18. DYSPEPSIA AND PEPTIC ULCER DISEASE

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The development of quality indicators for dyspepsia and peptic ulcer disease (PUD) diagnosis and treatment was based on a MEDLINE search of the English language review literature published between 1992 and 1996. This was supplemented by identification of more specific review articles and clinical studies in areas of controversy, or in areas where benefit to selected diagnostic or therapeutic measures has been documented.

DYSPEPSIA

IMPORTANCE

Dyspepsia is a persistent symptom of epigastric discomfort or a feeling of gnawing hunger that is sometimes associated with meals, and with nausea, belching, or bloating (Barker et al., 1991). It may also be defined as pain or discomfort localized in the upper abdomen (Talley, 1993), or simply as symptoms that the physician believes are referable to the upper gastrointestinal (GI) tract (Pound and Heading, 1995). Figures on the prevalence of dyspepsia vary, with some citing a prevalence of seven percent in the U.S. (Barker et al., 1991), and others citing a six-month prevalence of over 35 percent (Pound and Heading, 1995). Differences in estimates probably depend on how dyspepsia is defined or elicited, and on the time window employed.

SCREENING

Only one in four of all patients with dyspepsia consult their general practitioner, and fewer than one in five of those age 20 to 40 do so (Pound and Heading, 1995). Because there are no data to indicate that all individuals with dyspepsia should consult their general practitioner. Our indicators do not address routine screening of individuals for dyspepsia.

DIAGNOSIS

Eliciting subjective details about the discomfort is not a highly reliable way to distinguish ulcer from nonulcer dyspepsia. Because ulcers are not the sole source of dyspepsia, the severity, timing, location of discomfort, and information on current bowel habits are often used to direct the diagnosis and guide use of further evaluative studies and treatment. Causes of nonulcer dyspepsia include: irritable bowel syndrome, which is classically associated with diffuse abdominal pain, altered bowel habits, and relief with defecation; cholelithiasis, which may be associated with discrete episodes of right upper quadrant pain; gastroesophageal reflux, which is associated with "heartburn" and a sensation of acid backwash; and chronic pancreatic disease, which is commonly associated with more severe pain and steatorrhea. Cases of nonulcer dyspepsia that defy these classifications are termed essential dyspepsia, in which approximately 50 percent will have *Helicobacter pylori* gastritis (Barker et al., 1991). Unfortunately, clinical diagnosis may not accurately predict endoscopic diagnosis in patients with dyspepsia (Muris et al., 1994). Although the majority of patients with chronic dyspepsia do not have concurrent ulceration, up to 40 percent of patients with chronic dyspepsia may have chronic peptic ulceration. However, symptoms alone are not sensitive and specific enough to make the diagnosis in most cases (Talley, 1993). One study suggests that 30 percent of patients with a major pathological lesion are misclassified, including 50 percent of ulcer patients. The chance-corrected validity of nonulcer dyspepsia was only slightly better than chance (Bytzer et al., 1996). Because of the questionable utility of symptom characteristics, no indicator requires that details of the character of the dyspeptic symptoms be elicited.

Use of current medications should be determined in patients with dyspepsia because this may influence the likelihood of diagnosing ulcer disease, ulcer complications, or drug-induced dyspepsia. Use of aspirin or nonsteroidal antiinflammatory drugs (NSAIDs) is particularly important, as these agents are widely used and may predispose patients to "NSAID gastritis" or ulcers (Griffin et al., 1988; Griffin et al., 1991; Clearfield, 1992; Walt, 1992; Rex, 1994; Lee, 1995). Each year,

nearly 70 million prescriptions for NSAIDs are written (Lee, 1995) and more than 30 billion NSAID pills are consumed in the U.S. (Loeb et al., 1992). The global market for NSAIDs is estimated at $2 billion per year (Lee, 1995). An estimated 1.2 percent of the population take NSAIDs regularly, and many more take them intermittently (Loeb et al., 1992). One study found that upper GI symptoms occurred in 38 percent of patients within one month after assignment to a common NSAID (Bianchi Porro et al., 1991), and in 37 percent of chronic NSAID patients in the two months prior to questioning. The two to four percent overall risk of ulcers in patients taking NSAIDs is twice that of the general population (Ebell, 1992) and four to five times higher than that of age-matched controls in the elderly (Griffin et al., 1988; Griffin et al., 1991). The prevalence of gastric ulcers among NSAID users may be five to ten times higher than in the general population (Lee, 1995).

The risk of hospitalization or major adverse GI events is approximately three to ten times greater in patients who take NSAIDs than in those who do not (Clearfield, 1992; Ebell, 1992; Loeb et al., 1992). Patients who take NSAIDs are more likely to require emergency surgical intervention for hemorrhagic or perforated peptic ulcers, and one study found they had an increased mortality from PUD in comparison with a matched control group (Loeb et al., 1992). Although NSAIDs are not significantly associated with chronic duodenal ulcers, ulcer complications of duodenal or gastric origin are equally common (Loeb et al., 1992). Medical costs of GI complications from NSAIDs have been estimated at $3.9 billion per year (Loeb et al., 1992).

