HEPATITIS AND PHYSIOLOGY OF LIVER CELLS - A REVIEW

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ABSTRACT

Hepatitis means inflammation of the liver, with accompanying damage to liver cells. Hepatitis is classified into chronic and acute hepatitis and the different types are hepatitis A, B, C, D and E. However, their causes, modes of transmission, incubation periods, signs and symptoms, diagnosis, treatments and preventions were also discussed. Hepatitis causes liver diseases such as liver cirrhosis, hepatocellular carcinoma, and jaundice. It is reviewed that when chronic hepatitis C or B goes untreated, it causes scarring to the liver (cirrhosis) and an increased chance of liver cancer and liver failure, ending in death. Hepatitis viruses, especially Hepatitis A Virus (HAV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection are endemic in Nigeria and constitute a public health menace, the prevalence of HBV in some professional group was found to be highest among the female sex workers (FSWs). Global prevalence of chronic HAV and HBV infection is highest in Africa, Asia and Western Pacific; intermediate in Southern and Eastern Europe and Lowest in Western Europe, North America and Australia. Pregnant women, in the 3rd trimester of gestation are found to be more likely to be infected than those in the 1st and 2nd trimester, thus, the virus can be transmitted from the infected mother to the offspring during birth. The group of people who stood the high risk of contracting both HAV and HBV infections were also revealed. It is recommended that hepatitis screening should be incorporated in the routine antenatal check up, and government at all levels should be proactive in innovation and immediate implementation of a general child and adolescents immunization against HBV to prevent further spread of this virus.

Keywords: Hepatitis, Liver cell, cirrhosis, jaundice, hepatocellular carcinoma

INTRODUCTION

Despite the availability of a safe and effective vaccine against hepatitis infection for over two decades now, the overall burden of the disease remains enormous with over two billion people infected worldwide and approximately one million deaths occur annually from hepatitis related diseases (Lavanchy, 2004). Several studies have demonstrated that hepatitis especially hepatitis B virus (HBV) is endemic in Nigeria and have the seroprevalence among various groups (Olubuyide et al., 1997; Belo, 2000; Odemuyiwa et al., 2001; Cobelens et al., 2004). Most of the information of HBV prevalence in Nigeria is available from blood donors (Otgbayo et al., 2003; Ejele and Ojule, 2004). It is highly prevalent among the female sex workers (FSW) and pregnant women in Nigeria. Hepatitis is one of the diseases in pregnancy that causes jaundice in women, and if left untreated may lead to the birth of babies with low intelligent quotient (IQ).

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are major public health concern (Wasley and Alter, 2000; Modi and feld, 2007). Like in the case of HIV, the highest incidence of the acute hepatitis is among the young adults. Therefore, as a result of all these burdens the disease cause to human, I deem it right to undertake this study to discuss on the hepatitis and the physiology of liver cells.

General Overview of Hepatitis

The word hepatitis was coined from two Greek words hepatitis - liver and its- inflammation. Thus, hepatitis means inflammation of the liver, with accompanying damage to liver cells (BMA, 2008). Hepatitis is a general term meaning inflammation of the liver and can be caused by a variety of different viruses such as hepatitis A, B, C, D and E. Hepatitis B virus (HBV) infection is endemic in Nigeria and constitutes a public health menace (Ndams et al., 2008). WHO (1990) reported that Nigeria is a highly endemic area with a prevalence greater than 8 %. The prevalence of HBV in normal population in Nigeria ranges from 2.7 % to 13.3 % (Kulkarnii et al., 1986; Muula, 2000). HBV spot surveys amongst pregnant women in the country revealed a prevalence of 4.3 % in Port Harcourt (Akani et al., 2005), 15.1 % in Jos (Egah et al., 2007), 8.3 % in Zaria (Luka et al., 2008), 11.6 % in Maiduguri (Harry et al., 1994), 13.8 % in Lagos (Nasidi et al., 1993), 5.7 % in Ilorin (Agbede et al., 2007) and 2.19 % in Benin City (Onakewhor et al., 2008). Prevalent rate in other cities in Nigeria are yet to be investigated.

Similar studies in other parts of the world reported a prevalence of 10% in Hong Kong (Kong et al., 1997), 10% in India (Sharma et al., 1995), 12 % in Taiwan (Lin et al., 2003), 17.3 % in Burkino Faso (Collenberg et al., 2006), 11 % in Papua New Guinea (Clegg, 1991) and 3.7 % in Ethiopia (Awol and Gebre-Slassie, 2005). According to Juszozyk (2000), the global prevalence of chronic hepatitis B virus (HBV) infection varies, being highest in Africa, Asia and Western Pacific (>8%), intermediate (2-7%) in southern and Eastern Europe and lowest (<2%) in Western Europe, North America and Australia.

A hepatitis B positive mother also confers the risk of passing the infection to her offspring. Siriprakash and Anil (1997), reported that neonates who contact HBV infection will almost have 90 % risk of developing chronic hepatitis and cirrhosis. Otgbayo et al. (2008) reported that there is overlap in risk factor for HIV, HBV and HCV. HIV co-infection with HBV and /or HCV is associated with increased risks of liver-related morbidity and mortality among the HIV/AIDS patients (Garcia et al., 2001; Thio et al., 2002).

According to WHO (2003), the global burden of HCV and HBV is 170 million and 400 million respectively. As at 2010, China has 120 million infected people, followed by India and Indonesia with 40 million and 12 million respectively. So far, in March 2002, 151 countries have introduced hepatitis B vaccine within their national immunization programmes (Kane, 1998; VHPB, 1996; VHPB, 1998). In other countries, universal vaccination is still being postponed. The reasons for this are the weakness of a social commitment to preventive medicine and vaccines, the lack of medical and public awareness, the view of hepatitis B infection as a limited public health problem that does not justify the expense and other efforts of

Liver Cells

A hepatocyte is a cell of the main tissue of the liver. Hepatocytes make up 70-80% of the liver's cytoplasmic mass. These cells are involved in Protein synthesis, Protein storage, Transformation of carbohydrates, Synthesis of cholesterol, bile salts and phospholipids and detoxification, modification, and excretion of exogenous and endogenous substances. The hepatocyte also initiates formation and secretion of bile. Liver is the largest organ in the body, contributing about 2% of the total body weight, or about 1.5 kg in the average adult human (Guyton and Hall, 2006). It is a roughly wedge-shaped, red-brown structure lies in the upper abdominal cavity, directly below the diaphragm (BMA, 2002). The liver is divided into two main lobes (right and left lobe) both containing 50,000 to 100,000 individual lobules in human (BMA, 2002). The lobules are surrounded by branches of the hepatic artery, which supplies the liver with oxygenated blood, and the portal vein, which supplies nutrient-rich blood (BMA, 2002). Some biochemical parameters are contained in the liver which helps in the normal processes of the liver cells. Some of these parameters include Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), total and direct serum bilirubin, total protein, alkaline phosphatase (ALP), prothrombin time, albumin etc. Under normal liver conditions, the laboratory results shows elevated levels of some of the parameters stated above. The normal values of AST in adult male and female is 14 – 20 U/L and 10-36 U/L respectively, ALT levels are 10-40 U/L and 7-35 U/L in male and females respectively (Chernecky and Berger, 2008). Total bilirubin in normal adult is 0.3-1.0 mg/dl, Urea is 2.5-7.5 mmol/L.

Moreover, under abnormal conditions, may be when someone gets hepatitis, the liver will no longer perform the above functions as supposed to be and can be affected to varying degrees (Guyton and Hall, 2006). When this happens, some of the biochemical parameters in the liver (liver panels) such as bilirubin, ALT, AST, albumin, total proteins etc., will vary either above or below normal levels (Robinson, 1995; Hollinger and Liang, 2001). The varying levels of the liver panels indicate that liver has been impaired, this may result to liver cirrhosis, liver cancer, jaundice etc.

