Approach to the adult with dyspepsia

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INTRODUCTION

Dyspepsia is a common symptom with an extensive differential diagnosis and a heterogeneous pathophysiology. It occurs in up to 20 percent of the population, although prevalence rates are lower using different iterations of the Rome criteria [1,2]. Most affected people do not seek medical evaluation for their symptoms [1,2]. Although dyspepsia does not affect survival, it is responsible for substantial health care costs and significantly affects quality of life [3-6].

This topic will review the definition, etiology, and general approach to the evaluation and management of the patient with dyspepsia. The evaluation and recommendations are largely consistent with the American College of Gastroenterology and American Gastroenterological Association guidelines for the evaluation of dyspepsia [7,8].

ETIOLOGY

Approximately 20 to 25 percent of patients with dyspepsia have an underlying organic cause (table 1). However, up to 75 to 80 percent of patients have functional (idiopathic or nonulcer) dyspepsia with no underlying cause on diagnostic evaluation [9]. (See 'Diagnostic strategies and initial management' below.)

Dyspepsia secondary to organic disease — Although there are several organic causes for dyspepsia, the main causes are peptic ulcer disease, *Helicobacter pylori*, gastroesophageal reflux, medications (nonsteroidal antiinflammatory agents being the most common offender),

and gastric malignancy (table 1). Although gastric cancer as a cause of dyspepsia is a concern for both health care providers and patients, it is uncommon in North America [8].

- **Peptic ulcer disease** – Upper abdominal pain or discomfort is the most prominent symptom in patients with peptic ulcers. Although discomfort from ulcers is usually centered in the epigastrium, it may occasionally localize to the right or left upper quadrants [10]. While classic symptoms of duodenal ulcer occur when acid is secreted in the absence of a food buffer (ie, two to five hours after meals or on an empty stomach), peptic ulcers can be associated with food-provoked symptoms, and thus, the utility of using symptoms related to food ingestion to predict the presence of an ulcer is unreliable. Peptic ulcers can also be associated with postprandial belching, epigastric fullness, early satiation, fatty food intolerance, nausea, and occasional vomiting. (See "Peptic ulcer disease: Clinical manifestations and diagnosis".)

- **Gastroesophageal malignancy** – Gastroesophageal malignancy is an uncommon cause of chronic dyspepsia in the Western hemisphere, but the incidence is higher in Asian Americans, Hispanic Americans, and Afro-Caribbean Americans. The incidence of gastroesophageal malignancy increases with age. When present, abdominal pain tends to be epigastric, vague, and mild early in the disease but more severe and constant as the disease progresses. In addition, other symptoms and signs typically evolve with disease progression (eg, anemia, fatigue, weight loss). (See "Epidemiology and pathobiology of esophageal cancer", section on 'Epidemiology' and "Epidemiology of gastric cancer" and "Clinical features, diagnosis, and staging of gastric cancer", section on 'Clinical features'.)

- **Biliary pain** – Classic biliary pain is characterized by episodic intense dull pain located in the right upper quadrant, epigastrium, or (less often) substernal area that may radiate to the back (particularly the right shoulder blade). The pain is often associated with diaphoresis, nausea, and vomiting. The pain is constant and not colicky [11]. It is not exacerbated or reproduced by movement and is not relieved by squatting, belching, bowel movements, or passage of flatus. The pain typically lasts at least 30 minutes, plateauing within an hour. The pain then starts to subside, with an entire attack usually lasting less than six hours. (See "Approach to the management of gallstones" and "Overview of gallstone disease in adults".)

- **Drug-induced dyspepsia** – NSAIDs and COX-2 selective inhibitors can cause dyspepsia even in the absence of peptic ulcer disease. Other drugs that have been implicated in drug-induced dyspepsia include calcium channel blockers, methylxanthines, alendronate, orlistat, potassium supplements, acarbose, dabigatran, iron, vitamin D, selective serotonin reuptake inhibitors, sildenafil, sulfonylureas, and certain antibiotics, including

erythromycin [12,13]. (See "Nonselective NSAIDs: Overview of adverse effects", section on 'Gastrointestinal effects'.)

