INNOVARE JOURNAL OF AYURVEDIC SCIENCES

Vol 2, Issue 4 , 2014 ISSN:2321-6824

Review Article

HEPATITIS AND PHYSIOLOGY OF LIVER CELLS-A REVIEW

UGWU GODWIN CHIGOZIE, EJERE VINCENT CHIKWENDU, OKANYA CHINAGOROM LAURETE, EGBUJI JUDE VICTOR

DEPARTMENT OF ZOOLOGY AND ENVIRONMENTAL BIOLOGY, UNIVERSITY OF NIGERIA, NSUKKA, ENUGU STATE, NIGERIA. Email: godwinchigozie.gc@gmail.com

Received:19 August 2014, Revised and Accepted: 1 September 2014

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 adolescent 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 (Otegbayo *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 hepat- liver and itis–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 % (Kulkarinii *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 (Awole 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 chronic liver disease. Otegbayo *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

universal immunization, and the financial burden of national programmes (Iwarson, 1998; VHPB, 1996; VHPB, 1998).

Liver Cells

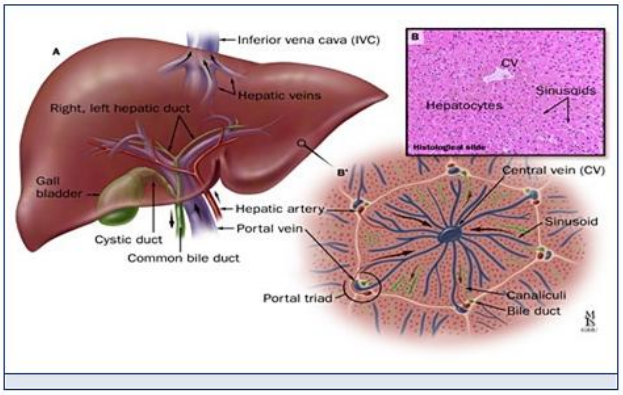


Fig. 1: A, Normal gross anatomy of a liver, B, histological slide, B', histological view.

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 e.t.c, 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). Binucleate 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. Stellate (Ito) cells store vitamin A and produce extracellular matrix and collagen; they are also distributed amongst endothelial cells but are difficult to visualise by light microscopy.

Hepatocytes are an important physiological example for evalutation 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, Catarrhal 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 1min, 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), ß-propriolactone (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; Koff, 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

HAV endemicity	REGIONS BY EPIDEMIOLOGICAL PATTERN	AVERAGE AGE OF PATIENTS (YEARS)	MOST LIKELY MODE OF TRANSMISSION
Very high	AFRICA, PARTS OF SOUTH AMERICA, THE MIDDLE EAST AND OF SOUTH-EAST ASIA	UNDER 5	PERSON-TO-PERSON, CONTAMINATED FOOD AND WATER
High	BRAZIL'S AMAZON BASIN, CHINA AND LATIN AMERICA	14-MAY	PERSON-TO-PERSON, OUTBREAKS/ CONTAMINATED FOOD OR WATER
Intermediate	SOUTHERN AND EASTERN EUROPE, SOME REGIONS OF THE MIDDLE EAST	24-MAY	PERSON-TO-PERSON, OUTBREAKS/ CONTAMINATED FOOD OR WATER
Low	AUSTRALIA, USA, WESTERN EUROPE	MAY-40	COMMON SOURCE, OUTBREAKS
Very low	NORTHERN EUROPE AND JAPAN	OVER 20	EXPOSURE DURING TRAVEL TO HIGH ENDEMICITY AREAS, UNCOMMON SOURCE

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

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

REGION	1990POPULATION (IN MILLIONS)	INCIDENCE (PER100,000 PER YEAR)	CASES (PERYEAR
North America	275	10	28,000
CentralandSouthAmerica	453	20-40	162,000
Europe	791	5-60	278,000
Africa and Middle East	827	20-60	251,000
Asia	2893	10-30	676,000
Oceania	28	15-30	5,000
Total			1,399,000

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 faeces 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; VHPB, 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 (VHPB, 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 Schneider, 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 of the world's population (i.e. more than 2 billion people) have been infected with HBV and millions are chronic carriers of the virus (Ferriara, 2000; Draton *et al*., 2004; Cheesbrough, 2006). Hepatitis B virus is the most virulent of the entire hepatitis viruses. It may lead to a condition called cirrhosis (permanent scaring of the liver) or liver cancer, both of which cause severe illness and even death. If a person lives with HBV infection for a number of years, it may develop to liver cancer, liver cirrhosis or chronic hepatitis. HBV is estimated to be 50 to 100 times more infectious than HIV (Barker *et al*., 1996).

