

# EFFECTIVENESS

## *Matters*

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### HELICOBACTER PYLORI AND PEPTIC ULCER

- H.pylori is a bacteria which is strongly associated with peptic ulcer.
- H.pylori can be reliably diagnosed and successfully eradicated.
- Eradication of H.pylori cures peptic ulcer and decreases relapses.
- Eradication of H.pylori reduces the need for acid-suppressing therapy, and so the total cost of treatment.
- Clinicians and managers need to ensure that the eradication of H.pylori is the basis of all local policies on the treatment of peptic ulcer.

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*Effectiveness Matters* is an update on the effectiveness of important health interventions for practitioners and decision makers in the NHS. It is produced by researchers at the NHS Centre for Reviews and Dissemination at the University of York, in collaboration with subject area experts. *Effectiveness Matters* is extensively peer reviewed.

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100 *H.pylori* positive patients with a duodenal ulcer treated using eradication therapy instead of conventional treatment would result in:

- 15 more patients whose ulcers heal
- 57 fewer patients whose ulcers recur within the first year

## BENEFITS OF ERADICATION

Eradication of *H.pylori* is effective in curing peptic ulcer.

The use of antimicrobial treatments to eradicate the bacterium:

- Increases ulcer healing rates from 78 per cent to 93 per cent;<sup>1</sup>
- Reduces the time patients spend with an active ulcer;
- Decreases first year ulcer recurrence rates from 66 per cent to nine per cent<sup>1</sup>.
- Eliminates the need (in most patients) for long-term acid-suppressing maintenance treatment once the ulcer has healed and so the total cost of treatment;

## BACKGROUND

*Helicobacter pylori* is a Gram negative spiral shaped bacteria. In humans, it colonises the stomach and the likelihood of infection increases with age. In the UK, half of those over 50 are infected<sup>2</sup>.

There is some evidence that *H.pylori* may be associated with gastric cancer. There is no convincing evidence, at present, for a relation between *H.pylori* and non-ulcer dyspepsia.

*H.pylori* infection by itself is not sufficient to cause peptic ulcers. Other factors are needed. These may include hypersecretion of acid, smoking and genetic predisposition.

## DIAGNOSIS OF H PYLORI

### Invasive tests (following endoscopy):

- *Rapid urease tests (CLO test)*  
The enzyme urease is detected using a commercial assay within the endoscopy suite. Results are available in minutes.
- *Histology*  
*H.pylori* like organisms can be identified on stained biopsy samples.
- *Culture*  
Microbiology laboratories routinely culture *H.pylori* from biopsy specimens. Culture may be prone to high false negative rates.

### Non-invasive Tests:

- *Serology*  
IgG antibodies against *H.pylori* can be detected in the serum using laboratory based and near-patient testing serology kits.
- *Breath tests*  
Isotopically labelled carbon dioxide can be detected in the breath of *H.pylori* positive individuals following ingestion of urea labelled with <sup>13</sup>C or <sup>14</sup>C.

### Conclusion

All these assay tests have sensitivities and specificities greater than 90 per cent<sup>3</sup>. Although near patient serology tests, might prove the most practical in primary care further evidence on their accuracy is needed.

## EFFECTIVE TREATMENTS

Treatment regimes which have been shown in randomised controlled trials (RCTs) to be most effective consist of two antibiotics combined with either bismuth or a proton pump inhibitor or H2-antagonist<sup>4</sup>. Three regimes are mentioned here:

### 1. "Standard" triple therapy

This is the most thoroughly tested option<sup>4</sup>, consists of a two week course of:

- bismuth subcitrate (4 x 120 mg daily) with
- metronidazole (3 x 400 mg daily) and
- tetracycline (4 x 500 mg daily)

It is cheap and has been shown to eradicate *H.pylori* in around 95% of patients. One week's treatment may be as good as two, but a direct comparison has not been performed.

This regimen has commonly been given alongside an H2-antagonist or proton pump inhibitor, but the benefits of this have not been conclusively evaluated. The H2-antagonist or proton pump inhibitor is stopped once healing has occurred.

### 2. Other triple therapies

A recent multi-centre clinical trial has evaluated five new regimes, and found two to achieve eradication rates of 95 per cent or over:

#### *One week of:*

- omeprazole (2 x 20 mg daily)
- amoxicillin (2 x 1000 mg daily)
- clarithromycin (2 x 500 mg daily)

#### *Alternatively, one week of:*

- omeprazole (2 x 20 mg daily)
- metronidazole (2 x 400 mg daily)
- clarithromycin (2 x 250 mg daily)

These treatments have not yet been compared directly to the "standard" triple therapy. Several other alternative regimes have been proposed and more continue to be published making the choice confusing.

