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AMPATHCHAT

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Helicobacter pylori: an update

Introduction

Helicobacter pylori is a highly prevalent curved gram-negative bacterium. Seropositivity rates in South-Africa range between 60% and 100%. It causes more than 90% of duodenal ulcers and up to 80% of gastric ulcers. Atrophic gastritis due to *H. pylori* can lead to gastric cancer. The World Health Organisation classifies *H. pylori* as a Group I carcinogen (a category that includes other carcinogens such as tobacco smoke and asbestos). Environmental, host and bacterial factors influence the progression to malignancy.

Pathogenesis

H. pylori produces urease, which assists with the colonisation of the acidic gastric mucosa. Colonisation leads to dysregulation of gastric acid secretion and mucosal damage. For the majority of patients, symptoms of colonisation are transient. Patients who become symptomatic may suffer from gastritis or dyspepsia.

Indications for testing

It is critical to know which patients should be tested, as an active infection requires treatment.

A test-and-treat strategy is appropriate in the following setting:

- Active peptic ulcer disease (PUD)
- A history of PUD if cure of *H. pylori* has not been documented
- Early gastric cancer or low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma
- Uninvestigated dyspepsia in patients <60 years without alarm features

The benefits to testing are unclear in the following groups: prior to giving chronic NSAID treatment or long-term low- dose aspirin, unexplained iron deficiency and adults with idiopathic thrombocytopaenia.

Laboratory testing

Invasive and non-invasive diagnostic tests are available and each has its own limitations (Tables 1 and 2).

Susceptibility testing can be performed using culture (invasive specimens) or molecular testing (non-invasive and invasive specimens).

Table 1: Non-invasive tests

Test	Performance	Advantages	Disadvantages
Urea breath test	Sensitivity: 90–100% Specificity: 90–95%	• Detects active infection • Useful as proof of eradication • Good positive predictive value	• Limited availability • Complex specimen collection • Requires preparation ahead of testing by patient
Stool antigen	Sensitivity: 90–95% Specificity: 90–95%	• Detects active infection • Can be used in paediatric patients • Useful as proof of eradication • Convenient specimen to collect • Inexpensive	• Patient may have to return later with the specimen • Regional performance variability between products
Serology	Sensitivity: 80–85% Specificity: 75–80%	• Convenient specimen to collect • Not affected by current PPI or antibiotic use • Useful for epidemiological profiling	• Cannot distinguish active from previous infection • Requires validation on local population for assay cut-off values
PCR	Refer to Table 3		

Table 2: Invasive tests: gastric tissue biopsy (corpus and antrum)

Test	Performance	Advantages	Disadvantages
Rapid urease test (RUT)	Sensitivity: 85–95% Specificity: 95–100%	• Rapid and inexpensive • Combining several tissues prior to RUT increases sensitivity	• Sensitivity can be decreased in a bleeding peptic ulcer • Formalin contamination of forceps used to collect the biopsy may reduce sensitivity
Histopathological examination	Sensitivity: 93% Specificity: 95–100%	• Detects active infection	• Routine stains are non-specific • Immunohistochemical stains are more expensive, but have increased specificity
Culture	Sensitivity: 24–85% Specificity: 100%	• Detects active infection • Allows for susceptibility testing of different antibiotic classes	• May require up to 5 days to grow • Insensitive method • Reference lab has better success at culture (fastidious organism with special transport and growth requirements)
PCR	Refer to Table 3		

Molecular diagnostics: detection and genotypic susceptibility testing

Clarithromycin resistance in H. *pylori* is increasing globally, leading to treatment failure. Clarithromycin should not be used empirically where the regional resistance rate is above 15%.

Limited South Africa data has documented primary clarithromycin resistance rates above 15% in different regions. Due to rising resistance, routine susceptibility testing may lead to more benefits than awaiting treatment failures before testing. Genotypic susceptibility testing is increasingly being used to guide antibiotic selection and can improve eradication rates.

Molecular testing (Table 3) provides excellent sensitivity and specificity for simultaneous detection of *H. pylori* as well as the genes associated with antimicrobial resistance to clarithromycin. This overcomes the barriers of traditional culture-based methods. Molecular testing can be performed on both tissue and stool, which provides a non-invasive clarithromycin testing option.

Resistance mutations have also been identified for the fluoroquinolones. Metronidazole resistance cannot be completely explained by the known mutations, and other mechanisms may possibly contribute. In these complicated cases, culture-based methods may still be indicated.

Table 3: Molecular testing (PCR)

Specimen types	Performance	Advantages	Disadvantages
• Stool • Gastric tissue biopsy: Ideally fresh tissue, but formalin-fixed specimens may be used	Sensitivity >95% Specificity >95%	• For both diagnosis and clarithromycin susceptibility testing • Rapid turnaround time • Can be used as proof of eradication • Recommended by international guidelines • Does not require strict transport conditions	• More costly • Requires access to a lab with molecular expertise • Novel resistance mutations will not be detected

Treatment

European guidelines have advised eradication of *H. pylori* when detected regardless of symptoms. *H.pylori* triple therapy consists of antibiotic combination therapy with a proton pump inhibitor (PPI) (Table 4).

Table 4: Treatment regimens

Standard triple therapy: clarithromycin, amoxicillin, PPI	Bismuth quadruple (BQ) therapy: bismuth, tetracycline, metronidazole,PPI
• Highly influenced by rate of clarithromycin resistance • Eradication rates may be below 80% due to growing resistance • In penicillin allergic patients, metronidazole replaces amoxicillin • Duration of treatment is 14 days	• Similar efficacy, compliance and tolerability compared to clarithromycin triple therapy • Metronidazole resistance has an effect on BQ, but it is not as profound as clarithromycin resistance on triple therapy • Recommended treatment choice in regions with high clarithromycin resistance or previous treatment with a macrolide for any reason • Duration of treatment is 10–14 days
Concomitant therapy: amoxicillin, clarithromycin, metronidazole,PPI	**Levofloxacin regimen: Levofloxacin, either metronidazole or amoxicillin, PPI**
• In an RCT comparing concomitant (481 patients) to triple therapy (503 patients), the intention to treat cure rates were 90% and 78% respectively (95% CI, 1.67–3.34; or 2.36). • European guidelines recommend that concomitant therapy is the preferred non-BQ therapy as it is the most effective in overcoming resistance. • Limited data suggests that clarithromycin resistance may reduce the efficacy of concomitant therapy, but to a lesser degree than clarithromycin triple therapy. • The ideal duration of therapy is not clear, but 10 to 14 days is suggested.	• Eradication rates vary geographically and are probably linked to fluoroquinolone resistance. • European guidelines advise the use of levofloxacin in scenarios where high dual clarithromycin and metronidazole resistance is present and bismuth is not available.

Proof of eradication

Post-eradication testing should be performed in all patients four weeks after completion of treatment. Tests for proof of eradication include stool antigen test, urease breath test and, recently, molecular testing.

References are available on request