In 2004, an estimated 350 million individuals were infected worldwide. National and regional prevalence ranges from over 10% in Asia to under 0.5% in the United States and northern Europe. Routes of infection include vertical transmission (such as through childbirth), early life horizontal transmission (bites, lesions, and poor sanitary habits), and adult horizontal transmission (sexual contact, intravenous drug use) (Custer *et al*., 2004). The primary method of transmission reflects the prevalence of chronic HBV infection in a given area. In low prevalence areas such as the continental United States and Western Europe, injection drug abuse and unprotected sex are the primary methods, although other factors may also be important (Redd *et al*., 2007). In moderate prevalence areas, which include Eastern Europe, Russia, and Japan, where 2–7% of the population is chronically infected, the disease is predominantly spread among children. In high prevalence areas such as China and South East Asia, transmission during childbirth is most common, although in other areas of high endemicity such as Africa; transmission during childhood is also significant (Alter, 2003). The prevalence of chronic HBV infection in areas of high endemicity is at least 8%. As at 2010, China had 120 million infected people, followed by 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

	% of population positive for		Infection	
AREA	**HBsAg**	**anti-HBs**	**NEONATAL**	**CHILDHOOD**
Northern, Western, and Central Europe, North America, Australia	0.2-0.5	4-6	Rare	Infrequent
Eastern Europe, the Mediterranean, Russia and the Russian Federation, Southwest Asia, Central and South America	2-7	20-55	Frequent	Frequent
Parts of China, Southeast Asia, tropical Africa	8-20	70-95	very frequent	very frequent

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), most 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 (Gitlin, 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 none sterilized equipment for tattooing, acupuncture or body piercing and through blood transfusion. (Sleinsenger *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 note worthy 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 4: Nomenclature of Hepatitis B

HBV	hepatitis B virus (complete infectious virion)	The 42 nm, double-shelled particle, originally called the Dane particle that consists of a 7 nm thick outer shell and a 27 nm inner core. The core contains a small, circular, partially double-stranded DNA molecule and an endogenous DNA polymerase. This is the prototype agent for the family Hepadnaviridae.
HBsAg	hepatitis B surface antigen (also called envelope antigen)	The complex of antigenic determinants found on the surface of HBV and of 22 nm particles and tubular forms. It was formerly designated Australia (Au) antigen or hepatitis-associated antigen (HAA).
HBcAg	hepatitis B core antigen	The antigenic specificity associated with the 27 nm core of HBV.
HBeAg	hepatitis B e antigen	The antigenic determinant that is closely associated with the nucleocapsid of HBV. It also circulates as a soluble protein in serum.
Anti-HBs, anti-HBc, and anti-HBe	Antibody to HBsAg, HBcAg, and HBeAg	Specific antibodies that are produced in response to their respective antigenic determinants.

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 or travelling to 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 child birth. 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 antidepressant (Agomelatine, Amitriptyline), antiarrythmic (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 (Nifidipine), antiepileptic (Phenytoine and Valproic acid), antiretroviral (Zidovudine), Hormonal contraceptives, Alloprinol, antibacterial (Isoniazid), acetaminophen (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 acreata)* 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 cyanobacterium (C*ylindrospermopsis 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 U/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

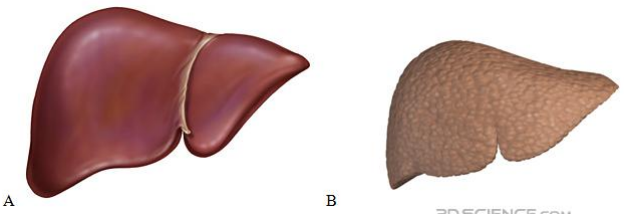


Figure 2: A) Normal liver B) Cirrohtic liver

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

.

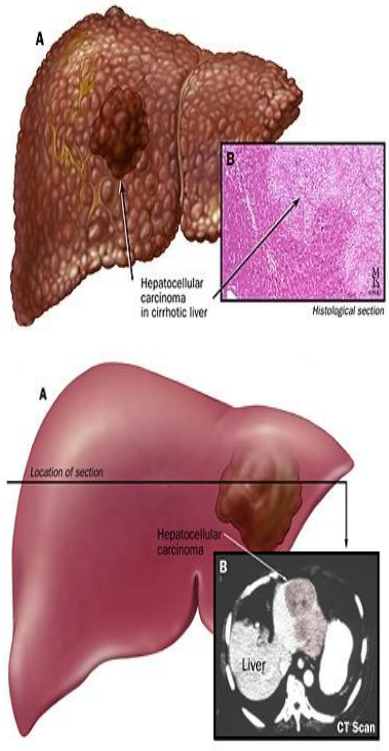


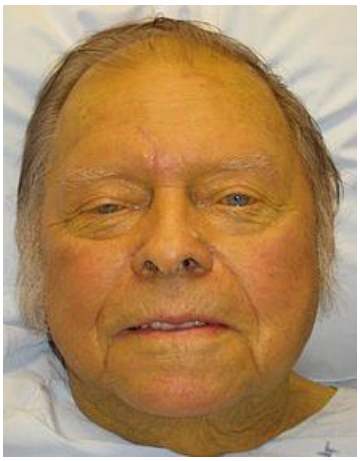
Fig. 3: A) Hepatocellular Carcinoma in Cirrhotic and normal liver. B) Histological appearance

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, pancrease or large intenstine) (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. The *α-foetoprotein* 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).