Drug-induced dyspepsia may also occur with corticosteroids (DePriest, 1995), theophylline, digoxin, oral antibiotics (especially ampicillin and erythromycin), or potassium or iron supplements (Pound and Heading, 1995). Use of Pepto Bismol or iron may lead to a history of black stools in a patient who is found to be hemoccult negative on physical examination. Because medications may influence the diagnosis and management of ulcer disease versus nonulcer dyspepsia (which may be more likely, for instance, if erythromycin was begun soon before symptom onset), the medical record should document medication use, or at least

the presence or absence of NSAID use, in all patients newly presenting with dyspeptic symptoms (Indicator 1).

Ascertainment of smoking status is appropriate but not mandatory. Smoking has been shown to stimulate acid secretion, to impair mucosal defenses by reduction of blood flow and prostaglandin synthesis, and to provide an environment favorable to *H. pylori* (Bateson, 1993; Ziller and Netchvolodoff, 1993; Lanas et al., 1995). Cigarette smoking is believed by some to be an important risk factor for the development of PUD (Ebell, 1992; Bateson, 1993; Ziller and Netchvolodoff, 1993; Lanas et al., 1995). Smokers do indeed appear to be twice as likely as nonsmokers to develop PUD (Ebell, 1992), which may in turn induce symptoms of dyspepsia. Nonetheless, the evidence regarding a causal connection between smoking and PUD is not persuasive. Screening and treatment of smoking for all patients are discussed in Chapter 5 of the Cardiopulmonary Conditions book.

Ascertainment of alcohol use is appropriate but not mandatory. Alcohol use in itself has not been shown to be consistently associated with either dyspepsia (Talley et al., 1994) or peptic ulcers (Ebell, 1992; Chou, 1994), even though some recommend cessation or moderation of alcohol use in patients with ulcer disease (Loeb et al., 1992) and concurrent use of alcohol and NSAIDs may substantially increase the risk of upper GI bleeding (Ebell, 1992). Therefore, while it is probably appropriate to elicit an alcohol history, since this may influence the likelihood of diagnosing upper GI bleed (particularly with concurrent NSAIDs), no indicator has been formulated to require that alcohol use be elicited in the context of dyspepsia.

TREATMENT

Dyspepsia Not Associated With NSAID Use

H. pylori and Dyspepsia: *H. pylori* is common in the general population, and increases with age. More than 50 percent of asymptomatic persons over age 60 in North America show evidence of past or active *H. pylori* infection (Feldman and Peterson, 1993). A particularly high incidence of *H. pylori* is evident in patients with PUD, estimated at 90 to 95 percent of patients with duodenal ulcer and

70 percent of those with gastric ulcer (Cave, 1992). Furthermore, the eradication of *H. pylori* greatly lowers relapse rates of PUD (Feldman, 1993). In one study, relapse after six to twelve months of follow-up occurred in 85 percent of *H. pylori*-positive individuals, and in only ten percent of those with successful *H. pylori* eradication (Soll, 1996). Therefore, treatment of PUD has shifted emphasis from acid reduction to eradication of *H. pylori*, although traditional antiulcer treatment is still used to alleviate symptoms and promote ulcer healing. Finally, eradication of *H. pylori* can effectively reduce the re-bleeding rates for the two years following peptic ulcer hemorrhage, according to preliminary studies (Jiranek and Kozarek, 1996).

Management Options in Non-NSAID Dyspepsia

Guidelines from the Practice Parameters Committee of the American College of Gastroenterology recognize three approaches for management of new-onset dyspepsia not due to NSAIDs (Soll, 1996), most of which arise in association with *H. pylori* infection. Trial data are insufficient as yet to distinguish among these options. The first approach for management of new onset dyspepsia not due to NSAIDs is a single, short-term trial of empiric antiulcer therapy. If symptoms do not improve within two to four weeks, endoscopy should be pursued. If symptoms improve, the trial is discontinued after six weeks, and endoscopy is pursued if symptoms recur (Soll, 1996). The second option is a definitive diagnostic evaluation, including endoscopy with testing for *H. pylori* (Indicator 2). Endoscopy is performed immediately if there are "alarm" markers including anemia, GI bleeding, anorexia, early satiety, recurrent vomiting, dysphagia, jaundice, palpable mass, guaiac-positive stool, or weight loss (Talley, 1993; Soll, 1996). Because the diagnostic yield for organic pathology with endoscopy is 60 percent in patients over age 60, these patients should also receive early endoscopy, preferably within four to six weeks of presentation, if symptoms have occurred for the first time (Barker et al., 1991) (Indicator 3). Indeed, some recommend early endoscopy for those over age 45 (Talley, 1993). The third option for managing non-NSAID dyspepsia is noninvasive testing for *H. pylori* followed by antibiotics

in *H. pylori*-positive patients. *H. pylori* treatment has potential side
effects, and should only be undertaken if presence of *H. pylori* is
confirmed. An exception may be made if *H. pylori* is highly probable, as
in a person with dyspepsia with a history of duodenal ulcer and absence
of NSAID use (Indicator 4). With empiric antibiotics in *H. pylori*-
positive dyspectic patients, the 15 to 30 percent who have an ulcer are
likely to respond well, but nonulcer dyspeptic study subjects have been
shown to have a variable response compared with subjects on placebo.
The potential advantage of this approach lies in reserving definitive
work-up and extended therapy for patients with recurrent symptoms after
a course of antibiotics has been tried (Soll, 1996). However, the cost
advantage of empiric therapy over prompt endoscopy is subject to debate.
One decision analysis found the choice of optimal management strategy a
"toss-up" (Silverstein et al., 1996), while another study reported frank
cost savings and improved patient satisfaction with prompt endoscopy
(Bytzer et al., 1994).

