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Gastritis and Peptic Ulcer Disease

Method of
Barry J. Marshall, MD

Gastritis

Gastritis literally means inflammation of the stomach. Gastritis is a nonspecific term because it can be used to describe:

- Symptoms related to the stomach
- An endoscopic appearance of the gastric mucosa
- Histologic change characterized by infiltration of the epithelium with inflammatory cells such as polymorphonuclear leukocytes (PMNs)

The last description is the most correct.

CLINICAL GASTRITIS

In lay terms, nausea and vomiting with epigastric pain might be called "an attack of gastritis," even though the exact pathology affecting the stomach is unknown. Use of the term gastritis in this situation is to be discouraged as symptoms correlate rather poorly with actual pathology present in the stomach.

ENDOSCOPIC GASTRITIS

Mucosal Redness (Erythema)

The appearance of the mucosa at endoscopy does not correlate well with the histologic diagnosis determined from a biopsy. Confusion can arise because almost every abnormality of the gastric mucosa is called gastritis by endoscopists.

The normal color of the gastric mucosa is pink, similar to the palm of your hand. An appearance of redness probably represents increased capillary blood flow in the mucosa, but does not necessarily mean that inflammatory cells are present. When bile is present, the redness often appears to be diffusely present throughout the stomach.

Redness (erythema) in the gastric mucosa may be localized to the antrum or the corpus. It may be homogeneous or mottled, or present in spots from petechia size to a few millimeters. Sometimes redness is present on the top of the gastric folds of the corpus. Often, red streaks radiate upward from the pylorus. In all cases it is appropriate for the endoscopist to refer to the appearance as *endoscopic gastritis*, accompanied by a description of gastric mucosa. General treatment of endoscopic gastritis is to treat the patient's symptoms, usually with acid reduction therapy and avoidance of foods or medications that might aggravate the problem. Specific treatment of endoscopic gastritis depends on a histologic diagnosis. Therefore, biopsies of the gastric mucosa are necessary.

Surface Irregularity (Chicken Skin, Gooseflesh, Cobblestones)

The cause of small lumps on the antral mucosa, which are referred to as *chicken skin*, *gooseflesh*, and *cobblestones*, is usually *Helicobacter pylori* gastritis.

Erosive Gastritis

Erosions are breaks in the mucosa that do not extend beyond the muscularis mucosa. All lesions less than 1 mm deep are erosions. The distinction between ulcers and erosions might not have much effect on patient management, because both can bleed and both are usually healed with acid blocking therapy.

Umbilicated lumps may be a variant of erosive gastritis. As with all erosive mucosal lesions of the gastrointestinal (GI) tract, viral causes should be considered in immunosuppressed patients.

Atrophic Gastritis and Gastric Atrophy

After many years of chronic gastritis, the gastric mucosa can become atrophic (i.e., thin and translucent), with the submucosal veins easily visible. In severe cases, the folds normally present in the upper half of the stomach (the corpus) are diminished or absent (gastric atrophy). Acid secretion diminishes and the condition predisposes to adenocarcinoma of the stomach. *H. pylori* and pernicious anemia are the two main causes.

Hypertrophic Gastritis (Ménétrier's Disease)

Rarely, gastric folds are massively increased in size because of hyperplasia and hypertrophy of the specialized acid-secreting mucosa. Excessive mucus secretion leads to a syndrome of hypoalbuminemia with diarrhea, edema, or a hypercoagulable state. *H. pylori* infection is one cause, other causes are idiopathic (so far).

Portal Gastropathy and Angiodysplasia

The red lesions caused by portal gastropathy and angiodysplasia give a pattern of *snake skin* and *watermelon stomach*, respectively, when severe. They may cause GI blood loss, but are usually asymptomatic. The former is associated with portal hypertension. The latter is idiopathic and is treated, when necessary, with argon plasma coagulation.

HISTOLOGIC GASTRITIS

Histologic gastritis is present when inflammatory cells infiltrate the mucosa. Diagnostic biopsies for detection of gastritis should be taken from intact mucosa, away from any focal lesion. At least one antrum and one corpus biopsy should be examined by histology because diseases can selectively affect only the mucus-secreting mucosa of the antrum, or only the parietal cell mucosa of the corpus.

