TABLE 348-6 GUIDE TO NSAID THERAPY

	No/Low NSAID GI Risk	NSAID GI Risk
No CV risk (no aspirin)	Traditional NSAID	Coxib *or* Traditional NSAID + PPI *or* misoprostol Consider non-NSAID therapy
CV risk (consider aspirin)	Traditional NSAID + PPI *or* misoprostol if GI risk warrants gastroprotection Consider non-NSAID therapy	A gastroprotective agent must be added if a traditional NSAID is prescribed Consider non-NSAID therapy

Abbreviations: CV, cardiovascular; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor.

Source: Adapted from AM Fendrick: Am J Manag Care 10:740, 2004. Reproduced with permission of INTELLISPHERE, LLC via Copyright Clearance Center.

of risk status, who is being considered for long-term traditional NSAID therapy, should also be considered for *H. pylori* testing and treatment if positive. Assuring the use of GI protective agents with NSAIDs is difficult, even in high-risk patients. This is in part due to underprescribing of the appropriate protective agent; other times the difficulty is related to patient compliance. The latter may be due to patients forgetting to take multiple pills or preferring not to take the extra pill, especially if they have no GI symptoms. Several NSAID gastroprotective-containing combination pills are now commercially available, including double-dose famotidine with ibuprofen, diclofenac with misoprostol, and naproxen with esomeprazole. Although initial studies suggested improved compliance and a cost advantage when taking these combination drugs, their clinical benefit over the use of separate pills has not been established. Efforts continue toward developing safer NSAIDs, including NO–releasing NSAIDs, hydrogen sulfide–releasing NSAIDs, dual COX/5-LOX inhibitors, NSAID prodrugs, or agents that can effectively sequester unbound NSAIDs without interfering with their efficacy.

APPROACH AND THERAPY: SUMMARY

Controversy continues regarding the best approach to the patient who presents with dyspepsia **(Chap. 54)**. The discovery of *H. pylori* and its role in pathogenesis of ulcers has added a new variable to the equation. Previously, if a patient <50 years of age presented with dyspepsia and without alarming signs or symptoms suggestive of an ulcer complication or malignancy, an empirical therapeutic trial with acid suppression was commonly recommended. Although this approach is practiced by some today, an approach presently gaining approval for the treatment of patients with dyspepsia is outlined in **Fig. 348-12**. The referral to a gastroenterologist is for the potential need of endoscopy and subsequent evaluation and treatment if the endoscopy is negative.

Once an ulcer (GU or DU) is documented, the main issue at stake is whether *H. pylori* or an NSAID is involved. With *H. pylori* present, independent of the NSAID status, triple therapy is recommended for 14 days, followed by continued acid-suppressing drugs (H_2 receptor antagonist or PPIs) for a total of 4–6 weeks. Selection of patients for documentation of *H. pylori* eradication (organisms gone at least 4 weeks after completing antibiotics) is an area of some debate. The test of choice for documenting eradication is the laboratory-based validated monoclonal stool antigen test or a urea breath test (UBT). The patient must be off antisecretory agents when being tested for eradication of *H. pylori* with UBT or stool antigen. Serologic testing is not useful for the purpose of documenting eradication because antibody titers fall slowly and often do not become undetectable. Two approaches toward documentation of eradication exist: (1) Test for eradication only in individuals with a complicated course or in individuals who are frail or with multisystem disease who would do poorly with an ulcer recurrence, and (2) test all patients for

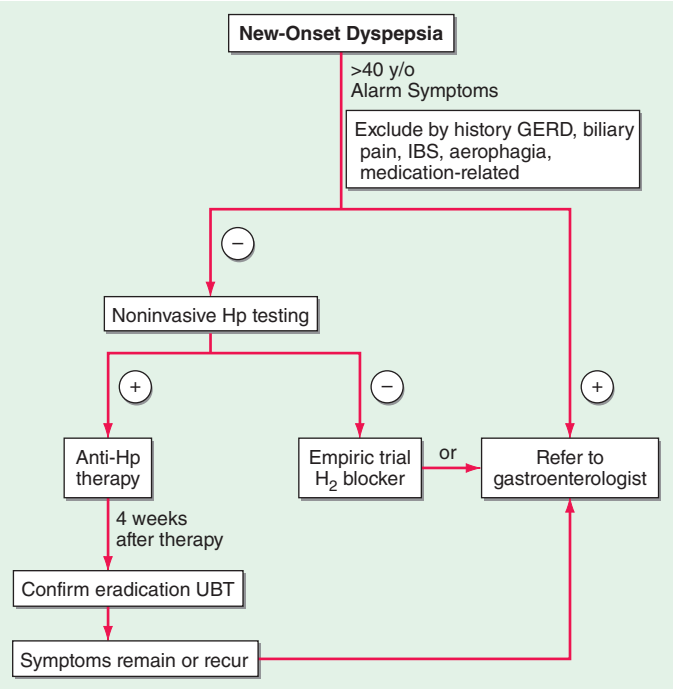

FIGURE 348-12 Overview of new-onset dyspepsia. GERD, gastroesophageal reflux disease; Hp, *Helicobacter pylori*; IBS, irritable bowel syndrome; UBT, urea breath test. *(Adapted from BS Anand and DY Graham: Endoscopy 31:215, 1999.)*

successful eradication. Some recommend that patients with complicated ulcer disease, or who are frail, should be treated with long-term acid suppression, thus making documentation of *H. pylori* eradication a moot point. In view of this discrepancy in practice, it would be best to discuss with the patient the different options available.

Several issues differentiate the approach to a GU versus a DU. GUs, especially of the body and fundus, have the potential of being malignant. Multiple biopsies of a GU should be taken initially; even if these are negative for neoplasm, repeat endoscopy to document healing at 8–12 weeks should be performed, with biopsy if the ulcer is still present. About 70% of GUs eventually found to be malignant undergo significant (usually incomplete) healing. Repeat endoscopy is warranted in patients with DU if symptoms persist despite medical therapy or a complication is suspected.

The majority (>90%) of GUs and DUs heal with the conventional therapy outlined above. A GU that fails to heal after 12 weeks and a DU that does not heal after 8 weeks of therapy should be considered refractory. Once poor compliance and persistent *H. pylori* infection have been excluded, NSAID use, either inadvertent or surreptitious, must be excluded. In addition, cigarette smoking must be eliminated. For a GU, malignancy must be meticulously excluded. Next, consideration should be given to a gastric acid hypersecretory state such as ZES (see "Zollinger-Ellison Syndrome," below) or the idiopathic form, which can be excluded with gastric acid analysis. Although a subset of patients have gastric acid hypersecretion of unclear etiology as a contributing factor to refractory ulcers, ZES should be excluded with a fasting gastrin or secretin stimulation test (see below). More than 90% of refractory ulcers (either DUs or GUs) heal after 8 weeks of treatment with higher doses of PPI (omeprazole, 40 mg/d; lansoprazole 30–60 mg/d). This higher dose is also effective in maintaining remission. Surgical intervention may be a consideration at this point; however, other rare causes of refractory ulcers must be excluded before recommending surgery. Rare etiologies of refractory ulcers that may be diagnosed by gastric or duodenal biopsies include ischemia, Crohn's disease, amyloidosis, sarcoidosis, lymphoma, eosinophilic gastroenteritis, or infection (cytomegalovirus [CMV], tuberculosis, or syphilis).