# LATEST APPROVED METHODS OF TREATMENT FOR THE PRACTICING PHYSICIAN

Edited by

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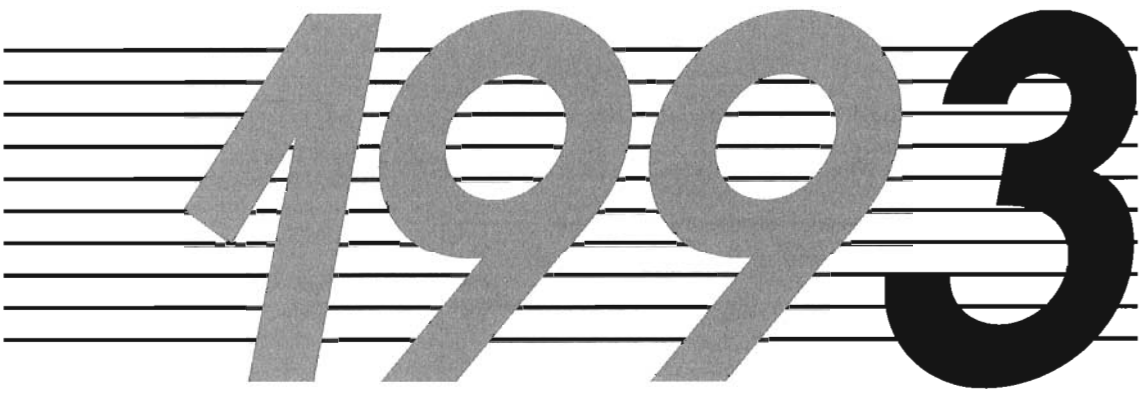


# Conn's Current Therapy

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Digital examination of the site to break down any loculations is important. Postoperatively, no packing is generally necessary and sitz baths twice daily are sufficient to allow the wound to heal. Careful follow-up examination and inspection of the wound within a week or 10 days is probably appropriate. Larger abscesses and higher abscesses generally require regional anesthetic or sedation in the operating room or outpatient facility to allow better drainage. Packing is rarely necessary in anal abscesses except for the initial 24-hour period for hemostasis. Repeated packing leads to increased scarring, slower healing, and more pain and discomfort on the part of the patient.

Occasionally, perianal abscesses and perianal infections can become potentially lethal because of synergistic activity, neglect in management, or delay in treatment. Such circumstances need aggressive surgical treatment, antibiotic therapy, and aggressive wound management. All abscesses should be drained soon, preferably the same day as diagnosis. Antibiotics have little role except in special circumstances and in a complementary fashion.

### Treatment of Fistulas

Perianal fistula management is surgical and complex. Differential diagnosis of fistulas from Crohn's disease is important. High fistulas, and those involving a lot of muscle, are challenging and require a good understanding of anatomy to minimize recurrence and incontinence. Occasionally, staged procedures with the use of a seton are necessary. This involves the use of a suture or portion of elastic to mark the site of a fistula to allow staged or gradual division of the fistula tract. Fistula surgery involves identification of the internal opening of the fistula along with good delineation of the fistula tract with proper drainage of the area. There has been controversy whether fistulotomy or fistulectomy is necessary for treatment of fistulas. Fistulectomy involves excision of the entire fistula tract, leading to a more complicated and larger wound. Although a fistulectomy may have some limited role, fistulotomy is sufficient to treat most fistulas. Proper postoperative care and careful management of the wound are as important as the surgical therapy.

Fistulotomy at the time of anal abscess drainage is probably indicated only in "low" fistulas, recurrent abscesses and fistulas, or fistulas that are coursing through small amounts of muscles. Generally, drainage of an anal abscess is followed by healing in approximately 50% of patients, with no subsequent recurrence. The other half of patients can be treated at a second stage with proper fistulotomy.

The use of dyes or fistulography to diagnose fistulas is rarely indicated. More complex fistulas with a horseshoe shape or high fistulas occurring above and around the anal sphincter mechanism are rare. Multiple fistulas and associated swollen skin tags, fissures, or ulcers are fairly pathognomonic of Crohn's disease. Classically, fistulas in Crohn's disease are relatively asymptomatic. Special therapy and care for Crohn's fistulas is necessary; rarely, primary surgical intervention is needed.

