INAUGURAL LECTURE SERIES 300

ERADICATING THE 'LITTLE FOXES' THAT DESTROY THE POWERHOUSE OF THE HUMAN BODY

By

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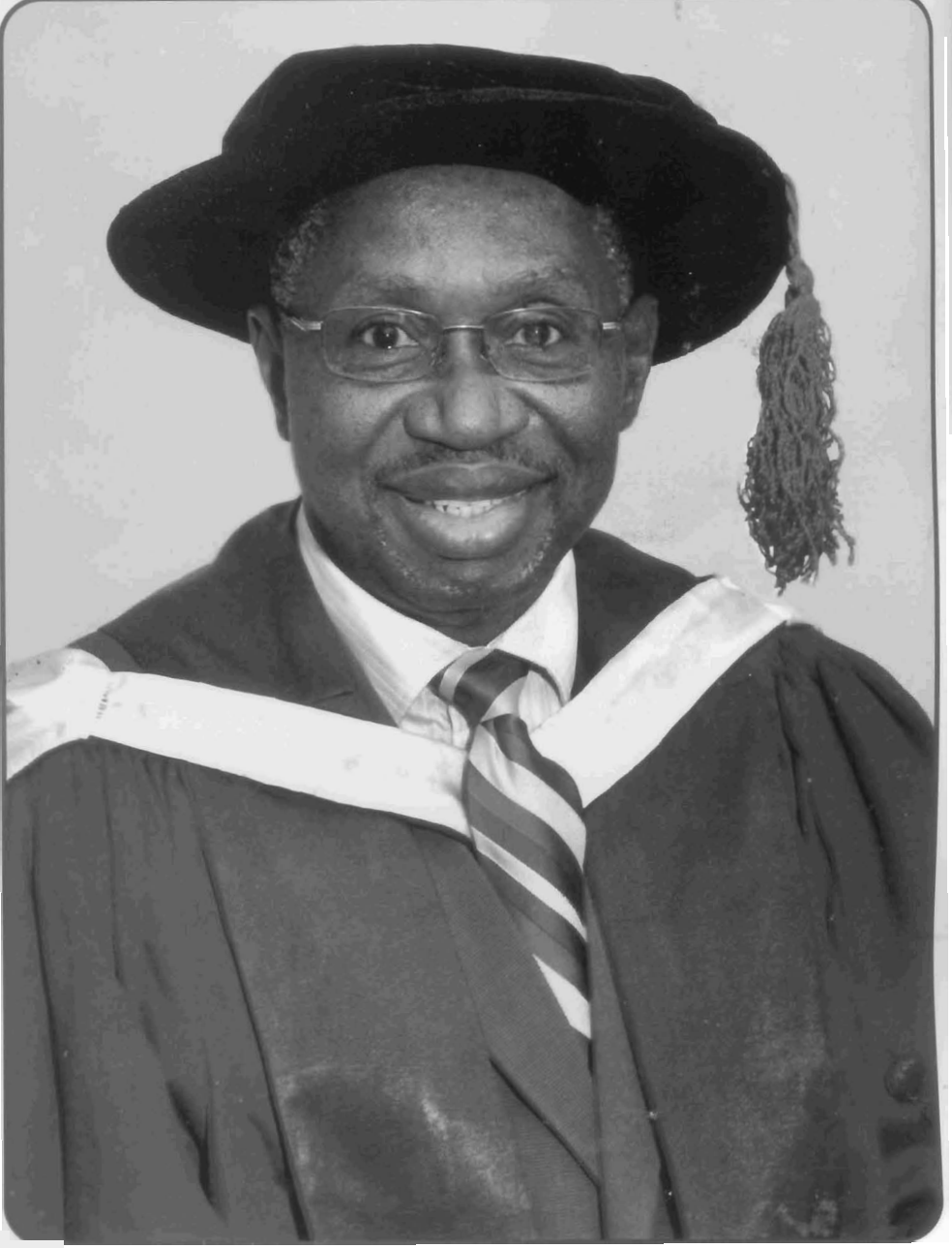
OBAFEMI AWOLOWO UNIVERSITY PRESS, ILE-IFE, NIGERIA.



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An Inaugural Lecture Delivered at Oduduwa Hall, Obafemi Awolowo University, Ile-Ife, Nigeria
On Tuesday, 28th March, 2017

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Inaugural Lecture Series 300

ISSN 0189-7848

Printed by

Obafemi Awolowo University Press Limited,
Ile-Ife, Nigeria.

Eradicating the 'Little Foxes' that Destroy the Powerhouse of the Human Body

1. Preamble

Mr. Vice-Chancellor Sir, I am eternally grateful to my Heavenly Father and Lord for not only making it possible for me to stand before you all today to give this inaugural lecture but also, and more importantly, for making me who I am today.

I would also like to pay tribute to my parents of blessed memory, Mr. & Mrs. Festus & Joy Ndububa. In particular, I remember the crucial role my father (Festus Ajuonuma Ndububa) played in my early life to place my foot on the path of academic success. He was among the pioneering staff of the then University College, Ibadan (now University of Ibadan) where I was born and brought up. He was a strict disciplinarian and a strong believer in academic excellence. In our primary school days, he would personally supervise the study of our books after returning from work. While other children played football and had fun he would ensure (with a whip on hand) that my siblings and I stay glued to our books! Even though the experience was painful before long the fruits began to manifest. My elder brother got admission into King's College, Lagos in the 1960s when it was run by British officials and my immediate junior brother was admitted into the equally prestigious Government College, Ibadan where he was the cynosure of eyes as he carted away prizes every year. In Lagelu Grammar School, Ibadan, where I attended, I took the third place position only once in my first year in the school. For the rest of my stay in the school till I graduated I took no other position but the first and in one particular year I won Dr. Lekan Are's trophy for the most promising science student in the entire school. Incidentally, that was the only year the trophy was awarded to my knowledge.

As Providence would have it, I had my university education at the University of Nigeria, Nsukka. My interest in the Specialty of Internal Medicine was kindled as far back as when I was an undergraduate in the University of Nigeria Medical School. We had quite a number of erudite and competent teachers but the two that made the greatest impression on me were Dr. P. I. Okolo and Dr. W. P. J. C. Onyeama. Dr. P. I. Okolo, a Consultant Physician, was the vintage teacher and repository of clinical information and skills while Dr. Onyeama, a Consultant Psychiatrist, held students spellbound with his knowledge, eloquence and great command of the Queen's English. Some of us simply dropped our pens just to listen and enjoy his lectures! It was no wonder, therefore, that I chose Internal Medicine when by God's determinate counsel I had to come to then Ife University Teaching Hospitals Complex, Ile-Ife, for my Residency Training Programme. In those days, resident doctors were few in number and the hospital had more units than now with the result that clinical workload was heavy. One teacher and senior colleague that kept me on my toes and never allowed me to lose focus was Dr. (later Professor) A. Akinsola. He was a mentor, motivator and goal-getter par excellence, intelligent and full of enthusiasm for his work. I am really grateful to him for the positive impact he made on me.

I entered the Senior Residency Training Programme of the West African College of Physicians in 1986. Since I chose Gastroenterology (i.e. study of the digestive system) as my sub-specialty of interest I had to work under the tutelage and supervision of Dr. S. O. Teniola who, at that time, was the first and only Consultant Gastroenterologist in the Department of Medicine. Dr. Teniola was based at the Wesley Guild Hospital, Ilesa (one of the constituent units of the teaching hospital) and so I had to join him at Ilesa. He taught me the basics of Hepatology (an arm of Gastroenterology) and under him I learnt and perfected the

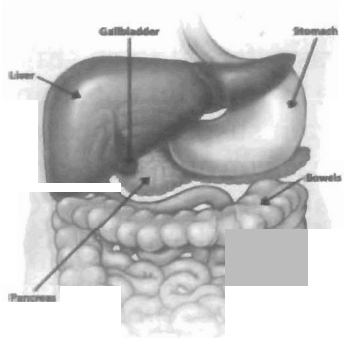


Figure 1. The Digestive System

liver biopsy procedure. At that time I also benefitted from the tutelage and experience of Professor M. A. Atoba, a Consultant Gastroenterologist on Sabbatical Leave at Ife from the University of Ibadan. I successfully completed the Residency Programme and joined the Obafemi Awolowo University as an academic staff during the period I was working in Ilesa.

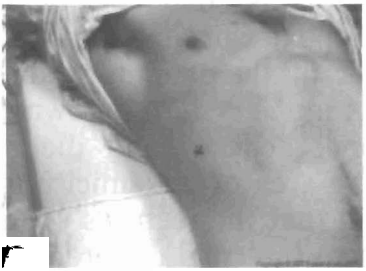


Figure 2. Position for Liver Biopsy

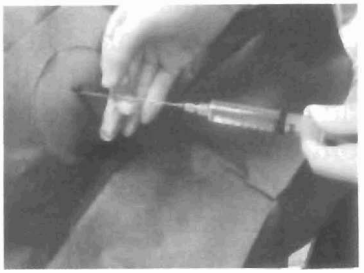


Figure 3. Liver Biopsy Procedure

2. Unravelling the Aetiopathogenesis of Seasonal Ataxic Syndrome ("Ijesha Shakes")

While working at Ilesa I began to see large numbers of patients presenting with generalized body tremors, ataxic (staggering) gait, autonomic dysfunction and varying levels of impaired consciousness usually after a meal. I later learnt that this condition occurred annually during the rainy season particularly among the Ijesa people and was called "Ijesha Shakes". For several years the cause of the illness remained

unknown. Initially, the condition was thought to be due to a viral infection and was referred to as "Encephalitis tremens" but viral studies done in 1973 did not support the hypothesis. A food poison was again suspected because sufferers usually gave a history of meal consumption prior to presentation. Also, because the peak period for the occurrence usually fell on the time of the new yam harvest, consumption of new yam was fingered as a probable cause. However, no single food item was found to be common to all the patients presenting with the disease.