Rakel and Bope: *Conn's Current Therapy 2006.*

If mononuclear cells are increased, chronic gastritis is present. If the PMNs are also increased, the gastritis is termed as active. In typical *H. pylori* infection, PMNs infiltrate the necks of the mucus-secreting glands of the gastric antrum causing active chronic gastritis.

Helicobacter pylori Gastritis

In the first week after infection, many PMNs and a few eosinophils infiltrate the mucosa. These are gradually replaced with the mononuclear cells. The presence of lymphoid follicles is called mucosa-associated lymphoid tissue (MALT). Rarely, MALT may become autonomous to form a low-grade, B-cell lymphoma called MALT lymphoma. When gastric tissue exists in the duodenal bulb (normally present in approximately 60% of persons), *H. pylori* may also colonize that location leading to active duodenitis.

When *H. pylori* is eradicated with antibiotics, PMNs disappear in a week or so, but reduction in the mononuclear cells is slow, often leaving mild chronic gastritis several years after *H. pylori* has disappeared.

In most countries with a high prevalence of *H. pylori*, gastric cancer is common, although diet probably also modulates the risk so that the association is not universal. Because *H. pylori* causes peptic ulcer and gastric cancer, nearly everyone with *H. pylori* chooses to be treated with antibiotics.

Non-*Helicobacter pylori* Gastritis

Because *H. pylori* is the most common cause of gastritis, and perhaps the most easily treated, non-*H. pylori* gastritis must be diagnosed with caution. Usually the *H. pylori* has been missed because of low numbers of organisms. This occurs when patients have recently taken antibiotics, or are taking proton pump inhibitors (PPIs), or have a patchy infection caused by intestinal metaplasia in the stomach (to which *H. pylori* cannot adhere). Therefore, as well as taking biopsies for urease test, histology, and culture, the physician should check serology before claiming a patient has *H. pylori*-negative histologic gastritis. Laboratory-based serologic tests are quite sensitive so can be used to confirm that *H. pylori* is not present and that the negative biopsy diagnosis is correct.

Rare causes of *H. pylori*-negative histologic gastritis are Crohn's disease, eosinophilic gastritis, gastric MALT lymphoma, as well as (very rarely) other viral and bacterial infections.

NONSTEROIDAL-INDUCED EROSIVE GASTRITIS AND ULCERS

Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) are corrosive. Aspirin and NSAIDs inhibit prostaglandin synthesis, which is essential for maintenance of the mucus and bicarbonate barrier in the stomach. The resulting gastric erosions are often asymptomatic but sometimes lead to gastric ulcer or duodenal ulcer.

The harmful effects of NSAIDs and *H. pylori* are not synergistic because *H. pylori* boosts the prostaglandin levels, thus partially negating the deleterious effect of the NSAID.

Eradication of *H. pylori* before or at the beginning of NSAID therapy is worthwhile. Once NSAID patients have developed an ulcer, provided that treatment of the ulcer with a PPI is continued, eradication of *H. pylori* is neither urgent nor essential.

DYSPEPSIA VERSUS GASTRITIS

Dyspepsia is defined here as discomfort in the upper half of the abdomen and lower chest that is somehow related to food. Symptoms and descriptions vary widely so the patient's ethnicity needs to be taken into account when taking a history.

Regurgitation refers to reflux of gastric contents into the mouth without discomfort. Gnawing is a feeling halfway between hunger and nausea, in which case the patient tends to have small snacks to ease the symptom without vomiting. Fullness and bloating are feelings of distension that contribute to early satiety in some patients so that they are unable to finish a normal-sized meal. Burning epigastric and lower thoracic pain that is quickly relieved by antacid is likely to be caused by gastroesophageal reflux disease (GERD), although it is wise to exclude a cardiac cause.

In general, dyspepsia correlates poorly with endoscopic findings. When endoscopy is freely available at no cost to the patient, endoscopy quickly defines a management plan and gives greater patient satisfaction, according to questionnaires given to patients 12 months later. However, endoscopy-first strategies are about 20% more expensive.

