvement in or even normalization of platelet counts. Potentially important but even more controversial associations are with ischemic heart disease and cerebrovascular disease. However, the strength of the latter associations is reduced if confounding factors are taken into account, and most authorities consider the associations to be noncausal. Several studies have shown an inverse association of *cagA*$^+$ *H. pylori* with childhood-onset asthma, hay fever, and atopic disorders. These associations have been shown to be causal in animal models, but causality in humans and the size of any effect have not been established.

DIAGNOSIS

Tests for *H. pylori* fall into two groups: tests that require upper gastrointestinal endoscopy and simpler tests that can be performed in the clinic (Table 188-1).

TABLE 188-1 TESTS COMMONLY USED TO DETECT *HELICOBACTER PYLORI*

Test	Advantages	Disadvantages
Tests Based on Endoscopic Biopsy		
Biopsy urease test	Quick, simple	Some commercial tests not fully sensitive before 24 h
Histology	May give additional histologic information	Sensitivity dependent on experience and use of special stains
Culture	Permits determination of antibiotic susceptibility	Sensitivity dependent on experience
Noninvasive Tests		
Serology	Inexpensive and convenient; not affected by recent antibiotics or proton pump inhibitors to the same extent as breath and stool tests	Cannot be used for early follow-up after treatment; some commercial kits inaccurate, and most less accurate than urea breath test
^{13}C urea breath test	Inexpensive and simpler than endoscopy; useful for follow-up after treatment	Requires fasting; not as convenient as blood or stool tests
Stool antigen test	Inexpensive and convenient; useful for follow-up after treatment; may be useful in children	Stool-based tests are disliked by people from some cultures

Endoscopy-Based Tests Endoscopy is usually unnecessary in the initial management of young patients with simple dyspepsia but is commonly used to exclude malignancy and make a positive diagnosis in older patients or those with "alarm" symptoms. If endoscopy is performed, the most convenient biopsy-based test is the biopsy urease test, in which one large or two small gastric biopsy specimens are placed into a gel containing urea and an indicator. The presence of *H. pylori* urease leads to a pH alteration and therefore to a color change, which often occurs within minutes but can require up to 24 h. Histologic examination of biopsy specimens for *H. pylori* also is accurate, provided that a special stain (e.g., a modified Giemsa or silver stain) permitting optimal visualization of the organism is used. If biopsy specimens are obtained from both antrum and corpus, histologic study yields additional information, including the degree and pattern of inflammation and the presence of any atrophy, metaplasia, or dysplasia. Microbiologic culture is most specific but may be insensitive because of difficulty with *H. pylori* isolation. Once the organism is cultured, its identity as *H. pylori* can be confirmed by its typical appearance on Gram's stain and its positive reactions in oxidase, catalase, and urease tests. Moreover, the organism's susceptibility to antibiotics can be determined, and this information can be clinically useful in difficult cases. The occasional biopsy specimens containing the less common non-*pylori* gastric helicobacters give only weakly positive results in the biopsy urease test. Positive identification of these bacteria requires visualization of the characteristic long, tight spirals in histologic sections; they cannot easily be cultured.

Noninvasive Tests Noninvasive *H. pylori* testing is the norm if gastric cancer does not need to be excluded by endoscopy. The best-established test (and a very accurate one) is the *urea breath test*. In this simple test, the patient drinks a solution of urea labeled with the nonradioactive isotope ^{13}C and then blows into a tube. If *H. pylori* urease is present, the urea is hydrolyzed, and labeled carbon dioxide is detected in breath samples. The *stool antigen test*, a simple and accurate test using monoclonal antibodies specific for *H. pylori* antigens, is more convenient and potentially less expensive than the urea breath test, but some patients dislike sampling stool. The simplest tests for ascertaining *H. pylori* status are *serologic assays* measuring specific IgG levels in serum by enzyme-linked immunosorbent assay or immunoblot. The best of these tests are as accurate as other diagnostic methods, but many commercial tests—especially rapid office tests—do not perform well.

Use of Tests to Assess Treatment Success The urea breath test, the stool antigen test, and biopsy-based tests can all be used to assess the success of treatment (Fig. 188-2). However, because these tests are dependent on *H. pylori* load, their use <4 weeks after treatment may yield false-negative results. Furthermore, these tests are unreliable if performed within 4 weeks of intercurrent treatment with antibiotics or bismuth compounds or within 2 weeks of the discontinuation of proton pump inhibitor (PPI) treatment. In the assessment of treatment success, noninvasive tests are normally preferred; however, after gastric ulceration, endoscopy should be repeated to ensure healing and to exclude gastric carcinoma by further histologic sampling. Serologic tests are not used to monitor treatment success, as the gradual drop in titer of *H. pylori*–specific antibodies is too slow to be of practical use.