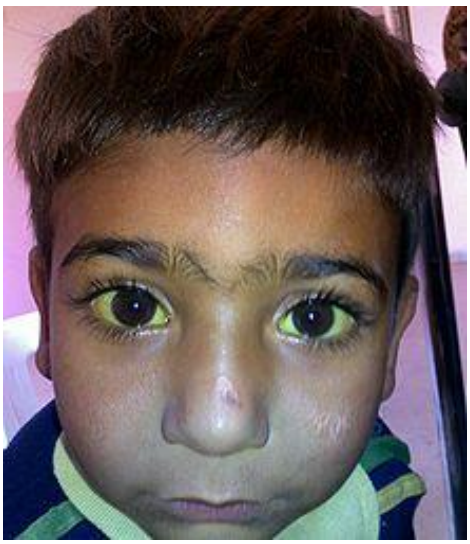
The incidence of HCC varies with geography, race, age, and sex. HCC is responsible for 90% of the primary malignant tumours of the liver observed in adults. Worldwide, it is the seventh most frequent cancer in males and ninth most common in females. Liver cancer is the cause of more than 500, 000 deaths 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 α-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 α-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 ultrasound 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 ultrasound 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 anticancer drugs.

Hepatocellular Jaundice



A



B

A) Jaundice of the skin caused by hepatic failure B) A 4-year-old boy with icteric (jaundiced) sclera

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). (>26μmol/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 intelligent 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 20× normal. GGT levels greater than 10x normal typically indicate cholestasis. Levels 5–10× tend to indicate viral hepatitis. Levels less than 5× normal tend to indicate drug toxicity. Acute hepatitis will typically have ALT and AST levels rising 20–30× 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, 1998). 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 (IgM and IgG) for assessment of immunity to HAV are not influenced by the passive administration of IG, because the prophylactic doses are below detection level (Lemon, 1997). At the onset of disease, the presence of IgG anti-HAV is always accompanied by the presence of IgM 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; Koff, 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. Three 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

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

Treatment of Hepatits 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 HBcAg. 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 (Hoolinger and Lau, 2006). Currently, there are seven medications licensed for treatment of chronic hepatitis B infection in the United States (Prammoolsinsop, 2002). These include antiviral drugs, Lamivudine (Epivir), Adefovir (Hepsera), Tenofovir (Viread), Telbivudine (Tyzeka) and Enticavir (Baroclude) and the two immune system modulators; interferon alpha-za and PEGylated interferon alpha-za. The 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; Tasspoulos, 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 (Tassapoulos, 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 EPIVIR®-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; Dienstay, 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 HBsAg carriers, but the effect is reversible, if therapy is stopped (Lai, 1997; Nevens, 1997; Gitlin, 1997; Mahoney and Kane, 1999; Dienstay, 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, Theradigm-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
Interferon	interferon-α	interferon-γ
Antiviral	lamivudine	acyclovir
	famciclovir	dideoxyinosine
		azudothymidine
		foscarnet
mmunomodulatory		prednisone
		interleukin-2
		thymosin
		levamisole

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 >51.3 μ mol/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 10^7/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

Manufacturer	Brand name§	Country	Type
Centro de Ingenieria Genetica Y Biotecnologia	Enivac-HB	Cuba	Recombinant DNA
Chiel Jedang	Hepaccine-B	South Korea	Plasma derived
Korea Green Cross	Hepavax B	South Korea	Plasma derived
Korea Green Cross	Hepavax-Gene	South Korea	Recombinant DNA
LG Chemical	Euvax B	South Korea	Recombinant DNA
Merck Sharp & Dohme	Recompivax H-B-Vax II	United States	Recombinant DNA
Merck Sharp & Dohme	Comvax	United States	Combined Hib and (recombinant)
Pasteur Mérieux Connaught	Genhevac B	France	Recombinant DNA (mammalian cell)
SmithKline Beecham	Engerix-B	Belgium	Recombinant DNA
SmithKline Beecham	Twinrix	Belgium	Combined hepatitis A and B (recombinant)
SmithKline Beecham	Tritanrix-HB	Belgium	Combined DTP and recombinant
SmithKline Beecham	Infanrix-HB	Belgium	Combined DTP (acellular P) and HB (recombinant)
Swiss Serum and Vaccines Institute	Heprecombe	Switzerland	Recombinant DNA (mammalian cell)

DTP- diphteria, tetanus and pertussis; HB - hepatitis B; Hib - *Haemophilus Influenza* type b

Toxic	Under evaluation
fialuridine	Interferon-β
adenine arabinoside	ribavirin
	lamivudine (long term)
	famciclovir (long term)
	adefovir
	entecavir
	adoptive immune transfer

Source: (Mahoney and Kane, 1999)

CONLUSION

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) 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 supposed to be 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 e.t.c, 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 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 (FSWs) 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 (Koziel 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.

