EDUCATIONAL COMMENTARY - VIRAL HEPATITIS

LEARNING OUTCOMES
On completion of this exercise, the participant should be able to

- discuss the causes, transmission, and symptoms of viral hepatitis infections.
- describe the laboratory tests performed to aid in the diagnosis and treatment of viral hepatitis.
- discuss hepatitis testing performed on blood donated for transfusion.

Introduction

Hepatitis is defined as inflammation of the liver and may be caused by toxins, alcohol, drugs, and bacterial or viral infections. Drugs may include prescription drugs, illicit drugs, and overuse of over-the-counter medications such as acetaminophen. Viral hepatitis may be acute or chronic. In acute cases, the infected person spontaneously recovers and produces protective antibodies that provide lifelong immunity. In chronic disease, the patient may develop scarring of liver tissue leading to cirrhosis or, in some cases, to hepatocellular cancer.

The liver is a large, vital organ located in the upper right portion of the abdomen. Its many functions include production of bile required for the digestion of fats, generation of cholesterol for hormones and cell wall integrity, storage of glycogen for energy, removal of waste products, production of amino acids, metabolism of drugs, and production of clotting factors. Oxygenated blood from the heart is delivered to the liver through the hepatic artery. The portal vein delivers nutrients and other substances from the digestive tract to the liver, where they are filtered before entering the circulation. Liver cells are capable of regeneration, but are unable to regenerate if too many cells are damaged. In cases where large areas of the liver are damaged and regeneration is not possible, cirrhosis or hepatocellular cancer occurs.

Hepatitis Viruses

There are six major hepatitis viruses (A, B, C, D, E, and G); other viruses such as cytomegalovirus, Epstein Barr virus, and herpes simplex virus may also cause hepatitis. The most prevalent types of viral hepatitis in the United States are hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV). HAV and hepatitis E virus (HEV) are spread through fecal-oral transmission by ingestion of contaminated food and water. These viruses usually result in spontaneous recovery and do not progress to chronic liver disease. HBV and HCV are spread through blood and body fluids. Infection with either of these viruses may lead to chronic disease. The major viral causes of chronic liver disease in the United States are HBV and HCV. Hepatitis D virus (HDV), also known as the delta virus, is rare in the United States. It is an incomplete virus and is incapable of infecting cells without the presence of HBV. A concurrent infection with HBV and HDV, is called a HBV/HDV coinfection. An HDV infection occurring in a patient already infected with HBV is known as a HBV/HDV superinfection. Coinfection or
superinfection increases the mortality rate from 0.5-1% in HBV alone to approximately 20%. HEV and hepatitis G virus (HGV) occur in third-world countries where living conditions are crowded and water supplies are contaminated. These types of hepatitis occur in the United States only in people who have traveled to endemic areas of the world.

For many years, HAV and HBV were recognized as the only types of hepatitis viruses. In the 1970s, it became apparent that another hepatitis virus existed. This virus was termed non-A, non-B hepatitis until it was identified in 1989 and named hepatitis C. An assay for anti-HCV was developed in 1990 and used to screen blood for transfusion. A third generation EIA procedure is currently used to screen blood donations for HCV.

HCV is a major health issue worldwide. Between 170 million and 200 million people, 3.2% of the world’s population, are infected with HCV. (CDC) According to sources at Dartmouth Medical School, there are as many cases of HCV as there are of human immunodeficiency virus. Currently, HBV and HCV are responsible for 75% of liver disease cases.

**Symptoms**

Viral hepatitis may be acute, asymptomatic, or chronic. Acute hepatitis manifests with flu-like symptoms, fatigue, nausea, vomiting, abdominal pain, and often jaundice and dark urine. The symptoms of HAV, HBV, and HCV are similar in the acute phase. The incubation period for HAV is about four weeks. During this period, large numbers viral particles are shed in the feces, and the patient is highly infectious. Symptoms of HAV persist from a few weeks to two months in most cases, but may last as long as six months. The infection is self-limiting and does not lead to chronic liver disease.

HBV has a longer incubation period, ranging from one to six months, and the acute phase of the infection usually persists for up to three months. At that point, protective antibodies are generated and the patient moves into the recovery phase. In approximately 10% of cases, HBV antigens persist, and protective antibodies are not generated within six months of the onset. These cases are classified as chronic active HBV and may progress to cirrhosis or hepatocellular carcinoma.