Management of Dyspepsia Associated With NSAID Use

In a patient with new dyspepsia who is taking NSAIDs, it is
probably prudent to discontinue NSAIDs, if possible, and then reassess
the patient (Soll, 1996). Although the incidence of dyspepsia is high,
the incidence of dyspepsia leading to physician visits is substantially
lower. If NSAIDs cannot be discontinued, dyspepsia or uncomplicated
ulcers are often treated with H2 blockers twice a day. Although the use
of H2 blockers may be appropriate, at present there is no convincing
evidence that agents other than misoprostol protect against NSAID-
induced ulcer disease; thus, no indicator will be formulated for use of
prophylactic antiulcer medication in dyspeptic patients continuing to
take NSAIDs.

FOLLOW-UP

The literature does not specify appropriate follow-up intervals for
patients with dyspepsia. Management and follow-up for PUD are discussed
below.

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PEPTIC ULCER DISEASE

IMPORTANCE

Peptic ulcer disease is a major health problem in the United States. There are more than four million prevalent cases annually according to the National Institutes of Health (NIH, 1989), and 200,000 to 400,000 new cases each year (Barker et al., 1991; Ziller and Netchvolodoff, 1993). One in ten people in the U.S. will be affected by PUD at some time in their lives (Barker et al., 1991; NIH Consensus Panel, 1994). Although the disease has relatively low mortality, it results in substantial suffering (NIH Consensus Panel, 1994). There are approximately 150,000 nonfederal, short-stay hospitalizations each year in the U.S. for evaluation and treatment of bleeding ulcers (Laine and Peterson, 1994; Jiranek and Kozarek, 1996). The direct and indirect costs associated with PUD represent a large percentage of costs for the treatment of all diseases of the digestive system (Ziller and Netchvolodoff, 1993).

Peptic ulcer disease is the leading cause of acute hemorrhage of the upper GI tract, accounting for about 50 percent of all cases (Laine and Peterson, 1994). Hospitalization and surgery rates for uncomplicated ulcers have declined in the U.S. and Europe over the past 30 years; however, the number of admissions for bleeding ulcers is relatively unchanged (Laine and Peterson, 1994), with approximately 150,000 hospital admissions for bleeding ulcers in the U.S. each year (Jiranek and Kozarek, 1996). Despite advances in treatment, overall mortality has remained at approximately six to eight percent for the past 30 years, due in part to increasing patient age and prevalence of concurrent illness (Laine and Peterson, 1994).

Until recently, ulcers were thought to be related to stress and diet. It is now recognized that most ulcers are produced by NSAIDs or by *H. pylori*. Ninety percent of patients with bleeding ulcers are taking NSAIDs or have active *H. pylori* infection (Jiranek and Kozarek, 1996). Eradication of *H. pylori*, if it is present, and avoidance of NSAIDs have been proven to cure more than 95 percent of patients with PUD (Jiranek and Kozarek, 1996). A minority of patients with ulcers

have etiologies distinct from NSAIDs and *H. pylori*, including gastrinoma and corticosteroid or "stress-related" ulcers.

SCREENING

Although *H. pylori* is strongly associated with PUD and highly prevalent in the population, screening asymptomatic individuals for ulcers and testing for *H. pylori* are not recommended.

PREVENTION

Treatment of *H. pylori*

Despite the strong association between *H. pylori* and PUD, treating asymptomatic patients who have *H. pylori* for primary prevention of ulcers is not recommended.

Discontinuation of NSAIDS

In patients with new dyspepsia taking NSAIDs, it is prudent to discontinue NSAIDs where possible (Soll, 1996). This may reduce the incidence of NSAID-associated ulcers in patients with NSAID-associated dyspepsia. However, dyspepsia is common in NSAID users in the absence of ulcers or ulcer complications, and ulcer complications of NSAIDs often occur in the absence of dyspeptic symptoms. Indeed, it is not known whether patients with NSAID-associated dyspepsia are at greater risk for serious NSAID-induced GI problems such as bleeding or perforation (Larkai et al., 1989). For this reason, we have not generated an indicator to discontinue NSAIDs if dyspepsia is present without documented ulcer disease, though this is probably appropriate.

Use of NSAIDs increases not only risk of ulcer but risk of hospitalization for ulcer and, in those patients with established ulcer disease, risk of major ulcer complications such as bleeding. Therefore, in patients treated with NSAIDs or aspirin who have endoscopically documented ulcers, the medical record should either state the reason for continuing NSAIDs or aspirin, or that the patient was advised to discontinue NSAIDs or aspirin (Indicator 5).

Prevention of NSAID-Induced Ulcers if NSAIDs are Continued

Misoprostol is the only drug approved by the FDA for prevention of NSAID-induced ulcers. Although proton pump inhibitors and H2 blockers have been used in practice and may be appropriate, no data are available to support this. Misoprostol co-therapy may be appropriate as secondary prevention in cases of continued NSAID use with prior clinical ulcer disease, or as primary prevention in cases with concurrent steroid or anticoagulant administration or with serious comorbid conditions that would increase risk for ulcer complications. Misoprostol is often difficult to tolerate because diarrhea and abdominal cramps limit patient compliance. In addition, cost effectiveness has not been established (Soll, 1996). No indicator is directed at use of misoprostol or other agents for prevention of NSAID-induced ulcers, though such an indicator may be appropriate in the future when more data are available.