The postoperative care of anal fistulas involves careful inspection of the wounds and patients in follow-up management. On occasion, it may take several months for anal abscesses and fistulas to heal. The use of sitz baths twice daily for 10 or 15 minutes is sufficient. Sterile dressings are not needed, and dressings are used simply to catch any drainage. As previously mentioned, packing the wounds is not generally necessary or indicated. Physicians who need to treat complex fistulas should refer to a good surgical textbook.

# GASTRITIS

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## CLINICAL APPEARANCE

Gastritis is the name given to conditions that cause an inflammation of the gastric mucosa. The inside of the stomach is not generally accessible for examination by the primary care physician, so the diagnosis of gastritis may be suspected, inferred, or proved, depending on what investigations have been performed.

Initially, a patient with upper gastrointestinal symptoms may be suspected of having gastritis. In many countries the term "gastritis" is synonymous with the clinical syndrome of "nonulcer dyspepsia." The patient may complain of a burning or gnawing sensation in the epigastrium, perhaps relieved by food and/or antacids. Other components of the discomfort may include bloating sensations after meals, flatulence, belching, abdominal distention, and epigastric tenderness. In more severe cases, nausea and vomiting may occur. Usually symptoms arising in the stomach are affected in some way by eating, the pain is located above the umbilicus, and disturbance of bowel habit is uncommon.

The clinical syndrome of gastritis does not correlate well with endoscopic and histologic appearances of the gastric mucosa. Patients with severe symptoms may have normal mucosa, and patients with no symptoms may have severe erosive gastritis. It is important

therefore to refer to a clinical impression of gastritis as "clinical gastritis" so that it is not confused with better-defined types of gastritis.

## ENDOSCOPY

At endoscopy, the normal gastric mucosa is a pink color, like the palm of the hand. The endoscopic appearance of gastric mucosa when gastritis is present can vary along a continuum from normality to redness, widespread erosion, hemorrhage, and ulceration.

Gastritis affects the antrum more severely than the body of the stomach. Degrees of redness are common, especially in the antral mucosa. Slight changes may be called "mild gastritis" by some gastroenterologists, but are regarded as a normal variant by many endoscopists and are not reported. When the mucosa is very red, all gastroenterologists mention gastritis on the endoscopy report.

When small areas of the epithelium are eroded, brown spots attributable to the presence of changed blood on the mucosa can be seen. These spots may not be associated with a visible macroscopic lesion; depending on the number present, "mild erosive gastritis" may be reported. An erosion is defined as an interruption of the epithelial layer that does not extend deeper than the muscularis mucosae (about 1 mm deep). More extensive lesions are called ulcers. Severe erosive gastritis occurs when the mucosa is diffusely affected and both microscopic and visible erosions are present.

It should be emphasized that endoscopic identification of gastritis does not reflect the histologic status of the mucosa. For example, in patients with extensive bleeding erosions resulting from nonsteroidal anti-inflammatory drug (NSAID) ingestion there may be a completely normal histologic appearance in mucosa not actually affected by an erosion.

Endoscopically apparent gastritis, therefore, is the macroscopic lesion seen at endoscopy. It is affected by recently ingested or retained food, coloring agents (premedication mixtures at endoscopy may be colored pink), the microvasculature (congestion, vasodilation), the integrity of the overlying mucosa (erosion, ulceration), the presence of bile (edema, vasodilation), bleeding (new or altered blood), and, in some cases, by the presence of pus cells in the gastric mucus.

Thus, endoscopic identification of gastritis is the sum total of many factors that may affect, or appear to affect, the gastric mucosa. More accurate diagnosis of the endoscopic lesion requires histologic examination of a mucosal biopsy specimen.

## HISTOLOGY

Histologic evidence of gastritis is an infiltration of the gastric mucosa with neutrophils, lymphocytes, and plasma cells. This is the most common form of gastritis, and there are two types.

