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Hepatitis And The Immune Responses

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Abstract

Immune responses explain the body's recognition and defense against viruses and other harmful materials. A strong immune system is important to protect the body from antigens like viruses and nonliving substances, including toxins and chemicals. Hepatitis is a condition involving the inflammation of the liver caused by different classes of viruses, including Hepatitis A, Hepatitis B, and Hepatitis C or toxins, alcohol, certain medications, and other medical conditions (CDC, 2021). The most prevalent condition is Hepatitis C, with almost 2.4 million people in the US living with it in 2018, and 50% are unaware they are infected. Approximately 24900 and 22600 new infections yearly for Hepatitis A and Hepatitis B, respectively (CDC, 2021). The infection by each type of virus is influenced by different virological and immunological factors . HAV induces an expression of a large proportion of IFNstimulated genes (ISGs). HBV does not induce ISG expression, but HAV minimally induces ISG expression. Human beings are the main natural hostof HBV (other Chimpanzees) and the only natural host for HCV (Rehermann & Nascimbeni, 2005). Immune-mediated mechanisms, including virus-specific T cells and nonspecific cells, influence liver injury in hepatitis virus infections. The immune-mediated liver injury is controlled by regulatory T cells and myeloid-derived suppressor cells. Hepatitis is a major public health issue due to its multiple causes, higher transmission risks, the vulnerability of various populations, and the associated health complications. The most critical is viral Hepatitis caused by HAV, HBV, and HCV. Unlike HBV and HCV, HAV does not cause chronic infection. HBV is also unique since it has vertical transmissions and a higher risk of infection in adulthood. There is no vaccine for HCV; hence, interventions are focused on treating the symptoms and delaying the occurrence of major healthcare complications. Treatmentof acute HAV, HBV, [1]and HCV involves support to manage the symptoms and ensure spontaneous alleviation of the infection. This is important to improve population immunity and reduce susceptibility to infections following increased risk factors.

Introduction

HEPATITIS AND THE IMMUNE SYSTEMS:

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Immune responses explain the body's recognition and defense against viruses and other harmful materials. A strong immune system is important to protect the body from antigens like viruses and nonliving substances, including toxins and chemicals (Shin, Sung, & Park, 2016). Hepatitis is a condition involving the inflammation of the liver caused by different classes of viruses, including Hepatitis A, Hepatitis B, and Hepatitis C or toxins, alcohol, certain medications, and other medical conditions (CDC, 2021). The most prevalent condition is Hepatitis C, with almost 2.4 million people in the US living with it in 2018, and 50% are unaware they are infected. Approximately 24900 and 22600 new infections yearly for Hepatitis A and Hepatitis B, respectively (CDC, 2021). The infection by each type of virus is influenced by different virological and immunological factors (Shin et al., 2016). HAV induces an expression of a large proportion of IFNstimulated genes (ISGs). HBV does not induce ISG expression, but HAV minimally induces ISG expression. Human beings are the main natural hostof HBV (other Chimpanzees) and the only natural host for HCV (Rehermann & Nascimbeni, 2005). Immune-mediated mechanisms, including virusspecific T cells and nonspecific cells, influence liver injury in hepatitis virus infections. The immunemediated liver injury is controlled by regulatory T cells and myeloid-derived suppressor cells (Shin et al., 2016).

Individuals can develop immunity against Hepatitis, including acquired immunity and passive immunity. The former involves immunity developed following exposure to the specific antigen. Passive immunity mainly involves the injection of antiserum, such as the immune serumglobulin, for immediate protection against the antigen when the risks are higher. Hepatitis A, Hepatitis B, and Hepatitis C differ in how long they last in the body. Hepatitis A can last for unprecedented period. Children aged 12-23 months should be vaccinated, and the 2-18 years (not previously immunized) should receive a "catch up" vaccination. Adults at risk of hepatitis A include international travelers, men who have sex with men, those who frequently inject drugs,occupational risks, and those who experience homelessness (CDC, 2021).