Smoking Cessation

Smoking is associated with increased incidence and prevalence of PUD (Hixson et al., 1992; Ziller and Netchvolodoff, 1993; Rex, 1994; Soll, 1996); delayed ulcer healing (in the pre-*H. pylori* eradication era); and increased risk of refractory and recurrent ulceration (in the pre-*H. pylori* eradication era) (Ebell, 1992; Bateson, 1993; Ziller and Netchvolodoff, 1993; Lanas et al., 1995). All patients who smoke will benefit from quitting and should be strongly encouraged to do so; however, additional evidence of selective benefit to PUD with smoking cessation, under current conditions of PUD treatment (including *H. pylori* eradication treatment), is lacking. Therefore, although it is appropriate to counsel all patients with PUD who smoke cigarettes to quit (Loeb et al., 1992), no indicator was constructed for this.

Alcohol Cessation

The role of alcohol use in ulcer disease is ill-defined. Although some recommend discontinuation of moderate-to-heavy use of alcohol in patients with a history of ulcers, as a way to prevent ulcer recurrence (Loeb et al., 1992), a causal relationship between alcohol use and ulcers has not been convincingly demonstrated (Ziller and Netchvolodoff,

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1993; Rex, 1994). While concurrent use of alcohol and NSAIDs may increase the risk of bleeding (Ebell, 1992), some studies show only modest or no increase in ulcer risk with alcohol use, and others actually suggest a possible protective effect. Therefore, while advice to curtail alcohol consumption is probably appropriate, no indicator will be directed at alcohol use in patients with PUD.

DIAGNOSIS

Endoscopy

Peptic ulcers are detected by the presence of a distinct crater that is visible on radiologic or endoscopic examination of the upper GI tract; they differ from erosions in that ulcers penetrate beyond the mucosa to the submucosa (Clearfield, 1992; Ziller and Netchvolodoff, 1993). Use of endoscopy to diagnose PUD is not recommended in the absence of symptoms, but may be appropriate in cases of dyspepsia or when evaluating GI bleeding. Indications for endoscopy to diagnose PUD are therefore listed in the management sections for dyspepsia and for GI bleeding.

Testing for *H. pylori* in PUD

Several tests are available for evaluating infection with *H. pylori*. Serological testing is sensitive and specific, and is the least expensive method (Walsh and Peterson, 1995). However, because serological testing does not distinguish between past and current *H. pylori* infection, it cannot be used to test for recurrence or for effect of treatment. Gastric mucosal biopsy -- by staining of biopsy materials, the Campylobacter-like organism test, or *H. pylori* culture -- and the ^{13}C-urea breath test may be used repeatedly to check for eradication of *H. pylori*. (*H. pylori* produces urease that hydrolyzes labeled urea, producing NH_3 and $^{13}CO_2$; $^{13}CO_2$ is identified in expired air by mass spectroscopy (Cave, 1992)). Culture is the least sensitive of the direct techniques (Walsh and Peterson, 1995). The urea breath test has the advantage of being noninvasive. These latter methods are sensitive to bacterial load and should be performed at least four weeks after use of bismuth or eradication therapy (Cave, 1992; Walsh and

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Peterson, 1995), because recent *H. pylori* suppression without eradication can lead to false negative results.

Testing for *H. pylori* may not be required in those ulcer patients in whom the likelihood of *H. pylori* is very high. In particular, patients with previously diagnosed duodenal ulcers with no history of NSAID use, no signs or symptoms of a hypersecretory state, and no history of antimicrobial treatment that might have cured a past infection, may not require testing for *H. pylori* (Walsh and Peterson, 1995) but may instead be candidates for empiric treatment. In patients with gastric ulcers, or those who are taking NSAIDs, however, the prevalence of *H. pylori* is lower and testing to identify or exclude *H. pylori* is indicated (Walsh and Peterson, 1995).

TREATMENT

Uncomplicated PUD

Management of uncomplicated PUD centers around removal of the identified cause (usually *H. pylori* or NSAIDs) and antiulcer therapy. Removal of contributing factors, such as cigarette smoking, has an ancillary role.

Antiulcer Therapy

Regardless of specific treatment for *H. pylori* or cessation of NSAID use, conventional ulcer therapy should be used for a minimum of four weeks to facilitate symptom relief and healing in documented ulcers (Indicator 6) (Soll, 1996).

There is no persuasive evidence to unequivocally favor one antiulcer regimen over another. Many randomized trials have shown comparable efficacy in treatment of duodenal ulcer for antacids, sucralfate, proton pump inhibitors (omeprazol or Prilosec), and H2 receptor antagonists such as cimetidine (Tagamet), ranitidine (Zantac), famotidine (Pepsid), and nizatidine (Axid) (Soll, 1996). Two meta-analyses and one large multicenter trial have found statistically more effective healing and a higher rate of symptom relief with omeprazole than with H2 receptor antagonists used to treat duodenal ulcers (Parent, 1994); however, there is no consensus that a difference in clinical efficacy is adequate to recommend omeprazole over other agents. Full

doses of H2 receptor antagonists offer effective initial therapy for gastric ulcers. Proton pump inhibitors and probably sucralfate, while not approved for gastric ulcer treatment in the U.S., may be effective alternatives (Soll, 1996).

