QUESTION 19
In patients with untreated post-transfusion hepatitis C, the lifetime risk of progression to cirrhosis best approximates:
A. 1%.
B. 5%.
C. 20%.
D. 50%.
E. 80%.

- Infection with the hepatitis C virus (HCV) can result in both acute and chronic hepatitis. The acute process is most often asymptomatic; if symptoms are present, they usually abate within a few weeks. Acute infection rarely causes hepatic failure.

- Acute HCV typically leads to chronic infection; 60 to 80 percent of cases develop chronic hepatitis (abnormal liver enzymes). Chronic HCV infection is usually slowly progressive; it may not result in clinically apparent liver disease in many patients if the infection is acquired later in life.

- Approximately 20 to 30 percent of chronically infected individuals develop cirrhosis over a 20- to 30-year period of time. Chronic HCV is the most common cause of chronic liver disease and the most frequent indication for liver transplantation in the United States.

- ACUTE HEPATITIS C — HCV is the cause of approximately 20 percent of cases of acute hepatitis in the United States. The presence of HCV RNA in serum or liver is the first biochemical evidence of HCV infection. HCV RNA is detectable in serum by PCR within days to eight weeks following exposure, depending in part upon the size of the inoculum. Serum aminotransferases become elevated approximately 6 to 12 weeks after exposure (range 1 to 26 weeks).

- The majority of acutely infected patients are asymptomatic and have a clinically mild course; jaundice is present in fewer than 25 percent. As a result, periodic screening for infection may be warranted in patients who are at high risk for infection. Additional symptoms are similar to those in other forms of acute viral hepatitis, including malaise, nausea, and right upper quadrant pain. In patients who experience acute symptoms, the illness typically lasts for 2 to 12 weeks. Fulminant hepatic failure due to acute HCV infection is very rare, but may be more common in patients with underlying chronic hepatitis B virus infection.

- CHRONIC HEPATITIS C — The risk of chronic infection after an acute episode of hepatitis C is high. In most studies, 80 to 100 percent of patients remain HCV-RNA positive, and 60 to 80 percent have persistently elevated liver enzymes. The rate of spontaneous clearance of virus after it has persisted for at least six months is very low. The mechanism responsible for the high prevalence of chronic infection is unclear (viral and host factors).

- Symptoms — Most patients with chronic infection are asymptomatic or have only mild nonspecific symptoms. The most frequent complaint is fatigue; other less common manifestations include nausea, anorexia, myalgia, arthralgia, weakness, and weight loss.

- Serum aminotransferases — There is wide variability in serum aminotransferase concentrations among individual patients with chronic HCV infection over time.

- Natural history — The natural history of chronic hepatitis C has been difficult to clearly define because of the long course of the disease. Several studies have provided estimates of the proportion of patients with chronic infection who develop cirrhosis within 20 years [39-52]. As a general rule, estimates from retrospective studies (17 to 55 percent) have been higher than prospective studies (7 to 16 percent), possibly reflecting referral bias in the retrospective studies. A consensus statement issued by the National Institutes of Health suggests that the actual risk is closer to that derived from the prospective studies (www.consensus.nih.gov/cons/116/116cdc_intro.htm).
• Hepatic decompensation — Cirrhosis is a prerequisite for most of the major complications of liver failure in patients with chronic HCV infection; however, not all patients with cirrhosis develop these complications.

• Hepatocellular carcinoma — Deaths associated with chronic hepatitis C in the United States are more likely to be due to end stage liver disease rather than hepatocellular carcinoma (HCC). However, HCV accounts for approximately one-third of HCC cases in the United States. Estimates of the risk of developing HCC once cirrhosis has developed have varied from 0 to 3 percent per year in various reports.

• In contrast to hepatitis B virus infection, HCC in patients with hepatitis C occurs almost exclusively in those with cirrhosis suggesting that it is cirrhosis that is the major risk factor.

• Alcohol intake — Alcohol promotes the progression of chronic HCV, even in patients with a relatively low alcohol intake. Alcohol increases HCV replication, and has also been linked to the acceleration of liver injury.

• Liver biopsy — The best clinical predictor of disease progression in chronic HCV infection is the amount of inflammation and fibrosis on liver biopsy.