Unimmunized infants have higher risks (90%) of developing chronic Hepatitis B than older children and adults (6%-10%). All infants, children, and adolescents (below 19 years) notimmunized, those at risk of infection from sex exposure, blood contact(injections), dialysis patients, diabetes patients (19-59 years), people with HIV, Hepatitis C, in prison should be vaccinated for Hepatitis B (CDC, 2021). Hepatitis C is critical since no vaccine is available to protect the people at risk (Shin et al., 2016). Responses to acute infections of Hepatitis involve epitope specific CD8+ T cell responses, successive in HAC and HBV but not in HCV infections (Shin et al., 2016). This paper explains Hepatitis, including the etiology, epidemiology, and immunology of the various types of Hepatitis infections.

Etiology and Pathophysiology of Hepatitis

Causes

Hepatitis can be classified into viral and non-viral Hepatitis based on the causes. Infectious Hepatitis is caused by parasitic, fungal, bacterial, and viral organisms. The most critical form is viral Hepatitis. This refers to the virally mediated liver inflammation in different classes, including Herpes simplex, Epstein-Barr, and Cytomegalovirus (Zarrin, 2022). The non-infectious Hepatitis is caused by autoimmune diseases, drugs, alcohol, and metabolic diseases (Mehta, & Reddivari, 2022). According to the Centers for Disease Control (CDC), non-viral Hepatitis is a condition were sudden liver inflation results in liver failure. The most common cause of Hepatitis is a viral infection, although an outbreak can result from a series of factors (Zarrin, 2022). HAV, HBV, and HCV are the primary causes of Hepatitis. Indeed, they account for 90% of acute viral Hepatitis in the US (Mehta, & Reddivari, 2022). Collectively the viruses enter the bloodstream, infect hepatocytes, and multiply and change the antigen structure.

Causes of Infectious Hepatitis

Hepatitis A

Hepatitis A is an RNA virus mainly present in high concentrations in the stool of infectedpersons. It is a member of the Picornaviridae family (Mehta, & Reddivari, 2022). The greatest viral load shedding is present at the end of the incubation period. The incubation period of Hepatitis A is 30 to 50 days (Zarrin, 2022). Secretion of the virus takes place for two weeks before the appearance of the symptoms and continues until three months later (OSU, n.d.). The primary mode of transmission of HAV is via the fecal-oral route. The transmission medium includes food, water, and other objects contaminated through fecal matter (Mehta, & Reddivari, 2022). There are different risk factors for the transmission of HAV via the fecal-oral route. In developing countries, poverty and poor sanitation increase transmission risks (OSU, n.d.). In the United States, international travel heightens the risk of transmission. A secondary transmission route for HAV is household contacts which account for 20% of the incidences and is a critical factor during HAV outbreaks (Mehta, & Reddivari, 2022). Highly crowded areas have higher risks of transmission of the virus. Secondary transmission routes for HAV are men who have sex with men and blood transfusion. HAV causes acute infections, and there are higher severity and mortality rates in adults than in children (Mehta, & Reddivari, 2022). There are no risks for chronic Hepatitis from HAVinfections, and only 1% of the incidences cause fulminant hepatic failure.

Hepatitis B

HBV is a DNA virus in 8 different genotypes and a member of the Hepadnaviridae family. The viral core of HAV is made up of hepatitis B core antigen (HBcAg) and nucleocapsid (Mehta, & Reddivari, 2022). However, Hepatitis B has eight different genotypes. They are not critical elements in determining the severity of the condition. HBV is commonly found in the tears, saliva, vaginal mucus, semen, and serum. Unlike HAV, it is not present in stool, urine, and sweat (Zarrin, 2022). HBV has unique transmission through vaginal secretion and semen, via blood through injections, or through close person-to-person contact (Mehta, & Reddivari, 2022). Unsafe medical practices, including transfusion, shared needles, wounds, and needlesticks, are also critical risk factors for the transmission of HBV.

Collectively the form of transmission of HBV, defined as vertical, occurs via contact with infected body fluids or mucous membranes. There are different risk factors for transmission of HBV in different locations influenced by various conditions of contact which are most present. The parenteral transmission of HBV within the healthcare environment is the most dominant transmission method in the United States. The individuals at highest risk of transmission of HBVare those born in the endemic areas, sexual partners of HBV carriers, individuals with multiple sexual partners, and patients with frequent blood transfusions. HBV is also transmitted perinatally, with infants of HBeAg-positive women having 70% to 90% chances of infections (Mehta, & Reddivari, 2022). Moreover, those who are infected have a 90% chance of developingchronic infections from HBV.

