Review Article

An Overview on Hepatitis and its Prevention

Shubhankar Saha*, Pranabesh Sikdar, D. Lavanya and M. Niranajan Babu

Department of Pharmacology and Pharmaceutical Chemistry, Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh, India.

ABSTRACT

Hepatitis means inflammation of the liver. The liver is just one of several organs that the viruses affect. There are several hepatitis viruses; they have been named types A, B, C, D, E and G. The most common types of viral hepatitis are HAV, HBV and HCV. The different hepatitis are transmitted by various routes such as Parenteral transmission, Sexual transmission, sporadic cases, Transmission via blood transfusion. There are some non viral causes such as Parental transmission, Alcohol. The different sign and symptoms observed in the hepatitis are fatigue flu-like symptoms dark urine pale stool abdominal pain loss of appetite. Hepatitis can be diagnosed in different methods such as Physical Exam, Liver Biopsy, Liver Function Tests, Ultrasound, Blood Tests and Viral Antibody Testing. Hepatitis vaccines are generally used to control the hepatitis caused by different modes.

Keywords: Hepatitis, Liver, Chronic Hepatitis A, Hepatitis B, Hepatitis C.

VIRAL HEPATITIS

Hepatitis means inflammation of the liver. Many illnesses and conditions can cause inflammation of the liver, for example, drugs, alcohol, chemicals, and autoimmune diseases. Many viruses, for example, the virus causing mononucleosis and the cytomegalovirus can inflame the liver. Most viruses, however, do not attack primarily the liver; the liver is just one of several organs that the viruses affect. There are several hepatitis viruses; they have been named types A, B, C, D, E and G. The most common hepatitis viruses are types A, B, and C. The focus of this review article is on these viruses that cause the majority of human viral hepatitis. [1, 2]

Hepatitis viruses multiply primarily in the liver cells. This can cause the liver to be unable to perform its functions. The following is a list of major functions of the liver:

1. The liver helps purify the blood by changing harmful chemicals into harmless ones. The source of these chemicals can be external, such as medications or alcohol, or internal, such as ammonia or bilirubin. These harmful chemicals are broken down into smaller chemicals to other chemicals that then are eliminated from the body in the urine or stool.
2. The liver produces many important substances, especially proteins that are necessary for good health. For example, it produces albumin, the protein building block of the body, as well as the proteins that cause blood to clot properly.
3. The liver stores many sugars, fats and vitamins until they are needed elsewhere in the body.
4. The liver builds smaller chemicals into larger, more complicated chemicals that are needed elsewhere in the body.

When the liver is inflamed, it does not perform these functions well, which brings about many of the symptoms, signs, and problems associated with any type of hepatitis.

EPIDEMIOLOGY

United States statistics

The Centers for Disease Control and Prevention conducts national surveillance for acute hepatitis A, B, and C. [3] In 2007, 2979 cases of acute symptomatic HAV infection were reported. This was the lowest incidence of HAV infection recorded to that point and represented a 90% decline from annual cases reported from 1995 through 2005. For HBV infection, 4519 acute, symptomatic cases were reported in 2007 also the lowest rate recorded to that point. With correction for asymptomatic cases and underreporting, the true number was estimated to be 43,000 new infections in 2007. The incidence of childhood HBV infection is not well

established, because more than 90% of such infections in children are asymptomatic.

Rates of HBV infection were highest in non-Hispanic blacks in 2007. Chronic HBV infection has a higher prevalence among Asian Pacific Islanders and non-Hispanic blacks. [4, 5]

The number of confirmed cases of acute hepatitis C increased slightly for 2007, from 802 reported cases in 2006 to 849 in 2007. The actual number of new HCV infections in 2007 was estimated to be around 17,000. About 70-90% of people infected progress to chronic HCV infection. Approximately 3.2 million people in the United States have chronic hepatitis C. [6]

International statistics

Worldwide, HAV is responsible for an estimated 1.4 million infections annually.HBV causes more than 4 million cases of acute hepatitis per year throughout the world, and it is estimated that approximately 350 million people are chronically infected with the virus. HBV leads to 1 million deaths annually as a result of viral hepatitis–induced liver disease.

COMMON TYPES OF VIRAL HEPATITIS

Currently there are 5 main varieties of these viruses and a sixth poorly characterised virus, causing distinct types of viral hepatitis:

Hepatitis A virus (HAV), causing a faecally-spread self-limiting disease.

Hepatitis B virus (HBV), causing a parenterally transmitted disease that may become chronic.

Hepatitis C virus (HCV) previously termed non-A, non-B (NANB) hepatitis virus involved chiefly in transfusion related hepatitis.