Functions of Hepatocyte

Liver plays a vital role in the body because it produces and processes a wide range of chemical substances (BMA, 2002). The substances include important proteins for blood plasma, such as albumin. The liver also produces cholesterol and special proteins that help the blood to carry fats around the body. In addition, liver cell secrete bile, which removes waste products from the liver and aids the breakdown and absorption of fats in the small intestine. Another major function is the processing of nutrients for use by cells. The liver also stores excess glucose as glycogen. Similarly, it controls the blood level of amino acids. If the level of amino acids is too high, the liver converts the excess into glucose, proteins, other amino acids, or urea (for excretion). Finally, the liver helps to clear the blood of drugs and poisons by breaking them down and excreted in the bile or urine (detoxification).

Histology of the Hepatocyte

Hepatocytes display an eosinophilic cytoplasm, reflecting numerous mitochondria, and basophilic stippling due to large amounts of rough endoplasmic reticulum and free ribosomes. Brown lipofuscin granules are also observed (with increasing age) together with irregular unstained areas of cytoplasm; these correspond to cytoplasmic glycogen and lipid stores removed during histological preparation. The average life span of the hepatocyte is 5 months; they are able to regenerate. Hepatocyte nuclei are round with dispersed chromatin and prominent nucleoli. Anisokaryosis is common and often reflects tetraploidy and other degrees of polyploidy, a normal feature of 30-40% of hepatocytes in adult human liver (Séverine Celton-Morizur et al., 2010). Binschoa cells are also common. Hepatocytes are organised into plates separated by vascular channels (sinusoids), an arrangement supported by a reticulin (collagen type III) network. The hepatocyte plates are one cell thick in mammals and two cells thick in the chicken. Sinusoids display a discontinuous, fenestrated endothelial cell lining. The endothelial cells have no basement membrane and are separated from the hepatocytes by the space of Disse, which drains lymph into the portal tract lymphatics. Kupffer cells are scattered between endothelial cells; they are part of the reticuloendothelial system and phagocytose spent erythrocytes. Steatite (fat) cells store vitamin A and produce extracellular matrix and collagen; they are also distributed among endothelial cells but are difficult to visualise by light microscopy.

Hepatocytes are an important physiological example for evaluation of both biological and metabolic effects of xenobiotics. They are separated from the liver by collagenase digestion, which is a two step process. In the first step, the liver is placed in an isotonic solution, in which calcium is removed to disrupt cell-cell tight junctions by the use of a calcium chelating agent. Next, a solution containing collagenase is added to separate the hepatocytes from the liver stroma. This process creates a suspension of hepatocytes, which can be cultured and plated on 96 well plates for immediate use, or cryopreserved by freezing (Li and Albert, 2011). They do not proliferate in culture. Hepatocytes are intensely sensitive to damage during the cycles of cryopreservation including freezing and thawing. Even after the addition of classical cryoprotectants, there is still damage done while being cryopreserved (Hamel, 2006).

Classes of Hepatitis

Hepatitis is grouped into two major classes, they are as follows:

- Acute hepatitis
- Chronic Hepatitis

Acute Hepatitis

Acute hepatitis is short-term inflammation of the liver. In some cases, acute hepatitis may progress to chronic hepatitis if left untreated, but it rarely leads to acute liver failure (BMA, 2002). Acute hepatitis is fairly common. The most frequent cause is infection with a hepatitis virus, but can be caused by other infections such as cytomegalovirus infection. It may also result from an overdose of halothane or paracetamol or exposure to toxic chemicals including alcohol. Symptoms range from mild to severe pain, fever and jaundice.

Chronic Hepatitis

This is a long term inflammation of the liver. It eventually causes scar tissues to form and leads to liver cirrhosis. Chronic hepatitis may develop following an attack of acute hepatitis. It is a leading cause of liver related deaths among patients with HIV/AIDS worldwide (Koziel and Peters, 2007). It may also occur as a result of autoimmune disorder or, more rarely due to a metabolic disorder, such as haemochromatosis or wilson’s disease. Chronic hepatitis may cause slight tiredness or no symptoms at all.
Types of Hepatitis

Five types of hepatitis exist, but the first three are the most common. They are Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D and Hepatitis E.

Hepatitis A

Hepatitis A, one of the oldest diseases known to humankind, is a self-limited disease which results in fulminant hepatitis and death in only a small proportion of patients. It is also called epidemic hepatitis. Hepatitis A was formerly called Infectious hepatitis, Epidemic hepatitis, Epidemic jaundice, Catarhal jaundice and Type A hepatitis, HA and caused by hepatitis A virus (HAV) (Stapleton and lemon, 1994 and Hollinger and Ticehurst, 1996). Hepatitis A is actually considered less destructive than some other hepatitis viruses. Unlike some other hepatitis viruses, hepatitis A virus rarely leads to a permanent liver damage. Also, HAV affects all age groups and, once someone has recovered from the infection, that person has immunity to the virus, and he or she may probably never get it again. However, it is a significant cause of morbidity and socio-economic losses in many parts of the world (Stapleton and lemon, 1994 and Hollinger and Ticehurst, 1996). Transmission of HAV is typically by the faecal-oral route (lemon, 1994; Stapleton; 1995; Hollinger and Ticehurst, 1996; Stapleton and Lemon, 1997). Infections occur early in life in areas where sanitation is poor and living conditions are crowded. With improved sanitation and hygiene, infections are delayed and consequently the number of persons susceptible to the disease increases. Under these conditions, explosive epidemics can arise from faecal contamination of a single source.

HAV is resistant to thermal denaturation (survives at 70°C for up to 10 min), acid treatment (pH 1 for 2 h at room temperature), 20% ether, chloroform, dichlorodifluoromethane, and trichlorotrifluoroethane, perchloracetic acid (300 mg/l for 15 min at 20°C), detergent inactivation (survives at 37°C for 30 min in 1% SDS) and storage at -20°C for years. Also, the virus (HAV) can be inactivated by heating to 85°C for 1 min, autoclaving (121°C for 20 min), ultraviolet radiation (1.1 W at a depth of 0.9 cm for 1 min), formalin (8% for 1 min at 25°C), 8-propiolactone (0.03% for 72 h at 4°C), potassium permanganate (30 mg/l for 5 min), iodine (3 mg/l for 5 min), chlorine (free residual chlorine concentration of 2.0 to 2.5 mg/l for 15 min), chlorine-containing compounds (3 to 10 mg/l sodium hypochlorite at 20°C for 5 to 15 min) and shellfish from contaminated areas should be heated to 90°C for 4 min or steamed for 90 sec before use.

Endemicity of Hepatitis A

Geographical areas can be characterized by high, intermediate, or low levels of endemicity patterns of HAV infection. The levels of endemicity correlate with hygienic and sanitary conditions of each geographical area (Melinick, 1995; Steffen, 1995; Hollinger and Ticehurst, 1996; VHPB, 1997; Roff, 1998). In developing countries with very poor sanitary and hygienic conditions (parts of Africa, Asia and Central and South America), infection is usually acquired during early childhood as an asymptomatic or mild infection. Reported disease rates in these areas are therefore low and outbreaks of disease are rare. Reported disease incidence may reach 150 per 100,000 per year.

Similarly, developing countries with transitional economies and some regions of industrialized countries where sanitary conditions are variable (Southern and Eastern Europe, some regions in the Middle East), children escape infection in early childhood. Paradoxically, these improved economic and sanitary conditions may lead to a higher disease incidence, as infections occur in older age groups, and reported rates of clinically evident hepatitis A are higher.

In developed countries (Northern and Western Europe, Japan, Australia, New Zealand, USA, Canada) with good sanitary and hygienic conditions, infection rates are generally low. In countries with very low HAV infection rates, disease may occur among specific risk groups such as travelers.