Four weeks is a reasonable minimum treatment duration. Twenty percent of duodenal ulcers fail to heal after four weeks of standard therapy. If treatment is continued for another four to eight weeks, ulcers will heal in 90 to 95 percent of patients. In patients who have failed *H. pylori* treatment, and perhaps in those who are *H. pylori* negative, treatment should probably be continued for six months, since most ulcer recurrences occur within this time (Soll, 1996).

NSAID-Associated Ulcers

In a patient with documented PUD who is taking NSAIDs, it is generally agreed that NSAIDs should be discontinued where possible, and the patient should be reassessed (Soll, 1996). This was reflected in Indicator 5 and no additional indicator is proposed.

H. pylori-Positive Ulcers

Recognition of the role of *H. pylori* in the pathogenesis of ulcer disease is recent, and new management strategies are in rapid flux. Broad spectrum antibiotic treatment is not without side effects (Hawkey, 1994). Therefore, in patients with peptic ulceration confirmed on endoscopy, *H. pylori* testing should be documented and recorded in the medical record before initiation of *H. pylori* treatment (Indicator 7). Because the presence of *H. pylori* predicts ulcer recurrence (Coghlan et al., 1987), and treatment of *H. pylori* hastens resolution of ulceration (Hosking et al., 1994) and reduces the ulcer relapse rate (Marshall et al., 1988) in randomized controlled trials, *H. pylori* eradication treatment should be initiated on endoscopic evidence of ulceration, and serological or pathologic evidence of *H. pylori* (Indicator 8). Many antibiotic regimens for treatment of *H. pylori* have been reported. These vary in cost, duration, side effects, and efficacy (Taylor et al., 1997). There is no evidence to support one regimen over all others (Taylor et al., 1997), and new regimens with adequate efficacy may soon be added to the list. At present, regimens should include at least two antibiotics with either colloidal bismuth (bismuth subsalicylate or

Pepto Bismol) or antisecretory agents (Soll, 1996). Common regimens
include bismuth and metronidazole combined with either tetracycline or
amoxicillin, with or without omeprazole; or omeprazole with any two out
of the following three antibiotics: metronidazole, amoxicillin, or
clarithromycin (Soll, 1996; Taylor et al., 1997).

Smoking Cessation

Data obtained in patients before the era of routine testing and
treatment for *H. pylori* indicated that smoking impedes ulcer healing
(Hixson et al., 1992; Ziller and Netchvolodoff, 1993; Rex, 1994; Soll,
1996). Healing rates in heavy smokers (those who smoke more than 1 1/2
packs per day) were about one-half the rates seen in nonsmokers after
eight weeks of therapy with an H2 blocker (Rex, 1994). In addition,
following standard antiulcer treatment (before *H. pylori* eradication
therapy), nonsmokers not on maintenance therapy had an ulcer relapse
rate of 40 to 50 percent at one year, whereas heavy smokers had a
relapse rate of 100 percent at three months. However, there is no
evidence that smoking cessation provides benefit (reduction of
recurrence or complications) in patients for whom *H. pylori* eradication
therapy is available. There is also no independent evidence of benefit
for smoking cessation with NSAID-associated ulcers. Therefore, although
it is appropriate to give strong recommendations to discontinue smoking
to all patients, there is no evidence of selective benefit from smoking
cessation in the context of current PUD management.

Gastric Ulceration

If gastric ulceration is noted on endoscopy, biopsy should be
performed to exclude gastric cancer. Either multiple biopsies should be
obtained at the time of initial endoscopy, or follow-up endoscopy for
gastric ulceration is indicated to confirm healing. If the ulcer
persists, multiple biopsies should again be obtained to exclude gastric
cancer (Soll, 1996) (Indicators 9, 10).

Complicated PUD

Complicated PUD is defined to include PUD with associated bleeding,
perforation, or obstruction. Gastrointestinal bleeding is the most

common of these complications. Management in patients with complicated PUD should also include the following.

Diagnosis

Emergency endoscopy: Endoscopy should be performed on an emergent basis, that is, within 12 hours, if nasogastric or orogastric lavage indicates continuous bleeding. In five percent of cases, active bleeding continues and the mortality rate in these instances approaches 30 percent.

Urgent endoscopy: There is consensus that endoscopy should be performed in patients presenting with GI bleeding with evidence of marked or continuing hemodynamic instability, despite adequate resuscitation efforts. However, because it is difficult to ascertain continuing hemodynamic instability from medical records, we will not address this area specifically in an indicator. Endoscopy can be justified in most cases of upper GI bleed, on the grounds that: 1) superficial lesions may heal quickly, and be missed with later endoscopy; 2) multiple lesions are present in approximately 25 percent of cases, and early endoscopy can identify the lesion actually responsible for the bleeding; and, most important, 3) endoscopy can identify subjects likely to rebleed, allowing them to be treated more aggressively. Although bleeding from peptic ulcers ceases spontaneously and does not recur in 70 to 80 percent of cases, rebleeding does occur in approximately 25 percent of cases, with a mortality well above ten percent (Qureshi and Netchvolodoff, 1993).