The alternative strategy is called test and treat, where patients are selected for initial endoscopy only if they have alarm signs, are older than 50 years of age, or are in a high-risk category for gastric cancer. Alarm signs are dysphagia, vomiting, weight loss, blood in the stool, a family history of gastric cancer, an abdominal mass, or virtually any abnormal laboratory test.

When dyspepsia is diagnosed but there is no peptic ulcer, the condition is called nonulcer dyspepsia (NUD) or functional dyspepsia. Many NUD patients actually have GERD. If GERD is suspected, a 7-day trial of double-dose PPI therapy is worthwhile.

For patients not obviously suffering from GERD, the possibility of peptic ulcer should be considered. Because most peptic ulcers are related to *H. pylori* infection, noninvasive tests for *H. pylori* can be used to determine ulcer risk. Patients who are *H. pylori*-negative on serology are unlikely to have peptic ulcer. This means that they can be managed by trial and error until symptoms respond to therapy. On the other hand, patients who are *H. pylori*-positive on serology should be regarded as possible ulcer candidates and should have the bacterium eradicated as the first step in management.

For patients who actually do have an ulcer, antibiotic therapy for *H. pylori* leads to clinical cure in approximately 70% of cases. Of the 30% who do not respond

clinically, 50% have persistent *H. pylori* and the remainder have *H. pylori*-negative dyspepsia (GERD, etc.). To differentiate these groups it is necessary to confirm cure of *H. pylori* in all patients who do not completely respond to *H. pylori* eradication. Cure is confirmed with a urea breath test. Follow-up breath test is also necessary in all patients with known peptic ulcer because these patients are at risk of ulcer relapse, with all its possible complications, if *H. pylori* persists. Because a nonendoscopic strategy does not separate ulcer from nonulcer patients at the beginning, there is a case for confirmation of *H. pylori* eradication in all patients, so that ulcer relapse never occurs.

GASTROESOPHAGEAL REFLUX DISEASE

Gastroesophageal reflux disease and symptoms related to the esophagus may be treated initially with acid reduction therapy, as needed. Antacid is used for immediate relief, and histamine-$_2$ receptor antagonists (H_2RAs) or PPIs may be given at the same time to diminish acid secretion over the next few hours. Combinations of these two are available as over-the-counter (OTC) medications in the United States. If dysphagia is present (difficulty swallowing), immediate endoscopy is advised, as this could be an early symptom of esophageal cancer or an acid-induced stricture.

If GERD symptoms do not completely respond, or if the patient requires the above treatment on a daily basis, then endoscopy is required. Endoscopy will indicate whether the patient's symptoms correlate with the disease severity. It is important to control both clinical and endoscopic GERD, because continued heartburn raises the lifetime risk of esophageal adenocarcinoma.

GERD patients should be given the following commonsense advice. Eat smaller meals, control obesity, and avoid tight clothing around the abdomen. Avoid liquids with meals, especially tea, coffee, colas, and beer. Do not eat large meals during the working day. Avoid bending or heavy work after meals. Eat the evening meal at least 3 hours before bedtime. Raise the head of the bed and sleep on the left side. Tablets that might damage the esophagus (aspirin, doxycycline, alendronate) should be taken before meals to ensure that they do not linger in the esophagus.

In spite of the above management, many patients continue to have symptoms, and endoscopic assessment reveals acid-induced esophageal damage. In this case lifestyle measures are rarely curative and long-term acid reduction with PPI is required. Since PPIs have long half-lives, once-daily therapy is usually sufficient. For severe GERD, start at double the usual dose then decrease after 3 months to a single daily maintenance dose. The aim of medical therapy is complete control of acidic symptoms. Advise patients that long-term medical treatment is usually necessary.

OTHER DYSPEPSIA

Because chronic dyspeptic symptoms unrelated to GERD or ulcer do not have a specific cause or defined therapy, it is worthwhile initially to search for another, more treatable diagnosis. Be certain to exclude cardiac causes of chest pain. Intermittent pain could be esophageal spasm, which can be diagnosed with esophageal manometry. Treat with PPI to abolish any GERD component, smooth muscle relaxants for the acute episode, and calcium channel blockers (CCBs). Note that therapy for angina is quite similar, so cardiac disease needs to be ruled out before treating esophageal spasm. Some of the above medical therapy causes side effects that make treatment hardly worthwhile in patients with intermittent spasm.