Type A gastritis is associated with pernicious anemia. It affects the parietal cells in the body of the stomach. It is uncommon and usually does not cause gastric symptoms because acid secretion is minimal or absent.

Type B gastritis is much more common. It affects the mucus-secreting epithelial cells that line the stomach. It is most severe in the antrum, where these cells are most plentiful. Type B gastritis is caused by chronic *Helicobacter pylori* infection.

Type B gastritis is referred to when the terms "acute," "active," "superficial," "chronic atrophic," and "nonspecific" are used by the pathologist. Other findings sometimes accompany Type B gastritis and may be sequelae of the disorder. Intestinal metaplasia is the replacement of the gastric mucus-secreting epithelial cells with intestinal-type (brush border and goblet) cells. The combination of chronic gastritis and intestinal metaplasia is associated with gastric carcinoma.

## SPECIFIC FORMS OF GASTRITIS

### Alcohol-Induced Gastritis

Acute gastritis, with or without erosions, may develop after the ingestion of any corrosive substance. Alcohol causes an acute erosive gastritis if it is consumed in excessive amounts, particularly as spirits. Occasionally, erosions and superficial ulcerations are also seen in the duodenum.

After the offending agent has been removed, the gastric mucosa heals rapidly. Symptoms and erosions therefore last no more than a few days after abstinence. Prolonged nausea or vomiting after 72 hours is more likely due to an underlying chronic gastritis, a peptic ulcer, or an associated metabolic disturbance. Alcohol in moderate amounts does not harm the gastric mucosa and is not implicated in the causation of chronic gastritis or peptic ulceration. Acute lesions due to alcohol do not lead to chronic gastritis or any kind of permanent mucosal defect.

Many alcoholics have chronic gastritis and peptic ulcer disease. It is now known that, in most cases, the chronic gastritis is caused by *H. pylori* infection (see later) so there is no need to invoke alcohol as a cause. *H. pylori* is more common in economically disadvantaged groups and, like other enteric infections, is more likely to be present in alcoholics. Conversely, alcoholics without *H. pylori* do not have chronic gastritis.

Hematemesis or coffee-ground vomitus is common after acute alcoholic binge drinking. Common causes are peptic ulcer disease, Mallory-Weiss tear, and erosive gastritis. It is important to ascertain whether the blood was present in the initial vomitus or if it was only noted in subsequent vomiting episodes. In Mallory-Weiss syndrome, the initial vomitus is normal and bright-red blood is seen in subsequent vomiting. If acute erosive gastritis or peptic ulcer is present, frank blood or coffee-ground vomitus is likely to be present in the initial vomitus. More serious lesions, such as bleeding esophageal varices, should be considered in the appropriate clinical setting.

**Treatment.** Symptoms should resolve rapidly after alcohol ingestion has ceased. Pain should be treated with antacids and $H_2$ receptor antagonists. If bleeding is present, an endoscopy within 12 hours is necessary to identify the site of bleeding. Later endoscopy may not detect rapidly healing small mucosal tears or small acute erosions. Mucosal biopsy should always be performed to check for chronic gastritis due to *H. pylori.*

### Aspirin-Induced Gastritis

Aspirin and NSAIDs together may be the most common causes of erosive gastritis. These drugs inhibit prostaglandin synthesis and so impair the ability of the mucosa to secrete mucus and withstand acid or peptic attack. Although NSAIDs may also have a directly "corrosive" effect on the mucosa, even persons taking NSAIDs rectally are prone to gastric erosions.

Aspirin-induced erosions may occur anywhere in the stomach, rather than being localized to the antrum as erosions related to peptic ulcer disease are (see later). Histologically, NSAID erosions are associated with little inflammation, not more than would be expected from natural healing of any epithelial disruption. Apart from discontinuity of the epithelial layer and hemorrhage, there may be no histologic abnormality. Away from the actual erosion, the mucosa is relatively normal.

Nearly all persons receiving long-term NSAID therapy have some degree of erosive gastritis. Not all erosions cause symptoms and not all progress to form a chronic peptic ulcer. If another predisposing cause is present, however, NSAID ingestion may be additive and result in expression of peptic ulcer disease. For example, in persons with *H. pylori* who take NSAIDs, the ulcer risk is additive. Apart from *H. pylori,* NSAIDs are the only common cause of peptic ulcer.