### Table 1: Worldwide Endemicity of Hepatitis A Infection

<table>
<thead>
<tr>
<th>Endemicity</th>
<th>Regions by Epidemiological Pattern</th>
<th>Average Age of Patients (Years)</th>
<th>Most Likely Mode of Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high</td>
<td>AFRICA, PARTS OF SOUTH AMERICA, THE MIDDLE EAST AND OF SOUTH-EAST ASIA, BRAZIL’S AMAZON BASIN, CHINA AND LATIN AMERICA</td>
<td>UNDER 5</td>
<td>PERSON-TO-PERSON, CONTAMINATED FOOD AND WATER</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>1-4 MAY</td>
<td>PERSON-TO-PERSON, OUTBREAKS/ CONTAMINATED FOOD OR WATER</td>
</tr>
<tr>
<td>Intermediate</td>
<td>SOUTHERN AND EASTERN EUROPE, SOME REGIONS OF THE MIDDLE EAST</td>
<td>2-4 MAY</td>
<td>PERSON-TO-PERSON, OUTBREAKS/ CONTAMINATED FOOD OR WATER</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td>MAY-40</td>
<td>OVER 20</td>
</tr>
<tr>
<td>Very low</td>
<td>NORTHERN EUROPE, AND JAPAN</td>
<td>OVER 20</td>
<td>EXPOSURE DURING TRAVEL TO HIGH ENDIMICITY AREAS, UNCOMMON SOURCE</td>
</tr>
</tbody>
</table>

Source: (VHPB, 1997; Barzaga, 2000; Cianciara, 2000; Tanaka, 2000; Tufenkeji, 2000)

### Table 2: Estimated Number of Cases of Hepatitis A per Continental Region

<table>
<thead>
<tr>
<th>Region</th>
<th>Population (in Millions)</th>
<th>Incidence (per 100,000 per Year)</th>
<th>Cases (per Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>275</td>
<td>10</td>
<td>28,000</td>
</tr>
<tr>
<td>Central and South America</td>
<td>453</td>
<td>20-40</td>
<td>162,000</td>
</tr>
<tr>
<td>Europe</td>
<td>791</td>
<td>5-60</td>
<td>278,000</td>
</tr>
<tr>
<td>Africa and Middle East</td>
<td>827</td>
<td>20-60</td>
<td>251,000</td>
</tr>
<tr>
<td>Asia</td>
<td>2893</td>
<td>10-30</td>
<td>676,000</td>
</tr>
<tr>
<td>Oceania</td>
<td>28</td>
<td>15-30</td>
<td>5,000</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>1,399,000</td>
</tr>
</tbody>
</table>

Source: Hadler (1991)

Modes of Transmission

HAV is transmitted from person-to-person via the faecal-oral route (Hollinger and Ticehurst, 1996; Lemon, 1997). As HAV is abundantly excreted in faeces, and can survive in the environment for prolonged periods of time. Thus, hepatitis A may be acquired from faecally contaminated food or water and from waste water-contaminated drills or water supplies (Lemon, 1994; Hollinger and Ticehurst, 1996). Direct person-to-person spread is common under poor hygienic conditions (Lemon, 1994). Occasionally, HAV is also acquired through sexual contact (anal/oral) and blood transfusions (Lemon, 1994). It is not transmitted from infected mothers to
newborn infants, as anti-HAV IgG antibodies present during initial tages of HAV infection across the placenta and provide protection to the infant after delivery.

**Incubation Period**

Once a person is exposed to the virus, it takes between 15 and 40 days to produce symptoms (BMA, 2002).

**Signs and Symptoms**

It is possible to experience mild or no symptoms whatsoever, but even if this is the case, the person's faces will still be infectious to others (Ryder and Beckingham, 2001). However, signs and symptoms of HAV include a shot, mild, flu-like illness, nausea, vomiting and diarrhea, loss of appetite, weight loss, jaundice (yellow skin and white of the eyes, darker yellow urine and pale faeces), Itchy skin and abdominal pain.

The infection usually clears in up to 2 months, but may occasionally reoccur or persists longer in some people.

**Risk Groups for Hepatitis A**

Certain groups can be defined as high risk for contracting HAV (Steffen, 1995; Hollinger and Ticehurst, 1996; Lemon, 1997; VHB, 1997; Koff, 1998). They include people in household/sexual contact with infected persons, medical and paramedical personnel in hospitals, international travelers from developed countries to regions of the world where HAV is endemic (3/1000 to 20/1000 people per month’s stay abroad), persons living in regions with endemic hepatitis A, persons residing in areas where extended community outbreaks exist, preschool children attending day-care centres, their parents and siblings, day-care centre employees, residents and staff of closed communities (institutions), refugees residing in temporary camps following catastrophes, homosexually active men, injecting drug users using unsterilized injection needles, persons with clotting factor disorders, persons with chronic liver disease, food-service establishments/food handlers and persons working with non-human primates.

Persons falling into any of the above mentioned categories should consider being vaccinated as a preventive measure. Risk factors remain unidentified in as much as 50% of hepatitis A cases (VHB, 1997; Koff, 1998). Hepatitis A is contracted at least 100 times more frequently than typhoid fever or cholera.

**Hepatitis B**

Hepatitis B is a serious and common infectious disease of the liver affecting millions of people throughout the world (Robinson, 1995; Chisari and Ferrari, 1997; Mahoney and Kane, 1999; Ganem and Schnider, 2001; Hollinger and Liang, 2001). Hepatitis B has also been called type B hepatitis, serum hepatitis, homologous serum jaundice (Robinson, 1995; Mahoney and Kane, 1999). Hepatitis B is an infectious illness caused by hepatitis B virus (HBV) which infects the liver of humans causing an inflammation which was originally known as serum hepatitis (Barker et al., 1996). The disease has caused epidemics in parts of Asia and Africa, and it is endemic in China (Williams, 2006). WHO (2009), reported that about a quarter million people every year are ill as a result of hepatitis B, with India and Indonesia with 40 million and 12 million people respectively (WHO, 2004). According to WHO, an estimated 600,000 people every year are ill as a result of related infection (HSRH, 2011). The rest of the world falls into the intermediate range of HBV prevalence, with 2 to 8% of a given population being HBV carriers.

**Table 3: Worldwide Prevalence of hepatitis B**

<table>
<thead>
<tr>
<th>AREA</th>
<th>% of population positive for HBsAg</th>
<th>% of population positive foranti-HBs</th>
<th>NEONATAL INFECTION</th>
<th>CHILDOOD INFECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Hemisphere</td>
<td>0.2-0.5</td>
<td>4-6</td>
<td>Rare</td>
<td>Infrequent</td>
</tr>
<tr>
<td>Western Hemisphere</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central Europe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediterranean</td>
<td>2-7</td>
<td>20-55</td>
<td>Frequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Russia and the Federation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southwest Asia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central and South America</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parts of China, Southeast Asia, tropical Africa</td>
<td>8-20</td>
<td>70-95</td>
<td>very frequent</td>
<td>very frequent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Zukerman (1996)

**Modes of Transmission**

HBV is transmitted from person to person through blood or other body fluids. The most important mode of HBV transmission globally is perinatal (i.e. from the mother to her newborn baby), mostly commonly during delivery. If a pregnant woman is HBV carrier and is also HBeAg-positive, her newborn baby has 90% likelihood to be infected and become a carrier. Among these children, 25% will die later from chronic liver disease or liver cancer (Hollinger and Liang, 2001). Another important mode of HBV transmission is from child to child during early life resulting from blood contact (Giffin, 1997). All patients with acute hepatitis B are HBeAg positive, and therefore highly infectious and careless contact with their blood or body fluids can lead to HBV infection.

However, there are several other ways HBV can be spread. These include through unprotected sex, sharing contaminated needles and other drug-injecting equipment, as well as by using non-sterilized equipment for tattooing, acupuncture or body piercing and through blood transfusion. (Steinseger et al., 2006; Kid-Ljunggren et al., 2006; WHO, 2009). Also, HBV is stable on environmental surfaces for at least 7 days, and indirect inoculation of HBV can occur via inanimate objects like toothbrushes, baby bottles, toys, razors, eating utensils, hospital equipment and other objects, by contact with mucous membranes or open skin breaks (Robinson, 1995).
It is noteworthy also that, HBV cannot be spread by casual contact such as holding hands, sharing eating utensils or drinking glasses, breast-feeding, kissing, hugging, coughing or sneezing (NIH, 2010).

