**Helicobacter pylori Infection and the new Stool Antigen Test**

**Introduction**

*Helicobacter pylori* (*H. pylori*) is a curved Gram-negative bacillus with the unique ability to exist on the surface of the gastric mucosa. A characteristic of the bacterium is the production of enormous amounts of the enzyme urease. It has been shown to cause both gastric and duodenal ulcers, not related to anti-inflammatory drugs. This organism has also been implicated in gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphomas.

Approximately half of the world’s population is infected with *H. pylori*. Though gastritis is a common histological finding, most infected persons manifest no symptoms; approximately 1 in 6 individuals with this infection will develop a peptic ulcer.

The role of *H. pylori* in nonulcer dyspepsia is contentious; some studies have shown symptomatic benefit from *H. pylori* eradication (i.e. complete eradication of dyspepsia, reduction in use of medication, and reduction of frank peptic ulcer disease during follow-up), whereas results from other studies have shown no or little benefit.

In this LAB-UPDATE, pros and cons of methods to diagnose *H. pylori* infection, including the new *H. pylori* stool antigen test, will be discussed in an attempt to demonstrate where each is most useful.

**Who should be tested?**

Testing should be restricted to patients who have symptoms compatible with *H. pylori* infection (i.e. dyspepsia, upper GI bleeding), and for whom treatment is being considered.

It is well known that only a small but significant number of infected subjects will develop complications such as peptic ulcers and/or gastric ulceration. Questions which need answers include:

- Should we wait for these conditions to develop or should we intervene early i.e. should we be treating infection or the disease?
- Will early intervention be cost-effective?
- Can patients be reassured that, as long as they remain asymptomatic, the infection is unlikely to have any deleterious effects, despite the persistence of the gastritis?

Until future studies have answered these questions, the current recommendations for antibiotic therapy should be followed, i.e. patients infected with H. pylori require antimicrobial treatment ONLY if:

- They have a peptic ulcer, or
- Recently, this recommendation has been updated to include selected patients with dyspepsia and no ulcers (nonulcer dyspepsia).

Which tests should be used?

A number of tests may be used to confirm the presence of H. pylori. These fall into 2 categories: those that rely on direct methods to detect infection and those which rely on indirect methods to detect infection.

The sensitivities and specificities of most of these tests are roughly comparable; thus the decision regarding which test to use should be based on other parameters, such as convenience and cost. The test of choice depends largely upon whether endoscopy is being considered in the patient's evaluation.

1. Tests that rely on direct methods to detect H. pylori infection
   a. Upper-GI endoscopy with biopsy for histology and biopsy for rapid urease test.
   b. Since evaluation is initiated in most patients because of dyspeptic symptoms for which an association with peptic ulcer disease is being sought, endoscopy is usually part of the work-up. At the time of endoscopy, unless an alternative diagnosis is obvious (e.g. bleeding oesophageal varices), biopsies are usually obtained for histological studies. Some endoscopists will also perform a rapid urease test on a biopsy. Since the rapid urease test is not as sensitive as histology for confirmation of H. pylori infection, a second biopsy should be submitted for histology, if the rapid urease test is negative. Culture on biopsy samples is rarely performed since this lacks sensitivity (70 - 80%) and it has long incubation periods (often as long as 14 days). (Culture is therefore reserved for rare cases or clinical trials when antibiotic sensitivity testing is required.)

   **Pros:** Upper GI-endoscopy is the only test that directly examines the gastric mucosa, allowing accurate diagnostic assessment. Histology of gastric biopsies is the most sensitive method to detect H. pylori (i.e. it is the "gold standard" diagnostic test).

   **Cons:** Inconvenient for the patient. Must be performed in a clinic or hospital setting. It is expensive: the cost of the endoscopy must be added to the cost of the rapid urease test and/or histology. Not practical for monitoring/assessing response to therapy. Since H. pylori is not evenly distributed throughout the stomach, single biopsies may on rare occasions miss the site of the infection. Multiple biopsies are therefore recommended for histology.
**Conclusion:** Endoscopy and biopsies for histology is the test of choice. Endoscopy should always be performed in elderly patients, if there is a long history of symptoms, a history of weight loss, gastrointestinal bleeding or anaemia, and persistent vomiting. However, there are circumstances, when endoscopy is either not available or not convenient, such as when evaluating children or pregnant women. In these situations, a number of other tests are available.

b. Detection of H. pylori in stool.

This is a non-invasive stool antigen test using ELISA methodology for detecting H. pylori infection. Studies have revealed sensitivities ranging from 96-100% and specificities of 93-100%.

**Pros:** A major advantage of this test over serological tests to detect antibodies, is its ability to confirm eradication of the organism within 4 weeks of completing treatment. A positive result confirms current infection, whereas antibody tests merely indicate past exposure to H. pylori and not necessarily current infection. The stool antigen test also provides a useful noninvasive means of diagnosing H. pylori infection, without the need for any sophisticated equipment. The test is FDA approved for both H. pylori diagnosis, and for test of cure.

**Cons:** The detection of H. pylori merely confirms infection. Endoscopy is the only technique which will reliably reveal the presence of peptic disease.

Conclusion: Of the non-endoscopic tests, the H. pylori stool antigen test offers the most accurate information regarding infection. It can be used successfully for pre-endoscopic screening of patients referred for investigation of dyspepsia, and for therapeutic monitoring after eradication therapy. It has the advantage of being non-invasive and is relatively inexpensive in comparison to endoscopic biopsy and breath test.

2. **Tests that rely on indirect methods to detect infection**

a. Urea breath test

The basis of this test is the measurement of 13C or 14C containing CO2 in the subject’s breath after oral administration of isotope labelled urea. Due to urease activity, H. pylori infected subjects will have higher levels of expired radiolabelled CO2 in the breath.

**Pros:** 13C and 14C breath tests are non-invasive. These assays are reliable tests for detection of active infection. The urease breath test can be used to identify continuing infection. With current treatment regimens, a test of cure is seldom necessary. Follow-up is only indicated in patients with persistent symptoms despite therapy.

**Cons:** Quite expensive because of the need for special equipment. In order to prevent false-negative results, the patient must discontinue antibiotics and bismuth for 4 weeks, and proton pump inhibitors for 2 weeks before taking the test. False-negative results can also occur in the setting of previous gastric surgery. False-positive results may occur from achlorhydia (bacterial overgrowth with other urease-producing bacteria). Not readily available in South Africa.
**Conclusion:** The urea breath test may become more acceptable in future, once the cost of the test decreases and required equipment is simplified and made more readily available.

b. Serology to detect (serum) antibodies to H. pylori.

**Pros:** Serology requires only venepuncture.

**Cons:** This is an unreliable test for active disease. Helicobacter serology to detect antibodies provides evidence of exposure to H. pylori, but is of limited value as a positive result does not distinguish between previous and current infection. Furthermore, antibody levels decline slowly after therapy – thus it is also not useful for follow-up.

**Conclusion:** The non-invasive stool antigen test offers more definitive information than do the presence of antibodies to H. pylori. However, serology may be useful in patients who do not have an endoscopic diagnosis of H. pylori infection and who are not able to provide a stool specimen for the preferred antigen test.

**Specimen requirements for stool H. pylori antigen test**

Stool, unpreserved, submitted in a sterile container within 24 hours of collection. (This may be kept at room temperature or at 4-8o C, but not frozen.)