REFERENCES

1. Koziel MJ, Peters MG. Viral hepatitis in HIV infection. *The New England Journal of Medicine* 2007; 356: 1445-1454.
2. Agbede OO, Iseniyi JO, Kolawole MO, Ojuowa A. Risk factors and seroprevalence of hepatitis B surface antigenemia in mothers and their preschool age children in Ilorin, Nigeria. *Therapy* 2007; 4(1):67-72.

3. Akani CI, Ojule AC, Opurum HC, Ejilemele AA. Seroprevalence of HBsAg in pregnant women in Port Harcourt, Nigeria. *Nigeria Postgraduate Medical Journal* 2005; 12(4): 266-270.
4. Alter M. Epidemiology and prevention of hepatitis B. *Seminars in liver disease* 2003; 23(1): 39–46.
5. André FE. Approaches to a vaccine against hepatitis A: development and manufacture of an inactivated vaccine. *Journal of Infectious Diseases* 1995; 171:S33-S39.
6. Awole M, Gebre-Selassie S. Seroprevalence of hepatitis B surface antigen and its risk factors among pregnant women in Jimma, Southwest Ethiopia. *Ethiopian Journal of Health and Development* 2005; 19(1):45-50
7. Barker LF. Transmission of serum hepatitis. *Journal of the American Medical Association* 1996; 276(10): 841–844.
8. Barzaga BN. Hepatitis A shifting epidemiology in South-East Asia and China. *Vaccine* 2000; 18(2): 61-64.
9. Bastida G, Nos P, Aguas M, Beltrán B, Rubín A, Dasí F, Ponce J. "Incidence, risk factors and clinical course of thiopurine-induced liver injury in patients with inflammatory bowel disease". *Aliment Pharmacology Therapy* 2005; 22(9): 775–82.
10. Battegay M, Gust ID, Feinstone SM. Hepatitis A virus. In: Mandell, G.L, Bennett, J.E, and Dolin, R, (Editors). *Principles and Practice of Infectious Diseases*. 4th Edition. Churchill Livingstone, New York; 1995.
11. Beckingham IJ, Ryder SD. "Investigation of liver and biliary disease". *British medical Journal(Clinical research ed.)* 2001; 322(7277): 33–36.
12. Belo AC. Prevalence of hepatitis B virus markers in surgeons in Lagos, Nigeria. *East Africa Medical Journal* 2000; 77: 283-285
13. British Medical Association Illustrated Medical Dictionary (BMA). First Edition. Dorling Kindersley Limited, UK; 2002.
14. Centers for Disease Control and Prevention. Hepatitis B virus: A comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the immunization practices advisory committee (ACIP). *Morbidity and Mortality Weekly Report* 1991; 40:1-19.
15. Centers for Disease Control and Prevention. Control measures for hepatitis B in dialysis centers, *http://www.cdc.gov/ncidod/hip/control.htm*; 1998. Accessed 2011-10-12
16. Cheesbrough M. *District Laboratory Practice in Tropical Countries*. 2nd Edition. Cambridge University Press, UK; 2006.
17. Chernecky CC, Berger BJ. *Laboratory Tests and Diagnostic Procedures*, 5th Edition. St. Louis, Saunders; 2008.
18. Chisari FV, Ferrari C. Viral Hepatitis. In: Nathanson, N, (Editor). *Viral Pathogenesis.* Lippincott – Raven, Philadelphia; 1997.
19. Cianciara J. Hepatitis A shifting epidemiology in Poland and Eastern Europe. *Vaccine* 2000; 18(2):68-70.
20. Clegg T. Hepatitis B surface and e antigen seropositivity in mothers and cord blood at Port Moresby General Hospital: implication for a control program. *Papua New Guinea Medical Journal* 1991; 34:234-237.
21. Cobelens FG, Van Schothorst HJ, Wertheim-Van Dillen PM. Epidemiology of hepatitis B infection among expatriates in Nigeria. *Clinical Infectious Disease*. 2004; 38: 370-376.
22. Collenberg E, Ouedraogo T, Ganame J, Fickenscher H, Kynast-Wolf G, Becher H, Kouyate B, Krausslich HG, Sangare L, Tebit DM. Seroprevalence of six different viruses among pregnant women and blood donors in rural and urban Burkina Faso: A comparative analysis. *Journal of Medical Virology* 2006; 78(5): 683-692.
23. Custer Sullivan S, Hazlet T, Iloeje U, Veenstra D, Kowdley K. "Global epidemiology of hepatitis B virus". *Journal of Clinical Gastroenterology* 2004; 38(10): 158–168.
24. Dienstag JL. Extended lamivudine retreatment for chronic hepatitis B: maintenance of viral suppression after discontinuation of therapy. *Hepatology* 1999; 30:1082-1087.
