



Dyspepsia H.pylori Peptic ulcer

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Case 1

42 y/o male with chronic pain and discomfort in the upper abdomen.
P/E is normal





Definition of dyspepsia (Rome II)

Pain or discomfort occurring in the upper abdomen

- Dyspepsia subgroups
 - Ulcer-like (predominantly pain)
 - Dysmotility-like (predominantly discomfort)
 - Unspecified (non-specific, no predominant symptom)

Dyspepsia covers a range of symptoms



Uninvestigated dyspepsia vs functional dyspepsia

Uninvestigated dyspepsia

 All symptomatic patients, regardless of whether a cause has been sought

Functional dyspepsia

 Symptomatic patients in whom an organic cause has been sought and excluded

Dyspepsia: the size of the problem

- 15–25% of the general population experience dyspepsia within a 12-month period
- Much more common than peptic ulcer
- Up to 5% of primary care visits are due to dyspepsia
- Most patients have no detectable abnormality on radiological upper GI series or endoscopy
- Endoscopy findings and symptoms do not correlate

Talley, J Clin Gastroenterol2001; **32**: 286–93. Locke, Ballieres Clin Gastroenterol1998; **12**: 435–42. Paré, Can J Gastroenterol1999; **13**: 647–54. van Bommelet al., Postgrad Med J 2001; **77**: 514–18. Talley et al., BMJ 2001; **323**: 1294–7.

Dyspepsia: pathogenic mechanisms



Talley et al., BMJ 2001; 323:1294–7. Tack et al., Curr GastroenterolRep 2001; 3: 503–8.

Causes of functional dyspepsia

Illness behaviour Psychosocial factors

Genetic predisposition

Intraluminal Noxious stimuli (Food allergy? *H. pylori*?)



Symptom perception

Spinal hyperalgesia

Altered motility Visceral hypersensitivity Gut wall inflammation

- The major organic diseases causing dyspepsia are:
- gastroduodenal ulcer
- atypical gastroesophageal reflux
- gastric cancer

Gastroesophageal reflux can cause burning epigastric pain that typically radiates up toward the neck, but this disease may be confused with functional dyspepsia.

Gastroduodenal ulcer disease is found in approximately 15 - 25 % of patients with dyspepsia but cannot be accurately distinguished from functional dyspepsia based on the symptom pattern

Up to 60% of patients with dyspepsia have no definite explanation and are classified as having functional dyspepsia. Between 30 - 60 % of these patients have Helicobacter pylori-induced gastritis, but it is unclear whether this infection causes the symptoms.

Differential diagnosis of dyspepsia

- Functional dyspepsia
- GORD
- PUD
- Gastric malignancy
- Pancreatitis
- Musculoskeletal pain
- IBS
- Cardiovascular disease
- Somatisation
- Pancreato-biliary disease

- Endoscopy is the test of choice to exclude gastroduodenal ulceration, reflux esophagitis, and upper gastrointestinal tract malignancy.
- Upper gastrointestinal radiographs have inferior diagnostic accuracy to upper endoscopy.

Dyspepsia: symptom assessment



What is your idea?

MANAGEMENT OF NEW-ONSET DYSPEPSIA?

Empiric medical therapy
Immediate diagnostic evaluation
Testing for H. pylori infection by serology

MANAGEMENT OF NEW-ONSET DYSPEPSIA

- Empiric medical therapy (eg, an antisecretory or prokinetic drug) with any subsequent investigation reserved for failures
- Immediate diagnostic evaluation in all cases, applying endoscopy preferably
- Testing for H. pylori infection by serology or urea breath test and reserving endoscopy for positive cases to look for ulcer disease or cancer
- Testing for H. pylori and treating all positive cases with antibacterial therapy to cure ulcer disease.