In a bid to unravel the enigma of "Ijesha Shakes", I entered into a collaborative study with my Neurologist colleague at Ile-Ife, Dr. Bola Adamolekun. Together we developed a detailed questionnaire and examination protocol which we then administered on the patients presenting with "Ijesha Shakes". We found that the condition (also referred to as "seasonal ataxic syndrome") occurred exclusively among individuals of low socio-economic status who subsisted almost exclusively on a monotonous diet of heavy carbohydrate meals. But while the type of carbohydrate meal differed from one patient to another, all the patients studied had consumed the dried larvae of *Anaphe venata* (known as *koni* in local parlance), a seasonal delicacy and dietary protein supplement common in the area of endemicity for the syndrome. It was also observed that the features of the condition were remarkably similar to the triad of cerebellar ataxia, ocular disturbances and encephalopathy seen in acute thiamine (vitamin B1, a component of the vitamin B complex group) deficiency. Based on these observations, it was therefore postulated that "Ijesha Shakes" could be a variant of Wernicke's disease and that individuals already marginally thiamine deficient due to monotonous consumption of heavy meals of carbohydrates containing thiamine-binding cyanogenetic glycosides suffered a seasonal exacerbation of thiamine deficiency from thiaminases or anti-thiamine factors putatively present in

the larvae of *Anaphae venata* (Adamolekun B & Ndububa DA, 1994).

As a means of proving that the nutritional status of an individual determined susceptibility to the ataxic syndrome, we conducted a controlled study of serum albumin levels as an index of protein nutriture in both "Ijesha Shakes" patients and their unaffected relatives who ate the same meals. The study revealed that the serum albumin level in patients on admission was significantly lower than at discharge and was also significantly lower than in unaffected relatives. This showed that low income people with critically low protein nutriture were particularly susceptible to the ataxic syndrome if they consumed the larvae of *Anaphae venata* (Adamolekun B *et al*, 1994). Thus our studies uncovered the cause of "Ijesha Shakes" and with this knowledge came a rapid decline in the incidence of the condition as people either avoided *koni* or ensured that they took adequate amounts of protein in their meals. Today, patients with "Ijesha Shakes" are hardly seen again in our medical wards.

3. The Body's Powerhouse

I would define the body's powerhouse as the system of the body that is involved in receiving and processing of food and nutrients with the eventual generation of energy and maintenance of good health. The stomach in conjunction with the rest of the gut and the liver largely represent the powerhouse of the human body.

The stomach is a J-shaped hollow organ that serves as an expandable "container" for temporary food storage. Partial digestion of food takes place in the stomach both by the physical churning action of its muscles and chemical breakdown of food by acid and enzymes secreted in the stomach juice. The processed food (crushed, mixed and liquefied to form chyme) is gradually released by the stomach into the small intestine via the pyloric canal in a controlled and regulated manner. The stomach also produces

certain factors (e.g. intrinsic factor) that aid vitamin absorption.

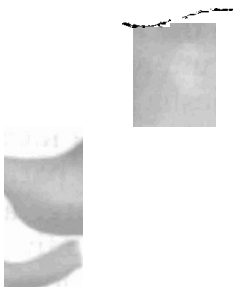


Figure 4. The Stomach

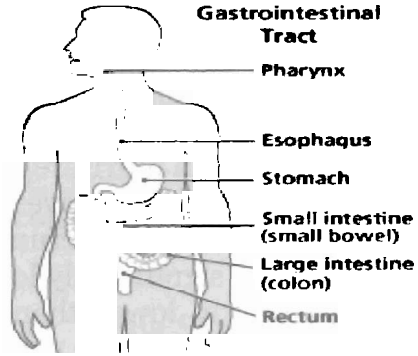


Figure 5. Gastrointestinal Tract

The liver is the second largest organ in the human body after the skin. However, it is the largest and heaviest gland, weighing an average of 1.5 Kg and shaped like a pyramid, wedge or prism. The liver has been described as a complex chemical "factory" that works throughout the 24 hours of the day. Virtually everything we eat, drink, breathe in, inject or rub on our skin is processed by the liver. It acts like a sieve for all absorbed substances carried to it in the blood from the small and large intestines. Over 500 different vital functions have been ascribed to the liver but here are just a few of them:

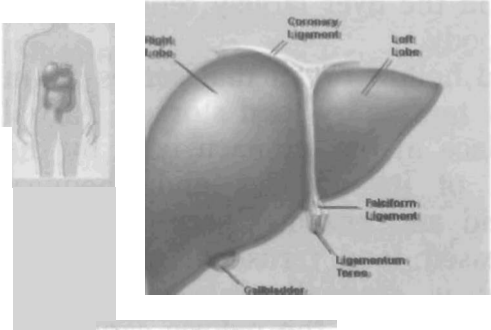


Figure 6. The Liver

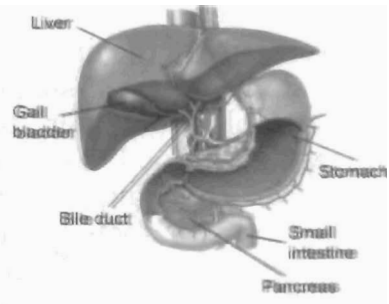


Figure 7. The Liver, Gall Bladder & Stomach

Table 1: Functions of the Liver

S/NO.	FUNCTION
1.	Detoxification and cleansing of blood: metabolism of drugs, chemicals & alcohol; neutralization & elimination of harmful toxic substances
2.	Body fuel supply: producing, storing and supplying fast energy in the form of glucose; production, storage and export of fat
3.	Manufacture of essential body proteins: e.g. albumin, clotting factors
4.	Manufacture and storage of vitamin D: essential for tooth and bone health
5.	Regulation and storage of iron and copper
6.	Defence against infections: it has specialized cells that engulf and destroy bacteria and other pathogens that enter the liver through its blood supply
7.	Produces bile which aids in the digestion of fat
8.	Production & regulation of body cholesterol which it also converts to other useful body substances
9.	Metabolism and regulation of sex hormones, thyroid hormones, cortisol and other adrenal hormones

The liver therefore combines the functions of body fuel supply, food & nutrient storage, metabolism of body proteins & hormones, detoxification of harmful substances and fighting of infections.

4. The 'Little Foxes'

In the Song of Solomon, chapter 2 verse 15, we read "Catch us the foxes, the little foxes that spoil the vines, for our vines have tender grapes" (NKJV Bible). These foxes were described as 'little' but they posed a great threat to the vines that carried delicate but valuable grapes. **This verse reads like a plea or cry for help from my numerous, hapless patients**. The cry is for us to catch or arrest the little foxes before they can wreck their havoc. These 'little foxes' represent the tiny organisms that undermine and

eventually destroy huge, vital and delicate organs of the human body. They enter the body unannounced but produce devastating outcomes when their work is done! The 'little foxes' that specifically attack the body's powerhouse are the hepatitis viruses (against the liver) and a bacterium called *Helicobacter pylori* (against the stomach). Since the discovery of these 'little foxes' as the causes of major hepatic and gastroduodenal diseases, Gastroenterologists the world over have been engaged in a battle not only to 'catch' but also to eliminate them.

5.0 Viral Hepatitis

Viral hepatitis refers to a diffuse inflammatory disease of the liver associated with hepatocyte (liver cell) necrosis secondary to infection with a virus. Viral agents that cause hepatitis have been categorized into 3 groups, namely, (1) Primary Hepatotropic Viruses, (2) Secondary Hepatotropic Viruses and (3) Exotic Hepatotropic Viruses

Table 2: **Hepatitis Viruses**

Category	**Member Viruses**
Primary Hepatotropic Viruses	Hepatitis A Virus (HAV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Hepatitis D Virus (HDV) & Hepatitis E Virus (HEV)
Secondary Hepatotropic Viruses	•Herpes viruses: Cytomegalovirus (CMV), Epstein virus (EBV), Herpes simplex virus (HSV) & Human herpes viruses 6,7,8 (HHV) •Varicella virus •Adenovirus •Enteroviruses •Paramyxovirus •Parvovirus •Rubella virus •Corona virus (agent that causes SARS)
Exotic Hepatotropic Viruses	•Flavi viruses: Dengue fever, Yellow fever

	•Filo viruses: Ebola virus, Marburg virus •Bunya viruses: Rift Valley fever virus, Crimea Congo haemorrhagic fever virus •Arenavirus: Lassa fever

The primary hepatotropic viruses have special affinity for the hepatocytes (liver cells) and specifically target them for infection. The secondary hepatotropic viruses cause inflammation of the liver as part of a multi-organ, systemic involvement especially in immunocompromised individuals while the exotic hepatotropic viruses cause the viral haemorrhagic fevers.