Symptoms are present in only a small percentage of cases of HCV. Approximately 80% of infections become chronic, i.e. HCV RNA is detectable more than six months after the onset of the infection. The patient may be asymptomatic and not display symptoms of liver damage for up to 20 years after being infected. According to the National Digestive Diseases Information Clearinghouse, HCV is responsible for more liver transplants than any other disease.

**Laboratory Testing**

All types of hepatitis may cause damage to the liver and result in elevations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin. Identification of the type of
hepatitis is accomplished using screening assays for the types of hepatitis that are most prevalent in the United States: HAV, HBV, and HCV. The screening tests are most commonly performed using enzyme immunoassay techniques.

- **HAV**

  If HAV is suspected, testing for HAV immunoglobulin M (IgM) and HAV Immunoglobulin G (IgG) will be performed. A patient who is currently infected will be positive for HAV IgM and HAV IgG antibodies. If the patient is HAV IgM negative and HAV IgG positive, the patient was infected with HAV in the past. HAV IgG is a protective antibody and prevents reinfection with HAV.

- **HBV**

  If HBV is suspected, a battery of assays may be performed, including tests for hepatitis B surface antigen (HBs), hepatitis B e antigen (HBe), antibody to hepatitis B core antigen (anti-HBc), antibody to HBeAg (anti-HBe), and antibody to HBs (anti-HBs). Depending on which of these assays are positive, the patient’s status may be determined. (See Table) In patients with chronic hepatitis B infections, the patient does not seroconvert, i.e. the protective antibody anti-HBs is not produced and the viral antigens HBsAg and HBeAg persist. As long as these antigens persist, liver damage continues to progress.

### Table.

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<th>HBe</th>
<th>Anti-HBc</th>
<th>Anti-HBe</th>
<th>Anti-HBs</th>
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<tbody>
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<td><strong>Early acute phase</strong></td>
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<td><strong>Acute phase</strong></td>
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<tr>
<td><strong>(Highly infective stage)</strong></td>
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<tr>
<td><strong>Convalescent phase</strong></td>
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<td><strong>Recovery</strong></td>
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<td><strong>Chronic disease</strong></td>
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• HCV

When HCV is suspected, an enzyme immunoassay for anti-HCV is performed. If positive, the result is confirmed using the HCV recombinant immunoblot assay or nucleic acid testing. HCV viral load testing is used to determine the number of viral RNA particles present in the blood. Quantitating the viral load helps the physician predict the success of interferon therapy as well as evaluate the patient’s prognosis. Patients with an HCV viral load of fewer than two million copies per milliliter are more likely to have a favorable response to therapy. Lower viral loads are associated with a lasting response to treatment. Another factor associated with the efficacy of therapy is the viral genotype. According to the World Health Organization, eleven different genotypes have been identified. The pathogenicity and virulence of the genotypes do not differ significantly, but there are significant variations in response to therapy. Individuals infected with genotypes 2 and 3 respond better to interferon therapy than those infected with genotypes 1, 4, and 5. Unfortunately, more than half of responders experience relapses after the completion of the therapeutic protocol. Combination of interferon with an antiviral drug such as ribavirin has increased the percentage of patients who experience a sustained response after cessation of therapy.

• HDV and HEV

An enzyme immunoassay for anti-HDV is performed only on patients who test positive for HBV. Since the symptoms for HEV are so similar to those of other types of hepatitis, serologic testing must be performed for its diagnosis. Testing may be performed for both HEV IgM and HEV IgG.

• Hepatitis in the Blood Supply

According to the American Red Cross, blood for transfusion has been screened for HBsAg since 1971 and for HBV core antibody since 1987. It was not until the 1990s that an assay for anti-HCV was available and screening blood donations for HCV began. Since people with HCV may remain asymptomatic for decades, all individuals who received blood transfusions before 1990 should be tested for HCV.

Conclusion

HBV and HCV cause liver infections that may lead to chronic active disease. The long term presence of HBV or HCV antigens leads to the death of liver cells and may progress to permanent scarring of the liver, or cirrhosis. Some cases progress to hepatocellular carcinoma. Assays for HBV and HCV are crucial aids to physicians in the diagnosis and treatment of these serious viral infections. Vaccines are available for HAV and HBV. Infants are vaccinated for both HAV and HBV, and vaccination for HBV is required for health care professionals. Currently, there is no available vaccine for HCV. Difficulties in
developing a vaccine rest in the ability of the virus to rapidly mutate. Until there is a vaccine, HCV will remain a serious health issue in the United States and worldwide.

References:


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