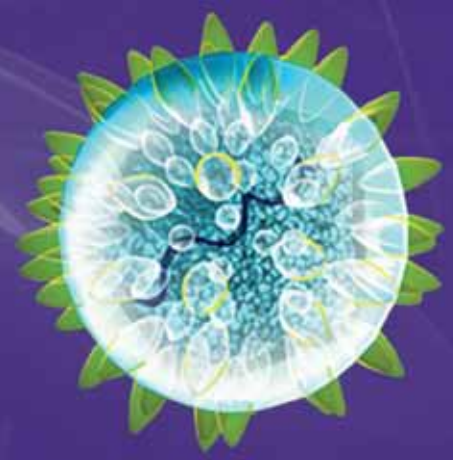


HEPATITIS C VIRUS (HCV): A MAJOR HEALTH PROBLEM



Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV). There are an estimated 180 million persons chronically infected with HCV globally.¹ In the United States, approximately 4.1 million people have been infected with HCV.¹ Up to 3.9 million of these people have chronic infection,² making it the most common chronic blood-borne infection in the country.³ More than three out of four, or 75 percent, of infected people are unaware that they are infected with HCV.⁴

HCV is transmitted through direct contact with the blood and bodily fluids of an infected person. Routes of infection include blood transfusions, needle sticks, and sharing contaminated needles, razors or tattooing instruments. The most common way that hepatitis C virus is spread is through sharing needles by injection drug use.⁵ Before 1992, widespread screening of donated blood was not performed. It is estimated that many of today's cases resulted from past transfusions of donated infected blood.⁵

HCV Disease Progression and Burden in the United States Although the number of new HCV cases in the US has declined due to safer needle practices and improved blood-donor screening, the burden of the disease will continue rising over the next two decades as those already infected with HCV experience disease progression. Baby boomers account for two out of every three cases of chronic HCV infection in the United States.⁴

Once HCV infection has become chronic, patients are at risk for developing fibrosis, which is when inflamed liver tissue begins to scar and replaces healthy liver tissue.⁶ Fibrosis can lead to cirrhosis, a process by which liver cells are either damaged or killed and replaced by scar tissue.⁶ In patients with HCV, the progression of cirrhosis is most common after the age of 60 years, regardless of how long the person has been infected.⁷ Therefore, early treatment of HCV infection is suggested.⁷

Cirrhosis and chronic liver disease are among the fifteen leading causes of death in the US.⁸ It is estimated that the number of patients with decompensated cirrhosis will increase from 30,000 to almost 150,000 over the next ten years.⁴ Over the next 20 years the number of patients with advanced liver disease will be more than four times greater than it is today.⁴

Hepatitis C is the leading cause of liver cancer in the US.⁵ Death rates increased for liver cancer during the past decade when most cancer death rates have declined.⁸ The American Cancer Society reported that between 1990 and 2003 there was a 47 percent increase in liver cancer death rates among males and between 1991 and 2003 there was a 27 percent increase among females. These were the largest increases in death rates reported for any cancer in this time period.⁸

Both advanced or decompensated cirrhosis and liver cancer can progress to end-stage liver disease, which is when the liver can no longer function properly and a liver transplant is necessary.⁶ In the United States, infection with HCV is the leading cause of liver transplantation and is reported to contribute to 4,600 to 12,000 deaths annually.⁷

In addition to the hepatic (related to the liver) manifestations of HCV (cirrhosis, liver cancer), it is possible for patients with HCV to develop extrahepatic (occurring outside the liver) conditions which affect other areas of the body, including the kidneys, skin and immune system.¹ Correlations have also been made between HCV and diabetes.⁹

ABOUT VERTEX

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical companies. Vertex's product pipeline is focused on viral diseases, cystic fibrosis, inflammation, autoimmune diseases, epilepsy, cancer, and pain. Vertex co-discovered the HIV protease inhibitor, Lexiva, with GlaxoSmithKline. .



Depression and Quality of Life HCV infection has also been associated with an increase in depression, the symptoms of which can intensify a patient's physical symptoms.¹⁰ In addition, psychiatric disorders including depression have been identified as a side effect of treatment, and are the most common reason patients discontinue therapy.¹⁰

Whether due to complications of advanced liver disease, extrahepatic manifestations, or disease-related depression, HCV has been linked to a decreased health-related quality of life in patients.¹¹ Studies have shown that health-related quality of life improves after patients have achieved a sustained virologic response (SVR), in which the virus remains undetectable six months after treatment has ended.¹¹

Economic Impact of HCV Economic burdens related to HCV are also expected to increase significantly during the next 20 years.⁴ Total medical costs for patients with HCV infection are expected to increase from \$30 billion in 2009 to over \$85 billion in 2024.⁴ If no changes are made to the HCV diagnosis and treatment paradigm overall health care costs would be expected to more than double over 20 years, the per-patient cost of people with chronic HCV infection will increase 3.5 times over 20 years, commercial and Medicare costs will more than double in 10 years and in 20 years, Medicare costs will increase 5-fold.⁴

UNMET MEDICAL NEED

Current therapies for HCV typically provide sustained benefit in about half of patients with genotype 1 HCV, the most common strain of the virus.¹ If treatment is not successful and patients do not achieve an SVR, they remain at risk for progressive liver disease.^{7,12,13,14} In a recent study, the risk of liver failure, cancer or death following unsuccessful HCV treatment was assessed at 23% after 4 years, and 43% after 8 years.¹² There is currently no vaccine available for HCV.⁵ New investigational antiviral therapies that directly target the HCV protease and polymerase, enzymes essential to the virus' replication, are currently in clinical development.

FACTS ABOUT HEPATITIS C AND DISEASE BURDEN

Fibrosis – Once HCV infection has become chronic, patients are at risk for developing fibrosis, which is when inflamed liver tissue begins to scar and replaces healthy liver tissue.⁶ This condition can lead to cirrhosis.⁶

Cirrhosis – For every 100 people infected with HCV, five to 20 will develop cirrhosis.⁵ A majority of HCV patients, if untreated, are expected to develop cirrhosis after the age of 60 years, regardless of age when infection occurred.⁷

Liver Cancer – In the US, HCV is the number one reason for liver cancer and has been linked to more than 50 percent of cases of hepatocellular carcinoma, the most common form of liver cancer.¹⁵

Diabetes – Research has shown a correlation between HCV infection and glucose abnormalities, and potential increased risk for the development of diabetes. Among a group of patients with diabetes risk factors who were followed for nine years, those with HCV infection were more than 11 times more likely than those without to develop diabetes.⁹

Depression – A study conducted among a group of patients awaiting treatment for HCV showed that HCV infection is associated with increased depression. Psychiatric disorders, including depression, are the most common reason patients discontinue therapy.¹⁰

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