### 3. Success of eradication therapy

Success depends on:

#### **Patient compliance**

Patients should be counselled concerning the importance of completing the whole course of therapy and warned of the side-effects they may experience

#### **The bacterium being sensitive to antibiotics**

Therapies involving metronidazole and tinidazole will be less effective in populations with a high resistance, including some ethnic minorities.

Alternative regimens have been proposed and more continue to be published making the choice confusing.

# Recommendations

**1** Clinicians and managers should ensure that a clear policy and treatment protocols are developed in primary and secondary care for the investigation, diagnosis and treatment of patients with suspected peptic ulcer and *H.pylori*. (Updated as evidence from trials becomes available). Adherence to such policies should be monitored through audit.

**2** All patients with proven non-NSAID related peptic ulcer presently on maintenance therapy should be offered a course of eradication therapy.

**3** All patients with newly diagnosed peptic ulcer (investigated according to locally agreed policy) should be offered a course of eradication therapy.

**4** Health authorities should ensure that there is adequate provision of diagnostic facilities for *H.pylori* for primary care.

**5** Clinicians should only use eradication treatments for which good evidence of cost-effectiveness exists. Unevaluated regimens should only be used within the context of randomised controlled trials.

**6** As the evidence in this field is accumulating rapidly, clinicians should maintain an awareness of the research in this area, particularly with respect to optimal eradication therapies and diagnostic strategies. There is at present no evidence that a policy of screening asymptomatic patients would be beneficial.

**7** Districts should monitor eradication rates and antibiotic resistance as these vary across the country.

## Conclusion

As the standard triple therapy has been proven to be very successful and is very cheap, this may be argued to possibly be the best choice. Future choice of eradication regimens should only be made on the basis of large randomised comparisons between new regimens and triple therapy. It is also important to assess cost-effectiveness

## MANAGING PEPTIC ULCER

In the light of this reliable evidence from systematic reviews, broadly speaking, there are four options:

- (1). Eradication therapy for patients with symptoms suggestive of peptic ulcer with. Investigations reserved for people whose symptoms fail to improve; OR
- (2). Non-invasive tests for H.pylori on symptomatic patients. Eradication therapy offered to those who are positive without further investigation for a definitive diagnosis of peptic ulcer; OR
- (3). Non-invasive test for H.pylori on symptomatic patients. Endoscopy for those who are positive, to establish a definitive diagnosis of peptic ulcer before eradication therapy is offered; OR
- (4). Endoscopy to establish a definitive diagnosis for all patients with suspected peptic ulcer with alongside a test for H.pylori. Eradication therapy offered to those with proven peptic ulcer and H.pylori infection.

It remains uncertain from present research which of these options, or combination of options is best, and the choice will also depend upon patient factors<sup>7</sup>, access to diagnostic services and costs.

The NHS Centre for Reviews and Dissemination (CRD) is a facility commissioned by the NHS Research and Development Division. Its aim is to identify and review the results of good quality health research and to disseminate actively the findings to key decision makers in the NHS and to consumers of health care services. In this way health care professionals and managers can ensure their practice reflects the best available research evidence.

The nucleus of this activity is the production of a number of core dissemination materials. One such project, the *Effective Health Care* series, produced jointly with colleagues in the University of Leeds, is already well known to many professionals within the NHS.

This new series, *Effectiveness Matters*, is produced to complement *Effective Health Care*. It covers topics in a shorter and more journalistic style and may summarise, as in this edition, the results of high quality systematic reviews that have not been undertaken or commissioned by the CRD. Both *Effective Health Care* and *Effectiveness Matters* are subject to extensive and rigorous peer review.

Both options 1 and 2 will result in a significant proportion of people with no ulcer being treated which is both costly and has no current evidence of benefit (and may in some cases be hazardous). For example studies have shown that only about 20-25 per cent of dyspepsia patients who are H.pylori positive will have a peptic ulcer.

Whilst options (3) and (4) would ensure that treatment was targeted on only those patients with an ulcer, they are more invasive and expensive and have potentially large consequences for endoscopy services. However even option (4), in which everyone has endoscopy, has been shown to be more cost effective than the more usual long-term use of H2 antagonists or proton pump inhibitors<sup>6</sup>.

Large randomised controlled trials are currently underway in primary care settings which will provide information on the effectiveness of different strategies.

### ASSESSMENT OF ERADICATION

*H. pylori* is defined as being eradicated when it is shown to be absent at least four weeks after completion of treatment<sup>3</sup>. Eradication can be assessed by the breath test, CLO test, histology or culture, but **not** by serology. In many cases there may be no benefit from verifying eradication in patients whose symptoms have resolved. Assessment may be important however in monitoring eradication rates and antibiotic resistance within an area.

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