HBV has an incubation period of 12 weeks. Only 1% of the patients have the risk of developing fulminant hepatic failure. Following the infections and as the acute condition resolves, infants and adults develop antibodies against HBV and fully recover (Zarrin, 2022). Only a small percentage of the patients develop chronic infections. Mehta and Reddivari (2022)

explain that 10% to 30% of patients exhibit the symptoms of chronic infections and extrahepatic manifestations of the conditions. About 20% of chronic condition patients develop cirrhosis and hepatic decomposition (Mehta, and Reddivari, 2022). Moreover, 5% of the victims have a high risk of hepatocellular carcinoma. The dynamic of HBV infections' acute and chronic conditions is explained further in the subsequent section. Typical symptoms of acute infection of HAV include Jaundice, vomiting, anorexia, and malaise.

Hepatitis C

HCV is an RNA virus and a member of the Flaviviridae family. The virus has more than six core genotypes and 80 subtypes. This extensive genetic has made it difficult to develop a vaccine to prevent HCV infection. HCV can be described as an adverse factor linked to blood transfusions. The incubation period of HCV is approximately 40 days. Although liver enzymes are elevated, there are usually no major symptoms to assist in the diagnosis of HCV infections. In other words, the conditions are asymptomatic in most cases, but 55% to 85% of the incidencesdevelop into chronic infections. Intravenous or intranasal actions such as drug use, sexual contact, and contaminated healthcare injections remain the fundamental mode of transmission of the virus (Zarrin, 2022). However, sexual contact and perinatal transmission are less common. Individuals who require transfusion or organ transplant are at higher risk of infection from the infected donors (Mehta, and Reddivari, 2022). Chronic infection of HCV increases the risks of hepatocellular carcinoma and subsequent mortality rates. Indeed, HCV is a contributing factor to over 20000 death annually (Zarrin, 2022).

Hepatitis D, Hepatitis E and Hepatitis G

Although the infections from Hepatitis D (HDV) and (HEV) are limited and For HepatitisG (HGV) is not certain they are significant factors in the epidemiology of liver inflammation .

Therefore, a unique factor is that HBV also infects individuals infected by HDV. The modes of transmission for HDV are like HBV, although perinatal transmission is uncommon (Mehta & Reddivari, 2022). HDV has an incubation period of 13 weeks, and infection only occurs for individuals with acute or chronic Hepatitis B. HDV infections cause similar symptoms as HBV. However, individuals with HDV and HBV infections have higher risks of progression to cirrhosis than patients with chronic Hepatitis B alone (Zarrin, 2022). When HDV infects patients with Hepatitis B, they have higher risks of developing superinfections. Superinfection causes fulminant hepatic failure (Mehta & Reddivari, 2022). Hepatitis E (HEV) is an RNA virus in the Hepevirus genus. It resembles HAV infections in most factors, although it can be asymptomatic. The most common mode of transmission is via fecally contaminated water. Therefore, HEV is a common infection in developing countries with water and sanitation challenges. Although it is usually rare, person-to-person transmission isalso a possible transmission mode. In some instances, maternal-neonatal transmission can also occur (OSU. (n.d.). The incubation period of HEV is approximately 2 to 10 weeks. Compared to Hepatitis B, acute Hepatitis E is less severe. However, pregnant women have a 25% risk of mortality associated with Hepatitis E infection. Moreover, Hepatitis E has risks of impairment of kidney functions or causing neurological symptoms (Mehta & Reddivari, 2022). Hepatitis G Virus (HGV) is an RNA virus of the Flaviviridae family in the Pegivirus A species. The transmission mode is infected blood and occurs mainly as a coinfection for individuals infected by HBV or HCV. According to Zarrin (2022), researchers have not established if HGV is an agent of Hepatitis, but its infection is greatly associated with acute and chronic liver diseases. The incubation period of HGV is 14 to 20 days. The HGV infection shows symptoms similar to other hepatitis viruses. Unlike in Hepatitis C, which relies on the viral load, the elevation of alanine aminotransferase (ALT) depends on viremia in Hepatitis G. Indeed, in Hepatitis C infection high viral load causes higher ALT (Mehta & Reddivari, 2022).

