There is ongoing debate in the literature about which is the best test to request for the detection of infection with *Helicobacter pylori*. The most appropriate test is influenced by several factors, such as the pre-test probability of *H. pylori* infection (reflected by prevalence), the patient’s specific clinical circumstances and the cost and availability of the test.\(^1\) In New Zealand, like many other countries, the advice has changed over recent years, however, the current thinking is that the *H. pylori* faecal antigen test is now the preferred option in patients who require investigation for *H. pylori* (see: “The New Zealand Schedule and Test Guidelines update, Page 2). Infection with *H. pylori* is known to increase the risk of peptic ulcer disease and gastric cancer due to chronic inflammation and atrophy of the stomach mucosa.\(^2\)
The prevalence of *H. pylori* in New Zealand is low by world standards

In New Zealand the overall prevalence of *H. pylori* is lower than many other developed countries, although there is limited data and prevalence differs throughout the country.\(^3\)  
A recent small study in South Auckland, traditionally an area with rates of *H. pylori* > 30%, recruited patients undergoing endoscopy, and reported an overall prevalence of *H. pylori* for adults of all ethnicities of 18.6%. However, rates varied between people from different ethnic groups: for New Zealand Europeans, prevalence was reported as 7.7%, which ranks among the lowest rates for *H. pylori* in the world,\(^4,5\) but a significantly higher prevalence was noted in Māori (34.9%), Pacific (29.6%), Asian (23.8%) and Indian (19.2%) peoples.\(^4\)

The overall global prevalence of *H. pylori* is > 50%. Prevalence has declined in many countries due to improvements in treatment and in standards of living, however, there continues to be a marked variation between, and within, countries.\(^5,6\) This is because infection with *H. pylori* is influenced by a number of factors, including ethnicity, socioeconomic status, gender and age.\(^5\) Rates remain higher in developing countries due to associations with increased transmission in areas with overcrowded living conditions, poor sanitation and unsafe drinking water.\(^1, 5, 6\)

*H. pylori* is typically acquired during childhood and does not usually resolve spontaneously. Infection tends to be acquired at a very young age in children in developing countries compared to developed countries.\(^1\) For example, in Bangladesh, 50 – 82% of children aged < 9 years are infected with *H. pylori* and this rises to > 90% in adults.\(^5\) In comparison, a rate of 7.1% is reported for young people aged 5 – 18 years in Canada, rising to 20 – 30% in adulthood.\(^3\)

Prevalence of *H. pylori* in adults is high in most Asian countries, e.g. Japan and China (50 –70%), South American, Eastern European and Middle Eastern countries, e.g. Chile (73%), Bulgaria (61.7%), Egypt (90%) and Saudi Arabia (80%).\(^5,6\) Lower rates are reported for countries such as the United Kingdom (13.4%), Switzerland (11 – 26%), and Australia (15 – 20%).\(^5,6\)

Do we still need to test patients for *H. pylori*?

The decreasing prevalence of *H. pylori*-related peptic ulcer disease and gastric cancer has begun to alter management recommendations when a patient presents with dyspepsia, or *H. pylori* is suspected.\(^7, 8\) It is suggested that testing for *H. pylori* may not be needed, or helpful, in people who live in areas with low prevalence,\(^8, 9\) which applies to people in many areas of New Zealand.

When a person first presents with dyspepsia, therefore, the clinician should consider how likely it is that *H. pylori* will be present, whether red flags are present (see: “Red flags”), if there are other factors that may be influencing their symptoms, such as NSAID use, and how the test result will influence the management of the patient.\(^9\) Routinely testing all patients with dyspeptic symptoms for *H. pylori* or prescribing empiric eradication treatment for *H. pylori* without testing is not recommended.\(^10\)

The decision to treat dyspeptic symptoms empirically with a proton pump inhibitor (PPI) in people who are less likely to have *H. pylori*, or to “test and treat” for *H. pylori* can be, in part, based on:

- Where they live – prevalence is generally higher in the north of New Zealand than in the south\(^3\)
- Their ethnicity – if the person is of New Zealand European ethnicity, the prevalence is likely to be approximately ≤7%, but in Māori, Pacific, Asian and Indian peoples prevalence will be much higher\(^4\)
- Where they were born – even allowing for expected differences due to ethnicity, if the person was born in New Zealand, the chance that they will have *H. pylori* is likely to be lower than many people born overseas (depending on their country of origin). If the person was born in a developing country, there is at least a 50% chance that they will have *H. pylori*, and research shows that adults who immigrate retain a prevalence of *H. pylori* similar to their country of origin.\(^11\)
- The presence of any red flags (see: “Red flags”)
There is also evidence that the majority of people with dyspeptic symptoms and an absence of red flags will have normal findings at endoscopy and that empiric treatment with a PPI for symptom control is considered an effective, safe strategy.\textsuperscript{12}

Taking these factors into account for an individual patient can help determine the most appropriate management strategy.