- **Other causes** – Celiac disease and chronic pancreatitis may rarely present with dyspeptic symptoms alone. Other rare causes for dyspepsia include infiltrative diseases of the stomach (eg, eosinophilic gastroenteritis [14], Crohn disease, sarcoidosis [15], lymphoma [16], and amyloidosis [17,18]), diabetic radiculopathy [19], metabolic disturbances (eg, hypercalcemia, heavy metal toxicity), hepatoma, steatohepatitis, celiac artery compression syndrome, superior mesenteric artery syndrome, abdominal wall pain [20], and intestinal angina (table 1). (See "Granulomatous gastritis", section on 'Crohn disease' and "Extrapulmonary manifestations of sarcoidosis", section on 'Gastrointestinal' and "Celiac artery compression syndrome" and "Superior mesenteric artery syndrome" and "Chronic mesenteric ischemia", section on 'Clinical presentations' and "Epidemiology, pathogenesis, and clinical manifestations of celiac disease in adults", section on 'Gastrointestinal manifestations'.)

Functional dyspepsia — The diagnosis of functional (idiopathic or nonulcer) dyspepsia requires exclusion of other organic causes of dyspepsia [21]. It is defined by the presence of one or more of the following: postprandial fullness, early satiation, epigastric pain, or burning, and **no** evidence of structural disease to explain the symptoms [22]. The pathophysiology, diagnosis, and management of functional dyspepsia are discussed in detail, separately. (See 'Diagnostic strategies and initial management' below and "Functional dyspepsia in adults".)

INITIAL EVALUATION

A history, physical examination, and laboratory evaluation are the first steps in the evaluation of a patient with new onset of dyspeptic symptoms. (See 'History' below and 'Physical examination' below and 'Laboratory tests' below.)

The goal of the initial evaluation is to identify alarm features for gastroesophageal malignancy (table 2), which will direct the diagnostic approach. (See 'Diagnostic strategies and initial management' below.)

History — A detailed history is necessary to determine the underlying cause and to identify patients with alarm features (table 2).

As examples:

- A dominant history of heartburn or regurgitation, is suggestive of gastroesophageal reflux disease (GERD), recognizing that some patients have overlapping GERD and functional dyspepsia [23,24]. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults", section on 'Clinical manifestations'.)

- Aspirin and other NSAID use raises the possibility of NSAID dyspepsia and peptic ulcer disease. Radiation of pain to the back or personal or family history of pancreatitis may be indicative of underlying chronic pancreatitis. (See "Nonselective NSAIDs: Overview of adverse effects", section on 'Gastrointestinal effects'.)

- Significant weight loss, anorexia, anemia, vomiting, dysphagia, odynophagia, and a family history of gastrointestinal cancers suggest the presence of an underlying gastroesophageal malignancy. (See "Clinical features, diagnosis, and staging of gastric cancer", section on 'Clinical features'.)

- The presence of severe episodic epigastric or right upper quadrant abdominal pain, usually in association with nausea or vomiting, lasting at least 30 minutes is suggestive of symptomatic cholelithiasis [25]. (See "Acute calculous cholecystitis: Clinical features and diagnosis", section on 'Clinical manifestations'.)

- Nausea and vomiting, with or without weight loss, occurring with recurrent or persistent upper abdominal pain raises the possibility of gastroparesis, especially in patients with risk factors. However, both the pathophysiology and symptom expression of functional dyspepsia and gastroparesis are quite similar [26]. An analysis of patients in a multicenter gastroparesis registry recognized the significant overlap in functional dyspepsia and gastroparesis symptoms [27].