25. Drosten C, Nipparaschk T, Manegold C, Meisel H, Brixner V, Roth WK, Adedjihou A, Gunther S. Prevalence of hepatitis B virus DNA in anti-HBV positive/HBsAg-negative sera correlates with HCV but not HIV serostatus. *Journal of Clinical Virology* 2004; 29:59-68.
26. Egah DZ, Banwat EB, Audu ES, Iya D, Mandong BM, Annele AA, Gomwalk NE. Hepatitis B surface antigen, hepatitis C and HIV antibodies in a low-risk blood donor group, Nigeria. *Eastern Mediterranean Health Journal* 2007; 13(4): 71-73.
27. Ejele OA, Ojule AC. The prevalence of hepatitis B surface antigen (HBsAg) among prospective blood donors and patients in Port Harcourt, Nigeria. *Nigerian Journal of Medicine* 2004; 13: 336-338.
28. Fattovich G. Long-term outcome of hepatitis B e antigen-positive patients with compensated cirrhosis treated with interferon alfa. European Concerted Action on Viral Hepatitis (EUROHEP). *Hepatology* 1999; 26:1338-1342.
29. Ferriara MS. Diagnosis and treatment of hepatitis. *Revista da Sociedade Brasileira de Medicina Tropical* 2000; 33:389-400
30. Gan SI, Devlin SM, Scott-Douglas NW, Burak KW. *Lamivudine for the treatment of membranous glomerulopathy secondary to chronic Hepatitis B infection* 2005; 19. pp. 625–9.
31. Ganem D, Schneider RJ. Hepadnaviridae: The Viruses and Their Replication. In: Knipe, D.M, (Editor). *Fields Virology.* 4th Edition. Lippincott Williams & Wilkins, Philadelphia; 2001.
32. Garcia-Samaniegorez Rodriguez M, Berenguer J, Rodriguez-Rosado R, Carbo J, Asensi V, Soriano V. Hepatocellular carcinoma in HIV-infected patients with chronic hepatitis C. *American Journal of Gastroenterology* 2001; 96: 179-183.
33. Gitlin N. Hepatitis B: diagnosis, prevention, and treatment. *Clinical Chemistry* 1997; 43:1500-1506.
34. Guyton MD, Hall JE. *Textbook of Medical Physiology.* Elsevier, Saunders; 2006.
35. Guyton MD, Arthur C, John E, Hall. *Textbook of Medical Physiology.* Elsevier, Saunders; 2005.
36. Hadler SC. Global impact of hepatitis A virus infection changing patterns. In: Hollinger, F.B., Lemon, S.M, and Margolis, H.S, (Editors). *Viral Hepatitis and Liver Disease*. Williams & Wilkins, Baltimore; 1991.
37. Hadziyannis SJ, Manesis EK, Papakonstantinou A. Oral ganciclovir treatment in chronic hepatitis B virus infection: a pilot study. *Journal of Hepatology* 1999; 31:210-214.
38. Hamel. "Wheat Extracts as an Efficient Cryoprotective Agent for Primary Cultures of Rat Hepatocytes": Wiley Interscience, Montreal; 2006.
39. Harry TO, Bajani MD, Moses AE. Heaptitis B virus infection among blood donors and pregnant women in Maiduguri, Nigeria. *East Africa Medical Journal* 1994; 70: 596-597.
40. Health A to Z. Hepatitis as a result of chemicals and drugs. http://web.archive.org/web/20060623141402/http://www.healthatoz.com/healthatoz/Atoz/dc/caz/infc/hepa/hepres.jsp 2006; Accessed 2011-10-01.
41. Healthcare stumbling in RI's Hepatitis fight. The Jakarta Post. *http://www.thejakartapost.com/news/2011/01/13/healthcare-stumbling-ri's-hepatitis-fight.html* 2011; Accessed 2011-01-13.
42. Hollinger FB, Lau DT. Hepatitis B: the pathway to recovery through treatment. *Gastroenterology Clinics of North America* 2006; 35(4):895–931.
43. Hollinger FB, Liang TJ. Hepatitis B Virus. In: Knipe, D.M., (Editors). *Fields Virology.* 4th Edition. Lippincott Williams & Wilkins, Philadelphia; 2001.
44. Hollinger FB, Ticehurst JR. Hepatitis A virus. In: Fields, B.N, Knipe, D.M, and Howley, P.M, (Editors). *Fields Virology*. 3rd Edition. Lippincott – Raven, Philadelphia; 1996.
45. Ikeda K. Interferon dicreases hepatocellular carcinogenesis in patients with cirrhosis caused by the hepatitis B virus: a pilot study. *Cancer* 1998; 82:827-835.
46. Iwarson S. Why the Scandinavian countries have not implemented universal vaccination against hepatitis B. *Vaccine* 1998; 16: 56-57.
47. Janssen HL. Interferon alfa for chronic hepatitis B infection: increased efficacy of prolonged treatment. *Hepatology* 1999; 30: 238-243.
48. Joint Committee on Vaccination and Immunisation. "Chapter 18 Hepatitis B". *Immunisation Against Infectious Disease 2006* (The Green Book). 3rd Edition. Stationery Office, Edinburgh; 2006.