Overwhelming majority of hepatitis cases seen in clinical practice are caused by the primary hepatotropic viruses. Hepatitis A and Hepatitis E viruses are transmitted through water or food contaminated by faecal matter (faeco-oral route) and they usually give rise to a self-limiting infection. As a result of this, they are endemic in the developing countries of the world with low standards in personal and environmental hygiene. Mortality rate in women could be, however, as high as 20-40% in Hepatitis E if the infection is contracted in pregnancy and it may occur in epidemics. Hepatitis B and hepatitis C virus infections are contracted through parenteral (blood-borne) and percutaneous (via breached skin & mucous membranes) routes and can lead to chronic liver disease (CLD), liver failure and cancer. Hepatitis D virus shares similar routes of transmission as HBV and HCV but can only infect those already positive for HBV infection.

5.1 Hepatitis B Virus Infection

The breakthrough in our understanding of hepatitis B came in 1965 when Dr. Baruch Samuel Blumberg [Fig. 8] identified an unusual antigen from the blood sample of an

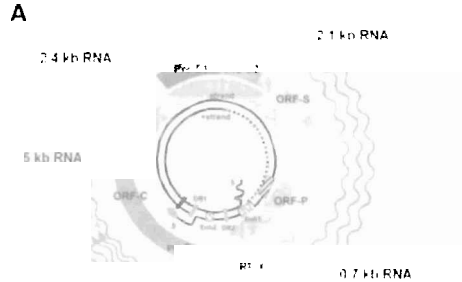
Australian Aborigine during a research on the genetics of disease susceptibility.

Figure 8. Dr. Baruch Blumberg

This unusual antigen was originally called "Australia antigen" because the Australian Aborigine's blood sample reacted with an antibody in the serum of an American haemophilia patient. After further research, this turned out to be the antigen that caused hepatitis B, now known as hepatitis B surface antigen (HBsAg). In 1969, Dr. Blumberg and his colleague, Dr. Irving Millman produced the hepatitis B vaccine. The United States' Food & Drug Administration (FDA) named it the first 'anti-cancer' vaccine because its prevention of chronic hepatitis B could in turn prevent the development of liver cancer. In 1976, Dr. Baruch Blumberg was awarded the Nobel Prize in Medicine in recognition of his discovery of HBV.

The hepatitis B virus (HBV) is a small virus that belongs to the *Hepadnaviridae* family. Its genome is a circular, partially double-stranded DNA composed of 3200 base pairs and has four overlapping open reading frames (ORF) or genes, namely, *S, C, P,* and *X*. The *S* gene encodes the hepatitis B surface antigen (HBsAg), the *C* gene encodes the hepatitis B core antigen (HBcAg) and the hepatitis B e antigen (HBeAg). The DNA polymerase enzyme is encoded

by the *P* gene while the *X* gene encodes the hepatitis B x antigen (HBxAg) which is thought to contribute to the oncogenic potential of the virus [Fig. 9].



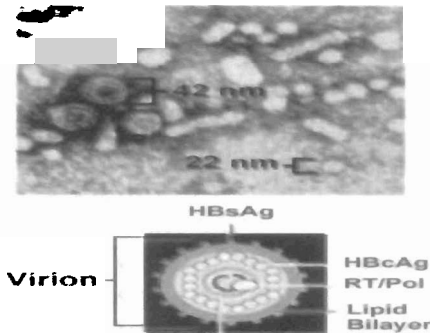


Figure 9. Hepatitis B Virus Genome

Figure 10. HBV Particles & Structure

The infectious HBV virion called the Dane particle is double-shelled and spherical in shape measuring 42 nm in diameter. This Dane particle consists of a lipid envelope containing HBsAg that surrounds an inner nucleocapsid composed of HBcAg complexed with polymerase and the viral genome [Fig. 10]. The various antigens of the HBV and their corresponding antibodies have diagnostic and prognostic implications [Table 3]

Table 3: Hepatitis B Virus Markers

HBV Marker	Significance
HBsAg	Evidence of HBV infection, acute or chronic
Anti-HBs	Evidence of immunity or marker of hepatitis B vaccination
HBeAg	High-level HBV replication and infectivity
Anti-HBe	Relatively low HBV replication and infectivity
Anti-HBc (IgM)	Acute or current HBV infection; could indicate a flare of chronic hepatitis B
Anti-HBc (IgG)	Chronic HBV infection or evidence of past infection with HBV
HBV DNA	Marker of viraemia, infectivity and response to therapy

Hepatitis B is a major global health problem with approximately two billion people worldwide having evidence of past or present infection with HBV. It is estimated that about 250 million people are chronically infected with HBV (defined as positive HBsAg for at least 6 months). Hepatitis B is a potentially life-threatening infection that puts infected individuals at a high risk of death from liver cirrhosis and liver cancer. HBsAg positive individuals have 12-300 times higher risk of developing liver cancer compared to those negative for the marker and up to 80% of the world's liver cancer is due to HBV infection. Almost 700,000 people die annually due to these complications of hepatitis B. The World Health Organization (WHO) has classified HBV as a Class 1 carcinogen (i.e. cancer-causing agent). In fact, HBV is the second most important carcinogen in the world, probably surpassed only by the cigarette smoke.

Based on HBsAg sero-prevalence rates, the world is categorized into low (<2%), intermediate (2-7%) and high prevalence areas (≥8%). High prevalence areas include sub-Saharan Africa and East Asia [Fig. 11].

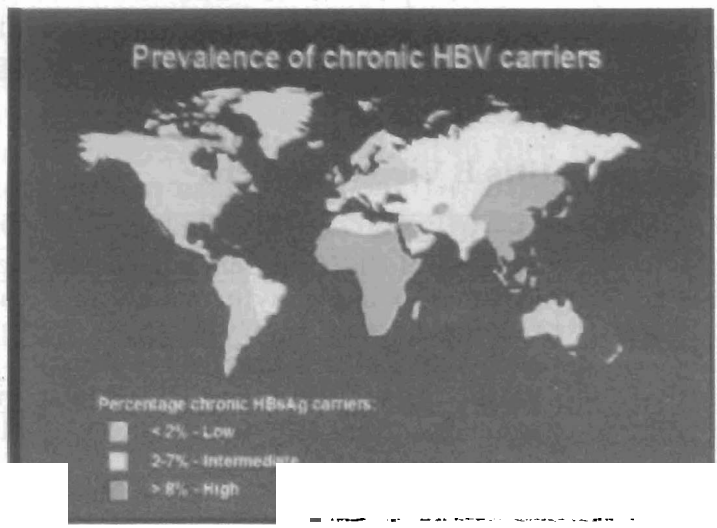


Figure 11. World Sero-Prevalence of HBsAg

In Nigeria, the prevalence rate for HBV ranges from 11% to 13.7% and with an estimated population of 170 million, this translates to about 20 million Nigerians chronically infected. Nigerians with sero-prevalence rates ≥25% include hospital (especially clinical) staff, persons with sexually transmitted infection, and commercial sex workers. However, based on the presence of at least one HBV serological marker, 76.6% (i.e. 130 million) of Nigerians have evidence of past or present infection. This endemicity and high prevalence rate of infection in Nigeria is mainly related to the age at infection. The rate of progression from acute to chronic HBV infection is about 90% when infection is acquired in early childhood (perinatal), 20-50% for infections between one and five years of age and ≤ 5% for infections acquired in adulthood. In Nigeria, as in other high prevalence areas in sub-Saharan Africa, the major modes of transmission of HBV are horizontal (child-to-child) and vertical (mother-to-infant) unlike in America, Western Europe and other developed countries where the infection is acquired mainly in adulthood through sexual exposure [Table 4]. This was confirmed by our study which found that sexual transmission was not an important risk factor for HBV infection in a Nigerian population of blood donors (Adekanle O, Ndububa, DA *et al*, 2010).

Table 4: Modes of Transmission of Hepatitis B Virus

- **Horizontal** (child-to-child during plays and scuffles)
- **Vertical** (mother-to-infant during perinatal period)
- **Sexual** (risk is high in individuals with multiple sexual partners, sexually transmitted infection or high risk behaviours)
- **Transfusion with unscreened blood** (especially from paid commercial donors)
- **Injection with re-cycled needle or from quacks**
- **Accidental needle stick or scalpel or clipper/razor injury** (if these sharp objects had already been used on an infected person)
- **Trado-medical procedures** (scarifications, circumcisions, tattoos, ear piercing and native surgeries done with unsterilized instruments)

A new syndrome, the acquired immunodeficiency syndrome (AIDS), was described for the first time in 1981 among gay men in the United States. In the mid-1980s, the first cases of HIV/AIDS were described in Nigeria and interest in this nascent epidemic began to grow. Since the HBV and the human immunodeficiency virus (HIV) shared similar routes of transmission, we screened blood donors at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife and members of the public including university students for HBV and HIV infection in the period of 1987-1989. We found that while the sero-prevalence rate for HIV in blood donors was 0.08%, the HBsAg sero-prevalence rate among them and the general populace was 7.3% and 8.8% respectively. We cautioned, therefore, that screening for HIV/AIDS should not be done at the expense of hepatitis B screening (Durosinmi MA, Ndububa DA *et al*, 1991). This study was instrumental in instituting hepatitis B screening of all potential blood donors in our hospital as an established, routine practice. However, while HIV/AIDS received a lot of public awareness and media campaign, no discernible interest was being shown in hepatitis B. It was not surprising, therefore, that in a study done among blood donors in OAUTHC ten years after the first one, the HBsAg sero-prevalence rate had climbed to 12% (Ojo OS *et al*, 1998). It is pertinent to mention here that HBV is 100 times more infectious and can survive for much longer periods (at least seven days) outside the human body than HIV.