For patients with dyspepsia who are at:

- **Lower risk of H. pylori infection** – the most pragmatic approach is to prescribe a PPI and review the patient in a month to assess whether their symptoms have improved. If the patient’s symptoms have not improved, reassess for the presence of red flags and consider testing for H. pylori. Ideally the PPI should be stopped for two weeks prior to testing for H. pylori to reduce the rate of false negative results.

- **Higher risk of H. pylori infection** – consider testing for H. pylori with a faecal antigen test. If the patient has a positive result for H. pylori, they should be prescribed eradication treatment. If the result is negative, empiric treatment with a PPI can be initiated after reassessing for red flag features.

**Faecal antigen testing is now recommended to detect H. pylori infection**

There are three non-invasive tests for H. pylori. These are the:

- Faecal antigen test
- Carbon-13 urea breath test
- Serum antibody test

Table 1 summarises the advantages and disadvantages of these three tests.

**Faecal antigen testing** is now included as a Tier 1 test on the New Zealand Laboratory Schedule, and is widely available throughout community laboratories in New Zealand. When faecal antigen tests for H. pylori were first introduced they relied on polyclonal antibodies and the results were often unreliable.\textsuperscript{13} The use of monoclonal antibody-based techniques to assess faecal samples has improved the accuracy of the test.\textsuperscript{13, 14} The test detects the presence of antigens to H. pylori in a faecal sample and can be used to diagnose active infection and, if required, to confirm that eradication treatment has been successful.\textsuperscript{14} Sensitivity and specificity of faecal antigen testing is similar to that reported

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**Red flags for people presenting with dyspepsia**

A patient with any of the following factors has an increased risk of significant organic disease and may require referral for endoscopy:\textsuperscript{3}

- Age \( \geq 50 \) years at first presentation (the incidence of gastric cancer increases with age)
- Age \( \geq 40 \) years at first presentation for people of Māori, Pacific or Asian descent (gastric cancer tends to occur a decade earlier in these groups)
- Family history of gastric cancer with age of onset < 50 years
- Dyspeptic symptoms that are severe or persistent
- Previous history of peptic ulcer disease, particularly if complicated
- The use of aspirin or NSAIDs (also check over-the-counter use)
- Signs and symptoms of chronic gastrointestinal bleeding, such as malaena, anaemia
- Iron deficiency anaemia
- Difficulty in swallowing
- Persistent regurgitation or protracted vomiting
- Palpable abdominal mass
- Unexplained weight loss

* If a person taking NSAIDs has no other red flags and symptoms are mild, initial management is to stop the NSAID and then reassess symptoms

For further information, see: “Managing dyspepsia and heartburn in general practice – an update”, BPJ 34 (Feb, 2011).
Table 1. Advantages and disadvantages for non-invasive tests for *H. pylori*.\(^{5,7,9,13,14}\)

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faecal antigen test</td>
<td>94 – 95%</td>
<td>94 – 97%</td>
<td>84%</td>
<td>Determines active infection</td>
<td>The accuracy of the test may be reduced if the patient has upper gastrointestinal bleeding or if the stool sample is unformed or watery. Patient should not have antibiotics for four weeks, or PPIs or bismuth for two weeks, prior to testing. Advice varies regarding whether H₂-receptor antagonists and antacids are able to be continued.</td>
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<td></td>
<td></td>
<td>Can be used as a test of cure</td>
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<td></td>
<td></td>
<td>No cost to patient as the test is funded in New Zealand</td>
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</tr>
<tr>
<td>Urea breath test</td>
<td>95%</td>
<td>96%</td>
<td>88%</td>
<td>Determines active infection</td>
<td>Cost to patient as test is not funded in New Zealand</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Can be used as a test of cure</td>
<td>Limited availability</td>
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<td>Patient needs to be fasted</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>The patient should not have antibiotics for four weeks, or PPIs for two weeks, or H₂-receptor antagonists for 24 hours, prior to testing.</td>
</tr>
<tr>
<td>Serology</td>
<td>85 – 92%</td>
<td>79 – 83%</td>
<td>64%</td>
<td>Convenient for the patient</td>
<td>No longer funded in New Zealand (however, the test is relatively inexpensive)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>The test is not affected by medicines such as antibiotics, PPIs or H₂-receptor antagonists</td>
<td>Variable specificity; most accurate if there is high prevalence of <em>H. pylori</em></td>
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<td></td>
<td>Cannot distinguish between past and present infection – a positive result means the patient has been exposed but may not mean the patient has active infection</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cannot be used as a test of cure</td>
</tr>
</tbody>
</table>

**Sensitivity** – reflects the ability of the test to correctly identify patients with the condition being tested for, therefore a test with high sensitivity reduces the likelihood of a false negative result.

