Evidence Report

Chapter 1: Introduction

Hepatitis C, a viral disease, is the most common blood-borne infection in the United States. According to the Centers for Disease Control and Prevention (CDC), approximately 36,000 cases of acute hepatitis C infection occur each year in the United States. Approximately 85 percent of those with acute hepatitis C develop a chronic infection.[1,2] Chronic hepatitis C is often asymptomatic but may cause progressive liver injury. The hepatitis C virus (HCV) infects over 170 million persons worldwide and over 4 million Americans.[1] Chronic hepatitis C has significant morbidity and mortality as it can lead to cirrhosis of the liver as well as hepatocellular carcinoma (HCC).

Approximately 15 to 25 percent of patients with chronic hepatitis C develop cirrhosis.[3,4] The time frame between infection and development of cirrhosis is affected by several factors including use of alcohol[5] and viral co-infection with HIV or hepatitis B[6-8] male sex, and older age at infection.[9-11] The prognosis of those with HCV-related cirrhosis often depends on development of two complications, hepatic decompensation and HCC. The 10-year survival of those with chronic hepatitis C is approximately 50 percent for those with uncomplicated cirrhosis.

Chronic hepatitis C is the leading cause of liver transplants and HCC in the United States, and it accounts for between 8,000 and 10,000 deaths per year. Without advances in treatment, the number of deaths could triple in the next 10 to 20 years.

The National Institutes of Health (NIH) conducted a Consensus Development Conference in 1997 regarding the management of hepatitis C. The Conference addressed several important questions on prevention, diagnosis, and management of hepatitis C. The conclusions of the 1997 Consensus Development Conference were as follows:

"Hepatitis C is a common infection with variable course that can lead to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The course of illness may be adversely affected by various factors, especially alcohol consumption. Therefore, more than one drink per day is strongly discouraged in patients with hepatitis C, and abstinence from alcohol is recommended. Initial therapy with interferon alfa (or equivalent) should be 3 million units three times per week for 12 months. Patients not responding to therapy after 3 months should not receive further treatment with interferon alone, but should be considered for combination therapy of interferon and ribavirin or for enrollment in investigational studies. Individuals infected with the hepatitis C virus should not donate blood, organs, tissues, or semen. Safe sexual practices, including the use of latex condoms, are strongly encouraged for individuals with multiple sexual partners. Expansion of needle exchange programs should be considered in an effort to reduce the rate of transmission of hepatitis C among injection drug users."[3]

Notably missing from the conclusions and recommendations is discussion of the utility of liver biopsy in determining the appropriateness of treatment or the best protocols for screening for hepatocellular carcinoma. Medical research has made significant progress in the past 5 years regarding treatment modalities for chronic hepatitis C, with peginterferon[12,13] showing promising results. In addition, research has shown that certain subgroups of patients may be more or less likely to benefit from treatment based on clinical factors such as ethnicity, HCV genotype, or initial response to therapy. In addition, a substantial number of patients treated with

initial therapies have either relapsed after treatment or never responded. The future treatment of these patients needs to be explored further.

In 2002, the National Institutes of Health will convene another Consensus Development Conference on the management of hepatitis C. The purpose of this conference will be to determine the state of the art regarding several questions:

- What is the natural history of hepatitis C?
- What is the most appropriate approach to diagnosis and monitoring of patients with chronic hepatitis C?
- What is the most effective therapy for hepatitis C?
- Which patients with hepatitis C should be treated?
- What recommendations can be made to patients to prevent transmission of hepatitis C?
- What are the most important areas for future research?[14]

To this end, the Johns Hopkins University Evidence-based Practice Center (JHU EPC) prepared this evidence report focusing on several key questions on the management of chronic hepatitis C that warranted a systematic review of the recent literature. The EPC intended for this evidence report to be a resource for the Consensus Development Conference Panel that will formulate recommendations regarding the management of hepatitis C. The report should also be a resource for clinicians and policy makers who must make decisions about management of patients with chronic hepatitis C.