Table 18-4 Simplified Diagnostic Criteria (2008) of the International Autoimmune Hepatitis Group

		Points*
Autoantibodies	ANA or ASMA or LKM > 1:80	2
	ANA or ASMA or LKM > 1:40	1
	SLA/LP Positive (>20 units)	0
IgG (or gamma-globulins)	>1.10 times normal limit	2
	Upper normal limit	1
Liver histology†	Typical for autoimmune hepatitis	2
	Compatible with autoimmune hepatitis	1
	Atypical for autoimmune	0
Absence of viral hepatitis	Yes	2
	No	0

*Definite autoimmune hepatitis (AIH): P7; probable AIH: P6.
†Typical: (1) Interface hepatitis, lymphocytic/lymphoplasmacytic infiltrates in portal tracts and extending in the lobule; (2) emperipolesis (active penetration by one cell into and through larger cell); (3) hepatic rosette formation.
Compatible: Chronic hepatitis with lymphocytic infiltration without features considered typical.
Atypical: Showing signs of another diagnosis like NAFLD.
ANA, antinuclear antibody; ASMA, anti–smooth muscle actin; LP, liver pancreas; LKM, anti-liver kidney microsomal antibodies; SLA, soluble liver antigen; IgG, immunoglobulin G; AIH, autoimmune hepatitis.
Adapted from Hennes EM, et al. Simplified criteria for the diagnosis of autoimmune hepatitis. Hepatology 48:169-176; 2008.

parenchymal destruction followed rapidly by scarring. Features considered typical of autoimmune hepatitis include:

- Severe necroinflammatory activity indicated by extensive interface hepatitis or foci of confluent (perivenular or bridging necrosis) or parenchymal collapse
- Plasma cell predominance in the mononuclear inflammatory infiltrates (Fig. 18-17)
- Hepatocyte "rosettes" in areas of marked activity

The disease may be rapidly progressive or indolent, both giving rise eventually to liver failure. Clinical evolution correlates with a limited number of histologic patterns, any of which may be seen at the time of initial diagnosis:

- Very severe hepatocyte injury with widespread confluent necrosis, but little scarring; this pattern is often seen as symptomatic acute hepatitis and represents the first sign of disease.
- A mix of marked inflammation and some degree of scarring, seen in early or later stage disease
- Burned-out cirrhosis, with little necroinflammatory activity, that has been preceded, presumably, by years of subclinical disease

An acute appearance of clinical illness is common (40%) and a fulminant presentation with hepatic encephalopathy within 8 weeks of disease onset may also occur. The mortality of patients with severe untreated autoimmune hepatitis is approximately 40% within 6 months of diagnosis and cirrhosis develops in at least 40% of survivors. In general, prognosis is better in adults than in children, possibly due to delay in diagnosis in the pediatric population. Hence, diagnosis and intervention are imperative. Immunosuppressive therapy is usually successful, leading to remissions in 80% of patients that permits long term survival. In end stage disease, liver transplantation is indicated. Ten-year survival rate after liver transplant is 75%, but recurrence in the transplanted organ may affect 20% of transplanted patients.

In a small subset of patients, there may be overlap with other autoimmune liver diseases, in particular primary biliary cirrhosis or, less commonly, primary sclerosing cholangitis. *Diagnosis of "overlap" syndromes requires full display of both clinical and histologic features of autoimmune hepatitis and the other, concomitant disease.*

KEY CONCEPTS

Autoimmune Hepatitis

- There are two primary types of autoimmune hepatitis:
  - Type 1 autoimmune hepatitis is most often seen in middle-aged women and is most characteristically associated with antinuclear and anti–smooth muscle antibodies (ANA and ASMA)
  - Type 2 autoimmune hepatitis is most often seen in children or teenagers and is associated with anti-liver kidney microsomal autoantibodies (anti-LKM1)
- Autoimmune hepatitis may either develop with a rapidly progressive acute disease or follow a more indolent path; if untreated, both are likely to lead to liver failure.
- Plasma cells are a prominent and characteristic component of the inflammatory infiltrate in biopsy specimens showing autoimmune hepatitis.

Drug- and Toxin-Induced Liver Injury

As the major drug metabolizing and detoxifying organ in the body, the liver is subject to injury from an enormous array of therapeutic and environmental agents. Injury may result from direct toxicity, occur through hepatic conversion of a xenobiotic to an active toxin, or be produced by immune mechanisms, such as by the drug or a metabolite acting as a hapten to convert a cellular protein into an immunogen. A diagnosis of drug- or toxin-induced liver injury may be made on the basis of a temporal

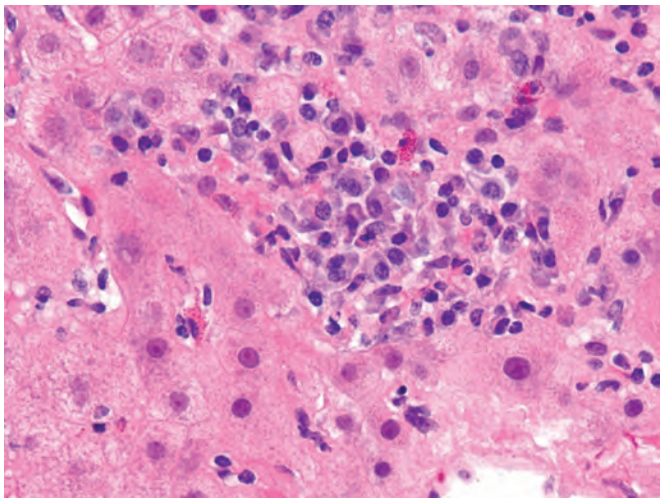

Figure 18-17 Autoimmune hepatitis. A focus of lobular hepatitis with prominent plasma cells typical for this disease.