Hepatitis delta virus (HDV) which is sometimes associated as super infection with hepatitis B infection.

Hepatitis E virus (HEV), causing water-borne infection.

Hepatitis G virus (HGV), is a recently discovered transfusion-transmitted hepatotropic virus but is not known to cause hepatitis.

All these human hepatitis viruses are RNA viruses except HBV which is a DNA virus.

Though a number of other viral diseases such as infection with Epstein-Barr virus (in infectious mononucleosis), arbovirus (in yellow fever), cytomegalovirus, herpes simplex and several others affect the liver but the changes produced by them are nonspecific; the term viral hepatitis is strictly applied to infection of the liver by the hepatitis viruses.

Table 1: Features of Various Types of Hepatitis Viruses

Feature	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Agent	HAV	HBV	HCV	HDV	HEV
Identified	1973	1965	1989	1977	1980
Viral particle	27 nm	42 nm	30-60 nm	35-37 nm	33 nm
Genome	RNA,	DNA,	RNA,	RNA,	RNA,
Spread	Faeco-oral	Parenteral,	Parenteral,	Parenteral,	Water-borne
Incubation	15-45 days	30-180 days	20-90 days	30-50 days	15-60 days
Antigen(s)	HAV	HBsAg	HCV RNA	HBsAg	HEV
		HBcAg	C 100-3	HDV	
		HBeAg	C 33c		
Antibodies	anti-HAV	anti-HBs	anti-HCV	anti-HBs	anti-HEV
		anti-HBc		anti-HDV	
		anti-HBe			

HEPATITIS A VIRUS

HAV accounts for an estimated 1,781 new infections per year according to the most recent CDC data. The hepatitis caused by HAV is an acute illness that never becomes chronic. At one time, hepatitis A was referred to as "infectious hepatitis" because it could be spread easily from person to person like other viral infections. Infection with hepatitis A virus can be spread through the ingestion of food or water, especially where unsanitary conditions allow water or food to become contaminated by human waste containing hepatitis A (the fecal-oral mode of transmission). Hepatitis A typically is spread among household members and close contacts through the passage of oral secretions (intimate kissing) or stool (poor hand washing). It also is common to have infection spread to customers in restaurants and among children and workers in day care centers if hand washing and sanitary precautions are not observed. The incubation period of HAV is 15-45 days (average, 4 weeks). The virus is excreted in stool during the first few weeks of infection, before the onset of symptoms. Young children who are infected with HAV usually remain asymptomatic. Acute hepatitis A is more severe and has higher mortality in adults than in children. The explanation for this is unknown. Typical cases of acute HAV infection are marked by several weeks of malaise, anorexia, nausea, vomiting, and elevated aminotransferase levels. Jaundice develops in more severe cases. Some patients experience a cholestatic hepatitis, marked by the development of an elevated alkaline phosphatase level, in contrast to the classic picture of elevated aminotransferase levels. Other patients may experience several relapses during the course of a year. Less than 1% of cases result in FHF. HAV infection does not persist and does not lead to chronic hepatitis. [7]

HEPATITIS B VIRUS

This type derives from an infection with the hepatitis B virus (HBV). This type is transmitted through puncture wounds or contact with infectious body fluids, such as blood, saliva, or semen. Injection drug use, having sex with an infected partner, or sharing razors with an infected person increase your risk of getting hepatitis B. Out of the approximately 5% of the world's population that is chronically infected with HBV, about 20% will eventually develop HBV-related cirrhosis or HCC. According to the World Health Organization, HBV is the 10th leading cause of death worldwide. [8] More than 10% of people living in sub-Saharan Africa and in East Asia are infected with HBV. Maintenance of a high HBsAg carriage rate in these parts of the world is partially explained by the high prevalence of perinatal transmission and by the low rate of HBV clearance by neonates. A pool of approximately 1.25 million chronic HBV carriers exists in the United States. Of these patients, 4000 die of HBV-induced cirrhosis each year, and 1000 die of HBV-induced HCC.

Parenteral transmission

The vast majority of HBV cases around the world result from perinatal transmission. Infection appears to occur during the intrapartum period, or, rarely, in utero. Neonates infected via perinatal infection are usually asymptomatic. Although breast milk can contain HBV virions, the role of breastfeeding in transmission is unclear.

Sexual transmission

HBV is transmitted more easily than human immunodeficiency virus or HCV. Infection is associated with vaginal intercourse, genital-rectal intercourse, and oral-genital intercourse. An estimated 30% of sexual partners of patients infected with HBV also contract HBV infection. However, HBV cannot be transmitted through kissing, hugging, or household contact (eg, sharing towels, eating utensils, or food). Sexual activity is estimated to account for as many as 50% of HBV cases in the US.