5.2 Hepatitis C Virus Infection

In 1975, American and British researchers identified a type of hepatitis that did not test positive to HAV antibodies (anti-HAV) and HBsAg. It was then called non-A, non-B hepatitis (NANB). In 1989, Hepatitis C virus (HCV) was identified by Centers for Disease Control & Prevention and Chiron Company as the major cause of the NANB hepatitis. HCV is a single stranded RNA virus that belongs to the *Flaviviridae* family (the same family to which Yellow Fever virus belongs). Its genome is 9.6 kb long and contains S and

NS regions that code for structural and non-structural proteins respectively.

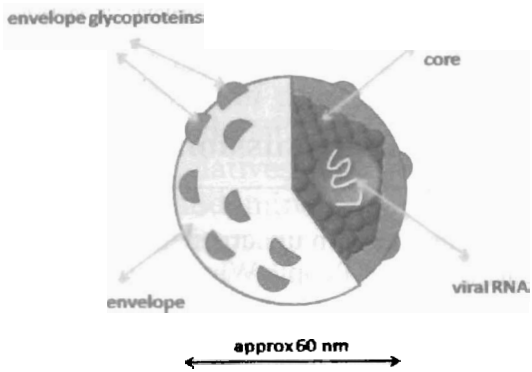


Figure 12. Structure of Hepatitis C Virus

HCV has six known genotypes (numbered 1 to 6). There are differences in the geographical distribution of these genotypes and the clinical outcome of HCV infection and response to treatment are also determined by the genotype involved [Table 5].

Table 5: HCV Genotypes and Geographical Locations

HCV Genotype	Geographical & Racial Distribution
1	United States, Europe, Nigeria
2	Europe
3	Europe
4	Egypt, Middle East, Central Africa
5	South Africa, France, Spain Belgium, Syria
6	Southeast Asia, Asian Americans, Asian Australians

More than 170 million people worldwide are chronically infected with HCV. Egypt has the world highest prevalence rates for HCV infection (up to 15%). The prevalence rate in Nigeria ranges from 0.5% to 4% with an average of 2.2%.

This translates to about 3.7 million Nigerians infected. The infection is transmitted principally through infected blood and the most common modes of transmission include transfusion with unscreened blood, injection drug use and haemodialysis [Table 6]

Table 6: Hepatitis C Transmission

1. Parenteral/Percutaneous
   - Blood transfusion with unscreened blood
   - Injection drug use (People Who Inject Drugs, PWID)
   - Haemodialysis
   - Occupational exposure by health workers
   - Tattooing
2. Non-Percutaneous
   - High-risk sexual practice (e.g. anal sex) by HIV positive persons and patients with STI
   - Multiple sexual partnership; risk is negligible in monogamous couples with no high-risk sexual practice
   - Mother-to-child: if the mother is HIV positive or has high viral load
   - Solid organ transplantation from an infected donor

Almost all cases of HCV infection are asymptomatic (give no complaints) and like chronic hepatitis B (CHB), the sequelae of chronic hepatitis C include cirrhosis, liver failure and liver cancer. In about 70-80% of cases, the infection progresses to liver cirrhosis within 20-30 years. In some patients, infection with HCV may produce extra-hepatic manifestations such as kidney disease, lichen planus, B-cell non-Hodgkin's lymphoma, cryoglobulinaemia, sicca syndrome and porphyria cutanea tarda. HCV infection is the most common indication for liver transplantation in the United States, Australia and most of Europe. Chronic viral hepatitis (both B & C) is responsible for 1.3 million deaths per year worldwide, which is comparable to the burden of HIV/AIDS, tuberculosis, and malaria put together.

In our study of individuals with chronic hepatitis (i.e. those harbouring HBV or HCV for more than six months or those with typical liver histology), we found that a large majority were asymptomatic and that the males were more affected than the females. Most of the subjects for this study were picked up at the Blood Bank as they attempted to donate blood for their sick relatives. The appearance of symptoms such as right upper abdominal pain, fatigue or weight loss, was found to signal the onset of liver cirrhosis or even cancer and this process was accelerated by alcohol consumption (Ndububa DA *et* al, 2005).

5.3 Treatment of Chronic Viral Hepatitis

Anti-viral therapy is now available for chronic viral hepatitis. For CHB, treatment is aimed at completely suppressing HBV replication, prevent HBV transmission and also prevent progression to liver cirrhosis, liver failure and liver cancer. Two drug groups are now available to achieve these aims, namely, the oral nucleos(t)ide analogues (NUCs) and the injectable interferons of which pegylated interferon-α (PegIFN) is the most widely available. Treatment with the oral NUCs is potentially lifelong as the treatment endpoint, the complete loss of HBsAg and development of anti-HBs, is achieved only by a small minority of patients after many years of continuous treatment. On the other hand, treatment with PegIFN has a finite period (48 weeks). However, there are stringent criteria to be met before choosing PegIFN and, in addition, the cost is exorbitant and there are major side effects to contend with. For both types of treatment, there are laboratory parameters to monitor and prominent among them are the serum HBV DNA and the HBeAg. Unfortunately, not all strains of HBV produce the HBeAg (HBeAg-negative CHB). Our research showed that two-thirds of Nigerian CHB patients are negative for HBeAg. One implication of this is that serum HBV DNA will be a more reliable treatment monitoring index in Nigerian patients. This makes treatment more herculean as serum HBV DNA

test is very costly ranging from ₦29,000 to ₦50,000 per test depending on the laboratory. We found that only 37.5% of our patients responded to treatment and about the same proportion (34.4%) were lost to follow-up principally due to the high cost of investigation and treatment (Ndububa DA *et al*, 2014).

Table7: Drugs for the Treatment of Chronic Hepatitis B

Nucleos(t)ide Analogues
1. Lamivudine
2. Adefovir dipivoxil
3. Telbivudine
4. Entecavir
5. Tenofovir
Interferon-alpha
1. Pegylated interferon α-2a

The treatment of chronic hepatitis C (CHC) has been revolutionized by the recent introduction of the oral directly acting anti-virals (DAAs). A number of these DAAs are effective against all the six genotypes of HCV (pangenotypic). Most cases of CHC without cirrhosis are now treated for only three months and for those who have developed cirrhosis treatment may be extended for another three months. Response rates of over 95% are being achieved with these DAAs and CHC has now become a curable disease. However, the management of CHC is equally expensive. Serum HCV RNA test costs between ₦50,000 and ₦70,000 and the 3-month course of DAAs costs about ₦300,000 - ₦400,000. From all these, it can be seen that the treatment of chronic viral hepatitis is unaffordable for a great majority of our patients and for this reason many who are eligible for treatment stay untreated.

Table 8: Drugs for the Treatment of Chronic Hepatitis C

Directly Acting Antivirals (DAAs)
1. Simeprevir
2. Sofosbuvir
3. Ledipasvir
4. Daclatasvir
5. Dasabuvir
6. Grazoprevir/Elbasvir
7. Paritaprevir/Ritonavir/Ombitasvir
8. Glecaprevir
9. Pibrentasvir
10. Velpatasvir
Interferons
1. *Pegylated interferon α-2a
2. Pegylated interferon α-2b
*Usually given with Ribavirin

6.0 Liver Cirrhosis and Cancer

Liver cirrhosis simply means the scarring of the liver with distortion of its shape, structure and blood supply following a chronic injury. When cirrhosis is fully established the features of liver insufficiency supervene and these include muscle wasting, abdominal swelling due to accumulation of fluid in the peritoneal cavity, jaundice (yellowness of the eyes) among others.

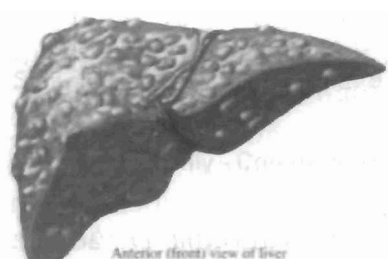


Figure 13. Liver Cirrhosis

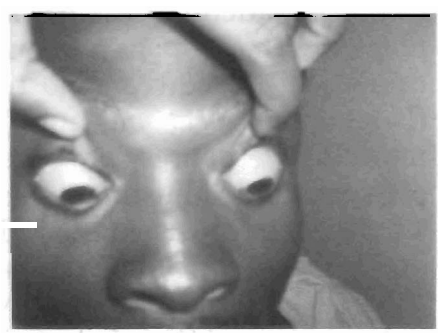


Figure 14. Jaundice

Liver cirrhosis may progress to or co-exist with liver cancer and for those patients who do not develop cancer the five-year survival rate is only 20-30%. The severity of liver disease in cirrhosis is usually graded using the Child-Pugh classification. This classification is based on the scoring of specific clinical parameters, namely, jaundice, ascites, encephalopathy, serum albumin, and prothrombin time. The sum of the scores classifies a patient into grade A, B or C [Table 9]