Physical examination — The physical examination in patients with dyspepsia is usually normal, except for epigastric tenderness. The presence of epigastric tenderness cannot accurately distinguish organic dyspepsia from functional dyspepsia. Abdominal tenderness on palpation should be evaluated for the presence of Carnett's sign to determine if it is due to pain arising from the abdominal wall rather than due to inflammation of the underlying viscera. The presence of increased local tenderness during muscle tensing (positive Carnett's sign) suggests the presence of abdominal wall pain. However, if the pain is decreased (negative Carnett's sign), the origin of pain is not from the abdominal wall and likely from an intra-abdominal organ, as the tensed abdominal wall muscles protect the viscera. (See "Anterior cutaneous nerve entrapment syndrome", section on 'Diagnostic approach'.)

Other informative findings on physical examination include a palpable abdominal mass (eg, hepatoma) or lymphadenopathy (eg, left supraclavicular or periumbilical in gastric cancer),

jaundice (eg, secondary to liver metastasis), a bruit (celiac artery compression syndrome), a succussion splash (gastric outlet obstruction), or pallor secondary to anemia. Ascites may indicate the presence of peritoneal carcinomatosis. Patients with an underlying malignancy may have evidence of muscle wasting, loss of subcutaneous fat, and peripheral edema due to weight loss.

Laboratory tests — Routine blood counts and blood chemistry including liver function tests, serum lipase, and amylase, should be performed to identify patients with alarm features (eg, iron deficiency anemia) and underlying metabolic diseases that can cause dyspepsia (eg, diabetes, hypercalcemia) (table 2). (See "Clinical manifestations of hypercalcemia", section on 'Gastrointestinal' and "Diabetic autonomic neuropathy of the gastrointestinal tract".)

DIAGNOSTIC STRATEGIES AND INITIAL MANAGEMENT

The approach to, and extent of, diagnostic evaluation of a patient with dyspepsia is based on the clinical presentation, the patient's age, and the presence of alarm features (table 2). An approach to the evaluation of a patient with dyspepsia is outlined in the algorithm (algorithm 1) [28]. Our approach is largely consistent with the American College of Gastroenterology and Canadian Association of Gastroenterology guidelines [8].

The optimal age cut-off for endoscopic evaluation in patients with dyspepsia is controversial and is supported by limited evidence that suggests that the risk of malignancy in most United States populations below the age of 60 years is low. Guidelines also suggest that the age cutoff may vary between countries, depending upon the prevalence of gastric cancer. The American Gastroenterological Association guidelines suggest that it may be reasonable in some resource-rich countries to consider the age of 60 or 65 years as the threshold age at which endoscopy should be offered to all new dyspeptic patients, while an age cutoff of 45 or 50 years may be more appropriate for Asian Americans, Hispanic Americans, and Afro-Caribbean Americans due to an increased risk for gastric cancer, or in populations with a high incidence of gastric cancer in young individuals [11]. A European consensus statement recommends endoscopy in adults older than 45 years old who present with persistent dyspepsia [29]. These recommendations highlight the fact that diagnostic evaluation of the patient with dyspepsia need to be individualized based on symptoms, age, ethnic background, family history, nationality, and regional incidence of gastric cancer. (See "Clinical features, diagnosis, and staging of gastric cancer".)

Patient age ≥60 years

Upper endoscopy — We perform an upper endoscopy to evaluate dyspepsia in patients age ≥60 years [8]. Biopsies of the stomach should be obtained to rule out *H. pylori*. Patients with *H. pylori* should receive eradication therapy in addition to treatment based on the underlying diagnosis (eg, peptic ulcer disease). After *H. pylori* treatment, eradication should be assessed. (See "Medical management of gastroesophageal reflux disease in adults" and "Peptic ulcer disease: Treatment and secondary prevention", section on 'Initial management' and "Treatment regimens for Helicobacter pylori in adults".)