Endoscopic Therapy

Several types of endoscopic treatment are available, including Nd:Yag laser, heater probe, bipolar (Bicap) electrode, or injection treatment with agents such as hypertonic saline, epinephrine, or pure ethanol (Sugawa and Joseph, 1992; Qureshi and Netchvolodoff, 1993). Injection treatment achieves permanent hemostasis in more than 80 percent of cases (Qureshi and Netchvolodoff, 1993); however, studies and meta-analyses comparing these techniques have not consistently shown any one to be superior (Sacks et al., 1990; Sugawa and Joseph, 1992).

Not all patients with internal bleeding require endoscopic treatment or, where endoscopic treatment is not available, surgery.

Whether or not patients require such treatment is based in part on the risk of recurrent upper GI bleeding, as assessed by endoscopic findings (Qureshi and Netchvolodoff 1993). The risk of recurrent bleeding is less than two percent for those with a clean ulcer base; less than 10 percent for those with a black or red spot; 35 percent for those with oozing from an adherent clot; 40 percent with a nonbleeding visible vessel or "sentinel clot" (a pigmented protuberance that represents a fibrin clot plugging a side hole in an artery that runs parallel to the base of the ulcer) (NIH Consensus Statement, 1989); 80 percent with a visible vessel and hypotension; and approximately 100 percent with active bleeding (Qureshi and Netchvolodoff, 1993). Endoscopic treatment was shown to reduce further bleeding, surgery, and mortality in patients with high-risk endoscopic features of active bleeding or nonbleeding visible vessels in two meta-analyses of 25 and 30 randomized controlled trials (Sacks et al., 1990; Cook et al., 1992). This has buttressed the belief, previously articulated in the 1989 NIH Consensus Statement on therapeutic endoscopy and bleeding ulcers, that endoscopic treatment is merited if there is active oozing or spurting of blood, or a visible vessel (Qureshi and Netchvolodoff, 1993) (Indicator 11). Surgery is an acceptable alternative where endoscopic therapy is not available. Data for ulcers with a clean base or for nonbleeding ulcers with an adherent clot do not show clear evidence of benefit with endoscopic treatment.

H. pylori **Testing and Treatment**

Bleeding ulcers differ from uncomplicated peptic ulcers in that up to 25 percent of patients with bleeding ulcers who are not taking NSAIDs may not be infected with *H. pylori*; therefore, the presence of infection should be documented before eradication is attempted (Laine and Peterson, 1994). Thus, in patients with ulcer complication not documented to be associated with NSAIDs, *H. pylori* testing should be performed. This may be done by obtaining specimens for histology at the time of endoscopy, or if this is not done, by serological testing (provided the patient has not received prior eradication therapy). *H. pylori* eradication in patients with complicated PUD has been shown to reduce the rate of rebleeding in randomized controlled trials (Graham et al., 1993; Rokkas et al., 1995). In those who test positive for *H.*

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pylori, an eradication regimen for *H. pylori* should be initiated (Indicator 12).

FOLLOW-UP

Confirmation of *H. pylori* Eradication

Confirmation of successful *H. pylori* cure by endoscopic biopsy or urease breath test is important in patients with a history of ulcers complicated by bleeding, perforation, or obstruction, or ulcers that recur after *H. pylori* eradication therapy (Soll, 1996) (Indicator 13). Successful eradication of *H. pylori* has been clearly shown to reduce bleeding recurrences, while *H. pylori* persistence after therapy is associated with continued risk of rebleeding (Labenz and Borsch, 1994). Confirmation of eradication remains controversial in patients with uncomplicated ulcers who remain asymptomatic after antibiotic therapy (Soll, 1996).

Maintenance Therapy

Maintenance therapy with H2 receptor antagonists is indicated in high-risk patients with PUD who have *H. pylori*-negative ulcers or who fail *H. pylori* cure. Efficacy of maintenance therapy has not been explicitly tested in these groups, but is presumed to parallel that of patients evaluated before *H. pylori* testing was available, most of whom were likely to have been *H. pylori*-positive. Maintenance therapy has been shown to reduce duodenal ulcer recurrences at one year from 60 to 90 percent to 20 to 25 percent (Soll, 1996). The risk of subsequent recurrent ulceration after initial healing is not diminished after completing one year of maintenance therapy; however, continued maintenance therapy with H2 blockers remains effective in reducing ulcer recurrence for two to five years. Because no data are yet available in the populations for whom maintenance treatment would currently be considered, there is no consensus regarding duration of maintenance treatment. Because the relevant populations are a small subset of ulcer patients, no indicator has been generated regarding use of maintenance therapy.

Review of Follow-up Treatment

In subjects with an ulcer history requiring maintenance therapy, and in those with past ulcer complications, *H. pylori* identification should be pursued (Soll, 1996) (Indicator 14). As previously noted, *H. pylori* identification followed by *H. pylori* eradication reduces ulcer recurrence (Marshall et al., 1988), negates the need for maintenance treatment in most individuals, and reduces the rate of rebleeding in those with a history of bleeding ulcer (Graham et al., 1993; Labenz and Borsch, 1994; Jaspersen et al., 1995; Rokkas et al., 1995).