Causes of Non-Infectious

Hepatitis is also caused by non-infectious factors, including autoimmune Hepatitis, alcohol, and other toxins (Zarrin, 2022, CDC. (2021). Generally, the etiology of non-infectious Hepatitis in children and adults is complex and associated with various factors. For instance, a recent incidence of acute non-viral Hepatitis in children was associated with drinking alkaline water (CDC, 2021). Autoimmune Hepatitis has unknown risk factors,

although some conditions, such as Epstein-Barr virus infections, environmental agents, and drugs, can trigger the autoimmune response (Mehta & Reddivari, 2022). Victims of autoimmune Hepatitis develop autoantibodies which are more common in individuals with chronic hepatitis C virus infections (Zarrin, 2022). Some drugs, such as methyldopa, adalimumab, minocycline, infliximab, and nitrofurantoin, are key triggers of autoimmune Hepatitis (Mehta & Reddivari, 2022). Therefore, when a patient stops to use infectious drugs, the hepatitis condition improves. Autoimmune Hepatitis is associated with increased concentrations of gammaglobulin and circulating autoantibodies. Although the research findings are not clearly defined, patients who develop the conditions havea genetic predisposition. The condition is often secondary to viral infection or an idiosyncratic reaction to the drug. Another common non-infectious hepatitis is Alcoholic Hepatitis (Mehta & Reddivari, 2022). Although various factors which induce alcoholic Hepatitis are not clearly defined, a combination of processes are involved in triggering it. Most significant include oxidative injuries, genetic factors, malnutrition, and immunologic factors influencing Alcoholic Hepatitis (Zarrin, 2022). The mechanism of Alcoholic Hepatitis is highly complex and multifactorial, resulting from the interactions between inflammation, ethanol metabolism, and innate immunity.The most critical factor in hepatotoxicity is the cytokines and tumor necrosis (Mehta & Reddivari, 2022). There are other possible causes of non-infectious Hepatitis, which include chemicals (pesticides, paint thinners, solvents, and metals), wild-growing mushrooms and plants, traditionalor home remedies, contaminated water or food, and dietary or herbal supplements (CDC, 2021). Toxic Hepatitis is also a significant form of noninfectious Hepatitis. The symptoms of acute non-viral Hepatitis are similar to those of viral Hepatitis. The most common symptoms includeyellow skin or eyes, dark urine, loss of appetite, vomiting, nausea, light-colored stools and abdominal pain, fatigue, and fever (CDC, 2021). Non-infectious Hepatitis can cause liver cirrhosis, liver failure, and death. Diagnosis of non-infectious Hepatitis involves examining the possible risk factors for the symptom. Some of the important tests include CT scans and biopsies.

Health Consequences

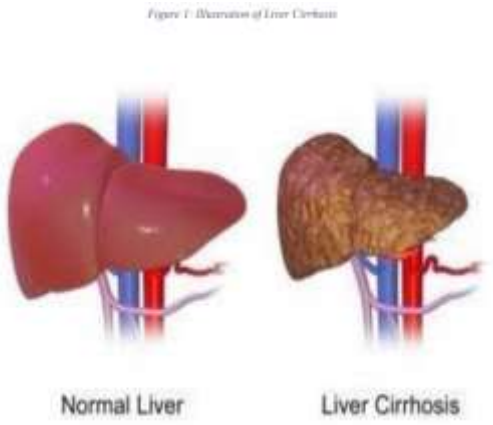
Depending on the causes and the nature of the condition, the symptoms of Hepatitis can be acute or chronic, ranging from mild to severe illness. As described, all types of Hepatitis have critical health complications. For instance, HEV infection is associated with various deaths annually, especially in developing countries (Krain et al., 2014). However, the health consequences depend on the type of infection and the geographical location. Most of the mortality incidences associated with this Hepatitis occur in the resource-poor countries of Africa and Asia. Moreover, the human associated HEV genotypes increase the prevalence of these conditions (Krain et al., 2014).

Symptoms

Acute and chronic conditions of Hepatitis result in different symptoms. Symptoms vary depending on the three stages of Hepatitis: prodromal, icteric, and convalescent. In the prodromal phase, the virus in the blood releases chemicals that cause symptoms such as nausea, fatigue, headache, fever, joint pains, skin rashes, and vomiting (OSU, n.d.).