49. Juszozyk J. Clinical Course and consequence of Hepatitis B infection. *Vaccine* 2000; 18:23-25.
50. Kane MA. Status of hepatitis B immunization programmes in 1998. *Vaccine* 1998; 16: 104-108.
51. Kidd-Ljunggren K, Holmberg A, Bläckberg J, Lindqvist B. "High levels of hepatitis B virus DNA in body fluids from chronic carriers". *The Journal of Hospital Infection* 2006; 64(4): 352–7.
52. Koff RS. Hepatitis A. *Lancet* 1998; 341: 1643-1649.
53. Kong KL, Cho Y, Lee SS. The declining HbsAg carriage rate in pregnant women in Hong Kong. *Epidemiology and Infections* 1997; 199: 281-283.
54. Kulkarimi S, Alowola FO, Wayo GG. Prevalence of hepatitis B surface antigen in Northern Nigerian blood donors. *Vox Sangunis* 1986; 50: 151-153.
55. Lai CL. Lamivudine is effective in suppressing hepatitis B virus DNA in Chinese hepatitis B surface antigen carriers: a placebo-controlled trial. *Hepatology* 1997; 25:241-244.
56. Lai CL. A one-year trial of lamivudine for chronic hepatitis B. Asia Hepatitis Lamivudine Study Group. *New England Journal of Medicine* 1998; 339:61-68.
57. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment and current and emerging prevention and control measures. *Journal of viral Hepatitis* 2004; 11: 97-107.
58. Lemon SM. Hepatitis A virus. In: Webster, R.G and Granoff, A, (Editors). *Encyclopedia of Virology*. Academic Press Ltd, London; 1994.
59. Lemon SM. Type A viral hepatitis: epidemiology, diagnosis, and prevention. *Clinical Chemistry* (1999; 43(8B): 1494-1499.
60. Li, Albert P. "Screening for human ADME/Tox drug properties in Drug Discovery". *Drug Discovery Today* 2001; 6(7): 357-366
61. Li XM, Shi MF, Yang YB, Shi ZJ, Hou HY, Shen HM, Teng BQ. "Effect of hepatitis B immunoglobulin on interruption of HBV intrauterine infection". *World Journal of Gastroenterology* 2004; 10(21): 3215–7.
62. Li XM, Yang YB, Hou HY, Shi ZJ, Shen HM, Teng BQ, Li AM, Shi MF, Zou L. "Interruption of HBV intrauterine transmission: a clinical study". *World Journal of Gastroenterology* 2003; 9(7): 1501–3.
63. Lin HH, Kao JH, Chang TC, Hsu HY, Chen DS. Secular trend of age-specific Prevalence of hepatitis B surface and antigenemia in pregnant women in Taiwan. *Journal of Medical Virology* 2003; 69:466-470.
64. Luka SA, Ibrahim MB, Iliya SN. Seroprevalence of hepatitis B surface antigen among pregnant women attending Ahmadu Bello University Teaching hospital, Zaria, Nigeria. *Nigerian Journal of Parasitology* 2008; 29(1): 38-41.
65. Mahoney FJ, Kane M. Hepatitis B vaccine. In: Plotkin, S.A., Orenstein, W.A, (Editors). *Vaccines*. 3rd Edition. W.B. Saunders Company, Philadelphia; 1999.
66. Melnick JL. History and epidemiology of hepatitis A virus. *Journal of Infectious Diseases* 1995; 171(1): 2-8.
67. Modi AA, Feld JJ. Viral hepatitis and HIV in Africa. *AIDS reveal* 2007; 9(1): 25-39.
68. Muula AS. Tackling HIV/AIDS in Africa-another perspective. *African Health* 2000; 23(1): 5-6
69. Nadir A, Reddy D, Van, Thiel DH. "Cascara sagrada-induced intrahepatic cholestasis causing portal hypertension: case report and review of herbal hepatotoxicity". *America Journal of Gastroenteroly* . 2000; 95(12): 3634–7.
70. Nasidi A, Harry TO, Vyazor SO, Numumbe GMR, Azzan BB, Ancinlev VA. Prevalence of Hepatitis B infection marker in two different geographical areas of Nigeria. *Proceedings of the first international conference* 1983; *12-15 December 1983,* Lagos, Nigeria.
71. National Institute of Health. "Hepatitis B". http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001324*;* 2010. Retrieved 2011-10-23.
72. Ndams IS, Joshua IA, Luka SA, Sadiq HO. Epidemiology of Hepatitis B Infection Among Pregnant Women in Minna, Nigeria. *Science World Journal* 2008; 3(5-8).
73. Nevens F. Lamivudine therapy for chronic hepatitis B: a six-month randomized dose-ranging study. *Gastroenterology* 1997; 113:1258-1263.