Table 9: Child-Pugh Classification

Parameter	1 Point	2 Points	3 Points
Albumin (g/dl)	> 3.5	2.8 – 3.5	< 2.8
Ascites	Absent	Mild	Moderate
Bilirubin (mg/dl)	< 2.0	2.0 – 3.0	> 3.0
Hepatic encephalopathy	Absent	Grades 1 & 2	Grades 3 & 4
PT (seconds prolonged)	< 4	4 – 6	> 6
Child-Pugh Class A = 5 - 6 points, B = 7 - 9 points, C = 10 – 15 points			
PT = Prothrombin Time			

6.1 Our Studies on Liver Cirrhosis

We found that about one-quarter of our patients with chronic liver disease have liver cirrhosis (Ojo OS, Ndububa DA *et al*, 1998). About two-thirds of our liver cirrhosis patients were in the Child-Pugh grade C, which is the worst grade on the scale of disease severity, by the time they were presenting in the hospital. This showed that most Nigerian cirrhosis patients present with very advanced disease. They not only have poor prognosis, they are also poor-risk candidates for both diagnostic and therapeutic interventions (Ndububa DA *et al*, 2005). A high rate of psychiatric morbidity (depression, generalized anxiety disorder, delirium and adjustment disorder) was found in patients with liver cirrhosis compared to patients with hypertension and normal controls (Aghanwa HS & Ndububa D, 2002). Women with liver cirrhosis who become pregnant suffer a deterioration of their liver function and run the risks of post-partum haemorrhage, gastrointestinal bleeding and stillbirth

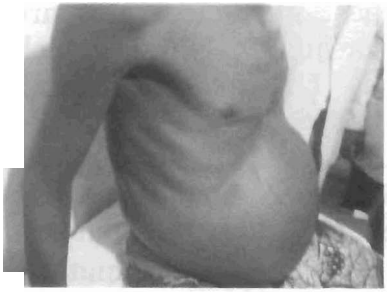


Figure 15. Abdominal Swelling in Cirrhosis

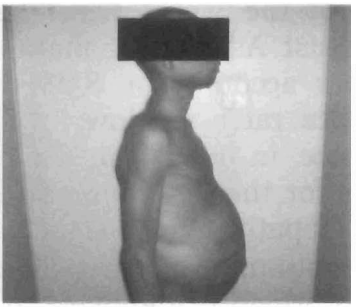


Figure 16. Patient with Liver Cirrhosis

among others (Ndububa DA *et* al, 2002). In another study, we found that sexual desire, performance and satisfaction were all significantly impaired in patients with liver cirrhosis and cancer when compared to age and sex-matched controls and that these dysfunctions were most pronounced in those individuals with Child-Pugh class C liver disease (Adekanle O, Ndububa DA *et al,* 2014). Liver cirrhosis patients also showed cognitive dysfunction especially in the domains of language, memory, attention/calculation and praxis (Adekanle O *et al*, 2012).

Primary liver cancer or hepatocellular carcinoma (HCC) is a malignant tumour of the liver cells. Worldwide, it is the fifth most common cancer in men and eighth most common cancer in women (749,000 new cases per year). However, it is the third cause of cancer-related death (500,000 to 1 million deaths per year).

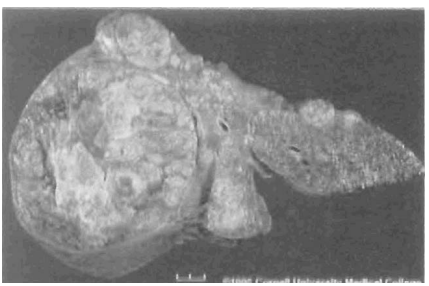


Figure 17. Liver Cancer

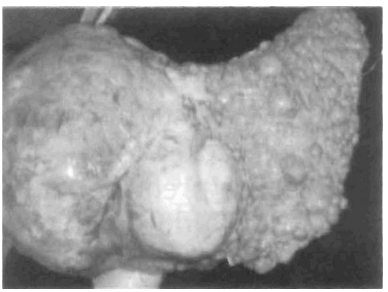


Figure 18. Liver Cancer with Cirrhosis

Areas of the world with the highest incidence rates are South-east Asia, sub-Saharan Africa and Melanesia which together account for 85% of cases. On the other hand, incidence rates are low in developed countries, the crude incidence in European Union being 8.29/100,000. Risk factors for the development of liver cancer include chronic viral hepatitis (B & C), alcohol, dietary aflatoxin consumption, α_1-antitrypsin deficiency, haemochromatosis (iron overload in the liver), non-alcoholic fatty liver disease (NAFLD), cigarette smoking and HIV co-existing with chronic viral hepatitis [Table 10].

Table 10: Aetiological Risk Factors for Liver Cancer

1. Hepatitis B Virus infection
2. Hepatitis C Virus infection
3. Aflatoxin consumption (eating mouldy foods & grains)
4. Alcohol consumption
5. Non-alcoholic fatty liver disease (NAFLD)
6. α_1-antitrypsin deficiency
7. Haemochromatosis (iron overload)
8. Cigarette smoking
9. HIV co-existing with chronic viral hepatitis
10. Chemicals, e.g. X-ray contrast media (thorotrast), arsenic, etc.

6.2 Liver Cancer Situation in Nigeria

Nigeria belongs to the region of the world with a moderately high incidence for liver cancer (11-20/100,000). Our studies, which are in agreement with others done in various parts of the country, show that middle-aged Nigerians in the 40-59 years age bracket (though the tumour has been seen in teenagers) are predominantly affected with a male to female ratio of 3.7:1 (Ndububa DA *et* al, 1999 & Ndububa DA *et* al, 2001). It is probably the most common cancer in young to middle-aged males in Nigeria.

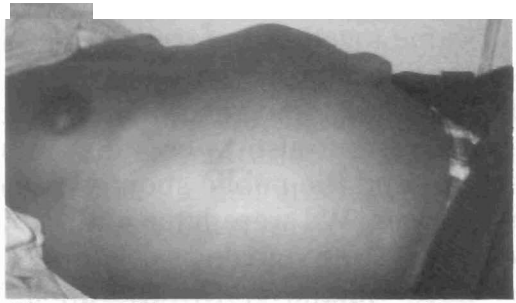


Figure 19. Young Man with Liver Cancer

Table 11: IARC Classification of Liver Cancer Incidence in Males*

Category	Incidence	Country/Region
Very High	> 20/100,000	China, Central/East Africa, Japan
Moderately High	11-20/100,000	West Africa, South-east Asia
Intermediate	5-10/100,000	Europe, North America
Low	< 5/100,000	Australia, New Zealand, S. America

• With an incidence in males of 15.3/100,000, West Africa falls into the moderately high incidence category
IARC = International Agency for Research on Cancer
*Gomaa AI *et al*, World J Gastroenterol 2008

One major downside of my medical practice has been to watch helplessly as Nigerians are being cut down in their prime of life by this relentless and aggressive tumour. An overwhelming majority of them present to the hospital with advanced, terminal disease and the three most common symptoms are abdominal pain, weight loss and abdominal swelling. Hardly any week passes without having at least two liver cancer cases on admission in the ward. Death occurs within an average period of four months from the onset of symptoms making the diagnosis of liver cancer a virtual death sentence.

7. The Ife Liver Disease Study Group

Disturbed by the ravaging effects of chronic viral hepatitis and its often fatal sequelae of cirrhosis and cancer on our

people, Dr. (now Professor) Segun Ojo of the Department of Morbid Anatomy & Forensic Medicine, Dr. Toun Lawal (now Dr. (Mrs.) A. A. Ejilemele) of the Department of Chemical Pathology and I came together to form the Ife Liver Disease Study Group in 1992. The group not only sought to promote the study of liver diseases and mentor junior colleagues in the field of hepatology but also to create awareness among health professionals and the public about viral hepatitis and its tragic consequences. We were later joined by Professors Gbenga Adeodu, Augustine Agbakwuru, Muheez Durosinmi, B. J. Olasode, Bayo Adetiloye, Dr. Olorunda Rotimi, Dr. Andy Fakoya and Dr. O. C. Famurewa. One of the first tasks we set for ourselves was to determine the aetiology (cause) of liver cancer in our patients. We developed a study proposal and with it we were able to attract a research grant from Glaxo SmithKline (GSK) (Nig.) Limited. We studied not only the blood but also the liver tissue of 130 patients with chronic liver disease (mainly cirrhosis and cancer) for markers of HBV. Using special stains we were able to demonstrate the presence of the antigens of HBV (HBsAg & HBcAg) in the liver tissue in over 70% of the patients studied. This study was first of its kind in Nigeria. We thus conclusively established the aetiological role of HBV infection in the development of liver cancer among Nigerian patients (Ojo OS, Ndububa DA *et al*, 1998). We also showed that 90% of patients with chronic liver disease (CLD) had evidence of current or past infection with HBV. On the other hand, the contribution of HCV and hepatitis D virus (HDV) to the development of CLD in Nigerian patients especially in the Southwest was found to be much less important as only 4% of them were positive to these viruses (Ojo OS *et al*, 1995). In another study of risk factors for the development of liver cancer in Nigerians, HCV infection did not appear important (Igetei R *et al*, 2010).