Complications of Hepatitis

Hepatitis can cause significant morbidity and mortality (Mehta, & Reddivari, 2022). Acute Hepatitis is liver inflammation lasting for less than six months. In most instances, acute Hepatitis is self-resolving, but depending on its etiology, it can result in liver failure (Mehta, & Reddivari, 2022). When the condition lasts for six more months, it is termed chronic Hepatitis. The complication of chronic Hepatitis includes liver damage ranging from hepatocellular carcinoma, cirrhosis, liver fibrosis, and portal hypertension. Figure 1 below shows the distinctionbetween a normal liver and liver cirrhosis.



Since the liver is a vital organ involved in digestion and nutrition, including bile production, emulsification and absorption, and other metabolic functions, liver damage affects different body parts. Some of the liver's key metabolic functions include converting glucose into glycogen, detoxification, and synthesizing nutrients into forms that can be absorbed into the body (OSU, n.d.). The liver also plays a critical function in removing ammonia through conversion into urea excreted via the urine. Liver damage results in high bleeding risks, reducing protein production and detoxification. A build-up of toxins in the body is a major cause of hepatic encephalopathy. Moreover, the failure to release conjugated bilirubin can result in Jaundice.

Treatment and Management of Hepatitis

Treatment of various types of Hepatitis is important to reduce the risks of morbidity andmortality. There is no intravenous procedure for HAV infection, so the patients should be admitted and closely monitored. The type of treatment also depends on the symptoms. Those patients who have nausea or symptoms require intravenous procedures to rehydrate them. Complications such as hepatic encephalopathy require more sophisticated treatment procedures. A major precaution for patients is to avoid hepatotoxic substances, including alcohol and medications like acetaminophen, to manage the various symptoms (Mehta, & Reddivari, 2022).

Moreover, patients with viral infections should avoid vigorous physical activity and explore constant medical checkups before they resume those activities. Treatment of Hepatitis B and Hepatitis C is categorized into acute and chronic infection treatment (Zarrin, 2022). For acute HBV, the treatment should be supportive similar to acute HAV infection (Mehta, & Reddivari, 2022).

Lamivudine exhibits good results in the treatment of severe cases of acute hepatitis B virus. Early interferon therapy is an effective procedure to treat acute Hepatitis C when it is detected (Zarrin, 2022). Since the patient can alleviate the infection spontaneously, antiviral therapy should begin at least six months after the infection. The primary treatment goals for chronic Hepatitis B and chronic Hepatitis C are to inhibit viral replication andto eradicate the hepatitis C virus respectively (Mehta, & Reddivari, 2022). The secondary treatment goal is to reduce symptoms and delay the progression of liver cirrhosis and other complications. Developments in the diagnostic procedures for various viral Hepatitis are important in the treatment and prevention (Pawlotsky et al., 2020). For instance, there are various HCV drug combinations with a clearly defined safety profile to enhance high positive outcomes. The most effective drugs for the treatment of HCV infections include Sofosbuvir (one tablet once daily), Sofosbuvir/velpatasvir (one tablet once daily), Sofosbuvir/velpatasvir/voxilaprevir (one tablet once daily with food), Glecaprevir/pibrentasvir (three tablets once daily with food), and Grazoprevir/elbasvir (one tablet once daily) (Pawlotsky et al., 2020). However, the choice of therapy is selected based on patient profile, preference, and drug resistance.