**Incubation Period**

Once a person is exposed to HBV, the first signs and symptoms occur between 1 to 6 weeks.

**Signs and Symptoms**

Acute infection with hepatitis B virus begins with general ill-health, loss of appetite, nausea, vomiting, body aches, mild fever, dark urine, and then progress to development of jaundice. The illness lasts for a few weeks and then gradually improves in most affected people. The infection may be entirely asymptomatic and may go unrecognized (Terrault, 2005).

Chronic infection with HBV may be either asymptomatic or may be associated with a chronic inflammation of the liver, leading to cirrhosis over a period of several years. This dramatically increases the incidence of hepatocellular carcinoma (liver cancer). HBV has been linked to the development of membranous glomerulonephritis (Gan et al., 2005).

<table>
<thead>
<tr>
<th>Table 4: Nomenclature of Hepatitis B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
</tr>
<tr>
<td>HBsAg</td>
</tr>
<tr>
<td>HBeAg</td>
</tr>
<tr>
<td>Anti-HBs, Anti-HBc, and Anti-HBeAg</td>
</tr>
</tbody>
</table>

**Source:** Hollinger and Liang (2001)

**Risk Groups for Hepatitis B**

Frequent and routine exposure to blood or serum is the common denominator of healthcare occupational exposure. Surgeons, dentists, oral surgeons, pathologists, operating room and emergency room staff and clinical laboratory workers who handle blood are at the highest risk (Robinson, 1995). However, according to Hollinger and Liang (2001) and Robinson (1995), groups of people who are at risk of contracting HBV include infants born to infected mothers, young children in day-care or residential settings with other children in endemic areas, sexual/household contacts of infected persons, health care workers, people sharing unsterile medical or dental equipment, people providing or receiving acupuncture and/or tattooing with unsterile medical devices, sexually active heterosexuals and homosexuals. Similarly, patients and employees in haemodialysis centres (CDCP, 1998; VHPB, 1998), injection drug users sharing unsterile needles (VHPB, 1998) and persons living in regions with high HBV transmission risk include infants born to infected mothers, young children in day-care or residential settings with other children in endemic areas, sexual/household contacts of infected persons, health care workers, people sharing unsterile medical or dental equipment, people providing or receiving acupuncture and/or tattooing with unsterile medical devices, sexually active heterosexuals and homosexuals. Similarly, patients and employees in haemodialysis centres (CDCP, 1998; VHPB, 1998), injection drug users sharing unsterile needles (VHPB, 1998) and persons living in regions with endemic hepatitis B (WHO, 1999) are also at risk of contracting the Virus.

**Hepatitis C**

Hepatitis C like other types of hepatitis causes inflammation of the liver. It is caused by hepatitis C virus (HCV). Like hepatitis B, Hepatitis C can lead to cirrhosis and liver cancer though; it is not as common as other types of hepatitis. Hepatitis C is the most serious type of hepatitis (Rockstroh, 2011). It is now one of the most common reasons for liver transplant in adults. It is transferred primarily through blood, and is more persistent than hepatitis A or B (Pollack, 2011).

**Mode of Transmission**

Hepatitis C can be transmitted from person to person by sharing drug-injecting equipment (needles, heating spoons etc), by using non-sterilized equipment for tattooing, acupuncture or body piercing, as well as by sharing equipment used to snort cocaine, because it can be contaminated with blood from a person’s nose. It can also be transmitted through exposure to blood during unprotected sex and through blood transfusion.

It is rarely transmitted from an infected mother to her baby during childbirth. However, the risk may be greater if the mother is also infected with HIV. Similarly, hepatitis C cannot be passed on by hugging, sneezing, coughing, sharing food or water, sharing cutlery or casual contact (NIH, 2010).

**Incubation Period**

A person who is infected with HCV begins to have first signs and symptoms between 6 to 12 months.

**Signs and Symptoms**

People with hepatitis C often get symptoms similar to those caused by other viral infections. Occasionally, a person will not develop any symptom and their immune system will successfully clear the virus without their knowledge, but can still act as a carrier and pass the virus on to others. However, symptoms may include a short, mild, flu-like illness, nausea and vomiting, diarrhea, loss of appetite, weight loss, jaundice, itching skin etc.

Chronic infection with HCV may cause mild or no symptoms at all and may develop some complications such as liver cirrhosis and liver cancer if the person lives with it for a number of years.

**Causes of Hepatitis**

A group of viruses known as hepatitis viruses cause most cases of hepatitis worldwide. However, there are other factors that can cause hepatitis. These include alcohol consumption, utilization of some drugs, industrial organic solvents and plants, metabolic disorder, obstructive, autoimmune disease and ischemic hepatitis.

**Alcoholic Induced Hepatitis**

This is a hepatitis caused by alcohol. Ethanol mostly in alcoholic beverages is a significant cause of hepatitis (Parveen et al., 2005). Usually, alcoholic hepatitis results after a period of increased alcohol consumption. Hepatitis caused by alcohol is characterized by variable symptoms, which may include feeling unwell, enlargement of the liver, development of fluid in the abdomen ascites and modest elevation of liver enzymes. Long term alcohol consumption leads to development of hepatitis C. The combination of HCV and alcohol consumption accelerates the development of cirrhosis.

**Drug Induced Hepatitis**

A large number of drugs can cause hepatitis (Health A to Z, 2006). Such drugs include antidepressants (Agomelatine, Amitriptyline), antiarrhythmic (Amiodarone), anesthetic gas (Halothane), nonsteroidal anti-inflammatory drugs (NSAIDs)(Ibuprofen and
Indomethacin, antifungal (Ketoconazole), antihistamine (Loratadine), immune suppressant (Methotrexate), antihypertensive (Methyldopa), tetracycline antibiotics (Minocycline), antihypertensive (Nifedipine), antiepileptic (Phenytione and Valproic acid), antiretroviral (Zidovudine), Hormonal contraceptives, Allopurinol, antibacterial (Isoniazid), acetyaminophen (Paracetamol) and antidiabetic (Troglitazone), but troglitazone was withdrawn in the year 2000 for causing hepatitis. It is note worthy that Paracetamol can only cause hepatitis when taken in an overdose

According to Nadir et al. (2000) and Bastida et al. (2005), Atomoxetine and Azathioprine respectively can cause hepatitis. However, the clinical cause of drug induced hepatitis is quiet variable; it depends on the drug and the patient’s tendency to react to the drug. For example, hormonal contraception can cause structural changes in the liver (Health A to Z, 2006), halothane induced hepatitis can range from mild to fatal as can INH-induced hepatitis, while Amiodarone induced hepatitis can be untreatable since it has a long half life of up to 60 days, which means that there is no effective way to stop exposure to the drug (Health A to Z, 2006). Statins can cause elevations of liver function blood tests normally without indicating an underlying hepatitis. However, human variability is such that any drug can be a cause of hepatitis.

**Industrial Organic Solvents and Plants induced Hepatitis**

Some other toxins can cause hepatitis. Examples are as follows:

- Amatoxin-containing mushroom, including the death cap (Amanita phalloides), the destroying angel (Amanita acerea) and some species of Galerina (Parveen et al, 2005). It is noteworthy that a portion of single mushroom can be enough to be lethal
- White phosphorous (an industrial toxins and war chemical)
- Carbon tetrachloride, chloroform, trichloroethylene and all chlorinated hydrocarbon, cause steatohepatitis (hepatitis with fatty liver)
- Cylindrospermopsin, a toxin from the cyanobacteria (Cylindrospermopsia raciborskii) and other cyanobacteria.

**Metabolic Disorder Induced Hepatitis**

This is a group of disorder in which some aspect of body chemistry is disturbed (BMA, 2002). Some metabolic disorders result from an inherited malfunction or deficiency of an enzyme. Others result from under or overproduction of a hormone that controls metabolic activity, such as occurs in diabetes mellitus and hypothyroidism. Also, Hemochromatosis (due to iron accumulation) and Wilson’s disease (copper accumulation) can cause liver inflammation and cirrhosis. All these and other metabolic disorders cause different forms of hepatitis.