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RECOMMENDED QUALITY INDICATORS FOR DYSPEPSIA AND PEPTIC ULCER DISEASE

The following indicators apply to men and women age 18 and older with dyspepsia or PUD.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Dyspepsia: Diagnosis				
1. Patients presenting with a new episode of dyspepsia[1] should have the presence or absence of NSAID[2] use noted in the medical record on the date of presentation.	II-2	Lee, 1995; Clearfield, 1992; Rex, 1994; Walt, 1992; Bianchi-Porro, 1991; Larkai, 1989; Ebell, 1992; Loeb, 1992; Griffin, 1991, 1988	Reduce dyspeptic symptoms. Reduce development of ulcers and ulcer complications.	Use of NSAIDs[2] increases symptoms of dyspepsia, risk of erosions and ulcers, and PUD complications.
Dyspepsia: Treatment of Non NSAID-Associated Dyspepsia				
2. Patients prescribed empiric antiulcer treatment[3] for dyspepsia who were not using NSAIDs[2] within the previous month should have at least one of the following within 8 weeks: • documentation in medical record that symptoms have improved; • endoscopy; • H. pylori test.[4]	III	Soll, 1996; NIH, 1994	Direct effective treatment. Reduce symptoms and complications of PUD.	To guide successful therapy (e.g., for *H. pylori*) and thereby prevent complications, identification of the cause is needed when empiric treatment fails.

	Indicator	Quality of Evidence	Literature	Benefits	Comments

3.	Patients with new dyspepsia[1] who have any of the following "alarm" indicators on the date of presentation should have endoscopy performed within 1 month, unless endoscopy has been performed in the previous 6 months:
	  a. anemia;[5]
	  b. early satiety;
	  c. significant unintentional weight loss (exceeding 15 pounds in the past 3 months);
	  d. guaiac-positive stool;
	  e. dysphagia;
	  f. over age 60.
		II-2
		III
			Soll, 1996	Detect gastric cancer.
				Direct correct treatment.
				Reduce morbidity from ulcer complications.
					Patients over age 60 and those with "alarm" symptoms have an increased incidence of positive findings on endoscopy. Older patients may be more likely to have gastric cancer, which can be treated if detected early.

4.	Patients who are prescribed *H. pylori* eradication antibiotic treatment[6] within 3 months after presentation for a new episode of dyspepsia[1] should have one of the following noted in the medical record before start of antibiotic treatment: • prior positive test for H. pylori;[4] • both a history of documented duodenal ulcer and absence of NSAID[2] use.	III	Hawkey, 1994; Soll, 1996; Walsh, 1995	Prevent drug side effects.	Antibiotic treatment is not without risks, and treatment should not be given without prior testing except in cases where the probability of *H. pylori* as a causal agent is extremely high.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Peptic Ulcer Disease: Secondary and Tertiary Prevention				
5. For patients with endoscopically documented PUD who have been noted to use NSAIDs[2] within 2 months before endoscopy, the medical record should indicate, within 2 months before or 1 month after endoscopy, one of the following: • a reason why NSAIDs[2] or aspirin will be continued; • advice to the patient to discontinue NSAIDs[2] or aspirin.	II-2	Clearfield, 1992; Lee, 1995	Reduce symptoms of dyspepsia. Reduce ulcer occurrence. Reduce hospitalization. Reduce mortality.	Use of NSAIDs[2] increases risk of ulcer, hospitalization for ulcer, PUD complications,[8] and delay of healing in existing ulcer.
Peptic Ulcer Disease: Treatment of Uncomplicated PUD				
6. Patients in whom peptic ulceration is confirmed on endoscopy should have antiulcer treatment[3] for a minimum of 4 weeks.	III	Soll, 1996	Assist ulcer healing. Reduce symptoms.	Antiulcer treatment[3] should be provided to assist ulcer healing even if specific therapy is given (e.g., *H. pylori* eradication treatment[6]).
7. Patients with endoscopically confirmed gastric or duodenal ulcer should have *H. pylori* testing[4] within 3 months before or 1 month after endoscopy, unless the medical record, in the same time period, documents a past positive *H. pylori* test[4] for which no *H. pylori* eradication treatment[6] was given.	III	Marshall, 1988; Graham, 1993	Prevent recurrence. Prevent side effects.	Testing allows identification or exclusion of *H. pylori*, which permits initiation of effective treatment to prevent recurrence, or avoidance of such treatment and its attendant side effects.
8. Eradication therapy for *H. pylori* should be offered within 1 month when all of the following conditions are met: • documentation of history of positive *H. pylori* test at any time in the past; • documentation of endoscopically confirmed ulceration of the duodenum at any time in the past.	I	Coghlan, 1987; Marshall, 1988	Prevent recurrence.	Recurrence of duodenal ulcer is predicted by presence of *H. pylori*. Recurrence of duodenal and gastric ulcer is markedly decreased after eradication of *H. pylori* infection.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Peptic Ulcer Disease: Treatment				
9. Patients with a gastric ulcer confirmed by endoscopy should have one of the following: • a minimum of 3 biopsies during endoscopy; • follow-up endoscopy within 3 months.	III	Soll, 1996	Detect and treat gastric cancer.	Gastric ulceration and *H. pylori* are associated with increased incidence of gastric cancer. Failure to heal (identified on follow-up endoscopy) may indicate presence of gastric cancer, and biopsies should be obtained to exclude this possibility. It is preferable that follow-up endoscopy occur at least 4 weeks after discontinuing antibiotics, proton pump inhibitors, or bismuth if repeat *H. pylori* testing[4] will be performed.
10. Patients with endoscopically documented gastric ulcer who have follow-up endoscopy within 6 months should have one of the following at the follow-up endoscopy: • complete healing of the gastric ulcer noted; • a minimum of 3 biopsies of the ulcer.	III	Soll, 1996	Identify gastric cancer. Treat early gastric cancer.	Gastric ulceration that fails to heal may represent gastric carcinoma, which requires different treatment than does PUD alone. Gastric cancer may be cured if identified early.
Peptic Ulcer Disease: Treatment of Complicated Peptic Ulcer Disease				
11. Patients with endoscopically documented PUD should be offered endoscopic treatment[7] or surgery within the next 24 hours if either of the following are documented in the endoscopy note: a. continued oozing, bleeding, or spurting of blood; b. a visible vessel (or "pigmented protuberance").	I III	Sacks, 1990; Cook, 1992; NIH Consensus Statement, 1989	Reduce rebleeding. Reduce blood transfusions. Reduce need for emergency surgery. Improve survival.	A meta-analysis showed that endoscopic treatment reduced further bleeding, surgery, and mortality in patients with high-risk features of active bleeding or nonbleeding visible vessels.

