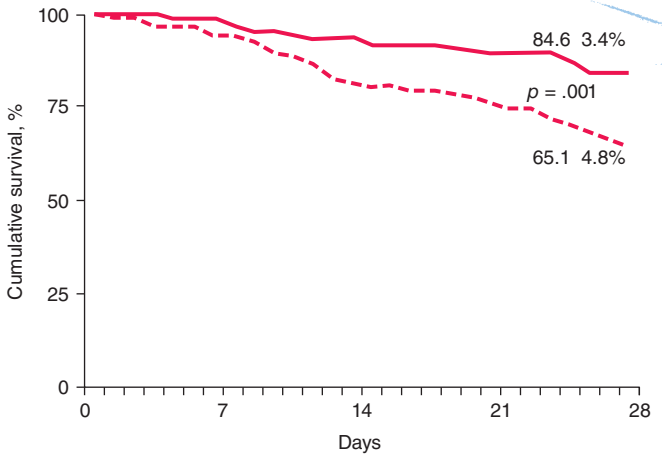

FIGURE 363-1 Effect of glucocorticoid therapy of severe alcoholic hepatitis on short-term survival: the result of a meta-analysis of individual data from three studies. Prednisolone, solid line; placebo, dotted line. *(Adapted from P Mathurin et al: J Hepatol 36:480, 2002, with permission from Elsevier Science.)*

period of sobriety. Patients presenting with alcoholic hepatitis have been largely excluded from transplant candidacy because of the perceived risk of increased surgical mortality and high rates of recidivism following transplantation. Recently, a European multidisciplinary group has reported excellent long-term transplant outcomes in highly selected patients with florid alcoholic hepatitis. General application of transplantation in such patients must await confirmatory outcomes by others.

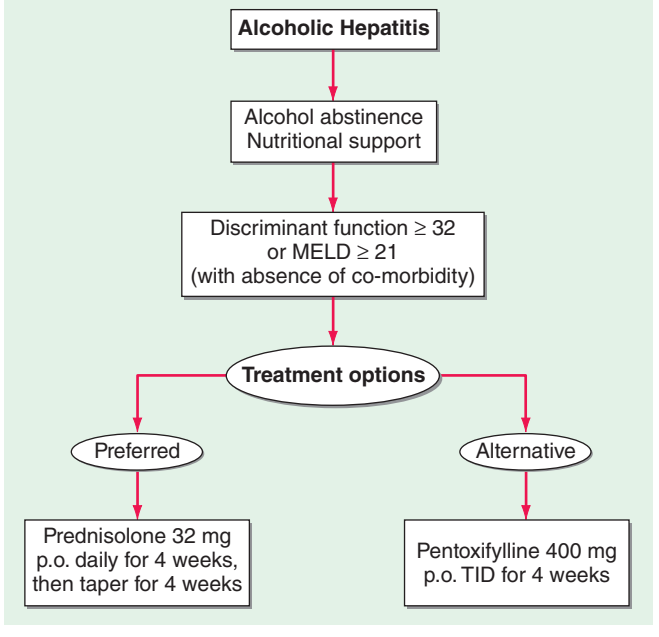

FIGURE 363-2 Treatment algorithm for alcoholic hepatitis. As identified by a calculated discriminant function >32 (see text), patients with severe alcoholic hepatitis, without the presence of gastrointestinal bleeding or infection, would be candidates for either glucocorticoids or pentoxifylline administration.

364 Nonalcoholic Fatty Liver Diseases and Nonalcoholic Steatohepatitis

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INCIDENCE, PREVALENCE, AND NATURAL HISTORY

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in many parts of the world, including the United States. Population-based abdominal imaging studies have demonstrated fatty liver in at least 25% of American adults. Because the vast majority of these subjects deny hazardous levels of alcohol consumption (defined as greater than one drink per day in women or two drinks per day in men), they are considered to have NAFLD. NAFLD is strongly associated with overweight/obesity and insulin resistance. However, it can also occur in lean individuals and is particularly common in those with a paucity of adipose depots (i.e., lipodystrophy). Ethnic/racial factors also appear to influence liver fat accumulation; the documented prevalence of NAFLD is lowest in African Americans (~25%), highest in Americans of Hispanic ancestry (~50%), and intermediate in American whites (~33%).

NAFLD encompasses a spectrum of liver pathology with different clinical prognoses. The simple accumulation of triglyceride within hepatocytes (hepatic steatosis) is on the most clinically benign extreme of the spectrum. On the opposite, most clinically ominous extreme, are cirrhosis **(Chap. 365)** and primary liver cancer **(Chap. 111)**. The risk of developing cirrhosis is extremely low in individuals with chronic hepatic steatosis, but increases as steatosis becomes complicated by histologically conspicuous hepatocyte death and inflammation (i.e., nonalcoholic steatohepatitis [NASH]). NASH itself is also a heterogeneous condition; sometimes it improves to steatosis or normal histology, sometimes it remains relatively stable for years, but sometimes it results in progressive accumulation of fibrous scar that eventuates in cirrhosis. Once NAFLD-related cirrhosis develops, the annual incidence of primary liver cancer is 1%.

Abdominal imaging is not able to determine which individuals with NAFLD have associated liver cell death and inflammation (i.e., NASH), and specific blood tests to diagnose NASH are not yet available. However, population-based studies that have used elevated serum ALT as a marker of liver injury indicate that about 6–8% of American adults have serum ALT elevations that cannot be explained by excessive alcohol consumption, other known causes of fatty liver disease **(Table 364-1)**, viral hepatitis, or drug-induced or congenital liver diseases. Because the prevalence of such "cryptogenic" ALT elevations increases with body mass index, it is presumed that they are due to NASH. Hence, at any given point in time, NASH is present in about 25% of individuals who have NAFLD (i.e., about 6% of the general U.S. adult population has NASH). Smaller cross-sectional studies in which liver biopsies have been performed on NASH patients at tertiary referral centers consistently demonstrate advanced fibrosis or cirrhosis in about 25% of those cohorts. By extrapolation, therefore, cirrhosis develops in about 6% of individuals with NAFLD (i.e., in about 1.5–2% of the general U.S. population). The risk for advanced liver fibrosis is highest in individuals with NASH who are older than 45–50 years of age and overweight/obese or afflicted with type 2 diabetes.

To put these data in perspective, it is helpful to recall that the prevalence of hepatitis C–related cirrhosis in the United States is about 0.5%. Thus, NAFLD-related cirrhosis is about three to four times more common than cirrhosis caused by chronic hepatitis C infection. Consistent with these data, experts have predicted that NAFLD will surpass hepatitis C as the leading indication for liver transplantation in the United States within the next decade. Similar to cirrhosis caused by other liver diseases, cirrhosis caused by NAFLD increases the risk for primary liver cancer. Both hepatocellular carcinoma and intrahepatic cholangiocarcinoma (ICC) have also been reported to occur in NAFLD patients without cirrhosis, suggesting that NAFLD per se may be a premalignant condition. NAFLD, NASH, and NAFLD-related cirrhosis are not limited to adults. All have been well documented in children. As in adults, obesity and insulin resistance are the main risk