EPIGASTRIC DYSPEPSIA AND GASTROPARESIS

Always try to find the definitive causes of epigastric dyspepsia and gastroparesis, as this allows better planning of therapy and more accurate prognosis. Endoscopy often rules out any macroscopic lesion such as an ulcer or a tumor, allowing trials of medical therapy to proceed.

If the patient has symptoms of GERD, but does not respond completely to therapy, he/she may be a rapid metabolizer of PPI. If starting with once-daily omeprazole (Prilosec), double the dose to twice daily, use a more powerful drug (esomeprazole [Nexium]), choose one with a longer half-life (pantoprazole [Protonix]), or use a drug that is less affected by metabolizer status (rabeprazole [AcipHex]). At endoscopy, avoid PPI on the day of the test and measure gastric-juice pH to see if the patient maintains a pH above 4 for the complete 24 hours after a dose. If pH is above 4.0, then the cause of the continued symptoms might not be acid reflux.

Symptoms of nausea and/or vomiting are unlikely to be caused by esophageal disease. Gastric mucosal problems or gastric outlet obstruction need to be considered. The two should be considered separately because disorders such as acute viral gastroenteritis and food poisoning cause nausea, but motility is normal. Similarly, patients with chronic gastroparesis are worse off if they also have a mucosal disease such as *H. pylori* causing the nausea.

If *H. pylori* is present it should be treated. If patients cannot take antibiotics because of nausea, try to settle them with high-dose PPI as this will suppress *H. pylori* in 50% of cases.

Delayed gastric emptying (gastroparesis) may be diagnosed with an isotope gastric emptying study. When present, gastroparesis is usually a chronic disorder with relapses and remissions. Eradication of *H. pylori* often decreases nausea and settles the condition somewhat, but relapses still occur in most patients. Promotility agents such as metoclopramide (Reglan) and cisapride (Propulsid)* should be used (cisapride is no longer available in the United States because it has caused fatal arrhythmias). Small doses of erythromycin[1] (25 mg per day before meals) may improve gastric peristalsis as this drug is a motilin agonist. As long as obstruction is not present, a soft or liquid diet will usually empty from

*Investigational drug in the United States.
[1]Not FDA approved for this indication.

the stomach, even when motility is poor. Posturing the patient to stay vertical after meals, with an inclination toward the right side, should help gastric contents drain through the pylorus. Avoid uncooked vegetables because skins and salad leaves take many hours to leave the stomach. A low-residue diet is preferred whenever motility is impaired.

Management of Dyspepsia

I usually include a *test and treat* strategy for *H. pylori* as part of any dyspepsia management plan. I also search for and treat GERD with PPI. Lesser symptoms of GERD or vague dyspepsia may respond (if needed) to H_2 blocker such as ranitidine (Zantac), 150 mg once or twice daily. In addition, patients can carry antacid tablets for immediate relief. Antacid-H_2RA combinations are available OTC in the United States, and these are very effective. The complete algorithm for management of dyspepsia is shown as Figure 1.