8. Aflatoxin and Liver Cancer

In the 1990s, interest was generated in aflatoxin as an important aetiological factor for liver cancer in sub-Saharan

Africa. Aflatoxin, especially aflatoxin B_1 (AFB_1), is a mycotoxin elaborated by the fungi (mould) *Aspergillus flavus* and *Aspergillus parasiticus* and is found in large quantities in improperly stored grains and foodstuff. Studies from southern Africa and parts of West Africa showed significant amounts of AFB_1 in the staple diets above the maximum allowed concentration (MAC) and in the urine of liver cancer patients. Further studies revealed that AFB_1 was genotoxic (gene-damaging) and, in particular, it caused codon 249 hot-spot mutation of the p53 tumour suppressor gene in liver cancer. In 1994, I won a Research Fellowship award of the Association pour la Recherche sur le Cancer (ARC) under the auspices of the Ife Liver Disease Study Group to study the aetiological contribution of aflatoxin to the development of liver cancer in Nigeria. This research was conducted at Centre Léon Bérard hospital, Lyon, France, under the supervision of Prof. Mehmet Ozturk who is a world renowned authority on p53 tumour suppressor gene mutations. I extracted DNA from liver cancer tissues brought from Nigeria and tested them for codon 249 mutation using nested polymerase chain reaction (nPCR). Only one (5.5%) of the liver cancer tissues demonstrated codon 249 mutation thereby suggesting that aflatoxin played a limited role in hepatocarcinogenesis (liver cancer formation) in Nigeria (Ndububa DA *et al*, 2001). This finding was later corroborated by another study of ours which showed p53 codon 249 mutation in the plasma DNA of only 7.6% of liver cancer patients from another part of southwestern Nigeria (Igetei R *et al*, 2008).

9. Alcohol and Liver Cancer

Alcohol is a major cause of liver cirrhosis which may eventually transform into liver cancer. Also, the risk of liver cancer is greatly increased if an individual with HBV or HCV infection regularly drinks alcohol in addition. Alcohol-related liver disease is a common problem in the developed countries where the drink is readily available and affordable. In our study of the contribution of alcohol to the

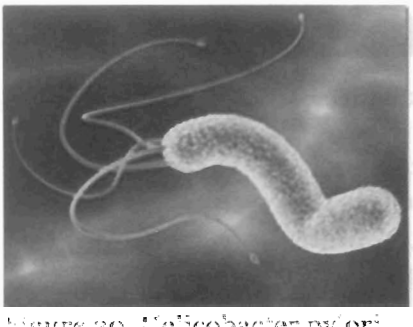
development of CLD we found that only the affluent abused alcohol and that the males were predominantly involved. Even though the proportion of CLD directly attributable to alcohol was found to be low (4%), we were able to show that the burden of liver cirrhosis and cancer was related to the amount of alcohol consumed with time (Ndububa *et al*, 2010).

10. Nigerian Association for the Study of the Liver

Having realized that viral hepatitis-related liver disease constituted the greatest proportion of liver disease burden in Nigeria and that viral hepatitis was preventable, we decided to enlarge the vision of the Ife Liver Disease Study Group and provide a wider platform for viral hepatitis control advocacy. We successfully sold the vision to doctors and other health professionals interested in liver diseases in Nigeria and in November 1994 the Nigerian Association for the Study of the Liver (NASL) was born right here in Ile-Ife. For several years NASL engaged the Federal Ministry of Health (FMOH) on the incorporation of hepatitis B vaccine into the National Programme on Immunization (NPI). A number of national workshops on viral hepatitis were held at Abuja under the auspices of NASL and the funding assistance of GSK (Nig.) Ltd. FMOH officials were invited to participate in these workshops. The efforts of NASL eventually paid off when in 2003 the hepatitis B vaccine became fully integrated into the NPI and in 2004 actual immunization was started in all Local Government Areas (LGAs) of the Federation. With this development we are looking forward to a progressive decline in the incidence of HBV infection as future generations of Nigerians become immune against the infection. The NASL was later re-named the Association for the Study of the Liver In Nigeria (ASLIN) in compliance with registration requirements from the Corporate Affairs Commission (CAC), Abuja.

11.0 Peptic Ulcer Disease

Peptic ulcer refers to a specific, circumscribed loss or breach of gut epithelial lining of those parts of the gastrointestinal system exposed to gastric (stomach) acid and pepsin secretion. The areas of the gut where peptic ulcers occur most are the lower oesophagus, stomach and the first part of the duodenum. The inside (lumen) of the stomach is very acidic (pH could be as low as 1.0-1.5) and, ordinarily, it is expected that the stomach lining would be damaged by the corrosive effects of the acid. There are, however, mucosal 'defensive forces' that prevent this damage from happening and these include mucus-bicarbonate barrier, rich gastric mucosal blood flow, epithelial tight junctions, prostaglandins and effective epithelial renewal/regeneration. Conditions and substances that undermine these 'defensive forces' often result into peptic ulcer formation. Peptic ulcer may therefore be caused by non-steroidal anti-inflammatory drugs (NSAID, e.g. aspirin), cigarette smoking, acute severe physical stress (e.g. burns injury, multiple fractures, head injury, etc.) and infection with *Helicobacter pylori*.



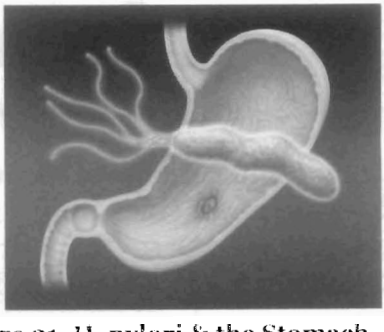


Figure 21. H. pylori & the Stomach

Table 12: Causative Factors for Peptic Ulcer Disease

1. Excessive Acid & Pepsin Secretion
2. Mucosal 'Defensive Factors' Weakened by
   - Non-steroidal anti-inflammatory drugs (NSAID)
   - *Helicobacter pylori* infection
   - Cigarette smoking
   - Acute physical stress (e.g. burns or head injury)
   - Duodeno-gastric bile reflux

The predominant symptom of peptic ulcer is epigastric (upper central) abdominal pain. The epigastric pain is often described as an aching, gnawing or peppery sensation frequently relieved by antacids or food. This symptom together with discomfort or sense of fullness or nausea constitutes what is known as dyspepsia. Dyspepsia is a common problem all over the world and contributes appreciably to job absenteeism, reduced quality of life and huge personal and national costs. The point prevalence of dyspepsia in the United States is estimated at 25%. The actual prevalence of dyspepsia in Nigeria is not known but it is a complaint for which a lot of patients visit the hospital.

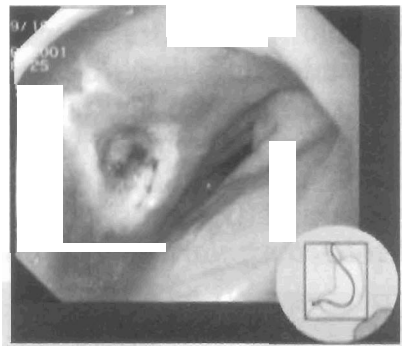


Figure 22. Peptic Ulcer

The complications of peptic ulcer include gastrointestinal haemorrhage (bleeding), free perforation into peritoneal cavity giving rise to peritonitis, penetration into another organ (e.g. pancreas) and gastric outlet obstruction. On occasions, patients present to the hospital for the first time with one or two of these complications.

11.1 Gastrointestinal Endoscopy

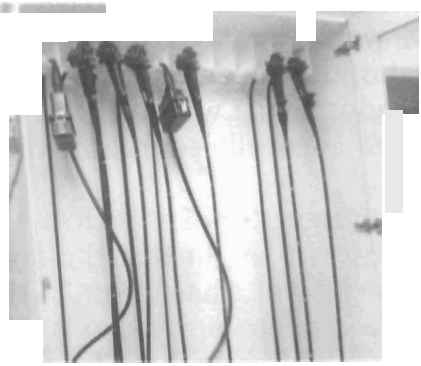


Figure 23. GIT Endoscopes

Endoscopy is the procedure for visualizing the internal body cavities. When the procedure is done to visualize the inside of the gastrointestinal tract it is called gastrointestinal (GIT) endoscopy and this could be upper (via the mouth) or lower (via the anus).

Figure 24. Endoscopy Suite

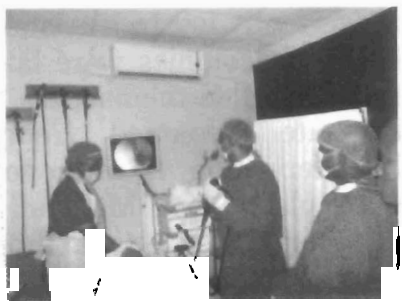


Figure 25. Endoscopy in Session

For a long time patients with peptic ulcer disease (PUD) were investigated with imaging (X-ray) techniques (e.g. Barium meal) but this modality was fraught with major shortcomings. Patients so investigated were exposed to radiation, ulcers or other lesions could not be directly visualized, inflammatory changes or erosions could not be demonstrated and biopsies were not possible. With the

advent of the flexible endoscope (fibreoptic or video-endoscope) these shortcomings have been completely circumvented. I would like to express my gratitude to Prof. Anthony Arigbabu, the doyen of Endoscopy in Nigeria, who taught me GIT endoscopy. I was really motivated by his great skills, patience and unparalleled passion for work.