Prevalence of Hepatitis (Epidemiology) Generally, viral Hepatitis is a public health issue causing significant incidences of mortality and morbidity (Mehta, & Reddivari, 2022). Global Prevalence of Hepatitis Approximately 20 million infections of Hepatitis occur globally each year (Krain et al., 2014). By 2009, more than 2 billion people were infected by HAV, HBV, and HCV. Some factors have increased the risks of viral Hepatitis in different countries. According to the World Health Organization (2020), Hepatitis remains a critical challenge in both developed and developing countries. HBV and HCV influence chronic infections and an estimated 354 million people live with Hepatitis B and Hepatitis C (WHO, 2020). They disproportionally affect certain countries. Since some of the viral infections can be prevented through vaccination between 2016 and 2030, there are global efforts to reduce hepatitis infection by 90% and the mortality rate by 65% (WHO, 2020). The primary goals include prevention (immunization), detection (improve surveillance systems), response (preparing for outbreaks), sustainability (immunization), and innovation (research and evaluation). Countries with the highest prevalence of HBV infections are in Africa at a prevalence rate of ≥ 8%. Most other African countries have a high intermediate Hepatitis B prevalence of 5% to 7% (CDC, 2021c). Countries in the developed regions of western Europe and North America mainly have a low intermediate prevalence of 2% to 4% for HBV (CDC, 2021c). According to recent statistics, in 2019 by WHO, about 296 million people lived with HepatitisB, while 58 million people lived with Hepatitis C (CDC, 2021c). Moreover, 1.5 million people are newly infected with chronic Hepatitis B and chronic Hepatitis C (3 million total) (CDC, 2021c).

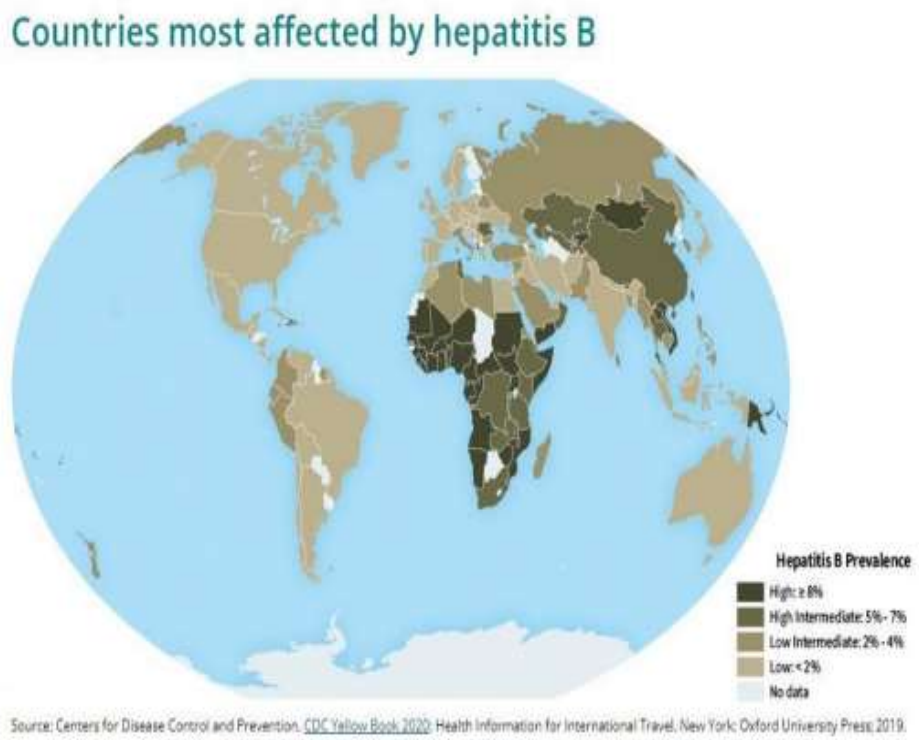


Figure 2: Global Prevalence of HBV infections (*CDC, 2021c)*

There are relatively similar trends in the prevalence of Hepatitis C. Some countries in Asia and Africa have a high prevalence of ≥ 5%. The majority of countries in Asia report a highmoderate prevalence of Hepatitis C (2% < 5%). Other countries have a low, moderate prevalence of Hepatitis C(1.5<2.0%). Figure 3 below highlights the prevalence of Hepatitis C in various countries, from high to very low (CDC, 2021).