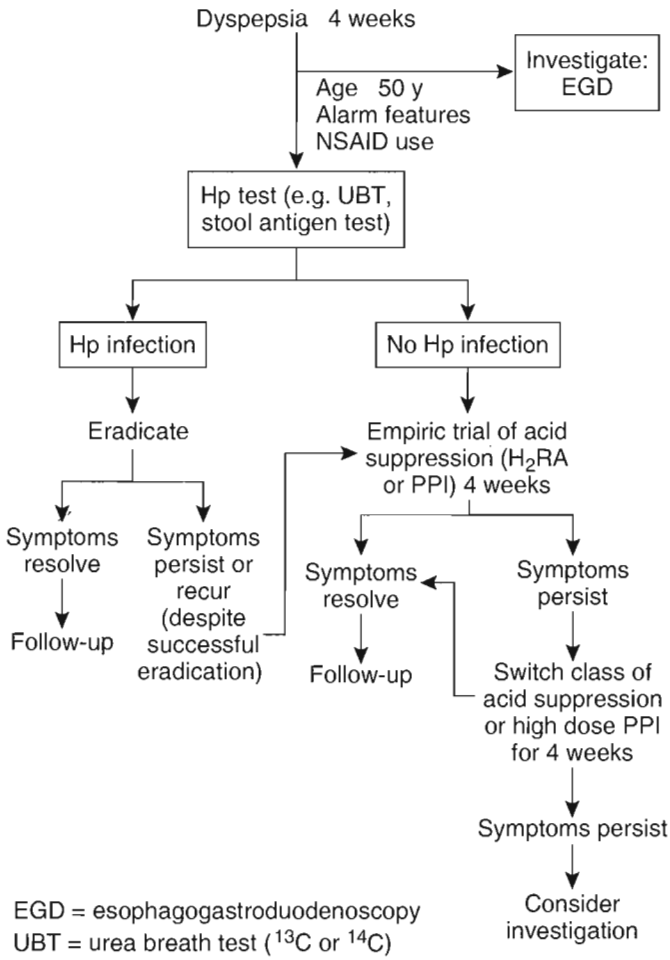

FIGURE 1. Management of uninvestigated dyspepsia.

Peptic Ulcer

Peptic ulcer is usually caused by *H. pylori*, NSAIDs, or a combination of the two. Rarely, hyperacidity is caused by a gastrinoma (Zollinger-Ellison syndrome) in which case a cause may not be found until serum gastrin is noted to be elevated. In any ulcer situation, resuscitate the patient and control acute bleeding endoscopically. At the first endoscopy, diagnostic biopsies should be taken for *H. pylori* (one urease test, one antrum, and one corpus for histology). If *H. pylori* is present, initiate treatment. *H. pylori* serology should be sent if the bacterium is not detected on biopsy because sometimes the acutely ill patient has taken medication, which suppresses *H. pylori* in the gastric mucosa, but has not eradicated the bacterium.

Ulcer patients without *H. pylori* usually have NSAIDs as the cause of the ulcer. In patients who have both *H. pylori* and NSAIDs, the sensible approach is to treat both. In most cases the NSAIDs will have been ceased and the patient given intravenous PPI, so antibiotic therapy is not the most important part of the acute therapy. Adding intravenous amoxicillin to an *H. pylori*-positive patient is an option to improve the healing rate of a dangerous ulcer. The normal oral *H. pylori* therapy can be completed a few days later when the patient tolerates a normal diet.

Peptic ulcers almost always heal once the initiating factor has been removed. However, it is usual to give H_2RA or PPI for 8 weeks to ensure a symptom-free healing period. During this time the *H. pylori* can be eradicated. At the end of 8 weeks, PPI can be changed to H_2RA, and a follow-up urea breath test can be done to confirm eradication of the bacterium. A stool antigen test is an alternative.

In patients who are unable to cease their NSAIDs, the drug should be changed to a cyclooxygenase (COX)-2 selective agent. In addition, full-dose PPI should be continued long term. Most ulcers will then heal and not relapse. Low-dose aspirin may remove the benefit of COX-2 selective NSAIDs so the relative benefits of aspirin should be reviewed in all patients. Prostaglandins are not a first choice ulcer therapy because of side effects, such as cramps (in women) and diarrhea; however, they do specifically protect against erosive gastritis and peptic ulcer caused solely by NSAIDs.

TREATMENT FOR *HELICOBACTER PYLORI*

In vitro testing does not correlate with in vivo success, so treatment combinations should be used that have been proven to work in each individual country. Treatment for less than 7 days has a low cure rate, but cure rates from day 7 to day 14 are similar, and more than 14 days of treatment is usually unnecessary. The first drug to use is a PPI in order to render the gastric pH neutral. This enhances the cure rate for the second drug, which is usually amoxicillin (Amoxil). Clarithromycin (Biaxin) is given as the third drug. Treatment and doses vary in each country; doses in Table 1 are typical for the United States and Australia.