**Specificity** – reflects the ability of the test to correctly identify patients without the condition, therefore a test with high specificity reduces the likelihood of a false positive result.

**Positive predictive value** – reflects the probability that if a result is positive, the patient does have the condition being tested for.

For further information see “Deciding when a test is useful: how to interpret the jargon”, Best Tests (Feb, 2013).
for carbon-13 urea breath testing. False negative results can occur if the patient has been taking medicines that may decrease the load of H. pylori in the stomach, or the contents of the stomach are less acidic, e.g. if a patient has been taking a PPI (Table 1). However, there is some limited evidence that monoclonal antibody-based faecal antigen tests may be less influenced by PPI use than urea breath tests.

Carbon-13 urea breath testing is still regarded in the literature as the gold standard for testing for H. pylori, however, the test is time consuming and expensive to perform. In New Zealand the test has limited availability and is not funded. The test provides an indirect measure of the presence of H. pylori-associated urease which is detected by a change in CO2 in the patient’s breath after ingestion of labelled urea. Both sensitivity and specificity of the test are comparatively high, although, as with faecal antigen testing, false negative results can occur with medicines that decrease the bacterial load or suppress gastric acid.

Serum antibody testing (serology) for H. pylori has previously been recommended as the most appropriate test in New Zealand. However, with the improved availability and accuracy of faecal antigen tests, serology is no longer the preferred test, and it is no longer funded in New Zealand. Serological testing detects the presence of IgG antibodies to the H. pylori bacteria. Although the sensitivity of the test is comparable with the other non-invasive tests, the specificity is variable and when prevalence of H. pylori is low the positive predictive value of the test declines. Serology also cannot distinguish between infection that is past or current, and because antibody levels decrease slowly over 6 – 12 months or longer after eradication treatment, it cannot be used as a test of cure.

Invasive testing for H. pylori requires endoscopy which can provide biopsy material for histology, rapid urease testing and culture.

Eradication treatment for H. pylori

If a positive result for H. pylori is obtained, the patient should be prescribed eradication treatment, i.e. “do not test if not intending to treat”. A recommended triple treatment regimen for the eradication of H. pylori is a seven day course of:

- Omeprazole 20 mg, twice daily
- Clarithromycin 500 mg, twice daily
- Amoxicillin 1 g, twice daily (or metronidazole 400 mg twice daily, if allergic to penicillin)

Other regimens using different dosing intervals, or other PPIs e.g. lansoprazole, can also be used.

Confirmation of eradication of H. pylori after a triple treatment regimen is not required for the majority of patients. A test of cure may be considered in patients with a recurrence of symptoms, a peptic ulcer complication or with important co-morbidities. Faecal antigen testing can give accurate confirmation of eradication if required.

Recently there have been concerns in New Zealand and worldwide about increasing resistance of H. pylori to the antibiotics used in the various eradication regimens. Resistance to clarithromycin and metronidazole was reported in a recent New Zealand study and, in particular, resistance to clarithromycin has doubled since the 1990s. Although the study was based on a small number of participants, rates of clarithromycin resistance varied with ethnicity – no resistance was reported in New Zealand Europeans while a rate of 25% was reported for Māori.

If an initial seven day eradication regimen has failed (i.e. symptoms have recurred) an alternative two week quadruple regimen can be used or referral for endoscopy considered. Bismuth-based quadruple treatment is comprised of:

- Omeprazole 20 mg, twice daily
- Tripotassium dicitratobismuthate 120 mg, four times daily (to be taken as: one dose 30 minutes before breakfast, midday meal and main evening meal, and one dose two hours after main evening meal)
- Tetracycline hydrochloride 500 mg, four times daily
- Metronidazole 400 mg, three times daily

In New Zealand, tripotassium dicitratobismuthate (or colloidal bismuth subcitrate) and tetracycline hydrochloride are unapproved medicines, supplied fully subsidised under Section 29. Tetracycline hydrochloride requires a Special Authority, which only applies to its use in this H. pylori eradication regimen. Doxycycline is not recommended as an alternative tetracycline as it results in a significantly lower eradication rate for H. pylori. Adhering to optimal timing of the medicines in the quadruple regimen can be challenging for patients.
References

ACKNOWLEDGMENT Thank you to Dr John Wyeth, Gastroenterologist, Clinical Leader, Capital & Coast DHB, Medical Director PHARMAC and Dr Rosemary Ikram, Clinical Microbiologist, Christchurch, for expert review of this article.