Multiple studies have evaluated the yield of upper endoscopy in patients with dyspepsia [30-33]. A meta-analysis of nine studies with 5389 patients found that the most prevalent findings in patients with dyspepsia were erosive esophagitis and peptic ulcer disease (pooled prevalence 6 and 8 percent, respectively) [34]. The diagnostic yield of upper endoscopy increases with age [30,32]. In the absence of warning signs, upper endoscopy in younger patients is unlikely to find a worrisome cause.

Additional evaluation and management — Most patients with a normal upper endoscopy and routine laboratory tests have functional dyspepsia. However, additional evaluation may be required based on symptoms. (See 'Laboratory tests' above and 'Evaluation of persistent symptoms' below and "Functional dyspepsia in adults".)

Patient age <60 years — Patients <60 years of age should be tested and treated for *H. pylori*, and upper endoscopy should be performed selectively. Patients who are *H. pylori* negative or who continue to have symptoms after successful eradication of *H. pylori* should be treated with antisecretory therapy with a proton pump inhibitor (PPI) (algorithm 1) [11,35]. In patients whose symptoms do not improve after eight weeks of PPI therapy, we initiate a therapeutic trial with a tricyclic antidepressant. Given the side effects associated with prokinetics and the limited evidence of efficacy, we reserve the use of prokinetics for patients who fail tricyclic antidepressants. (See 'Evaluation of persistent symptoms' below.)

Upper endoscopy in selected patients — Endoscopic evaluation of patients <60 years is reserved for patients with any one of the following:

- Clinically significant weight loss (>5 percent usual body weight over 6 to 12 months).
- Overt gastrointestinal bleeding.
- >1 other alarm feature (table 2).
- Rapidly progressive alarm features.

Alarm features include:

- Unintentional weight loss

- Dysphagia
- Odynophagia
- Unexplained iron deficiency anemia
- Persistent vomiting
- Palpable mass or lymphadenopathy
- Family history of upper gastrointestinal cancer

In such patients, upper endoscopy should be performed early, preferably within two to four weeks. Biopsies of the stomach should be obtained to rule out *H. pylori* and patients with evidence of infection should be treated with eradication therapy. (See 'Test and treat for Helicobacter pylori' below and "Treatment regimens for Helicobacter pylori in adults", section on 'Initial antibiotic therapy'.)

While prior guidelines have recommended upper endoscopy for all patients with alarm features regardless of age, the recommendation to selectively perform upper endoscopy in patients <60 years is based on evidence that individual alarm features have low positive predictive value for an upper gastrointestinal tract malignancy [8,36].

Test and treat for Helicobacter pylori — The rationale for *H. pylori* testing in patients with dyspepsia is based upon the recognition of *H. pylori* as an etiologic factor in peptic ulcer disease.

Mucosal biopsies for *H. pylori* should be obtained use the Sydney protocol, which includes specimens from the lesser and greater curve of the antrum within 2 to 3 cm of the pylorus, from the lesser curvature of the corpus (4 cm proximal to the angularis), from the middle portion of the greater curvature of the corpus (8 cm from the cardia), and one from the incisura angularis [37].

In patients who do not require an upper endoscopy or in whom biopsies were not performed at the time of upper endoscopy, testing for *H. pylori* should be performed with a test for active infection (eg, urea breath test or stool antigen assay). Serologic testing should not be used due to their low positive predictive value [38].

Patients who test positive for an infection with *H. pylori* should undergo treatment with eradication therapy. Most dyspeptic patients who are *H. pylori* positive and who are treated with appropriate antibiotic therapy persist with dyspeptic symptoms; the number needed to successfully relieve dyspeptic symptoms is estimated at one in seven. In a meta-analysis of two randomized trials in which 563 *H. pylori*- infected dyspepsia patients were assigned to eradication therapy or placebo, *H. pylori* eradication therapy resulted in a significant reduction in dyspepsia (RR remaining dyspeptic 0.81; 95% CI 0.70–0.94) with a number needed to treat of

seven [8,39]. (See "Treatment regimens for Helicobacter pylori in adults", section on 'Initial antibiotic therapy'.)