11.2 *Helicobacter pylori* Infection

For a long time it was thought that the inside of the human stomach was too acidic for a bacterium to survive there. Even though spiral shaped micro-organisms had been described in the human stomach by researchers from time to time since over 100 years, the reports were not taken seriously until the discovery and work of Drs. Barry Marshall and Robin Warren of Australia in 1982. Robin Warren, a Pathologist, had noticed what looked like bacterial organisms on the mucosa of the stomach specimens sent for histopathology and then invited Barry Marshall, a Resident Internist, to examine the organisms. Unsuccessful attempts were initially made to grow the bacteria until the culture plates were inadvertently left in the laboratory over the Easter holidays. Growth of colonies were later noticed on the culture plate and they called the bacteria *Campylobacter pyloridis* which was later renamed *Helicobacter pylori* after proper characterization. In order to prove that the bacteria caused peptic ulcer Barry Marshall swallowed *Helicobacter pylori* (*H. pylori*) culture. Even though he did not develop an ulcer, he developed severe gastritis (inflammation of the stomach) and so proved that *H. pylori* caused gastritis. The two researchers contended in their original publication that gastritis and most stomach ulcers were caused by bacterial infection and not by stress or spicy food as previously thought. Later studies not only showed that about 90% of duodenal ulcers (DU) and 70-80% of gastric ulcers (GU) were associated with *H. pylori* infection but also that treatment and eradication of the organism led to a cure of these ulcers. The organism has also been shown to be associated with gastric cancer and lymphoma. The WHO has

declared *H. pylori* to be a Class 1 carcinogen (cancer-causing bacterium) just like HBV. In recognition of their discovery, Barry Marshall and Robin Warren were awarded the Nobel Prize in Medicine and Physiology in 2005.

Figure 26. Barry Marshall & Robin Warren

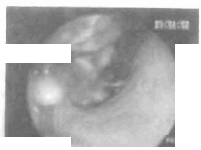


Figure 27. Stomach Cancer (Cardia)

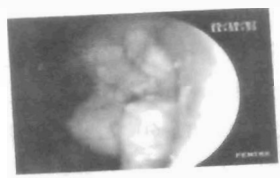


Figure 28. Stomach Cancer (Body)

Table 13: Gastroduodenal Diseases Associated with *H. pylori* Infection

1. Chronic active gastritis
2. Duodenal ulcer
3. Gastric ulcer
4. Gastric cancer (adenocarcinoma)
5. Mucosa-associated lymphoid tissue (MALT)
6. Low-grade B-cell lymphoma

Helicobacter pylori is a Gram negative, microaerophilic, flagellated bacterium that lives in the deep mucosal crypts of the human stomach. To survive in the acidic environment of the stomach, *H. pylori* burrows into the mucous lining of the stomach with its flagella and produces a urease enzyme that releases ammonia from the hydrolysis of urea thereby surrounding itself with an alkaline environment. The

presence of *H. pylori* in the stomach mucosa generates an inflammatory response that can eventually result in ulcer or even cancer depending on some ill-defined host and environmental factors.

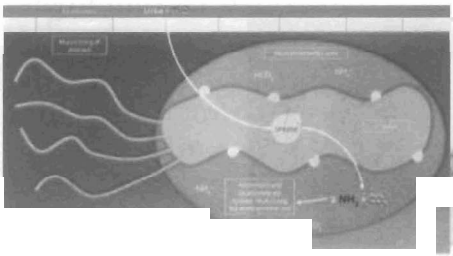


Figure 29. H. pylori Urease Production

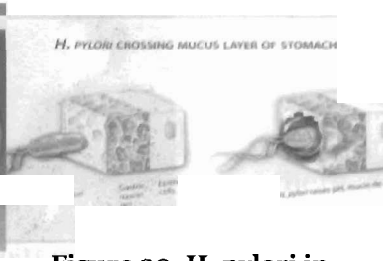


Figure 30. H. pylori in Stomach Mucus

H. pylori infection is probably the most common bacterial infection known to mankind as over 50% of the world's population are infected. Even though the precise mode of transmission of *H. pylori* is not clear, there is evidence to suggest that it is transmitted by the faecal-oral route and, possibly also, by the oral to oral route. High prevalence rates of infection occur in areas of crowded living conditions, poor personal and environmental sanitation, and poor water supply. This is why the infection rate approaches 80% among populations in the developing world.

11.3 Our Studies on *Helicobacter pylori* Infection

A number of studies in Nigeria had shown high sero-prevalence rates for *H. pylori* but ours was one of the earliest endoscopic studies. We showed that 73% of our patients with DU were positive for *H. pylori* and that certain endoscopic findings such as anterior DU and pyloric channel DU indicated massive *H. pylori* infection (Ndububa DA *et al*, 2001). The correlation between endoscopic findings of gastritis, GU and DU and positive rapid urease test for *H. pylori* infection was found to range from 76% to 100%. This very high correlation led to the conclusion that once any of these conditions is diagnosed on endoscopy, empirical treatment against *H. pylori* may be initiated where the rapid

urease test kits are unavailable (Agbakwuru EA, Ndububa DA *et al*, 2000).

We also contributed to knowledge in the area of diagnosis of *H. pylori* infection and its gene typing. We demonstrated that direct Gram stain of stomach mucosal biopsy was more sensitive than the rapid urease test and culture. The Gram stain technique is the cheapest of the three methods of diagnosis and can be easily undertaken in resource-poor and rural settings (Oyedeji KS *et al*, 2002). It had always been thought that the possession of the cytotoxin-associated gene (cagA) by a strain of *H. pylori* conferred pathogenicity on it. The cagA status of the *H. pylori* isolates from our patients was virtually the same in both those with active peptic ulcer and those with non-ulcer dyspepsia. We thus demonstrated not only the heterogeneity of *H. pylori* but also that other factors must be present before an individual infected with *H. pylori* can come down with active peptic ulcer (Smith SI *et al*, 2003).

Endoscopy Session

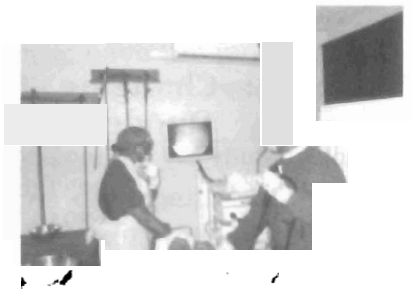


Figure . Inserting the gastroscope

H. pylori was shown to be the main aetiological agent for intestinal metaplasia (a pre-cancer condition of the stomach lining), mucosa-associated lymphoid tissue (MALT) and even stomach cancer with *H. pylori* infection rates of up to 90% in these lesions (Ndububa DA *et al*, 2007). In a study spanning over a period of 16 years, stomach cancer was found to account for 5.3% of all cancers, males were more affected, peak age group was 41-60 years and overwhelming majority (97.4%) presented in advanced stage. Only about

50% of the patients could undergo surgery and there was a poor 5-year survival rate of 14% (Alatise OI *et al*, 2007).

With the discovery of *H. pylori* and its association with peptic ulcer disease the eradication of *H. pylori* became an important goal of treatment of peptic ulcers. This was achieved in most cases by the combination of one anti-ulcer drug with two antibiotics. There is evidence to show that with the widespread use of this strategy the prevalence of *H. pylori* infection, DU and its complications have begun to decline. In our recent study of over 700 patients with dyspepsia, 18.5% of them had DU while 8.4% had GU (Ndububa DA *et al*, 2016). When compared with a similar study we did over a decade earlier, this result represents a 50% decline in DU prevalence but a proportionate rise in GU prevalence (Ndububa DA *et al*, 2001) [Table 14]. The rise in GU prevalence may be indicative of the fact that gastric erosions and ulcerations due to NSAID ingestion have not been affected by the *H. pylori* eradication therapy.

Table 14: Changing Trends in the Diagnosis of Duodenal and Gastric Ulcers

Period of Study	1992-1999 (n=834)	2006-2012 (n=726)
Duodenal ulcer	323 (38.7%)	134 (18.5%)
Gastric ulcer	39 (4.7%)	61 (8.4%)
Ratio (DU:GU)	8.3:1	2.2:1

However, going by the findings of our study showing that *H. pylori* had acquired resistance to all the commonly prescribed antibiotics this decline in DU prevalence may be reversed in the near future. This situation may not be unconnected with the widespread and indiscriminate use of antibiotics due to their availability over the counter (Aboderin OA *et al*, 2007).

12. My Contribution to the Training of Gastroenterologists in Nigeria

Soon after I completed my specialist training and joined the staff of the university and the teaching hospital the brain drain in the Nigerian health sector began. Many specialist doctors including Gastroenterologists left the country for greener pastures in the Middle East and Western countries. The onus was, therefore, on the few Gastroenterologists left to guide and train junior colleagues interested in specializing in the sub-specialty. At this time Ife was already known for endoscopy and the Ife Liver Disease Study Group had started making impact in the field of hepatology. As a result our Gastroenterology Unit began to receive a steady stream of senior resident (graduate) doctors wanting to specialize in Gastroenterology & Hepatology. We accommodated as many as were willing to undergo the training we provided and today I make bold to say that I have personally trained and mentored not less than twenty-four Gastroenterologists working at the Consultant level in hospitals all over the country. The result is that we now have far more centres in Nigeria offering a wide range of endoscopic services (both diagnostic and therapeutic) than ever before.