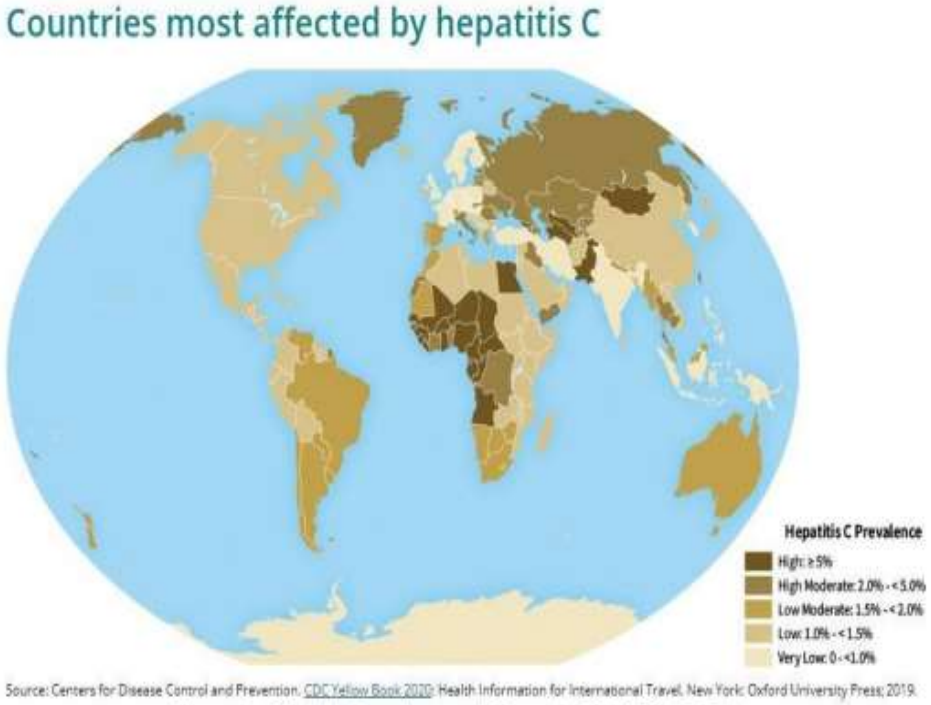
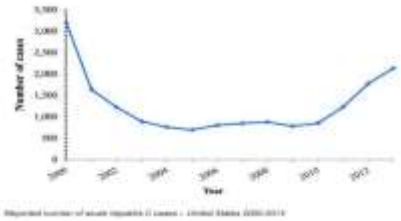


Figure 3: Global Prevalence of Hepatitis C (*CDC, 2021c)*

Prevalence of Hepatitis in the United States Developed countries, including North America, have high-risk conditions for adult HAV infections since they are not contracted in childhood to develop immunity (Xiridou et al., 2013). Particularly when individuals travel to developing countries where the virus circulates widely, there are higher risks of infections. Access to safe drinking water and stronger economic levels decreases the prevalence of Hepatitis A. Approximately 24000 cases of Hepatitis A are diagnosed annually in the United States (Mehta, & Reddivari, 2022). According to the Department of Health and Human Services, many Americans live with viral Hepatitis even though some do not exhibit the symptoms (HHS.gov., 2021). There is a high prevalence of Hepatitis C, ranging from 2.4 million to 4.7 million.

A significant 850000 individuals are living with hepatitis B, but the actual number could range from 730000 to 2.2 million (HHS.gov., 2021). Approximately 22600 new infections of Hepatitis B were recorded in 2018 (Mehta, & Reddivari, 2022). Americans are at higher risk of liver failure and liver cirrhosisdue to limited diagnosis of the infection. Moreover, there are higher risks of transmission of the virus to others. The prevalence of Hepatitis in the US also varies by race, with Pacific Islanders and Asian Americans at the highest risk (HHS.gov., 2021). While they make up 5% of the US population, they represent half of the population infected with Hepatitis B. Available statistics also show the prevalence of Hepatitis C in the US has been increasing with a significant 250% increase from 2010 to 2014, as shown in figure 4 below.

Figure 4: Trends in Prevalence of Hepatitis C in the US (HHS.gov., 2021)



Incidences of Hepatitis C were four times higher in 2018 than in 2010. With increased heroin and opioid use in North America, there is also a significant increase in hepatitis B. From 2006 to 2013, Hepatitis B incidences increased by 114% in West Virginia, Kentucky, and Tennessee, as illustrated below. In 2018 approximately 50300 new infections of Hepatitis C were recorded, reaching a significant number of 2.4 million people who live with Hepatitis C (Mehta, & Reddivari, 2022).