Antisecretory therapy — Antisecretory therapy with a PPI can relieve dyspepsia symptoms [11]. This was illustrated in a meta-analysis of six randomized controlled trials that included 2709 patients with dyspepsia who were assigned to PPI therapy or control (placebo or antacid therapy) [8]. Dyspepsia symptoms were present in a significantly lower proportion of the PPI group as compared with controls (50 versus 73 percent). PPIs are also likely to be more effective at relieving symptoms of dyspepsia as compared with H2 receptor antagonists (H2RA) [40,41]. Although a meta-analysis of seven randomized trials that included 2456 patients with dyspepsia did not demonstrate a statistically significant difference between PPIs and H2RAs in providing symptom relief, the meta-analysis was limited by significant heterogeneity between studies [8]. Studies have shown that a twice-daily PPI is not more effective than a once-daily PPI at relieving dyspeptic symptoms [42]. (See "Antiulcer medications: Mechanism of action, pharmacology, and side effects", section on 'Antisecretory agents'.)

Other therapies

Tricyclic antidepressants and azapirones — Patients who test negative for *H. pylori* or remain symptomatic after its eradication and have inadequate response to a PPI can be considered for therapy with a tricyclic agent (algorithm 1). For patients with persistent symptoms, the tetracyclic antidepressant mirtazapine may prove beneficial [43]. Alternatively, low-dose buspirone (an azapirone) before meals may improve post-prandial symptoms [44].

Prokinetics — Treatment with prokinetic agents (most evaluated agents are unavailable in North America) is discussed in detail separately [45]. (See "Functional dyspepsia in adults", section on 'Prokinetic agents' and "Functional dyspepsia in adults", section on 'Antidepressants'.)

Evaluation of persistent symptoms — Despite the approaches described above, some patients continue to have symptoms of dyspepsia. Patients with continued symptoms of dyspepsia fall into the following categories: patients with persistent *H. pylori* infection, patients with an alternate diagnosis, and patients with functional dyspepsia. (See "Functional dyspepsia in adults".)

Patients with continued symptoms of dyspepsia should be carefully reassessed, paying specific attention to the type of ongoing symptoms, the degree to which symptoms have improved or worsened, and compliance with medications.

An upper endoscopy should be performed in patients with persistent dyspepsia (algorithm 1). During upper endoscopy, biopsies for *H. pylori* should be performed in patients who have not previously been tested, while culture and sensitivity testing should be performed in patients previously treated for *H. pylori*. Biopsies of the duodenum should also be performed to rule out celiac disease or inflammatory conditions.

In patients with a normal upper endoscopy, further evaluation should be performed selectively based on the type of ongoing symptoms (eg, abdominal imaging with an ultrasound or computed tomography scan in patients with concurrent jaundice or pain suggestive of a biliary/pancreatic source, a four-hour solid-phase scintigraphic gastric emptying scan for those with persistent nausea and vomiting). Approximately 75 percent of patients with dyspepsia have functional (idiopathic or nonulcer) dyspepsia with no underlying cause on diagnostic evaluation. (See "Functional dyspepsia in adults".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Dyspepsia".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Stomach ache and stomach upset (The Basics)")
- Beyond the Basics topic (see "Patient education: Upset stomach (functional dyspepsia) in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Etiology –** Dyspepsia is defined as one or more of the following symptoms: postprandial fullness, early satiation, epigastric pain, or burning. Approximately 25 percent of patients with dyspepsia are found to have an underlying organic disease on diagnostic evaluation (table 1). However, approximately 75 percent of patients have functional (idiopathic or nonulcer) dyspepsia.

- **Initial evaluation –** A detailed history, physical examination, and laboratory studies are necessary to determine the underlying etiology and identify alarm features that may warrant additional evaluation (table 2).