TABLE 1 Treatment Options for *Helicobacter pylori*

Group		Duration
A*	**BISMUTH**	
	Ranitidine bismuth citrate[2] (RBC) 400 mg bid	14 days
	Bismuth subsalicylate (Pepto-Bismol)* 525 mg (2 tabs) qid	14 days
	Bismuth subcitrate[1,†] (De-Nol) 120 mg (1 tab) qid	14 days
B	**PENICILLIN**	
	Amoxicillin 1 g bid	7, 10 or 14 days
C	**MACROLIDE**	
	Clarithromycin (Biaxin) 500 mg bid	7, 10 or 14 days
	Josamycin[1,2,†] 1000 mg bid	7 days
D	**NITROIMIDAZOLE**	
	Metronidazole (Flagyl)[1] 500 mg bid or tid	7, 10 or 14 days
	Tinidazole[1,2] 1000 mg qd	7, 10 or 14 days
E	**TETRACYCLINE**	
	Tetracycline[1] 500 mg qid	14 days
F	**QUINOLONE**	
	Ofloxacin (Floxin)[1] 1000 mg[3] qd	7-14 days
	Levofloxacin (Levaquin) 500 mg qd	7-14 days
	Ciprofloxacin (Cipro)[1] 500 mg bid	14 days
G	**NITROFURAN**	
	Furazolidone (Furoxone)[1] 100 mg qid	7, 10 or 14 days
H	**ANSAMYCIN**	
	Rifabutin (Mycobutin)[1] 150 mg bid	14 days
I	Proton pump inhibitors (use double a normal dose)	
	Omeprazole (Prilosec) 20 mg bid	
	Esomeprazole (Nexium) 40 mg bid	
	Lansoprazole (Prevacid) 30 mg bid	
	Pantoprazole (Protonix) 40 mg bid	
	Rabeprazole (AcipHex) 20 mg bid	

[1]Not FDA approved for this indication.
[2]Not available in the United States.
[3]Exceeds dosage recommended by the manufacturer.
*When Pepto-Bismol is not available, substitute De-Nol, 1 tablet qid. RBC is not available in all countries.
Side effects are likely as doses of clarithromycin, metronidazole, and furazolidone increase.
Treatment combination priorities are normally: IBC → IBD → IBEG. For penicillin allergy choose ICD or IAED → IFH.
†Investigational drug in the United States.
Abbreviations: bid = twice daily; qd = once daily; qid = four times daily; tid = thrice daily.

One month after completing therapy, ensure that the patient is not taking PPI for 7 days, and then perform a urea breath test (UBT). Serology remains positive after treatment so it is not useful to prove eradication. If the UBT shows persistent infection, re-treat with a different regimen. As a second therapy, you may use PPI and amoxicillin again, since *H. pylori* does not develop resistance to amoxicillin. The third drug should change to metronidazole (Flagyl).[1] Always repeat the UBT after therapy.

If two therapies fail, the *H. pylori* is resistant to both clarithromycin[1] and metronidazole[1]; therefore, alternatives must be chosen. In addition, the motivation of the patient and physician need to be reassessed as compliance may be an issue. A third treatment changes the PPI to a much higher dose and/or a drug less affected by the metabolizer status of the patient. Rabeprazole (AcipHex), 20 mg twice daily, might be a good choice. Amoxicillin is given as before. In addition, add ofloxacin (Floxin)[1] or levofloxacin (Levaquin)[1] plus rifabutin (Mycobutin),[1] with all four drugs being given for 14 days.

An alternative and inexpensive regimen is bismuth (Pepto-Bismol) with tetracycline,[1] metronidazole (Flagyl),[1] and a PPI. This is also called bismuth quad therapy. It is useful also when patients are allergic to penicillin. Allergic patients might also try PPI with clarithromycin (Biaxin)[1] and metronidazole[1] as the initial therapy. If patients are unable to take oral antibiotics because of nausea, start with a harmless drug such as PPI or bismuth, and then add tetracycline[1] or amoxicillin (Amoxil). After 1 week, by which time symptoms have improved, add the clarithromycin[1] or metronidazole.[1] If all else fails, high-dose PPI will suppress *H. pylori* in 30% to

[1]Not FDA approved for this indication.

[1]Not FDA approved for this indication.

50% of patients. Alternatively, because biopsy and culture with antibiotic sensitivity testing are necessary, refer patients to a gastroenterologist specializing in *H. pylori*.