Sporadic cases

In approximately 27% of cases, the cause of HBV infection is unknown. Some of these cases, in fact, may be due to sexual transmission or contact with blood.

HEPATITIS C VIRUS

The CDC reported that there were about 16,500 reported new cases per year of hepatitis C. HCV hepatitis was previously referred to as "non-A, non-B hepatitis," because the causative virus had not been identified, but it was known to be neither HAV nor HBV. HCV usually is spread by shared needles among drug abusers, blood transfusion, hemodialysis, and needle sticks. Approximately 90% of transfusion-associated hepatitis is caused by HCV. HCV is the most frequent cause of parenteral non-A, non-B hepatitis worldwide. Hepatitis C is prevalent in 0.5-2% of populations in nations around the world. The highest rates of disease prevalence are found in patients with hemophilia and in

IDUs. In the 1980s, as many as 180,000 new cases of HCV infection were described each year in the United States by 1995, there were only 28,000 new cases each year. [9] The decreasing incidence of HCV was explained by a decline in the number of cases of transfusion-associated hepatitis and by a decline in the number of cases associated with IV drug use.

Transmission via blood transfusion

Screening of the US blood supply has dramatically reduced the incidence of transfusion-associated HCV infection. [10, 11] Before 1990, 37-58% of cases of acute HCV infection (then known as NANB) were attributed to the transfusion of contaminated blood products; today, only about 4% of acute cases are attributed to transfusion. HCV is estimated to contaminate 0.01-0.001% of units of transfused blood. Acute hepatitis C remains an important issue in dialysis units, where patients' risk for HCV infection is about 0.15% per year.

Transmission via intravenous and intranasal drug use

IV drug use remains an important mode of transmitting HCV. The use of IV drugs and the sharing of paraphernalia used in the intranasal snorting of cocaine and heroin account for approximately 60% of new cases of HCV infection. More than 90% of patients with a history of IV drug use have been exposed to HCV.

Transmission via occupational exposure

Occupational exposure to HCV accounts for approximately 4% of new infections. On average, the chance of acquiring HCV after a needle-stick injury involving an infected patient is 1.8%. Reports of HCV transmission from healthcare workers to patients are extremely uncommon.

Sexual transmission

Approximately 20% of cases of hepatitis C appear to be due to sexual contact. In contrast to hepatitis B, approximately 5% of the sexual partners of those infected with HCV contract hepatitis C.

The US Public Health Service recommends that persons infected with HCV be informed of the potential for sexual transmission. Sexual partners should be tested for the presence of antibodies to HCV (anti-HCV). Safe-sex precautions are recommended for patients with multiple sex partners. Current guidelines do not recommend the use of barrier precautions for patients with a steady sexual partner. However, patients should avoid sharing razors and toothbrushes with others. In addition, contact with patients' blood should be avoided.

Parenteral transmission

Parenteral transmission of HCV appears to be uncommon. It is observed in fewer than 5% of children born to mothers infected with HCV. The risk of perinatal transmission of HCV is higher in children born to mothers co infected with HIV and HCV. [12] Available data show no increase in HCV infection in babies who are breastfed. The USPHS does not advice against pregnancy or breastfeeding for women infected with HCV.

HEPATITIS D VIRUS

This is also called delta hepatitis. Hepatitis D is a serious liver disease caused by the hepatitis D virus (HDV). HDV is contracted through puncture wounds or contact with infected blood. Hepatitis D is a rare form of hepatitis that occurs in conjunction with hepatitis B infection. It's very uncommon in the United States. HDV requires the presence of HBV to replicate; thus, HDV infection develops only in patients who are positive for HBsAg. [13] Patients may acquire HDV as a co infection (at the same time that they contract HBV), or the HDV may super infect patients who are chronic HBV carriers. Although hepatitis D is not a reportable disease, the CDC estimates that it results in 7500 infections each year. Approximately 4% of cases of acute hepatitis B are thought to involve co infection with HDV.

HDV is believed to infect approximately 5% of the world's 350 million HBsAg carriers. The prevalence of HDV infection in South America and Africa is high. Italy and Greece are areas of intermediate endemicity and are well studied. Only about 1% of HBV-infected individuals in the United States and Northern Europe are co infected with HDV.