**Treatment.** As for alcohol-induced erosive gastritis, erosions due to NSAID ingestion should ideally be treated by withdrawing the offending drug. If the NSAID can be ceased, the mucosa repairs itself in a few days. Peptic ulcers caused by NSAIDs require a month or so to heal, as do all ulcers.

Symptoms should be treated with antacids and $H_2$ receptor antagonists for 3 to 14 days. If symptoms persist, another cause of gastritis should be suspected, e.g., *H. pylori* and/or peptic ulcer disease.

In many patients, the NSAID cannot be discontinued owing to a chronic rheumatic complaint. For example, rheumatoid arthritis is difficult to manage without the use of NSAIDs, all of which have ulcerogenic potential. There are several ways to approach this problem.

Misoprostol, a prostaglandin analogue, protects against NSAID-induced gastric lesions. Misoprostol should not be given to women of reproductive potential, and it may cause diarrhea, but it can be given on a long-term basis to many patients, allowing them to continue receiving the NSAID. The dosage is 100 to 200 μg four times a day. It is best to start with the lower dose and give the drug with food.

$H_2$ receptor antagonists, sucralfate, or antacids given in ulcer-healing dosages may heal erosions and prevent the progression to frank peptic ulcer. These are drugs of choice in those who cannot take prostaglandins.

Because *H. pylori* and NSAIDs produce additive deleterious effects on the gastric mucosa, it may be possible to destroy *H. pylori* and permit healing of symptomatic gastritis, erosions, or ulceration. If patients must continue taking an NSAID, one should check for the presence of *H. pylori* and treat *H. pylori*–associated gastritis if present (see later). Some patients improve clinically and are able to continue taking the NSAID.

### *Helicobacter pylori* Gastritis

*H. pylori* is the most common cause of gastritis. There are two clinical syndromes: the acute infection (hypochlorhydric gastritis) and the chronic infection (active chronic or Type B gastritis).

#### *Acute Hypochlorhydric Gastritis*

Acute hypochlorhydric gastritis (AHG) should be suspected when gastritis symptoms appear in a previously well person in whom there is no history of alcohol or aspirin ingestion. Three to 7 days after ingestion of the organism, the patient develops epigastric pain; feels bloated, anorectic, and nauseated; and may vomit very mucous clear fluid, which has reduced acidity (pH $>$ 4.0). This fluid also contains reduced amounts of urea because *H. pylori* urease enzyme destroys urea present in the gastric juice. Normal gastric juice contains 2 to 5 mM of urea, whereas the concentration is usually less than 1.0 mM if *H. pylori* is present.

Diagnosis is difficult if *H. pylori* has been suppressed with bismuth or antibacterial therapy. *H. pylori* may be detected at endoscopy, by examination of a gastric mucosal biopsy specimen with a rapid urease test, by histologic examination (Giemsa's stain of antral mucosa), or by a urea breath test (available in some centers).

In the United States, acute *H. pylori* infection is uncommon, but may be expected in children or

young adults who are in intimate contact with another person (spouse, parent, or grandparent) who has *H. pylori*. Thus, new members of families with a history of dyspepsia or peptic ulcer disease are prone to be infected with *H. pylori* and develop the acute syndrome. (Acute hypochlorhydric gastritis is a well-known syndrome in gastroenterology research volunteers infected during acid secretion studies. In addition, the syndrome has been confirmed in experiments in which *H. pylori* was deliberately administered to healthy subjects.)

Symptoms usually subside in 3 to 5 days, after which time chronic gastritis is present in most persons. After the acute stage, acid secretion remains low and the patient may be asymptomatic for months, for years, or indefinitely. When acid secretion returns, dyspeptic symptoms may appear, owing to the action of acid on the inflamed gastric mucosa.

The acute syndrome is usually short-lived and responds to simple measures such as a clear fluid diet, small snacks instead of regular meals, and administration of metoclopramide, antacids, and analgesics (avoid aspirin). Bismuth subsalicylate (Pepto-Bismol in the United States) or bismuth subcitrate (De-Nol)* is specific therapy for *H. pylori* gastritis and suppresses the infection.