After *H. pylori* eradication, symptoms are still present in most patients, but improve gradually over 3 to 6 months. GERD symptoms may temporarily worsen, so I treat these symptoms with H_2 blockers initially because this does not interfere with the follow-up UBT. If symptoms persist then the patient is managed as *H. pylori*-negative dyspepsia as per the algorithm in Figure 1.

Acute and Chronic Viral Hepatitis

Method of
Fritz-Henry Volmar, MD, and Dilip Moonka, MD

Outbreaks of acute hepatitis and the ever-increasing number of patients diagnosed with chronic liver disease, cirrhosis, and hepatocellular carcinoma continue to fuel interest in the field of viral hepatitis. Viral hepatitis is the leading cause of liver disease. The past decade has yielded significant advances in our understanding of the natural history and molecular biology of the hepatotrophic viruses. Expanding efforts to prevent and treat viral hepatitis have led to the development of effective vaccines and therapies. The current section will focus on these advances as well as identify areas where further progress is necessary.

Hepatitis can be caused by a number of viruses. The overwhelming majority of cases of viral hepatitis are caused by the human hepatotropic viruses designated by the letters A, B, C, D, and E (Table 1). Although each of these can cause acute hepatitis, the hepatitis A virus (HAV) and hepatitis E virus (HEV) infections do so exclusively. The hepatitis B virus (HBV) and the hepatitis C virus (HCV) primarily lead to morbidity in that they cause chronic infection and chronic liver disease. Less common causes of viral hepatitis include herpes simplex, Epstein-Barr, cytomegalovirus, coxsackie, echovirus, adenovirus, rubella, and the mumps virus. Although these viruses will not be discussed in any detail, they should be included in the differential diagnosis of patients with acute hepatitis especially in those with compromised immune systems. It should also be noted the term hepatitis F was applied to a putative virus that was subsequently shown to be artifact. Hepatitis G virus (HGV) is present in 1% to 2% of the U.S. population but does not clearly cause disease in humans. Its primary distinction is that patients co-infected with HIV and HGV appear to have a more indolent form of the HIV infection.

Acute Hepatitis

All of the five lettered viruses listed previously can cause acute hepatitis, which is generally a self-limited illness. Although the majority of patients remain asymptomatic, those who develop symptoms will often attribute them to a nonspecific viral illness especially if jaundice is absent. The illness is clinically silent in most infected children and is more likely to be symptomatic in the elderly and immunocompromised. Symptomatic patients may complain of fever, malaise, fatigue, anorexia, nausea with or without vomiting, and abdominal discomfort localizing to the right-upper quadrant. Jaundice, if present, may be associated with darkening of the urine or pale stools. These symptoms will typically last several weeks. Rarely, acute hepatitis may lead to severe hepatic dysfunction manifesting as encephalopathy and coagulopathy. Mortality from fulminant hepatic failure is high, and the degree of liver injury may necessitate liver transplantation.

Chronic Hepatitis

Patients who have persistent symptoms or signs of liver disease 6 months after the acute infection are classified as having chronic hepatitis. As mentioned earlier, this is seen with HBV, HCV, as well as HDV. The clinical course of chronic viral hepatitis is highly variable and depends on viral and host factors. Persistent chronic inflammation can result in fibrosis, which can lead to cirrhosis and

TABLE 1 Common Hepatotropic Viruses

	HAV	HBV	HCV	HDV	HEV
Size	27-32 nm	42 nm	55 nm	35 nm	32 nm
Genome	ssRNA	dsDNA	ssRNA	ssRNA	ssRNA
Transmission	Fecal–oral	Percutaneous, sexual	Percutaneous, sexual	Percutaneous, sexual	Fecal–oral
Incubation	15-45 d	60-180 d	15-160 d	21-140 d	15-60 d
Acute infection	Yes	Yes	Yes	Yes	Yes
Chronic liver disease	No	<5% adults, >90% infants	70%-85%	Superinfection ~80%, coinfection <5%	No

Abbreviations: dsDNA = double-stranded DNA; HAV = hepatitis A virus; HBV = hepatitis B virus; HCV = hepatitis C virus; HDV = hepatitis D virus; HEV = hepatitis E virus; ssRNA = single-stranded RNA