The sharing of contaminated needles in IV drug use is thought to be the most common means of transmitting HDV. IDUs that is also positive for HBsAg have been found to have HDV prevalence rates ranging from 17% to 90%. Sexual transmission and perinatal transmission are also described. [14]

HEPATITIS E VIRUS

Hepatitis E is a waterborne disease caused by the hepatitis E virus (HEV). Hepatitis E is mainly found in areas with poor sanitation and is

typically caused by ingesting fecal matter. This disease is uncommon in the United States. [15,16] However, cases of hepatitis E have been reported in the Middle East, Asia, Central America, and Africa, reports the CDC. Hepatitis A and E are normally contracted from eating contaminated food or drinking contaminated water. Hepatitis B, C, and D are contracted through contaminated blood. These forms of hepatitis can be either acute or chronic. Types B and C usually become chronic. HEV is the primary cause of enterally transmitted NANB hepatitis. It is transmitted via the fecal-oral route and appears to be endemic in some parts of the less-developed countries, where most outbreaks occur. HEV can also be transmitted vertically to the babies of HEV-infected mothers. It is associated with a high neonatal mortality. [17] In one report, anti-HEV antibodies were found to be present in 29% of urban children and 24% of rural children in northern India. [18] Sporadic infections are observed in persons traveling from Western countries to these regions with hepatitis C infection. Some cases have progressed to cirrhosis. [19, 20]

HEPATITIS G VIRUS was recently discovered and resembles HCV, but more closely, the flaviviruses; the virus and its effects are under investigation, and its role in causing disease in humans is unclear. [21]

PATHOGENESIS

The exact mechanism by which hepatitis A occurs is not established clearly. It may occur due to cytoplasmic or immunological hepatocyte damage. hepatocyte damage may be due to natural killer cells or lymphokine activated killer cells. These cells stimulate the cytotoxic T lymphocytes to cause destruction of the liver cells. Subsequent death of hepatocytes releases virus and finally leads to the development of the disease. The mechanism by which hepatitis B develops is immunological hepatocyte destruction which is similar to that occurring with HAV. The mechanism by which hepatitis C develops is either direct or indirect immunological responses produced by HCV. Direct mechanism involves the accumulation of viral proteins or intact virus in the hepatocytes. Indirect mechanism the virus stimulates liver CD8+ lymphocytes via antigen independent pathway that activates cytotoxic T lymphocyte and initiates hepatocyte destruction. A very small role is played by autoimmune mechanism like anti-liver kidney microsomal antibodies to bring about hepatic damage. Hepatitis D virus causes hepatitis mainly via immune mediated response. It is mainly caused by the auto antibodies associated with HDV.

Pathogenesis of Hepatitis E and G virus not clearly described. It may be due to self limited episode. [22]

CAUSES OF NONVIRAL HEPATITIS

Alcohol

Hepatitis can be caused by liver damage from excessive alcohol consumption. This is sometimes referred to as alcoholic hepatitis. The alcohol causes the liver to swell and become inflamed. Other toxic causes include overuse of medication or exposure to poisons. [23]

Autoimmune Disease

The immune system may mistake the liver as a harmful object and begin to attack it, hindering liver function.

Common symptoms of Hepatitis

Signs and symptoms of acute hepatitis appear quickly. They include:

- fatigue
- flu-like symptoms
- dark urine
- pale stool
- abdominal pain
- loss of appetite
- unexplained weight loss
- yellow skin and eyes, which may be signs of jaundice

HEPATITIS DIAGNOSIS

Diagnosis of viral hepatitis is based on symptoms and physical findings as well as blood tests for liver enzymes, viral antibodies, and viral genetic materials. [24]

Symptoms and physical findings

Diagnosis of acute viral hepatitis often is easy, but diagnosis of chronic hepatitis can be difficult. When a patient reports symptoms of fatigue, nausea, abdominal pain, darkening of urine, and then develops jaundice, the diagnosis of acute viral hepatitis is likely and can be confirmed by blood tests. On the other hand, patients with chronic hepatitis due to HBV and HCV often have no symptoms or only mild nonspecific symptoms such as chronic fatigue. Typically, these patients do not have jaundice until the liver damage is far advanced.

Blood tests

There are three types of blood tests for evaluating patients with hepatitis: liver enzymes, antibodies to the hepatitis viruses, and viral proteins.