- Referral for early upper endoscopy is always indicated in older patients presenting with new-onset dyspepsia ; a threshold of 45 years is recommended.
- However, in populations where the age-specific incidence of gastric cancer is greater in younger age groups, a lower age threshold should be applied.
- Patients with alarm symptoms (eg, weight loss, recurrent vomiting, dysphagia, evidence of bleeding, or anemia) should be referred for prompt endoscopy.
- Patients whose symptoms have failed to respond to empiric therapeutic approaches also should undergo endoscopy.
- If endoscopy has been competently performed once, there is no indication to repeat it unless new alarm symptoms have developed that require investigation.

- After endoscopy, treatment should be targeted at the underlying diagnosis, but the majority of patients will be labeled as having functional (or nonulcer) dyspepsia; these patients may respond to reassurance and explanation followed, if necessary, by a course of <u>antisecretory or prokinetic</u> therapy.
- Although the role of H. pylori in functional dyspepsia remains uncertain, in those who have documented infection, <u>eradication therapy</u> is reasonable after fully explaining the risks and limitations.
- In patients with persistent symptoms, other treatments that may be considered include <u>behavioral therapy</u>, <u>psychotherapy</u>, or <u>antidepressant therapy</u>, but these approaches are not of established value.

In younger patients with no alarm features who have not been investigated previously, it is recommended that a locally validated noninvasive <u>H. pylori test</u> (eg, serology or urea breath test) is undertaken to determine if the patient is infected

A breath test is more costly but has greater accuracy for documenting current H. pylori infection

- If there is H. pylori infection, then an empiric trial of anti-H. pylori therapy is recommended.
- The rationale is that ulcer disease will heal and the ulcer diathesis will be abolished. A follow-up visit is recommended within four to eight weeks. If symptoms fail to respond or rapidly recur or alarm features develop, then prompt upper endoscopy is indicated.
- It is unlikely that an early (and hence curable) gastric cancer would progress to advanced cancer within one to two months of presentation; hence, follow-up within this time period is recommended.

- A trial of noninvasive testing followed by empiric therapy for H. pylori assumes that background prevalence of infection is not universally high and gastric cancer is not common.
- In regions where there is a high background incidence of gastric cancer, a strategy of H. pylori testing and endoscopy of those who test positive for the infection (to definitely exclude malignancy) may be preferable to a test and treat strategy, although data are unavailable.

- Treatment of H. pylori is appropriate for patients in whom an ulcer has been diagnosed, and it may be considered for patients in whom an ulcer has not been excluded.
- However, the benefit of treating H. pylori in patients who do not have an ulcer is unclear. The majority of studies have found that curing H. pylori in patients who have dyspepsia but do not have an ulcer does not significantly improve the symptoms of dyspepsia.

- In younger patients with no alarm features who are H. pylori negative, it is recommended that :
- A trial of antisecretory therapy (eg, H2-blocker or proton pump inhibitor) or a prokinetic be prescribed for one month.
- If this fails to relieve symptoms, therapy may be switched between the antisecretory and prokinetic classes.
- If after eight weeks of therapy symptoms persist or rapidly recur on stopping treatment, then endoscopy is recommended.

Rome IV Diagnostic Criteria for Functional Dyspepsia

Presence of ≥ 1 of:

Postprandial fullness (3 days per week)
 Early satiety (3 days per week)
 Epigastric pain (1 day per week)
 Epigastric burning (1 day per week)

and

🗹 No evidence of structural disease

Note: Criteria must be present for at least the past 3 months, with symptoms starting at least 6 months before diagnosis



Did you know? There are 2 types of Functional Dyspepsia!



PPIs and Functional dyspepsia

- We treat patients with functional dyspepsia who test negative for *H. pylori* and those with persistent symptoms four weeks after eradication of *H. pylori* with a proton pump inhibitor (PPI).
- In the systematic review of PPI therapy for functional dyspepsia, only two studies compared the efficacy of PPIs with H2AAs, and no difference was evident

PPIs and Functional dyspepsia

- PPIs appear to be moderately effective Low- and standard-dose PPIs had similar effectiveness
- Twice daily PPI use has not been shown to be better than once daily use.
- In patients with functional dyspepsia who respond to PPI therapy, attempts should be made to discontinue PPIs every 6 to 12 months to minimize long-term risk of therapy.

