

- The vowels (hepatitis A and E) never cause chronic hepatitis, only Acute hepatitis, except HEV in immunocompromised hosts and pregnant females.
- Only the consonants (hepatitis B, C, D) have the potential to cause chronic disease (C for consonant and for chronic).
- Hepatitis B can be transmitted by blood, birthing, and “bonking” (as they say in the United Kingdom).
- Hepatitis C is the single virus that is more often chronic than not (almost never detected acutely; 80% or more of patients develop chronic hepatitis, 20% of whom will develop cirrhosis).
- Hepatitis D, the delta agent, is a defective virus, requiring hepatitis B co-infection for its own capacity to infect and replicate.
- Hepatitis E is endemic in equatorial regions and frequently epidemic.
- The inflammatory cells in both acute and chronic viral hepatitis are mainly T cells; it is the pattern of injury that is different between the two time courses, not the nature of the infiltrate.
- Biopsy assessment in chronic viral hepatitis is most important for grading and staging of disease, which are used to decide whether a patient undergoes often arduous antiviral treatments.
- Patients with long-standing HBV or HCV related cirrhosis are at increased risk for the development of hepatocellular carcinoma.

### Bacterial, Parasitic, and Helminthic Infections

**A multitude of organisms can infect the liver and biliary tree, including bacteria, fungi, helminths and other parasites, and protozoa.** Several bacteria can infect the liver directly, including *Staphylococcus aureus* in toxic shock syndrome, *Salmonella typhi* in typhoid fever, and *Treponema pallidum* in secondary or tertiary syphilis. Bacteria may also proliferate in the biliary tree especially when outflow is compromised by partial or complete obstruction. The intra-biliary bacterial composition reflects the gut flora, and the acute inflammatory response within the intrahepatic biliary tree is called *ascending cholangitis*.

Bacteria may give rise to abscesses by spreading from extrahepatic sites, through the vascular supply, or from adjacent infected tissues. Liver abscesses are associated with fever and, in many instances, right upper quadrant pain and tender hepatomegaly. Jaundice may result from extrahepatic biliary obstruction. Although antibiotic therapy may control smaller lesions, surgical drainage is often necessary for the larger lesions. In the past almost 90% of the patients succumbed to the disease, but with early recognition and management, as many as 90% of patients can survive. Extrahepatic bacterial infections, particularly sepsis, can induce mild hepatic inflammation and varying degrees of hepatocellular cholestasis (see later).

Fungi (e.g., histoplasmosis) and mycobacteria can also infect the liver in disseminated disease, with histology showing classical granulomas. Organisms are usually not visible histologically, even with special stains, although serologic studies and tissue or blood cultures can often identify the causative agent.

Parasitic and helminthic infections are major causes of morbidity worldwide, and the liver is frequently involved (Chapter 8). These diseases include malaria, schistosomiasis, strongyloidiasis, cryptosporidiosis, leishmaniasis, echinococcosis, amebiasis, and infections by the liver flukes *Fasciola hepatica*, *Opisthorchis* species, and *Clonorchis sinensis*. *Schistosomiasis*, most commonly found in Asia, Africa, and South America, especially in those areas where the water contains numerous freshwater snails as a vector, is particularly associated with insidious sequelae of chronic liver disease. The liver flukes, most common in Southeast Asia, are notorious for causing a very high rate of cholangiocarcinoma. *Hydatid cysts* are usually caused by echinococcal infections (Chapter 8). They often have calcifications in the cyst walls which may aid radiologic diagnosis. In developed countries, hydatid cysts are uncommon. Cystic liver degeneration or abscesses can be caused by amebas and other protozoal and helminthic organisms. The incidence of amebic infections is low in developed countries and is usually found in immigrants from endemic regions.

### Autoimmune Hepatitis

**Autoimmune hepatitis is a chronic, progressive hepatitis with all the features of autoimmune diseases in general: genetic predisposition, association with other autoimmune diseases, presence of autoantibodies, and therapeutic response to immunosuppression.** Strong HLA-associations for autoimmune hepatitis support a genetic predisposition. In Caucasians, there is a frequent association with DRB1\* alleles. As with most other autoimmune diseases, the mechanistic basis of the HLA association are not clear. Triggers for the immune reaction may include viral infections or drug or toxin exposures.

**Clinicopathologic Features.** The annual incidence is highest among white northern Europeans at 1.9 per 100,000, but all ethnic groups are susceptible. There is a *female predominance* (78%). The diagnostic features are summarized in [Table 18-4](#). As can be seen, a point system is used for the diagnosis of definite and probable autoimmune hepatitis. *Autoimmune hepatitis is classified into types 1 and 2, based on the patterns of circulating antibodies.* Type 1, more common in middle-aged to older individuals, is characterized by the presence of antinuclear (ANA), anti-smooth muscle actin (SMA), anti-soluble liver antigen/liver-pancreas antigen (anti-SLA/LP) antibodies, and less commonly, anti-mitochondrial (AMA) antibodies. In type 2, usually seen in children and teenagers, the main serologic markers are anti-liver kidney microsome-1 (anti-LKM-1) antibodies, which are mostly directed against CYP2D6, and anti-liver cytosol-1 (ACL-1) antibodies.

### MORPHOLOGY

Although autoimmune hepatitis shares patterns of injury with acute or chronic viral hepatitis, the time course of histologic progression differs. In viral hepatitis, fibrosis typically follows many years of slowly accumulating parenchymal injury, whereas in autoimmune hepatitis, there is an early phase of severe