Liver enzymes

Among the most sensitive and widely used blood tests for evaluating patients with hepatitis are the liver enzymes, called aminotransferase. They include aspartate aminotransferase (AST/SGOT) and alanine aminotransferase (ALT/SGPT). These enzymes normally are contained within liver cells. If the liver is injured the liver cells spill the enzymes into the blood, raising the enzyme levels in the blood and signaling that the liver is damaged. The normal values for AST is from 5 to 40 units/ liter of serum while the normal range of values for ALT is from 7 to 56 units/liter of serum. Patients with acute viral hepatitis can develop very high AST and ALT levels, sometimes in the thousands of units per liter. These high AST and ALT levels will become normal in several weeks or months as the patients recover completely from their acute hepatitis. In contrast, patients with chronic HBV and HCV infection typically have only mildly elevated AST and ALT levels, but these abnormalities can last years or decades. Since most patients with chronic hepatitis are asymptomatic (no jaundice or nausea), their mildly abnormal liver enzymes are often unexpectedly encountered on routine blood screening tests during yearly physical examinations or insurance physicals. Elevated blood levels of AST and ALT only means that the liver is inflamed, and elevations can be caused by many agents other than hepatitis viruses, such as medications, alcohol, bacteria, fungi, etc. In order to prove that a hepatitis virus is responsible for the elevations, blood must be tested for antibodies to each of the hepatitis viruses as well as for their genetic material.

Viral antibodies

Antibodies are proteins produced by white blood cells that attack invaders such as bacteria and viruses. Antibodies against the hepatitis A, B, and C viruses usually can be detected in the blood within weeks of infection, and the antibodies remain detectable in the blood for decades thereafter. Blood tests for the antibodies can be helpful in diagnosing both acute and chronic viral hepatitis. In acute viral hepatitis, antibodies not only help to eradicate the virus, but they also protect the patient from future infections by the same virus, that is, the patient develops immunity. In chronic hepatitis, however, antibodies and the rest of the immune system are unable to eradicate the virus. The viruses continue to multiply and are released from the liver cells into the blood where their presence can be determined by measuring the viral proteins and genetic material. Therefore in chronic hepatitis, both antibodies to the viruses and viral proteins and genetic material can be detected in the blood. tests for viral antibodies are: anti-HAV, antibody to hepatitis B core, an antibody directed against the inner core material of the virus, antibody to hepatitis B surface, an antibody directed against the outer surface envelope of the virus, antibody to hepatitis B e, an antibody directed against the genetic material of the virus, hepatitis C antibody, the antibody against the C virus

Viral proteins test

Hepatitis B surface antigen, hepatitis B DNA, hepatitis B e antigen, hepatitis C RNA

Other tests

Obstruction of the bile ducts, from either gallstones or cancer, occasionally can mimic acute viral hepatitis.

Physical Exam

During a physical examination, doctor may press down gently on abdomen to see if there's pain or tenderness. Doctor may also feel to see if our liver is enlarged. If our skin or eyes are yellow, doctor will note this during the exam.

Liver Biopsy: A liver biopsy is an invasive procedure that involves the doctor taking a sample of tissue from your liver. This is a closed procedure. In other words, it can be done through the skin with a needle and doesn't require surgery. This test allows your doctor to determine if an infection or inflammation is present or if liver damage has occurred.

Ultrasound: An abdominal ultrasound uses ultrasound waves to create an image of the organs within the abdomen. This test will reveal fluid in the abdomen, an enlarged liver or liver damage.

Table 2: Standard Liver tests, their origin and disease

Parameter	Origin	Disease
AST	Liver, skeletal muscle, cardiac muscle, red blood cells, brain, pancreas, lungs	Hepatocellular injury of any cause, myopathies, myocardial infarct, hemolysis
ALT	Liver, kidneys, skeletal muscle	Hepatocellular injury of any cause, myopathies
AP	Liver, bone, placenta, kidneys, intestines	Cholestatic liver disease; sarcoidosis; pregnancy; lymphoma; bone, kidney, and intestinal diseases
γ-Glutamyl transferase	Biliary epithelial cells, kidneys, pancreas, prostate	Biliary or pancreatic disease, myocardial infarct, renal diseases, chronic lung disease, diabetes
Conjugated bilirubin	Hemolysis, insufficient excretion from the liver	Severe liver injury from any cause Rotor syndrome, Dubin-Johnson syndrome
Unconjugated bilirubin	Hemolysis	Hemolysis, Gilbert syndrome, Crigler-Najjar syndrome
Albumin	Produced in hepatocytes	Low in nephrotic syndrome, malnutrition, protein-losing enteropathy
Prothrombin time	Clotting factors produced in hepatocytes	Prolonged in liver disease, vitamin K deficiency, fat malabsorption, pancreatic insufficiency

HEPATITIS TREATMENT

Acute hepatitis

Patients with acute viral hepatitis, the initial treatment consists of relieving the symptoms of nausea, vomiting, and abdominal pain. Careful attention should be given to medications or compounds, which can have adverse effects in patients with abnormal liver function only those medications that are considered necessary should be administered since the impaired liver is not able to eliminate drugs normally, and drugs may accumulate in the blood and reach toxic levels. Moreover, sedatives and "tranquilizers" are avoided because they may accentuate the effects of liver failure on the brain and cause lethargy and coma. The patient must abstain from drinking alcohol, since alcohol is toxic to the liver. It occasionally is necessary to provide intravenous fluids to prevent dehydration caused by vomiting. Patients with severe nausea and/or vomiting may need to be hospitalized for treatment and intravenous fluids.