Tricyclic antidepressant (TCA) and functional dyspepsia

- In patients with functional dyspepsia whose symptoms do not improve after eight weeks of PPI therapy, we initiate a therapeutic trial with a tricyclic antidepressant (TCA).
- For patients with a partial clinical response to a PPI, a TCA can be initiated as combination therapy.
- For patients who fail to improve on a PPI, the PPI should be stopped and a TCA initiated

Tricyclic antidepressant (TCA) and functional dyspepsia

- We usually continue the TCA for 8 to 12 weeks before stopping, if it is ineffective.
- If the patient responds, we usually continue the drug for appropriately six months and then consider slowly tapering the medication off.

Prokinetic agents

We reserve the use of prokinetics (eg, metoclopramide 5 to 10 mg three times daily one-half an hour before meals and at night for four weeks), to patients in whom other therapies have failed and limit their duration to four weeks before discontinuing treatment



- If postprandial nausea is a predominant symptom, trials of other antiemetic agents can be employed (eg, promethazine, prochlorperazine, meclizine)
- Fundic relaxant drugs ; buspirone
- Antinociceptive agents (eg, carbamazepine, tramadol, or pregabalin)

Dietary modification

population case-control study failed to find an association between various foods and functional gastrointestinal disorders



Approach to the evaluation and management of dyspepsia in adults



H. pylori: Helicobacter pylori.

* Gastric mucosal biopsies should be obtained at the time of upper gastrointestinal endoscopy to rule out infection with *H. pylori*.

Additional evaluation may be required based on symptoms (eg, abdominal imaging in patients with concurrent jaundice or pain suggestive of a billiary/pancreatic source).

∆ Refer to UpToDate topic reviews.

◇ Patients with continued symptoms of dyspepsia for 3 months with symptom onset at least 6 months before diagnosis and no evidence of structural disease to explain the symptoms should be diagnosed and treated as functional dyspepsia.

§ Eradication of *H. pylori* infection can be confirmed with a urea breath test, stool antigen testing, or upper endoscopy-based testing performed 4 weeks after completion of antibiotic therapy. The choice of test depends on the need for an upper endoscopy (eg, follow-up of bleeding peptic ulcer) and local availability. *H. pylori* serology should not be used to confirm eradication of *H. pylori*. Refer to UpToDate topic on diagnostic tests for *H. pylori*.

 $\ensuremath{\mathtt{4}}$ Allow 8 to 12 weeks before reassessing symptomatic response.

For patients with a partial clinical response to a proton pump inhibitor, a tricyclic antidepressant can be initiated as combination therapy with a proton pump inhibitor.

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GP management of uninvestigated dyspepsia



Treatment options in functional dyspepsia



When to refer

- Presence of alarm symptoms
- Failure to respond to appropriate therapy
- Patients ≥45 years of age with new-onset symptoms

Talley et al., Gut 1999; 45(SuppHI): II37-42. Talley et al., BMJ 2001; 323: 1294-7. Bytzer & Talley, Ann InternMed 2001; 134: 815-22.



What is your idea? NATURAL HISTORY OF DYSPEPSIA?

NATURAL HISTORY OF DYSPEPSIA

- Patients with functional dyspepsia typically have a relapsing condition
 - In one report, 65 % of those with dyspepsia at study entry reported the same symptom three years later.
 - A U.S. study found that 86 % still reported dyspepsia after 12 to 20 months
 - British study found dyspepsia was present in 74 % of the cases after two years.
- Chronic peptic ulcer is also a relapsing disease unless H. pylori is eradicated or maintenance therapy is given; symptomatic relapse occurs in 50 - 80 % of patients over one year in both duodenal and gastric ulcer disease.
- Most cases of reflux esophagitis are also probably chronic and will relapse in approximately 50 - 80 % of cases over a year if medical treatment is ceased

NATURAL HISTORY OF DYSPEPSIA

The relapse of functional dyspepsia, ulcer disease, and esophagitis must therefore be taken into account in any management guidelines