- **Approach to diagnostic testing –** The approach to and extent of diagnostic evaluation of a patient with dyspepsia is based on the presence or absence of alarm features, patient age, and the prevalence of *H. pylori* infection (table 2 and algorithm 1).

  - Patients ≥60 years of age with dyspepsia should undergo an upper endoscopy. Most patients with a normal upper endoscopy and routine laboratory tests have functional dyspepsia. However, additional evaluation may be required based on symptoms (eg, abdominal imaging with an ultrasound or computed tomography scan in patients with concurrent jaundice or pain suggestive of a biliary/pancreatic source). (See 'Patient age ≥60 years' above.)

  - In patients <60 years, indications for upper endoscopy include (see 'Patient age <60 years' above and 'Upper endoscopy in selected patients' above):

    - Clinically significant weight loss (>5 percent usual body weight over 6 to 12 months)
    - Overt gastrointestinal bleeding
    - >1 alarm feature (table 2)
    - Rapidly progressive alarm features

  - Patients <60 years of age who do not have indications for upper endoscopy should be tested for *H. pylori* using alternative methods (stool antigen or urea breath test). Patients who test positive for an infection with *H. pylori* should undergo treatment with eradication therapy. (See 'Test and treat for Helicobacter pylori' above.)

- **Initial management –** In patients who test negative for *H. pylori* and for those with persistent symptoms after *H. pylori* eradication, we suggest treatment with antisecretory

therapy with a proton pump inhibitor for four to eight weeks (**Grade 2A**). Treatment options in patients who test negative for *H. pylori* or remain symptomatic after its eradication and have inadequate response to a proton pump inhibitor include a tricyclic agent and prokinetics. (See 'Test and treat for Helicobacter pylori' above and 'Antisecretory therapy' above and 'Other therapies' above.)

- **Additional evaluation in patients with refractory symptoms –** Patients with persistent dyspepsia despite a trial of a tricyclic antidepressant and prokinetic should undergo endoscopic evaluation with an upper endoscopy and biopsies, if not previously performed (algorithm 1). Further evaluation for an alternate diagnosis should be performed selectively based on the patient's symptoms. Patients with continued symptoms of dyspepsia for three months with symptom onset at least six months before diagnosis and no evidence of structural disease to explain the symptoms should be diagnosed and treated as functional dyspepsia. (See 'Evaluation of persistent symptoms' above and "Functional dyspepsia in adults".)

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Topic 20 Version 47.0

GRAPHICS

Differential diagnosis of dyspepsia

Diagnosis
Functional dyspepsia
Dyspepsia caused by structural or biochemical disease
Peptic ulcer disease
Helicobacter pylori gastritis
Gastroesophageal reflux disease (GERD)
Biliary pain
Chronic abdominal wall pain
Gastric or esophageal cancer
Gastroparesis
Pancreatitis
Carbohydrate malabsorption
Medications (including potassium supplements, digitalis, iron, theophylline, oral antibiotics [especially ampicillin and erythromycin], nonsteroidal antiinflammatory drugs [NSAIDs], glucocorticoids, niacin, gemfibrozil, narcotics, colchicine, quinidine, estrogens, levodopa)
Infiltrative diseases of the stomach (eg, Crohn disease, sarcoidosis)
Metabolic disturbances (hypercalcemia, hyperkalemia)
Hepatocellular carcinoma
Ischemic bowel disease, celiac artery compression syndrome, superior mesenteric artery syndrome
Systemic disorders (diabetes mellitus, thyroid and parathyroid disorders, connective tissue disease)
Intestinal parasites (*Giardia*, *Strongyloides*)
Abdominal cancer, especially pancreatic cancer

Adapted from:

1. *Talley NJ, Silverstein MD, Agreus L, et al. American Gastroenterological Association (AGA) technical review: evaluation of dyspepsia. Gastroenterology 1998; 114:582.*
2. *Fisher RS, Parkman HP. Management of nonulcer dyspepsia. N Engl J Med 1998; 339:1376.*

