



**Figure 1-1.** The natural history of patients following chronic HCV. Numbers in parentheses reflect the percentage of the total group of persons with chronic HCV infection.

patient with recently diagnosed chronic HCV. As already noted above, the vast majority of patients with chronic HCV will not develop end-stage liver disease. It is therefore imperative that the physician be able to recognize which patients with chronic HCV are at increased risk to develop cirrhosis and to counsel all patients accordingly.

The natural history of chronic HCV and cirrhosis is now well established. Our understanding of this is based upon prospective long-term natural history studies initiated in the 1970s prior to the development of interferon therapy and cross-sectional studies of patients with chronic HCV being evaluated for HCV treatment. As depicted in Figure 1-2, patients with chronic HCV can be divided into one of three groups: (1) patients who will never develop any fibrosis; (2) patients with rapid fibrosis progression who develop cirrhosis within 20 to 30 years after being exposed to HCV; and (3) patients with slow fibrosis progression who would eventually develop cirrhosis but at much slower rates, which would require 30 years or more following exposure. Many persons in this later category may endure 50 to 60 years of chronic HCV infection before they develop cirrhosis. Chronic HCV may therefore not cause morbidity or contribute to mortality in these patients until they reach the seventh or eighth decades of life. During this entire time the great majority of patients with chronic HCV infection are asymptomatic.

The use of liver biopsy and examination of liver histology has traditionally been utilized to assess the risk of developing cirrhosis. The role of liver biopsy in the assessment of patients with chronic HCV is discussed in Question 3. The largest prospective study to evaluate fibrosis progression was initiated in the 1970s prior to the identification of HCV.<sup>2</sup> This study enrolled patients with non-A, non-B hepatitis, over 95% of whom tested positive for HCV when this assay became available in the early 1990s. After an initial liver biopsy, these patients were followed prospectively for 20 years. Repeat liver biopsy was performed after 10 and 20 years or when these patients were thought to have developed cirrhosis based upon clinical grounds. All patients with bridging fibrosis on the initial