Acute HBV is not treated with antiviral drugs. Acute HCV though rarely diagnosed can be treated with several of the drugs used for treating chronic HCV. Treatment of HCV is recommended primarily for the 80% of patients who do not eradicate the virus early. Treatment results in clearing of the virus in the majority of patients.

Chronic hepatitis

Treatment of chronic infection with hepatitis B and hepatitis C usually involves medication or combinations of medications to eradicate the virus. Doctors believe that in properly selected patients, successful eradication of the viruses can stop progressive damage to the liver and prevent the development of cirrhosis, liver failure, and liver cancer. Alcohol aggravates liver damage in chronic hepatitis, and can cause more rapid progression to cirrhosis. Therefore, patients with chronic hepatitis should stop drinking alcohol. Smoking cigarettes also can aggravate liver disease and should be stopped. [25, 26]

Medications for chronic hepatitis C infection include: [27]

1. injectable alpha interferons
2. oral ribavirin
3. oral boceprevir
4. simeprevir
5. oral sofosbuvir
6. oral simeprevir

Medications for chronic hepatitis B infection include: [28, 29,]

1. injectable alpha interferons
2. oral lamivudine
3. oral adefovir
4. oral entecavir

Ongoing research and development of new antiviral agents, the current list of medications for chronic hepatitis B and C infections is likely to change every year. Many of those drugs which are currently available are rarely used because of newer, safer, and more effective alternatives. In addition, recent research has shown that combination of certain antiviral medications result in a cure in many patients with chronic hepatitis C. [30, 31] Further studies and FDA approval is pending.

HEPATITIS VACCINATIONS

Hepatitis A

Two hepatitis A vaccines are available in the US, hepatitis A vaccine (Havrix, Vaqta). Both contain inactive hepatitis A virus. For adults, two doses of the vaccine are recommended. After

the first dose, protective antibodies develop in 70% of vaccine recipients within 2 weeks, and almost 100% of recipients by 4 weeks. After two doses of the hepatitis A vaccine, immunity against hepatitis A infection is believed to last for many years. Individuals at increased risk for acquiring hepatitis A and individuals with chronic liver disease should be vaccinated. Although individuals with chronic liver disease are not at increased risk for acquiring hepatitis A, they can develop serious liver failure if they become infected with hepatitis A and, thus, they should be vaccinated. Protective antibodies take weeks to develop; travelers to countries where infection with hepatitis A is common should be vaccinated at least 4 weeks before departure. The Centers for Disease Control recommends that immunoglobulin be given in addition to vaccination if departure is prior to 4 weeks. Immunoglobulin provides quicker protection than the vaccines, but the protection is short-lived.

Hepatitis B

For active vaccination, a harmless hepatitis B antigen is given to stimulate the body's immune system to produce protective antibodies against the surface antigen of hepatitis B. Vaccines that are currently available in the U.S. are made using recombinant DNA technology. [8] These recombinant hepatitis B vaccines, hepatitis B vaccine (Energix-B and Recombivax-HB) are constructed to contain only that part of the surface antigen that is very potent in stimulating the immune system to produce antibodies. The vaccine contains no viral component other than the surface antigen, and therefore, cannot cause HBV infections. Hepatitis B vaccines should be given in three doses with the second dose 1 to 2 months after the first dose and the third dose 4 to 6 months after the first dose. For the best results, the vaccinations should be given in the deltoid muscles and not in the buttocks. Hepatitis B vaccines are 95% effective in healthy adults. Five percent of vaccinated individuals will fail to develop the necessary antibodies for immunity after the three doses. Patients with weakened immunity older patients, and patients undergoing kidney hemo dialysis are more likely to fail to respond to the vaccines. All pregnant women should have a blood test for the antibody to hepatitis B virus surface antigen. Women who test positive for hepatitis B virus risk transmitting the virus to their infants during labor, and, therefore, infants born to mothers with hepatitis B infection should receive HBIG in addition to hepatitis B vaccine at birth. The reason for giving both immunoglobulin and vaccine is that even though hepatitis B vaccine can offer long lasting, active immunity, immunity takes weeks or months to develop. Until active immunity develops, the short-lived, passive antibodies from the HBIG protect the infant.

Hepatitis C and D

There is currently no vaccine for hepatitis C. Development of such a vaccine is difficult due to the six different forms of hepatitis C. No vaccine for hepatitis D is available. However, HBV vaccine can prevent an individual not infected with HBV from contracting hepatitis D because hepatitis D virus requires live HBV to replicate in the body.