**Autoimmune Disorder Induced Hepatitis**

Bacteria, Viruses and drugs may play a role in initiating an autoimmune disorder, but in most cases the trigger is unknown. Anomalous presentation of human leukocyte antigen (HLA) class II on the surface of hepatocyte possibly due to genetic predisposition or acute liver infection; causes a cell-mediated immune response against the body’s own liver, resulting in autoimmune hepatitis (BMA, 2002). Initial treatment for any autoimmune disorder is to reduce the effects of the disease by replacing hormones that are not being produced (BMA, 2002). But, in most cases in which the disease is having widespread effect, treatment is also directed at diminishing the activity of the immune system while maintaining the body’s ability to fight disease. Corticosteroid drugs are most commonly used but may be combined with other immunosuppressant drugs

**Ischemic Hepatitis**

Ischemia is the insufficient supply of blood to a specific organ or tissue (BMA, 2002). Ischemic hepatitis is therefore caused by decreased circulation to the liver cells (hepatocytes). Usually this is due to decreased blood pressure (or shock), leading to the equivalent term "shock liver". This is usually result from disease of the blood vessels such as atherosclerosis but, may also result from injury, constriction of vessel due to spasm of the muscles in the vessel wall, or inadequate blood flow due to insufficient pumping of heart. Patients with ischemic hepatitis are usually very ill due to the underlying cause of shock. Rarely, ischemic hepatitis can be caused by local problems with the blood vessels that supply oxygen to the liver (such as thrombosis, or clotting of the hepatic artery which partially supplies blood to liver cells and sickle cell crisis) (Raurich et al., 2009). Blood testing of a person with ischemic hepatitis will show very high levels of transaminase enzymes (AST and ALT), which may exceed 1000 IU/L (Raurich et al., 2009). The elevation in these blood tests is usually transient (lasting 7 to 10 days). It is rare that liver function will be affected by ischemic hepatitis.

People who develop ischemic hepatitis may have pain in the right upper part of the abdomen, but they usually feel more unwell because of the serious reason that they developed the ischemia, than due to the ischemic hepatitis itself (Raurich et al., 2009). Ischemic hepatitis is related to another condition called congestive hepatopathy or nutmeg liver, which is a backflow condition due to poor drainage of the liver, usually due to heart failure. As a result, the two entities can co-exist. Treatment may include vasodilator drug to widen the blood vessels or in more seven cases, an angioplasty or bypass operation (BMA, 2002).

**Effects of Hepatitis on Liver Cells**

The hepatitis virus mainly enters into the liver cell. The hepatitis cell latches onto the protein membrane and eases its way into the liver cell. Once inside the cell, this virus gene is free to take over the normal function of the liver cell. This causes the liver cell to become weak and then it dies. Before it dies the virus cell has used the liver cell to reproduce itself thousands of times. These new and multi virus cells now live and begin to take over all of the healthy liver cells. The whole process can take place in a matter of hours. This process must occur many times before a person begins to show signs of liver damage. It is when chronic hepatitis C or B goes untreated that it causes scarring to the liver (cirrhosis) and an increased chance of liver cancer, and liver failure ending in death. When hepatitis B or C virus enters the liver, it begins to invade the cells and grow. As it does this, the number of cells that are scarred and damaged increased. The person may not even feel any symptoms until so much damage has occurred, that their liver is unable to function any longer. This can take 10 to 40 years. This depends on the individual, genetics, and how well you take care of your liver. This however, may results to the following disease conditions:

- Liver cirrhosis
- Liver cancer
- Jaundice and
- Variations in Liver Panels

**Liver cirrhosis**

Cirrhosis is the end result after necrosis of the hepatocytes, with destruction of the normal lobular structure by fibrous septa and regenerative nodules of hepatocytes. The clinical picture includes liver failure and signs of portal hypertension such as oesophageal varicose veins and ascites. The terminal stage is hepatic coma. Cirrhosis is scarring of the liver. It causes the formation of scar tissue on the liver because of injury or long-term disease. The most
common causes are chronic alcoholism and hepatitis. Other causes include disorder of bile duct, haemochromatosis, wilson’s disease, cystic fibrosis and heart failure (BMA, 2002). Two pathological types of liver cirrhosis are considered, they include Micronodular cirrhosis which is characterized by nodules less than 3 mm in diameter. This disorder was previously termed Laennec’s cirrhosis (after a French pathologist). The cause is alcohol abuse (alcoholic cirrhosis) or biliary tract disease (biliary cirrhosis) and Macronodular cirrhosis characterized by larger nodules sometimes including normal lobules. The cause is acute and chronic hepatic infection (hepatitis B virus, hepatitis C virus, hepatitis D virus) often in carriers.

In cirrhosis, liver cells die and are progressively replaced with fibrotic tissue leading to nodule formation. The internal structure of the liver is deranged leading to the obstruction of blood flow and decrease in liver function. This damage is caused by recurrent immune responses stimulated by the presence of the virus. Cirrhosis can lead to Easy bruising or bleeding, or nosebleeds, swelling of the abdomen or legs, extra sensitivity to medicines, high blood pressure in the vein entering the liver, enlarged veins in the esophagus and stomach and kidney failure. Cirrhosis may go unrecognized until symptoms such as mild jaundice, oedema, and vomiting of blood develop. There may be enlargement of the liver and spleen and, in men, enlargement of the breasts and loss of body hair due to an imbalance in sex hormones caused by liver failure. Complications include ascites, oesophageal varies and hepatoma. Treatment is focused on slowing the rate at which liver cells are being damaged, by treating the cause for instance, hepatitis. In some cases, if the condition progresses, liver transplant is the next option.

Liver cancer

*Chigozie et al.*


The a-fetoprotein is raised in the blood plasma. Other risk factors for hepatocellular carcinoma are alcoholic damage, haemochromatosis, aflatoxin from peanuts, androgens, and oestrogens. A number of HBV patients with chronic hepatitis will develop hepatocellular carcinoma (Robinson, 1995; Hollinger and Liang, 2001). Persons at increased risk of developing HCC, are those who contracted hepatitis B in early childhood (Mahoney and Kane, 1999). Only about 5% of patients with cirrhosis develop HCC. On the other hand, between 60 and 90% of HCC patients have underlying cirrhosis (Robinson, 1994; Robinson, 1995; Hollinger and Liang, 2001).

The incidence of HCC varies with geography, race, age, and sex. HCC is responsible for 90% of the primary malignant tumours of the liver observed in adults. Worldwide, it is the seventh most frequent cancer in males and ninth most common in females. Liver cancer is the cause of more than 500,000 deaths annually throughout the world, with a male to female ratio of 4:1. The frequency of HCC follows the same general geographic distribution pattern as that of persistent HBV infection. The age distribution of patients with clinically recognized tumours suggests that these tumours appear after a mean duration of about 35 years of HBV infection (Robinson, 1995; Hollinger and Liang, 2001). Patients who develop HCC as a result of malignant transformation of hepatocytes have a mean of 5-year survival rate of 25 to 60% (Hollinger and Liang, 2001). This variation depends on the symptoms, the size of the tumour, its resectability, and the presence or absence of a-fetoprotein (AFP).

Non-resectable tumours have a mean survival rate of 5 months for AFP-positive tumours and of 10.5 months for AFP-negative tumours (Hollinger and Liang, 2001). When serum a-fetoprotein (AFP) followed serially in HBSAg carriers rises significantly above the patient’s own baseline (>100 μg/ml), HCC can often be detected by liver scanning or ultrasonic procedures at a stage when the tumour can be cured by surgical resection (Robinson, 1995). The diagnosis may be confirmed by liver biopsy. This suggests that HBSAg carriers should have regular serial serum AFP determinations and ultrasonic examinations (at 6 months intervals for those above 40 years). Both these tests are recommended to be repeated regularly for all HBSAg carriers with cirrhosis (Robinson, 1995).