74. Ng F, Chan M, Chan H, Cheng C, Leung H, Chen N, Ren C. "Host heterogeneous ribonucleoprotein K (hnRNP K) as a potential target to suppress hepatitis B virus replication" (Free full text). *PLOS medicine* 2005; 2(7):163.
75. Niederau C. Long-term follow-up of HBeAg-positive patients treated with interferon alfa for chronic hepatitis B. *New England Journal of Medicine* 1996; 334:1422-1427.
76. Odemuyiwa SO, Oyedele OI, Forbi JC. Hepatitis B surface antigen (HbsAg) in the sera of medical, nursing and microbiology students in Ibadan, Nigeria. *Africa Journal of Medical Science* 2001; 30: 333-335.
77. Olubuyide IO, Ola SO, Aliyu B. Prevalence and epidemiological characteristics of hepatitis B and C infections among doctors and dentists in Nigeria. *East Africa Medical Journal* 1997; 74: 357-361.
78. Onakewhor JUE, Offor E, Okonofua FE. Maternal and neonatal seroprevalence of Hepatitis B surface antigen (HBsAg) in Benin City. *Journal of Obstetrics and Gynaecology* 2001; 21(6): 583-586.
79. Otegbayo JA, Fasola FA, Abja A. Prevalence of hepatitis B surface and antigens, risk factors for viral acquisition and serum transaminase among blood donors in Ibadan, Nigeria. *Tropical Gastroenterology* 2003; 24: 196-197, 2003.
80. Otegbayo JA, Taiwo BO, Akingbola TS, Odaibo GN, Adedapo, KS, Penugonda S, Adewole IF, Olaleye DO, Morphy R, Kanki P. Prevalence of hepatitis B and C seropositivity in a Nigerian cohort of HIV-infected patients. *Annals of Hepatology* 2008; 7(2): 152-156.
81. Parveen MD, Kumar, Michael Md. Some causes of acute parenchymal damage. *Clinical Medicine: with student consult Access*. W.B. Saunders Company, Philadelphia; 2005.
82. Pashankar D, Schreiber RA. "Jaundice in older children and adolescents". *Pediatrics in Review* 2001; 22(7): 219–226.
83. Pollack A. Merck's Hepatitis C Drug Wins F.D.A Approval. *The New York Times;* 2011.
84. Pramoolsinsup C. Management of viral hepatitis B. *Journal of Gastroenterology and Hepatology* 2002; 17:125–45.
85. Raurich JM, Pérez O, Llompart-Pou JA, Ibáñez J, Ayestarán I, Pérez-Bárcena J. "Incidence and outcome of ischemic hepatitis complicating septic shock". *Hepatology Research* 2009; 39(7): 700–5
86. Redd J, Baumbach J, Kohn W, Nainan O, Khristova M, Williams I. "Patient-to-patient transmission of hepatitis B virus associated with oral surgery". *The Journal of infectious diseases* 2007; 195(9): 1311–1314.
87. Robinson WS. Hepatitis B viruses. General Features (human). In: Webster, R.G and Granoff, A, (Editors). *Encyclopedia of Virology,* Academic Press Ltd, London; 1994.
88. Robinson WS. Hepatitis B virus and hepatitis D virus. In: Mandell, G.L, Bennett, J.E, Dolin R, (Editors). *Principles and Practice of Infectious Diseases.* 4th Edition. Churchill Livingstone, New York; 1995.
89. Rockstroh JK. The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel. *AIDS*, 25; 2011.
90. Ryder S, Beckingham I. "ABC of diseases of liver, pancreas, and biliary system: Acute hepatitis". *British Medical Journal* 2001; 322(7279): 151–153.
91. Séverine Celton-Morizur, Grégory Merlen, Dominique Couton, Chantal Desdouets. "Polyploidy and liver proliferation". *Cell Cycle* 2010; 9 (3): 460-466.
92. Sharma R, Malik A, Rattan A, Iraqi A, Maheshwari V, Dhawan R. Hepatitis B Virus Infection in Pregnant Women and its Transmission to Infants. *European Journal of Public Health* 1995; 5(3): 223-225.
93. Shi Z, Li X, Ma L, Yang Y. "Hepatitis B immunoglobulin injection in pregnancy to interrupt hepatitis B virus mother-to-child transmission-a meta-analysis". *International Journal of Infectious Diseases (IJID): Official Publication of the International Society for Infectious Diseases* 2010a; 14(7): 622–34.
94. Shi Z, Yang Y, Ma L, Li X, Schreiber A. "Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B