New Drugs Part of a New Front in Treating Hepatitis C

Epclusa is the latest antiviral drug to get FDA approval, but like other medications it comes with a price. Epclusa is a single pill taken once a day for 12 weeks. It is the first drug to clear all six strains of the virus in up to 99 percent of patients. It also is the latest direct acting antiviral a drug that stops the virus from replicating itself. Previous drugs worked by helping the body fight off the infection. [32]

Hepatitis E

There are currently no specific medical therapies to treat hepatitis E. Because the infection is often acute, it typically resolves on its own. People with this type of infection are often advised to get adequate rest, drink plenty of fluids, get enough nutrients, and avoid alcohol. [33]

COMPLICATIONS OF HEPATITIS

Chronic hepatitis B or C can often lead to more serious health problems. Because the virus primarily affects the liver, people with chronic hepatitis B or C are at risk for

1. chronic liver disease
2. cirrhosis (scarring of the liver)
3. cancer of the liver (in rare cases) [34]

When the liver stops functioning normally, liver failure can occur. Complications of liver failure include:

1. bleeding disorders
2. a buildup of fluid in the abdomen
3. increased blood pressure in portal veins that enter the liver
4. kidney failure
5. hepatic encephalopathy, which can involve fatigue, memory loss, and

diminished mental abilities due to the buildup of toxins that affect the brain (especially ammonia)

6. hepatocellular carcinoma, which is a form of liver cancer[]

People with chronic hepatitis C are encouraged to avoid alcohol because it can accelerate liver disease and failure. Certain supplements, prescription, and over-the-counter medications can also affect liver function.

Medications for Hepatitis

Five new drugs are quickly becoming the standard for treating hepatitis

- Ombitasvir, paritaprevir, dasabuvir, ritonavir
- Simeprevir
- Sofosbuvir

Simeprevir and sofosbuvir both need to be combined with the older hepatitis C drugs interferon and ribavirin but are now replacing boceprevir and telaprevir as the combination with interferon and ribavirin. Sofosbuvir can also be used without interferon for some types of the disease.

Elbasvir-grazoprevir and ledipasvir-sofosbuvir can be taken on their own. The Viekira pack means taking two ombitasvir, paritaprevir, ritonavir tablets once daily in the morning and one dasabuvir tablet twice daily morning and evening for at least 12 weeks. It can be used with or without ribavirin, but it is not recommended in patients with underlying liver disease.

CONCLUSION

Hepatitis is one of the dreadful disease the human kind is fighting with. The different methods of transmission and the different types of hepatitis have been discussed in the above review article. Vaccination for hepatitis plays a major role in the treatment for the hepatitis. The different drugs reported for the treatment of the hepatitis are Ombitasvir, paritaprevir, dasabuvir, ritonavir, Simeprevir and Sofosbuvir. Certain drugs such as discovered such as Epclusa which yet to approved by the FDA. The chronic condition can lead to the accumulation of water in the abdomen, kidney failure, hepatic encephalopathy and lastly liver cancer. The different medication used in case of chronic hepatitis A, B, C, D are alpha interferons, oral ribavirin, oral boceprevir, simeprevir, oral sofosbuvir, oral simeprevir. This article can be used as the review for further research of a more safer drug to treat hepatitis.

REFERENCES

1. Wasley A, Grytdal S, Gallagher, K, Surveillance for acute viral hepatitis--United States. 2006, 57(2), 1-24.
2. Previsani N, Lavanchy D. World Health Organization. Hepatitis B (WHO/CDS/CSR/LYO/2002.2). 2002.
3. Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR Recomm Rep. 2012, 61:1-32.
4. Keeffe E B, Dieterich D T, Han S H, Jacobson I M, Martin P, Schiff E R, *et al.* A treatment algorithm for the management of chronic hepatitis B virus infection in the United States. *Clin Gastroenterol Hepatol*. 2008, 6(12):1315-41.
5. Keeffe EB, Dieterich DT, Han SH, Jacobson IM, Martin P, Schiff ER, *et al.* A treatment algorithm for the management of chronic hepatitis B virus infection in the United States. *Clin Gastroenterol Hepatol*. 2004, 2(2):87-106.
6. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, *et al.* Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet. 2011, 378(9791):571-83.
7. Previsani N, Lavanchy D. World Health Organization. Hepatitis A (WHO/CDS/CSR/EDC/2000.7). 2000.
8. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat*. 2004, 11(2):97-107.
9. Alter MJ. Epidemiology of hepatitis C. *Hepatology*. 1997, 6:62S-65S.
10. Previsani N, Lavanchy D. World Health Organization. Hepatitis C (WHO/CDS/CSR/LYO/2003.). 2002.
11. Krawitt EL. Autoimmune hepatitis: classification, heterogeneity, and treatment. *Am J Med.* 1994, 96(1A):23S-26S.
12. Dienstag JL. Sexual and perinatal transmission of hepatitis C. *Hepatology*. 1997, 26: 66S-70S.
13. Adhami T, Levinthal G. Hepatitis D. The Cleveland Clinic Disease Management Project. 2002.