Indicator	Quality of Evidence	Literature	Benefits	Comments
12. Patients with a documented PUD complication[8] who have had a positive *H. pylori* test[4] within 3 months after the complication should be started on an *H. pylori* eradication regimen[6] within 1 month of the positive test.	I	Marshall, 1988; Labenz, 1994; Graham, 1993; Rokkas, 1995; Jaspersen, 1995	Reduce symptoms. Reduce rebleeding.	Identification and treatment of *H. pylori* reduces recurrences of *H. pylori*-associated bleeding ulcers. Testing may be warranted even in the presence of NSAID use.
Peptic Ulcer Disease: Follow-up				
13. Patients with endoscopically confirmed PUD whose symptoms of dyspepsia or documented ulcers recur within 6 months after eradication therapy for *H. pylori* should receive confirmatory testing for successful *H. pylori* cure by endoscopic biopsy or urease breath test within 1 month of symptom recurrence.	II	Soll, 1996; Labenz, 1994	Reduce symptoms and complications from PUD.	Patients in whom symptoms recur may have continued *H. pylori* infection. Complications are reduced with successful *H. pylori* eradication.
14. Patients with a history of PUD complications[8] in the past year should have results of *H. pylori* testing[4] documented in the medical record in the same time period.	I	Marshall, 1988; Labenz, 1994; Graham, 1993; Rokkas, 1995; Jaspersen, 1995	Prevent ulcer recurrence and rebleeding.	*H. pylori* treatment reduces rebleeding in PUD. Those with past complications should receive testing, and, where indicated, treatment for *H. pylori*.

Definitions and Examples

[1] New episode of dyspepsia: first visit for dyspepsia ever; or first visit for dyspepsia symptoms in the past year. Documentation of new onset or duration less than 3 months counts as a new episode.

[2] NSAIDs: Nonsteroidal antiinflammatory drugs. Selected short-acting NSAIDs include aspirin, diclofenac (Voltaren), ibuprofen (Advil, Motrin, Nuprin), indomethacin (Indocin), ketoprofen (Orudis), and tolmetin (Tolectin) (Clearfield, 1992). Selected long-acting NSAIDs include diflunisal (Dolobid), naproxen (Naprosyn), phenylbutazone (Butazolidin), piroxican (Feldene), and sulindac (Clinoril) (Clearfield, 1992).

[3] Antiulcer treatment may include sucralfate (Carafate); H2 receptor antagonists such as cimetidine (Tagamet), ranitidine (Zantac), famotidine (Pepsid), and nizatidine (Axid); proton pump inhibitors such as omeprazole (Prilosec); and antacids such as aluminum hydroxide, magnesium hydroxide, calcium carbonate, and sodium bicarbonate (Ebell, 1992).

[4] *H. pylori* test may include the following: serological test; 13-C or 14-C Urea breath test (may not be available commercially); endoscopy with gastic biopsy, followed by histological demonstration of organisms (Giemsa or Warthin-Starry stains or Hematoxylin and Eosin), direct detection of urease activity in the tissue specimen, or biopsy with culture of the *H. pylori* organism (NIH Consensus Conference, 1994).

[5] Anemia: Hematocrit less than 35 not due to other known cause.

[6] *H. pylori* eradication treatment: Antibiotic regimen including bismuth or omeprazole with at least two of the following: flagyl, ampicillin, tetracycline, or clarithromycin. Examples: BMT (1-2 wk); BMTO (1 wk); BMA (1-2 wk); BMA (2 wk); MOC (1 wk); AOC (1 wk); MOA (1-2 wk); (B = Bismuth subsalicylate, 2 tab qid with meals and at bedtime; T = Tetracycline, 500 mg qid with meals and at bedtime; M = metronidazole, 250 or 500 mg qid with meals and at bedtime; C = clarithromycin, 500 mg bid or tid with meals; A = amoxicillin (not ampicillin), 500 mg or 1 gm qid with meals and at bedtime; O = 20 mg bid before meals).

[7] Endoscopic treatment may include laser treatment; injection treatment with saline, ethanol, epinephrine, or polidocanol; or thermal treatment such as heater probe or bicap (bipolar electrocoagulation)

[8] PUD complications are bleeding, perforation, or obstruction.

Quality of Evidence Codes

I   RCT
II-1   Nonrandomized controlled trials
II-2   Cohort or case analysis
II-3   Multiple time series
III   Opinions or descriptive studies