virus: a systematic review and meta-analysis". *Obstetric Gynecology* 2010b; 116(1): 147–59.
95. Siriprakash I, Anil TP. Routine prenatal screening of Indian women for HBsAg: benefits derived versus cost. *Tropical Doctor* 1997; 107:10-15.
96. Sirisena ND, Njoku MO, Idoko JA. HBsAg in patients with human immunodeficiency Virus1 (HIV-1) infection in Jos, Nigeria. *Nigerian Medical Practitioner* 2002; 41:18-20.
97. Sleisenger MH, Feldman M, Friedman LS. *Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management.* 8th Edition. Saunders, Philadelphia; 2006.
98. Stapleton JT, Lemon SM. Hepatitis A and hepatitis E. In: Hoeprich, P.D, Jordan, M.C and Ronald, A.R, (editors). *Infectious Diseases* 5th Edition. Lippincott Co, Philadelphia; 1994.
99. Stapleton JT. Host immune response to hepatitis A virus. *Journal of Infectious Diseases* 1995; 171(1): 9-14.
100. Steffen R. Hepatitis A in travelers: the European experience. *Journal of Infectious Diseases* 1995; 171(1): S24-S28.
101. Tanaka J. Hepatitis A shifting epidemiology in Latin America. *Vaccine* 2000; 18(2): 57-60. .
102. Tassopoulos NC. Recombinant interferon-alpha therapy for acute hepatitis B: a randomized, double-blind, placebo-controlled trial. *Journal of Viral Hepatitis* 1997; 4:387-394.
103. Terrault N, Roche B, Samuel D. Management of the hepatitis B virus in the liver transplantation setting: A European and an American perspective. *Liver Transplantation* 2005; 11(7):716-732.
104. Thio CL, Seaberg EC, Skolasky R Jr, Phair J, Visscher B, Munoz A, Thomas DL. Multicnter AIDS Cohort Study. HIV-1, hepatitis B virus and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet* 2002; 360: 1921-1926.
105. Tufenkeji H. Hepatitis A shifting epidemiology in the Middle East and Africa. *Vaccine* 2000; 18(2):65-67.
106. Van Damme P, Kane M, Meheus A. Integration of hepatitis B vaccination into national immunisation programmes. *British Medical Journal* 1997; 314:1033-1037.
107. Vázquez-Martínez JL, Coreño-Juárez MO, Montaño-Estrada LF, Attlan M, Gómez-Dantés H. Seroprevalence of hepatitis B in pregnant women in Mexico. *Salud publication México* 2003; 45: 165-170, 2003.
108. Viral Hepatitis Prevention Board. Antwerp VHPB Report. Editorial. Control of viral hepatitis in Europe. *Viral Hepatitis* 1996; 4(2).
109. Viral Hepatitis Prevention Board. News from the VHPB meeting in St. Julians, Malta. *Viral Hepatitis* 1996; 6(1).
110. Viral Hepatitis Prevention Board. Universal HB immunization by 1997: where are we now?, (Fact Sheet VHPB/ 1998/2). *http://hgins.uia.ac.be/esoc/VHPB/vhfs2.html*; 1997. Accessed 2011-10-10
111. Viral Hepatitis Prevention Board. Ensuring injection safety and a safe blood supply. (Fact Sheet VHPB/ 1998/3). *http://hgins.uia.ac.be/esoc/VHPB/vhfs3.html*; 1998. Acessed 2011-09-20
112. Walton J, Barondess JA, Lock S. *The Oxford Medical Companion.* Oxford, Oxford University Press, London; 1994.
113. Wasley A, Alter MJ. Epidemeology of hepatitis C: geographic differences and temporal trends. *Seminar in Liver Diseases* 2000; 20: 1-16.
114. Williams R. "Global challenges in liver disease". *Hepatology (Baltimore, Md.)* 2006; 44 (3): 521–526.
115. World Health Organization. WHO / EPI Protocol for assessing prevalence of hepatitis B infection in antenatal patients. *WHO/EPI/GEN / 90.6*; 1990.
116. World Health Organization. The children's vaccine initiative and the global programme for vaccines and immunization: recommendations from the Special Advisory Group of Experts. *Wkly epidemiology Record* 1996; 71: 261-266.
117. World Health Organization. World health Organization (WHO) report, 2003. Shaping the future. *Geneva*; 2003.
118. World Health Organization. Hepatitis B vaccine. *Wkly epidemiology Record* 2004; 79: 255-263.
119. World Health Organization. Mortality and Burden of Disease Estimates for World Health Organization (WHO) Member States in 2002. http://www.who.int/entity/healthinfo/statistics/bodgbddeathdalyestimates.xls 2004; Accessed 2011-05-25
120. World Health Organization. "Hepatitis B". http://www.who.int/mediacentre/factsheets/fs204/en/index.html 2009; Retrieved 2011-10-19.
121. World Health Organization. Health risks and their avoidance - hepatitis B. In: International travel and health. *Vaccination requirements and health advice.* WHO, Geneva; 1999.
122. Zuckerman AJ. Hepatitis Viruses. In: Baron S, (Editors). *Medical Microbiology*. 4th Edition. The University of Texas Medical Branch at Galveston, Galveston; 1996.