Graphic 90590 Version 11.0

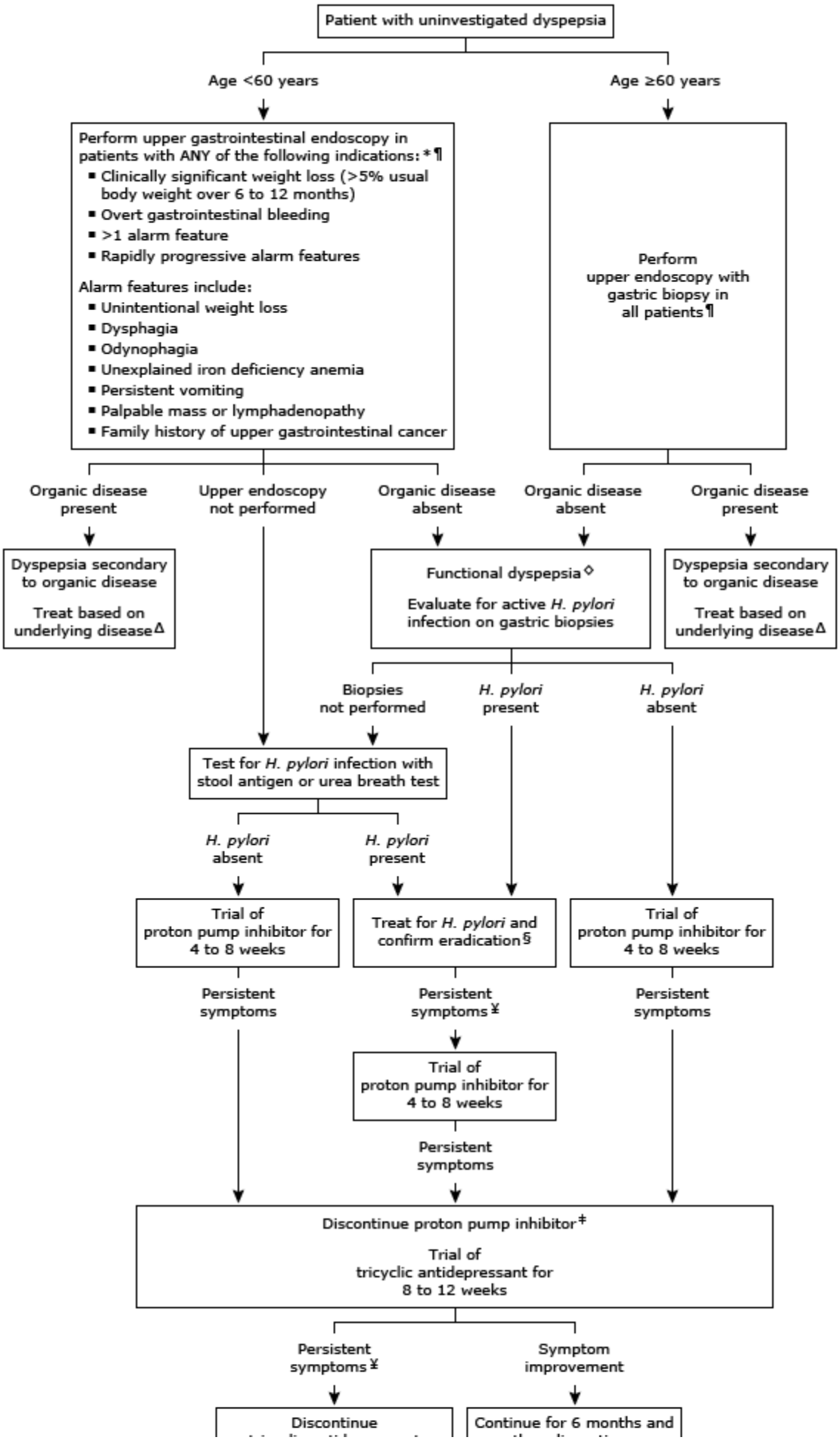
Alarm features in dyspepsia

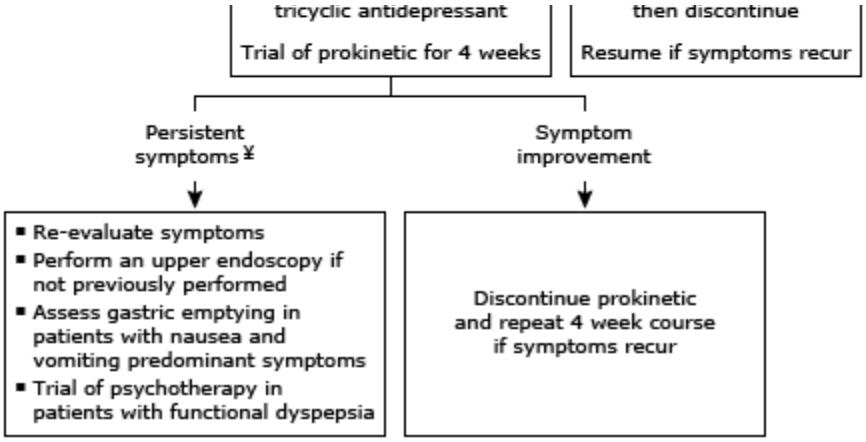
Unintentional weight loss
Dysphagia
Odynophagia
Unexplained iron deficiency anemia
Persistent vomiting
Palpable mass or lymphadenopathy
Family history of upper gastrointestinal cancer

Adapted from: Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology 2005; 129:1756.

Graphic 56585 Version 5.0

Approach to the evaluation and management of dyspepsia in adults


Patient with uninvestigated dyspepsia
Age <60 years
Age ≥60 years
Perform upper gastrointestinal endoscopy in patients with ANY of the following indications: *¶
Clinically significant weight loss (>5% usual body weight over 6 to 12 months)
Overt gastrointestinal bleeding
>1 alarm feature
Rapidly progressive alarm features
Alarm features include:
Unintentional weight loss
Dysphagia
Odynophagia
Unexplained iron deficiency anemia
Persistent vomiting
Palpable mass or lymphadenopathy
Family history of upper gastrointestinal cancer
Perform upper endoscopy with gastric biopsy in all patients ¶
Organic disease present
Upper endoscopy not performed
Organic disease absent
Organic disease absent
Organic disease present
Dyspepsia secondary to organic disease
Treat based on underlying disease Δ
Functional dyspepsia ◇
Evaluate for active H. pylori infection on gastric biopsies
Dyspepsia secondary to organic disease
Treat based on underlying disease Δ
Biopsies not performed
H. pylori present
H. pylori absent
Test for H. pylori infection with stool antigen or urea breath test
H. pylori absent
H. pylori present
Trial of proton pump inhibitor for 4 to 8 weeks
Treat for H. pylori and confirm eradication §
Trial of proton pump inhibitor for 4 to 8 weeks
Persistent symptoms
Persistent symptoms ¥
Persistent symptoms
Trial of proton pump inhibitor for 4 to 8 weeks
Persistent symptoms
Discontinue proton pump inhibitor ‡
Trial of tricyclic antidepressant for 8 to 12 weeks
Persistent symptoms ¥
Symptom improvement
Discontinue
Continue for 6 months and



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 biliary/pancreatic source).

Δ 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*.

¥ 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.

Graphic 115195 Version 3.0

Contributor Disclosures

George F Longstreth, MD No relevant financial relationship(s) with ineligible companies to disclose. **Brian E Lacy, MD, PhD** Consultant/Advisory Boards: Nestle [Functional dyspepsia]. All of the relevant financial relationships listed have been mitigated. **Nicholas J Talley, MD, PhD** Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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