### Chronic Gastritis

Chronic gastritis (Type B antral gastritis, ulcer-associated gastritis) is usually caused by *H. pylori* (>80%). It should be emphasized that most major "peptic" lesions in the stomach and duodenum occur in the region colonized by *H. pylori*—i.e., the distal lesser curve, the prepyloric antrum, the pyloric canal, and the first inch of the duodenal bulb. *H. pylori* lesions therefore affect the lower half of the stomach and display the full spectrum of clinical, endoscopic, and histologic findings of gastritis.

Chronic gastritis may be asymptomatic, with or without an endoscopic lesion. This is referred to as nonerosive chronic gastritis in some texts. Regardless of the endoscopic appearance, *H. pylori* gastritis is always associated with histologic changes called active chronic gastritis—i.e., infiltration of the mucosa with inflammatory cells. When pathologists call gastritis acute, they are usually referring to the presence of neutrophils in *H. pylori* gastritis. The changes are histologically acute, but not temporally acute. In some patients, they persist for many years.

Chronic *H. pylori* gastritis may lead to an endoscopically abnormal stomach, ranging from redness, through erosions, to ulcerations. One should remember that all ulcers must pass through the stage of redness and erosion and that most persons with chronic peptic ulcer disease have Type B gastritis, which remains even when the ulcer is healed.

Thus, patients with known or suspected peptic ulcer disease may have gastritis symptoms between episodes of frank ulceration. Typically, nausea is a prominent symptom in symptomatic patients who do not have a visible ulcer.

### Treatment

Symptomatic chronic gastritis due to *H. pylori* should be treated because it does not resolve spontaneously and may predispose the patient to peptic ulceration (20-fold risk) and, possibly, to gastric cancer. Before treatment, diagnosis must be confirmed.

Noninvasive methods of diagnosis include the urea breath test and serology. In the urea breath test, urea labeled with a carbon isotope is given orally. If *H. pylori* is present in the stomach, the urea is broken down by bacterial urease and the carbon isotope is quickly expired as $CO_2$ in the breath. Breath samples are read in a beta counter or a mass spectrometer. Serologic tests will be available in the United States after 1991. They are sensitive screening tests for *H. pylori* antibody. Nearly all infected patients have high levels of IgG and IgA against the bacterium.

More accurate methods of *H. pylori* detection involve endoscopic biopsy of the stomach and testing of a mucosal biopsy specimen with a rapid urease test (fastest and cheapest), culture (most specific, but less sensitive), or histologic Giemsa's staining (most sensitive, but slow and expensive).

Therapy for *H. pylori* is presently imperfect. The organism is always sensitive to bismuth, so bismuth subsalicylate, 525 mg four times daily (Pepto-Bismol regular strength liquid, 30 ml or 2 tablets four times daily on an empty stomach) should be given. Bismuth suppresses *H. pylori* and probably heals any associated mucosal lesions. After bismuth therapy has been commenced, the results of most diagnostic tests (except serologic studies) are normal for 1 to 3 weeks. One should try to confirm the diagnosis of *H. pylori* before instituting therapy.

In patients who cannot take bismuth, suppression of *H. pylori* with amoxicillin (2 grams daily), erythromycin (2 grams daily), or tetracycline (2 grams daily) may be tried. Without bismuth, cure of infection is difficult.

Cure of *H. pylori* infection requires that an antibiotic be given concurrently with bismuth subsalicylate (Table 1). The best antibiotic is metronidazole (Flagyl) in a daily dosage of 20 mg per kg (1 to 1.5 grams per day), with a 70% cure

*Not available in the United States.