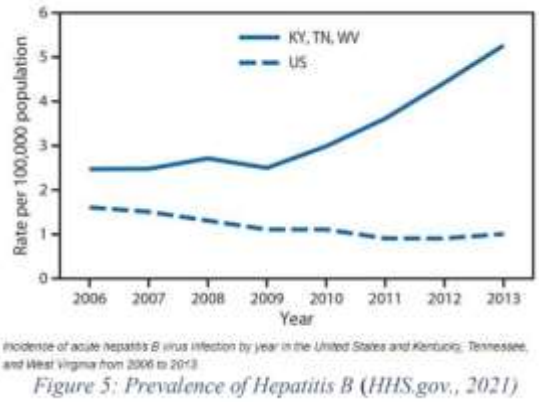


Figure 5: Prevalence of Hepatitis B (HHS.gov., 2021)

The high incidences of Hepatitis C and Hepatitis B are leading factors in higher rates of liver cirrhosis and premature deaths.

Immunology of Hepatitis

Immunology of Hepatitis A

Hepatitis A virus (HAV) does not develop into a chronic infection. HAV-specific antibodies offer a lifelong protective immunity to the infection that offers virus-neutralizing activity (Shin et al., 2016).

Control of acute infections is effective since virus-specific T-cellresponses are not delayed as in the case of HCV.

Immunology of Hepatitis B

Hepatitis B Virus (HBV) is effectively controlled in adults but can persist after neonatal infection. HBV is a double-stranded DNA virus. It is described as "enveloped, hepatotropic, oncogenic, hepadnavirus, noncytopathic for hepatocytes" (Vierling, 2007). The infection causes various outcomes influenced by the host's innate and adaptive immune responses. Moreover, its persistence or being cleared as a nonprogressive or progressive liver disease is influenced by a range of factors and characteristics of the virus and the host (Vierling, 2007). HBV has lifelong protective immunity from hepatitis B surface antigen (HBsAg)-specific antibodies which offer virus-neutralizing activity (Shin et al., 2016). Like HAV, there is effective control of the acute infection due to the robust and multiple virus-specific T-cell responses, which is otherwise not the case in HCV. However, sustained antigenic stimulation in chronic HBV infections leads to the virus-specific T cells being exhausted and functionally impaired, similar to chronic HCV infections. Chronic HBV is mainly through vertical transmission from the mother to the neonate.About 90% of individuals infected by HBV as adults recover (Rehermann & Nascimbeni, 2005). However, there are high reactivation risks for acute and chronic HBV infections following the replicative intermediates, which occur under immunologic control (Vierling, 2007). In the first week of infection, HBV does cause a detectable change in the expression of intrahepatic genes.

Immunology of Hepatitis C

The primary characteristic of the Hepatitis C Virus (HCV) is the establishment of a chronic persistent infection. HCV is a positive-stranded RNA virus. HCV causes high baseline ISGs in the liver, and the victims respond poorly to treatment leading to a severe lifelong infection. Particularly ISG15– ubiquitin-specific peptidase 18 (USP18)-mediated mechanism influences poor responses to interferon-α (IFNα)-based therapy (Shin et al., 2016). Even after spontaneous virus clearance, the HCV antibodies are not long-lasting. CV E1- and E2-specific antibodies' role in protective immunity and control of infection has not been elucidated, leadingto the increased risks of chronic infections. The virus-specific T-cell responses are remarkably delayed in acute infections, different in acute HAV and HBV, where the cell responses are robust. For chronic HCV infection, sustained antigenic stimulation causes the virusspecific T cells to be exhausted and functionally impaired (Rehermann & Nascimbeni, 2005). Only 20 to 40% of individuals infected by HCV as adults recover. In the first week of infection, HCV upregulates intrahepatic gene expression.

CONCLUSION:

Hepatitis is a major public health issue due to its multiple causes, higher transmission risks, the vulnerability of various populations, and the associated health complications. The most critical is viral Hepatitis caused by HAV, HBV, and HCV. Unlike HBV and HCV, HAV does not cause chronic infection. HBV is also unique since it has vertical transmissions and a higher risk of infection in adulthood. There is no vaccine for HCV; hence, interventions are focused on treating the symptoms and delaying the occurrence of major healthcare complications. Treatment of acute HAV, HBV, and HCV involves support to manage the symptoms and ensure spontaneous alleviation of the infection. This is important to improve population immunity and reduce susceptibility to infections following increased risk factors.

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