HBV causes 60-80% of the world’s primary liver cancer, and primary liver cancer is one of the three most common causes of cancer deaths in males in East and South-east Asia, the Pacific Basin, and sub-Saharan Africa (Robinson, 1995). Primary liver cancer is the eighth most common cancer in the world (Robinson, 1995). Up to 80% of liver cancers are due to HBV. When HCC presents clinically, the disease is fatal. The median survival frequency of HCC patients is less than 3 months. However, if the cancer is detected early, there is 85% chance of a cure. Treatment involves surgery, hepatic irradiation, and antinecancer drugs.

Hepatocellular Jaundice

Fig. 3: A) Hepatocellular Carcinoma in Cirrhotic and normal liver. B) Histological appearance

This is a cancerous tumour in the liver. The tumour may be primary (originating within the liver) or Secondary (having spread from elsewhere, often stomach, pancreas or large intestine) (BMA, 2002). There are two main types of primary tumour: a hepatoma, which develop in the liver cells, and a cholangiocarcinoma, which arises from cells lining the bile ducts. Seemingly healthy carriers of HBV and HCV are at risk of developing hepatocellular carcinoma.
Jaundice (also known as icterus; attributive adjective: icteric) is a yellowish pigmentation of the skin, the conjunctival membranes over the sclerae (whites of the eyes), and other mucous membranes caused by hyperbilirubinemia (increased levels of bilirubin in the blood) (Beckingham and Ryder, 2001). This hyperbilirubinemia subsequently causes increased levels of bilirubin in the extracellular fluid. Typically, the concentration of bilirubin in plasma must exceed 1.5 mg/dl (Guyton et al., 2005). (>26.5 \mu mol/L), three times the usual value of approximately 0.5 mg/dl for the coloration to be easily visible (Guyton et al., 2005). Jaundice comes from the French word jaune, meaning yellow. Jaundice is often seen in liver disease such as hepatitis or liver cancer. It may also indicate obstruction of the biliary tract, for example by gallstones or pancreatic cancer, or less commonly is congenital in origin.

Hepatocellular (hepatic) jaundice is one the disease condition resulting from liver damage. It can be caused by acute hepatitis, hepatotoxicity, and alcoholic liver disease. Cell necrosis reduces the liver’s ability to metabolize and excrete bilirubin leading to a buildup of unconjugated bilirubin in the blood. Other causes include primary biliary cirrhosis leading to an increase in plasma conjugated bilirubin because there is impairment of the liver for excretion of conjugated bilirubin into the bile. The blood contains abnormally raised amount of conjugated bilirubin and bile salts which are excreted in the urine. Jaundice seen in the newborn, known as neonatal jaundice, is common, occurring in almost every newborn as hepatic machinery for the conjugation and excretion of bilirubin does not fully mature until approximately two weeks of age (Pashankar and Schreiber, 2001). This form of jaundice is usually harmless and disappears within a week (BMA, 2002). Rarely, severe or persistent neonatal jaundice is caused by hepatitis or other infection. Neonatal jaundice may be treated with phototherapy but, in severe cases, exchange transfusion may be needed. In hepatic jaundice, there is invariably cholestasis. Jaundice can also be seen in pregnancy women, and if left untreated may lead to the birth of babies with low intelligence quotient (IQ).

Laboratory findings depend on the cause of jaundice.

- **Urine**: Conjugated bilirubin present, urobilirubin > 2 units but variable (except in children). Kernicterus is a condition not associated with increased conjugated bilirubin.
- **Plasma protein**: show characteristic changes.
- **Plasma albumin**: level is low but plasma globulins are raised due to an increased formation of antibodies.

**Variations in Liver Panels**

Hepatitis and some other liver related diseases cause serious variations in the liver panels. These variations may either be below or above normal levels. Most patients presenting with jaundice which causes increased bilirubin as a result of hepatitis will have various predictable patterns of liver panel abnormalities, though significant variation does exist (Beckingham and Ryder, 2001). The typical liver panel will include blood levels of enzymes found primarily from the liver, such as the aminotransferases (ALT, AST), and alkaline phosphatase (ALP); bilirubin (which causes the jaundice); and protein levels, specifically, total protein and albumin. Other primary lab tests for liver function include GGT and prothrombin time (PT).

ALP and GGT levels will typically rise with one pattern while AST and ALT rise in a separate pattern. If the ALP (10–45 IU/L) and GGT (18–85) levels rise proportionately about as high as the AST (12–38 IU/L) and ALT (10–45 IU/L) levels, this indicates a cholestatic problem (Beckingham and Ryder, 2001). On the other hand, if the AST and ALT rise is significantly higher than the ALP and GGT rise, this indicates a hepatic problem. Alcoholic liver damage may see fairly normal ALT levels, with AST 10x higher than ALT. On the other hand, if ALT is higher than AST, this is indicative of hepatitis. Levels of ALT and AST are not well correlated to the extent of liver damage. Low levels of albumin tend to indicate a chronic condition, while it is normal in hepatitis and cholestasis.

Lab results for liver panels are frequently compared by the magnitude of their differences, not the pure number, as well as by their ratios. The AST to ALT ratio can be a good indicator of whether the disorder is alcoholic liver damage (10), some other form of liver damage (above 1), or hepatitis (less than 1) (Guyton et al., 2005). Bilirubin levels greater than 10x normal could indicate neoplastic or intrahepatic cholestasis. Levels lower than this tends to indicate hepatocellular causes. AST levels greater than 15x tends to indicate acute hepatocellular damage. Less than this tend to indicate obstructive causes. ALP levels greater than 5x normal tend to indicate obstruction, while levels greater than 10x normal can indicate drug (toxic) induced cholestatic hepatitis or Cytomegalovirus (Beckingham and Ryder, 2001). Both of these conditions can also have ALT and AST greater than 20x normal. GGT levels greater than 10x normal typically indicate cholestasis. Levels 5–10x tend to indicate viral hepatitis. Levels less than 5x normal tend to indicate drug toxicity. Acute hepatitis will typically have ALT and AST levels rising 20–30x normal (above 1000), and may remain significantly elevated for several weeks (Chernecky and Berger, 2008). Acetaminophen toxicity can result in ALT and AST levels greater than 50x normal.

**DIAGNOSIS, TREATMENT AND PREVENTION OF HEPATITIS**

In this chapter, various ways through which hepatitis viruses could be diagnosed, treated and prevented are discussed.

**Diagnosis of Hepatitis**

The following are different ways through which various types of hepatitis can be diagnosed. They are as follows:

**Diagnosis of Hepatitis A**

Since both clinically and biochemically, acute hepatitis due to HAV cannot be distinguished from that due to the other hepatitis viruses, serologic tests are necessary for a virus-specific diagnosis (Hollinger and Ticehurst, 1996; Koff, 1998). Diagnosis of hepatitis is made by biochemical assessment of liver function (laboratory evaluation of urine bilirubin and urobilinogen, total and direct serum bilirubin, ALT and/or AST, alkaline phosphatase, prothrombin time, total protein, albumin, IgG, IgA, IgM, complete blood count). (Stepleton and Lemon, 1999; Hollinger and Ticehurst, 1996; Lemon, 1999; Koff, 1999). However, the specific routine diagnosis of acute hepatitis A is made by finding anti-HAV IgM in the serum of patients. A second option is the detection of virus and/or antigen in the faeces (Lemon, 1997; Koff, 1998).

Similarly, virus and antibody can be detected by commercially available RIA, EIA or ELISA kits. These commercially available assays
for anti-HAV IgM and total anti-HAV (IgG and IgG) for assessment of immunity to HAV are not influenced by the passive administration of IgG, because the prophylactic doses are below detection level (Lemon, 1997). At the onset of disease, the presence of IgM anti-HAV is always accompanied by the presence of IgG anti-HAV. As IgG anti-HAV persists lifelong after acute infection, detection of IgG anti-HAV alone indicates past infection (Stepleton and Lemon, 1994; Hollinger and Ticehurst, 1996; Koif, 1998). Virus may still be present in the absence of detectable HAV antigen, as demonstrated by the use of more sensitive methods (Hollinger and Ticehurst, 1996). If laboratory tests are not available, epidemiologic evidence can help in establishing a diagnosis.