TABLE 1. **Dose and Duration of Antibiotics Used in Combination with Bismuth**

| Drug | Dose | Times/ Day | Start Day | Duration of Therapy (days) |
|---|---|---|---|---|
| Metronidazole | 250 mg | 4–6 | 4 | 10 |
| Tetracycline | 500 mg | 4 | 1 | 10–14 |
| Erythromycin | 250–500 mg | 4 | 1 | 10–14 |
| Amoxicillin | 500 mg | 4 | 1 | 10–14 |

*Note:* Triple therapy with bismuth, tetracycline, and metronidazole cures 80 to 90% of *H. pylori* infections. If a metronidazole-resistant organism is present, replace the metronidazole with erythromycin. When bismuth cannot be used, treat with amoxicillin plus metronidazole. Amoxicillin has been associated with *Clostridium difficile* infection in 2% of patients.

rate if given from day 4 to day 10 of a 14-day course of bismuth subsalicylate. Other antibiotics are less successful in combination with bismuth. $H_2$ receptor antagonist therapy or other acid-reducing drugs (e.g., omeprazole) do not impair the efficacy of this therapy and may even enhance it. Addition of a third antibiotic may improve cure rates, but increases antibiotic side effects. Outside the United States, bismuth subcitrate (De-Nol) is used as an alternative to bismuth subsalicylate and gives about a 10% higher cure rate in combination with antibiotics. De-Nol is presently under evaluation in the United States.

### OTHER TYPES OF GASTRITIS

#### Bile Reflux (Alkaline Reflux) Gastritis

In patients who have had previous gastric surgery, dyspeptic symptoms are common. They may complain of bilious vomiting, as well as the usual symptoms of gastritis. Endoscopically, the gastric mucosa may appear quite red. This change is probably a vascular effect, inasmuch as histologic findings of inflammation are not present unless *H. pylori* infection is found. When other causes of gastritis are not present, the histologic examination may show a condition called "foveolar hyperplasia," which is associated with some edema and congestion.

Management principles are similar to those described earlier. First, one should exclude ingested agents as a cause and then exclude *H. pylori* infection (more than half of the patients have this and respond to appropriate therapy). Finally, some patients respond to surgical intervention with a Roux-en-Y bile diversion.

#### Hypertrophic Gastritis

This is a rare cause of diarrhea and protein loss in which massive hypertrophy of the gastric mucosa occurs and albumin is lost from the gastric mucosa. The cause is unknown. Diagnosis is by endoscopy and biopsy. In children, *H. pylori* can also cause excessive protein loss from the gastric mucosa.

### FURTHER READING

The understanding of gastritis has advanced a great deal since *H. pylori* was recognized as the most common cause. Review articles on *H. pylori* have appeared (Dooley CP, and Cohen H: The clinical significance of *Campylobacter pylori.* Ann Intern Med *108:*70–79, 1988; Peterson, WL: *Helicobacter pylori* and peptic ulcer disease. N Engl J Med *324:*1043–1048, 1991; and Hendrix TR, and Yardley JH: *Campylobacter gastritis* and associated disorders. South Med J *81:*859–862, 1988).

# ACUTE AND CHRONIC VIRAL HEPATITIS

method of
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Most commonly an infection by one of the hepatitis viruses (A, B, C, D, or E) is asymptomatic, and these individuals do not appear in physicians' offices or clinics. Among those who do develop clinical symptoms, the complaint may be nothing more than slight fatigue. Some have more severe problems, such as significant lassitude, nausea, and vomiting, with or without jaundice. Rarely, patients may progress to a state of overt liver failure, with coagulopathy and encephalopathy; this disease (fulminant hepatitis) has a high associated mortality.

Although some supportive measures can be provided until the disease runs its course, the major interventional thrust is to keep others from contracting the infection. Because the prophylactic measures differ for different viruses, each of these infections must be diagnosed early.

"Acute hepatitis" suggests a self-limited episode of symptoms (usually including jaundice), whereas "chronic hepatitis" may be perceived as a disease that inexorably progresses to end-stage liver disease (cirrhosis). However, the contrast is not that sharp. Patients with chronic viral hepatitis are usually asymptomatic; although some of them do ultimately (after many years or decades) progress to liver failure (variceal bleeding, ascites, chronic hepatic encephalopathy, etc.) or liver cancer, many others live normal lives, never bothered by any such hepatic problems. It is difficult to predict which patients will progress; all patients with chronic hepatitis have biochemical (abnormal aminotransferases) and histologic (chronic per-