I have also contributed in putting Gastroenterology practice in Nigeria on the world map. In 1997 an attempt was made to resuscitate the West African Society of Gastroenterology (WASOG) after several years of being moribund following the brain drain. After sometime, it became obvious that only the Nigerian chapter was active as all efforts to bring back our Gastroenterology colleagues from the other parts of West Africa, especially Ghana, failed. Therefore, in September 2007 there was a merger of the Association for the Study of the Liver In Nigeria (ASLIN) and the Nigerian Chapter of WASOG to form the Society for Gastroenterology and Hepatology in Nigeria (SOGHIN). Soon after its inauguration, SOGHIN became formally affiliated with the World Gastroenterology Organization (WGO).

Figure 33. Inauguration of SOGHIN in 2007

This affiliation has opened doors and opportunities for our members and colleagues to go for Fellowships, further skills training and workshops abroad. Our growing active participation in WGO programmes has also earned Nigeria global recognition as an Endoscopy Training Centre has now been established in Lagos by the WGO. By virtue of her affiliation with WGO, SOGHIN became a member of the Africa & Middle East Gastroenterology Association (AMAGE), a regional arm of WGO. In 2012, Nigeria successfully hosted the annual AMAGE conference in Calabar and today, one of us, Prof. Segun Ojo is the AMAGE President. No doubt, his tenacity of purpose, goal-oriented lifestyle, his disdain for mediocrity and unrepentant attachment to scholarship have earned him this honour and recognition.

13. Conclusion and Recommendations

Mr. Vice-Chancellor Sir, my research has clearly shown that infection with HBV is the main cause of liver cancer among Nigerians and that most of those infected do not give complaints; they only give complaints when liver cancer has already developed. Young and middle aged Nigerians are predominantly affected by liver cancer and those affected hardly survive beyond four months after the diagnosis has

been made. Whereas a lot of information is out there in the public domain concerning HIV/AIDS thanks to the electronic and print media blitz driven by funding from foreign donors, hardly anything is being said about HBV infection and its sequelae. Yet HIV/AIDS affects much less Nigerians than viral hepatitis (the 2014 national sero-prevalence rate was 3% which translates into 5 million Nigerians infected compared to 20 million Nigerians infected by HBV). Permit me to list here the other challenges facing viral hepatitis control (and by extension, liver cancer) in Nigeria.

1. Ignorance about the natural history and management of viral hepatitis even among general medical practitioners. Viral hepatitis patients have been wrongfully counselled by many uninformed medical practitioners that their infection is inconsequential or have been placed on wrong treatment only for the patients to present later with complications to the Specialist.
2. Medical quackery. A number of groups have sprung up in the country claiming to have the cure for viral hepatitis and deceiving the unsuspecting public. They do this mainly for profit and for treatment use unorthodox, unproven methods.
3. Limited and expensive diagnostic facilities. Only few centres exist in Nigeria that can do the full complement of investigations for the diagnosis of viral hepatitis. This is especially so with viral load estimation in the blood. Where the diagnostic tests are available, cost is a major constraint. For example, the cost of hepatitis B viral load ranges from ₦29,000 to ₦40,000 per test while hepatitis C viral load costs about ₦60,000 per test (excluding test for the HCV genotype). This laboratory charge is not covered by the National Health Insurance Scheme (NHIS) and so patients have to pay out of their pocket.

4. Availability and affordability of treatments. Even though potent drugs are now available for the treatment of both CHB and CHC, the treatments are very expensive due to the high cost of drugs. The treatment of CHB with pegylated interferon costs over ₦1.05m excluding the investigations. The estimated cost for the treatment of CHC has already been stated.
5. High cost of immunoprophylaxis for the prevention of mother to child transmission (PMTCT) of hepatitis B. **Transmission of HBV infection from an infected mother to her child during delivery and early childhood is the main reason for persisting high burden of CHB in endemic areas like Nigeria.** PMTCT is achieved by immunoprophylaxis using hepatitis B immune globulin (HBIG) plus HB vaccine on the baby within 12 hours of delivery and this provides 90-95% protection. Unfortunately, HBIG is very expensive and prices range from ₦65,000 to ₦90,000 depending on the retailer. As a result of this, many mothers cannot afford it making their babies vulnerable to infection with HBV.
6. Insufficient number of Specialists (Gastroenterologists/Hepatologists) to manage viral hepatitis and its complications. There are only about 100 Gastroenterologists to a population of 170 million Nigerians.

There are encouraging signs in the horizon that the world is now gearing up to fight the scourge of viral hepatitis as it is doing against HIV/AIDS. At the first ever World Hepatitis Summit held in Glasgow, Scotland in September 2015 and attended by delegates from 98 countries of the world, the Glasgow Declaration on Hepatitis was released. The summit was organized by WHO and World Hepatitis Alliance (WHA) in collaboration with the Scottish Government and agencies. The Declaration called on governments to develop and implement comprehensive, funded national hepatitis plans

and programmes in partnership with all stakeholders to set the goal and targets to eliminate viral hepatitis as a public health concern by the year 2030. This goal was predicated on the realization that "...there are highly effective measures to prevent new hepatitis B and C infections and highly effective treatments that can suppress hepatitis B virus replication and cure hepatitis C infection" (Appendix). Here in Nigeria very commendable preliminary steps have been taken by the Federal Ministry of Health in the fight against viral hepatitis. The National Policy for the Control of Viral Hepatitis in Nigeria was launched in 2015 and both the National Strategic Plan (2016-2020) for the Control and Guidelines for the Prevention, Treatment and Care of Viral Hepatitis in Nigeria were launched in 2016. These landmark achievements were facilitated by the contribution of SOGHIN in conjunction with other stakeholders and funding agencies. Right now the Technical Working Group of the viral hepatitis control programme, of which some of my SOGHIN colleagues and I are members, is in the process of training health professionals from various parts of the country and at the different levels of health care on the use of the viral hepatitis management guidelines. Meanwhile, I would recommend the following control measures for viral hepatitis:

1. Public awareness campaigns and education (by radio, TV programmes/adverts, posters, etc.). The World Hepatitis Day that comes up every July 28 can serve as an opportunity for this.
2. Mandatory pre-donation screening for viral hepatitis by all blood banks
3. Availability of the appropriate diagnostic facilities in all Teaching and Specialist hospitals
4. Screening of every pregnant woman for viral hepatitis (B & C) in all ante-natal clinics
5. Provision of hepatitis B immunoglobulin (HBIG) at affordable cost at hospitals and maternity centres

6. The National Health Insurance Scheme (NHIS) should be made to cover the treatment of chronic hepatitis B and chronic hepatitis C. In the alternative, government should subsidize the treatment.
7. Universal immunization of all newborn babies with the hepatitis B vaccine should be pursued with unrelenting zeal.

In regard to *H. pylori* infection and peptic ulcer disease there is a need to introduce regulatory measures in the prescription and use of antibiotics. Individuals who are aged 40 years and above who develop upper central abdominal pain or dyspepsia for the first time should report to the hospital for endoscopic examination.

14. Appreciation

Mr. Vice-Chancellor Sir, the Bible asked a question in the book of Proverbs chapter 31 verse 10 "Who can find a virtuous woman? for her price is far above rubies" (KJV). My answer is that I found one in Kofoworola Olumide, my wife of 31 years, my close confidant, friend and companion, my one and only precious Honey without whose understanding, encouragement, sacrifice and love I would not have been able to stand before this august gathering to give this lecture. Through our union God has blessed us with three wonderful children, Chidinma Oluwaseyi, Chinweike Oluwasegun and Uchechukwu Ifeoluwa and a lovely granddaughter, Esther Toluwalase. To the glory of God, I have been able to reproduce myself in one of my children, Dr. C. O. Ndububa!

I want to thank all my colleagues in the Department of Medicine for their contribution to what I may have achieved today and for the uncommon spirit of mutual respect and comradeship in the department. I will not also fail to register my gratitude to colleagues and friends in the pharmaceutical industry who contributed to my success both academically and professionally. In particular, I would like to thank Glaxo SmithKline (Nig.) Ltd., Roche Products (Nig.) Ltd., Mega

Life Sciences and Phillips Pharmaceuticals for their valuable support.

Mr. Vice-Chancellor, Sir, I feel highly honoured by the presence of this distinguished audience and I want to say thank you all for listening and God bless.

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APPENDIX

World Hepatitis Summit 2015

GLASGOW, SCOTLAND 2-4 SEPTEMBER

Glasgow Declaration on Viral Hepatitis

- Because there are 400 million people with hepatitis B or hepatitis C infection with no country or region unaffected
- Because there is a lack of global awareness and most persons with hepatitis remain undiagnosed
- Because 1.4 million people die every year from complications of viral hepatitis yet most of these deaths can be prevented
- Because there are highly effective measures to prevent new hepatitis B and C infections and highly effective treatments that can suppress hepatitis B virus replication and cure hepatitis C infection
- Because universal access to prevention, testing, diagnosis, care and treatment is a human right and promoting access to and affordability of these services is the responsibility of all stakeholders
- The participants of the inaugural World Hepatitis Summit believe it is possible and essential to set as a goal the elimination of both hepatitis B and C as public health concerns
- We therefore call upon governments in all jurisdictions, to develop and implement comprehensive, funded national hepatitis plans and programmes in partnership with all stakeholders and in line with the World Health Assembly Resolution 67.6; and, in collaboration with the World Health Organization, to define and agree on realistic yet aspirational goal targets for viral hepatitis prevention, testing, diagnosis, care and treatment.