Diagnosis of Hepatitis B

Diagnosis of hepatitis B is made by biochemical assessment of liver function. Initial laboratory evaluation should include total and direct bilirubin, ALT, AST, alkaline phosphatase, prothrombin time, total protein, albumin, serum globulin, complete blood count, and coagulation studies (Robinson, 1995; Hollinger and Liang, 2001). It is confirmed by demonstration in sera of specific antigens and/or antibodies. Clinical useful antigen-antibody systems have been identified for hepatitis B:

- a. hepatitis B surface antigen (HBsAg) and antibody (anti-HBs)
- b. antibody (anti-HBC IgM and anti-HBc IgG) and hepatitis B core antigen (HBcAg)
- c. hepatitis B e antigen (HBeAg) and antibody (anti-HBe)

HCV can be diagnosed by carrying out blood tests that detect HCV antibodies in the blood.

Treatment of Hepatitis B

Treatment of Hepatitis B is aimed at eliminating infectivity to prevent transmission and spread of HBV, at halting the progression of liver disease, the presence of IgM anti-HAV is always accompanied by the presence of IgG anti-HAV. As IgG anti-HAV persists lifelong after acute infection, detection of IgG anti-HAV alone indicates past infection (Stepleton and Lemon, 1994; Hollinger and Ticehurst, 1996; Koif, 1998). Virus may still be present in the absence of detectable HAV antigen, as demonstrated by the use of more sensitive methods (Hollinger and Ticehurst, 1996). If laboratory tests are not available, epidemiologic evidence can help in establishing a diagnosis.

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HCV can be diagnosed by carrying out blood tests that detect HCV antibodies in the blood.

Treatment of Hepatitis A

Hepatitis A has no specific treatment and specific cure. Most people fight it naturally, returning to full health within a couple of months.

Treatment of Hepatitis A

As no specific treatment exists for hepatitis A, prevention is the most effective approach against the disease (Stapleton and Lemon, 1994; Andre, 1995). Therapy should be supportive and aimed at maintaining adequate nutritional balance (1 g/kg protein, 30-35 cal/kg). Alcoholic beverages should not be consumed during acute hepatitis because of the direct hepatotoxic effect of alcohol. Hospitalization is usually not required (Stapleton and Lemon, 1994; Hollinger and Ticehurst, 1996).

Temporary auxiliary liver transplantation for sub acute liver failure may be a way to promote native liver regeneration (Stapleton and Lemon, 1994; Battegay et al., 1995; Hollinger and Ticehurst, 1996). Also, patients with HAV should have enough rest and should stay well hydrated by drinking lots of fluids.

Treatment of Hepatitis B

Treatment of chronic hepatitis B is aimed at eliminating infectivity to prevent transmission and spread of HBV, at halting the progression of liver disease and improving the clinical and histological picture, and at preventing HCC from developing, by losing markers of HBV replication in serum and liver like HBV DNA, HBeAg, and HBeAg. Normalization of ALT activity, resolution of hepatic inflammation, and the improvement of patients' symptoms usually accompany these virological changes (Mahoney and Kane, 1999; Hollinger and Liang, 2001).

There are two main classes of treatment:

- **Antivirals**: aimed at suppressing or destroying HBV by interfering with viral replication (Mahoney and Kane, 1999)

- **Immune Modulators**: aimed at helping the human immune system to mount a defense against the virus.

Acute hepatitis B does not usually require treatment because most adults clear the infection spontaneously (Hollinger and Lau, 2006). Currently, there are seven medications licensed for treatment of chronic hepatitis B infection in the United States (Prammookkiosop, 2002). These include antiviral drugs, Lamivudine (Epivir), Adefovir (Hepsera), Tenofovir (Viread), Telbivudine (Tyzeka) and Entecavir (Baroclude) and the two immune system modulators; interferon alpha-2a and Pegylated interferon alpha-2a. This treatment reduces viral replication in the liver, thereby reducing the viral load. Infant born to mothers known to carry hepatitis B can be treated with antibodies to the HBV (HBIG). Hepatitis B can also be treated by controlling the level of production of host-derived DNA building protein (Ng et al., 2005).

Currently, chronic hepatitis B is treated with interferons (Robinson, 1995; Gitlin, 1997; Mahoney and Kane, 1999; Hollinger and Liang, 2001). The only approved ones are interferon-α-2a and interferon-α-2b. Interferons display a variety of properties that include antiviral, immunomodulatory, and antiproliferative effects. They enhance T-cell helper activity, cause maturation of B lymphocytes, inhibit T-cell suppressors, and enhance HLA type I expression. To be eligible for interferon therapy, patients should have infection documented for at least six months, elevated liver enzymes (AST and ALT) and an actively dividing virus in their blood (HBeAg and/or HBV DNA positive tests). Patients with acute infection, end stage cirrhosis or other major medical problems should not be treated. Interferon-α produces a long-term, sustained remission of the disease in 35% of those with chronic hepatitis B, with normalization of liver enzymes and loss of the three markers for an active infection (HBeAg, HBV DNA, and HBsAg). Complete elimination of the virus is achieved in some carefully selected patients (Robinson, 1995; Tassopoulos, 1997; Mahoney and Kane, 1999; Hollinger and Liang, 2001).

Interferon therapy for patients with HBV-related cirrhosis decreases significantly the HCC rate, particularly in patients with a larger amount of serum HBV DNA. In patients with HBeAg-positive compensated cirrhosis, virological and biochemical remission following interferon therapy is associated with improved survival. In patients with chronic HBV infection, the clearance of HBeAg after treatment with interferon-α is associated with improved clinical outcomes (Niedarau, 1996; Ikeda, 1998; Mahoney and Kane, 1999; Fattovich, 1999; Hollinger and Liang, 2001). Interferon-α (Intron A (interferon-α-2b), Schering Plough, and Roferon, (interferon-α-2a) Roche Labs) is the primary treatment for chronic hepatitis B. The standard duration of therapy is considered after 16 weeks. Patients who exhibit a low level of viral replication at the end of the standard regimen benefit most from prolonged treatment (Tassopoulos, 1997; Janssen, 1999). Permanent loss of HBV DNA and HBeAg are considered a response to antiviral treatment, as this result is associated with an improvement in necro-inflammatory damage, and reduced infectivity. Interferon in high doses causes fever, fatigue, malaise, and suppression of white blood cell and platelet counts. These effects are reversible when the therapy is stopped (Robinson, 1995).

A new treatment introduced recently for chronic hepatitis B in adults with evidence of HBV viral replication and active liver inflammation is EPVIR®-HBV (lamivudine, Glaxo Wellcome). The recommended 100 mg oral dose once-daily in form of tablets is easy to take and generally well tolerated, although safety and effectiveness of treatment beyond 1 year have not been established (Gitlin, 1997; Nevans, 1997; Lai, 1998; Mahoney and Kane, 1999; Dienstag, 1999).

Lamivudine is a 2’, 3’-dideoxy cytosine analogue that has strong inhibitory effects on the HBV polymerase and therefore on HBV replication in vitro and in vivo. Lamivudine is well tolerated and suppresses HBV replication in HBeAg carriers, but the effect is reversible, if therapy is stopped (Lai, 1997; Nevans, 1997; Gitlin, 1997; Mahoney and Kane, 1999; Dienstag, 1999). Combination therapy with interferon-α and lamivudine for patients who failed interferon-α monotherapy is under investigation. Adoptive transfer of immunity to hepatitis B has been a novel approach to terminating HBV infection in the carrier after bone marrow transplantation from a hepatitis B immune donor (Gitlin, 1997; Hollinger and Liang, 2001).