14. Previsani N, Lavanchy D. World Health Organization. Hepatitis D. (WHO/CDS/CSR/NCS/2001.1). 2001.
15. Kumar A, Beniwal M, Kar P, Sharma JB, Murthy NS. Hepatitis E in pregnancy. *Int J Gynaecol Obstet*. 2004, 85(3):240-4.
16. Kamar N, Selves J, Mansuy JM, Ouezzani L, Péron JM, Guitard J, *et al.* Hepatitis E virus and chronic hepatitis in organ-transplant recipients. *N Engl J Med*. 2008, 358(8):811-7.
17. Khuroo MS, Kamili S, Khuroo MS. Clinical course and duration of viremia in vertically transmitted hepatitis E virus (HEV) infection in babies born to HEV-infected mothers. *J Viral Hepat*. 2009, 16(7):519-23.
18. Mathur P, Arora NK, Panda SK, Kapoor SK, Jailkhani BL, Irshad M. Sero-epidemiology of hepatitis E virus (HEV) in urban and rural children of North India. Indian Pediatr. 2001, 38(5):461-75.
19. Gérolami R, Moal V, Colson P. Chronic hepatitis E with cirrhosis in a kidney-transplant recipient. *N Engl J Med*. 2008, 358(8):859-60.
20. Kamar N, Mansuy JM, Cointault O, Selves J, Abravanel F, Danjoux M, *et al.* Hepatitis E virus-related cirrhosis in kidney- and kidney-pancreas-transplant recipients. *Am J Transplant.* 2008, 8(8):1744-8.
21. Adhami T, Levinthal G. Hepatitis E and Hepatitis G/GBV-C. The Cleveland Clinic Disease Management Project. 2002.
22. Mohan Harsh, Text book of Pathology.2010, 6th edition: 605-611.
23. Kerry Wilbur, Nonviral Hepatitis. J*ournal of Pharmacy Practice.* 2009, 22(4): 388-404.
24. Nathalie Boyer, Patrick Marcellin, Pathogenesis, diagnosis and management of hepatitis. *Journal of hepatology*. 2000, 32, (1): 98-112.
25. Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, *et al.* Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology*. 2008, 134(4):960-74.
26. Batts KP, Ludwig J. Chronic hepatitis. An update on terminology and reporting. *Am J Surg Pathol.* 1995 Dec. 19(12):1409-17.
27. Fattovich G, Giustina G, Sanchez-Tapias J, Quero C, Mas A, Olivotto PG, *et al.* Delayed clearance of serum HBsAg in compensated cirrhosis B: relation to interferon alpha therapy and disease prognosis. European Concerted Action on Viral Hepatitis (EUROHEP). *Am J Gastroenterol.* 1998, 93(6):896-900.
28. Liaw YF, Sung JJ, Chow WC, Farrell G, Lee CZ, Yuen H, *et al.* Lamivudine for patients with chronic hepatitis B and advanced liver disease. *N Engl J Med*. 2004, 351(15):1521-31.
29. Schmilovitz-Weiss H, Ben-Ari Z, Sikuler E, Zuckerman E, Sbeit W, Ackerman Z, *et al.* Lamivudine treatment for acute severe hepatitis B: a pilot study. Liver Int. 2004, 24(6):547-51.
30. Thomas DL, Thio CL, Martin MP, Qi Y, Ge D, O'Huigin C, *et al.* Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. *Nature.* 2009, 461(7265):798-801.
31. Ge D, Fellay J, Thompson AJ, Simon JS, Shianna KV, Urban TJ, *et al*. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. *Nature*. 2009, 461(7262):399-401.
32. FDA News Release. FDA Approves Rapid Test for Antibodies to Hepatitis C Virus. June 2010.
33. Previsani N, Lavanchy D. World Health Organization. Hepatitis E. (WHO/CDS/CSR/EDC/2001.12.). 2001.
34. Tabor E. The role of tumor suppressor genes in the development of hepatocellular carcinoma. In: Okuda K, Tabor E, eds. Liver Cancer. New York, NY: Churchill Livingstone; 1997,89-95.