Several new agents (e.g. Ritonavir, Adefovir, Dipivoxil, Lobucavir, Famvir, FTC, N-Acetyl-Cysteine (NAC), PC1323, TheraDig-HBV,
Thymosin-alpha, Ganciclovir (Hadziyannis and Manesis, 1999)) are in development, and some encouraging data are available.

### Table 5: Potential Drug Therapy for Chronic Hepatitis B

| Agent       | Effective   | Ineffective
<table>
<thead>
<tr>
<th></th>
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<tr>
<td>Interferon</td>
<td>interferon-α</td>
<td>interferon-γ</td>
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<tr>
<td>Antiviral</td>
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<td>acyclovir</td>
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<td></td>
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<td>foscarnet</td>
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<tr>
<td></td>
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<td>azidothymidine</td>
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<td></td>
<td></td>
<td>dideoxynosine</td>
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Table 6: Hepatitis B Vaccines Available Internationally

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Brand name</th>
<th>Country</th>
<th>Type</th>
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</thead>
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<tr>
<td>Centro de Ingenieria</td>
<td>Enivac-HB</td>
<td>Cuba</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Genetica Y Biotecnologia</td>
<td>Hepaccine-B</td>
<td>South Korea</td>
<td>Plasma derived DNA</td>
</tr>
<tr>
<td>Korea Cross</td>
<td>Hepavax B</td>
<td>South Korea</td>
<td>Plasma derived DNA</td>
</tr>
<tr>
<td>Korea Green Cross</td>
<td>Hepavax-Gene</td>
<td>South Korea</td>
<td>Recombinant DNA</td>
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<tr>
<td>LG Chemical</td>
<td>Euvax B</td>
<td>South Korea</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Merck Sharp &amp; Dohme</td>
<td>Recomipvax</td>
<td>United States</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Merck Sharp &amp; Dohme</td>
<td>Comvax</td>
<td>United States</td>
<td>Combined Hib and (recombinant) DNA</td>
</tr>
<tr>
<td>Pasteur Connaught</td>
<td>Genhevax B</td>
<td>France</td>
<td>DNA (mammalian cell)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Engerix-B</td>
<td>Belgium</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Twinrix</td>
<td>Belgium</td>
<td>Combined hepatitis A and B (recombinant)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Trratinix-HB</td>
<td>Belgium</td>
<td>Combined DTP and (recombinant)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Infanrix-HB</td>
<td>Belgium</td>
<td>Combined DTP (acellular P) and HB (recombinant)</td>
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<td>Swiss Serum and Vaccines</td>
<td>Heprecombe</td>
<td>Switzerland</td>
<td>Recombinant DNA</td>
</tr>
</tbody>
</table>

Source: (Gitlin, 1997)

### Contraindications of Interferon Therapy for Chronic Hepatitis B

Interferon therapy is contraindicated in a patient who have problems such as Hepatic decompensation (albumin <3.0 g/l, bilirubin >5.13 μmol/l [30 mg/l], prolonged prothrombin time >3.0 s), Portal hypertension (variceal bleed, ascites, encephalopathy), Hypersplenism (leukopenia (<2 x 10^9/l), thrombocytopenia (<7 x 10^9/l)), Psychiatric depression (severe, suicide attempt), Autoimmune disease (polyarteritis nodosa, rheumatoid arthritis, thyroiditis), Major system impairment (cardiac failure, obstructive airways A)

### Table 6: Hepatitis B Vaccines Available Internationally

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Brand name</th>
<th>Country</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centro de Ingenieria</td>
<td>Enivac-HB</td>
<td>Cuba</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Genetica Y Biotecnologia</td>
<td>Hepaccine-B</td>
<td>South Korea</td>
<td>Plasma derived DNA</td>
</tr>
<tr>
<td>Korea Cross</td>
<td>Hepavax B</td>
<td>South Korea</td>
<td>Plasma derived DNA</td>
</tr>
<tr>
<td>Korea Green Cross</td>
<td>Hepavax-Gene</td>
<td>South Korea</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>LG Chemical</td>
<td>Euvax B</td>
<td>South Korea</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Merck Sharp &amp; Dohme</td>
<td>Recomipvax</td>
<td>United States</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>Merck Sharp &amp; Dohme</td>
<td>Comvax</td>
<td>United States</td>
<td>Combined Hib and (recombinant) DNA</td>
</tr>
<tr>
<td>Pasteur Connaught</td>
<td>Genhevax B</td>
<td>France</td>
<td>DNA (mammalian cell)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Engerix-B</td>
<td>Belgium</td>
<td>Recombinant DNA</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Twinrix</td>
<td>Belgium</td>
<td>Combined hepatitis A and B (recombinant)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Trratinix-HB</td>
<td>Belgium</td>
<td>Combined DTP and (recombinant)</td>
</tr>
<tr>
<td>SmithKline Beecham</td>
<td>Infanrix-HB</td>
<td>Belgium</td>
<td>Combined DTP (acellular P) and HB (recombinant)</td>
</tr>
<tr>
<td>Swiss Serum and Vaccines</td>
<td>Heprecombe</td>
<td>Switzerland</td>
<td>Recombinant DNA</td>
</tr>
</tbody>
</table>

Source: (Gitlin, 1997)

### Conclusion

Liver is the largest organ in the body, contributing about 2% of the total body weight, or about 3-5 kg in the average adult human. (Guyton and Hall, 2006) and plays a vital role in the body because it produces and processes a wide range of chemical substances (BMA, 2002). From this study, it could be deduced that hepatitis viruses cause major effects in the physiology of liver cells. Moreover, Guyton and Hall (2006), stated that under abnormal conditions, may be when someone gets hepatitis, the liver will no longer perform the above functions as expected and can be affected to varying degrees and when this happens, some of the biochemical parameters in the liver (liver panels) such as bilirubin, ALT, AST, albumin, total proteins etc. will vary either above or below normal level (Robinson, 1995; Hollinger and Liang, 2001). The varying levels of the liver panels indicate that liver has been impaired; this may be as a result of liver cirrhosis, liver cancer, jaundice etc.

However, Sirisen (2000), classify Nigeria among the countries highly endemic for viral hepatitis. The major findings showed that hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most dangerous form of hepatitis that destabilizes the welfare of man. Research showed that the prevalence of HBV was highest among Nigeria female Sex workers (FSW) and among pregnant women who generally have depressed immunity. These findings corroborate reports of studies from Mexico which revealed that early age of sexual activity increases the risk of HBV infection (Vazquez-Martinez et al., 2003). This high prevalence among sex workers in Nigeria is indication that active sexual transmission is an important factor in the spread of HBV in this nation and that sex workers are a reservoir group for the maintenance and transmission of the virus. Research also revealed that chronic hepatitis is a leading cause of liver-related deaths among patients with HIV/AIDS worldwide (Kozel and Peters, 2007). The risk groups who are more likely to be susceptible to both HAV and HBV infections are also revealed.

In conclusion, since the viruses are usually transmitted through sexual contact or from infected mother to the offspring especially at birth, there is the need for proper screening of all pregnant women and infants born to HBV positive mothers. Similarly, Persons falling into any of the above mentioned categories of risk groups should consider being vaccinated as a preventive measure. Moreover, Government and non-governmental Organizations (NGOs) should intensify efforts to enlighten the general public on the public health importance of the disease, and incorporate hepatitis screening into the routine antenatal check up. Also, UNICEF, WHO, and several other international donor agencies should help developing countries to obtain HB vaccine and implement national programmes on universal vaccination against hepatitis virus. We also call for innovative and immediate implementation of a general child and adolescent immunization against hepatitis, to prevent the further spread of these viruses. Since the prevalence of hepatitis is higher among the female sex workers (FSWs) in Nigeria because of their frequent sexual contact and many sexual partners, we therefore quickly call for innovative programmes incorporating wide spread HBV education and vaccination among sex workers in Nigeria, to achieve immediate benefit within the targeted high risk population as an immediate first step to the global fight against HBV infection.

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