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An Inaugural Lecture delivered at the University of Ibadan
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UNIVERSITY OF IBADAN

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MR VICE-CHANCELLOR, DEAN OF THE FACULTY OF MEDICINE, DISTINGUISHED GUESTS, COLLEAGUES, LADIES AND GENTLEMEN,

I would like first of all to thank my Faculty for nominating me to give the Inaugural Lecture on their behalf. As you all know, my Faculty has many ably qualified persons on the waiting list who could have been called on to do the job. It would appear therefore as if I was jumping the queue. I am assured by my older colleagues that none of them wish to present a valedictory lecture for an inaugural one and I therefore have their mandate to talk to you this evening.

The definition of life found in the Concise Oxford Dictionary include "state of ceaseless change and functional activity peculiar to organized matter or an individual's actions or fortunes, that is, manner of existence". The liver is defined either as "a large glandular organ in vertebrates which secretes bile and purifies venous blood" or "one who lives in a specified way".

To many, it is a self-evident fact that an individual's manner of existence is dependent on the specified way he lives; that life depends on the liver. To others, this statement may be incomplete, as one's fortunes may be thought to depend on extraneous forces. I would show in this discourse that both the state of ceaseless change and functional activity peculiar to an individual and his actions or fortunes depend on his organ called the liver.

In the Bible, we find the following passage:

For the King Babylon stood at the parting of the way, at the head of the two ways, to use divination: he made his arrows bright, he consulted with images, he looked in the liver.
Ezekiel 21 : 21.

Thus from Babylonian times, the human and animal liver have been considered of great importance as a site for the soul and also for divination. The priest-physician therefore examined in

great details the livers of sacrificed animals for signs of significance from the gods.⁴⁴ In fact, the earliest known anatomical sculpture is a clay model of a sheep's liver with divinatory text dating from about 2000 B.C. which can be seen in the British Museum.

The concept that life depended on the liver was also firmly held by the Greeks.¹⁷ Adrastus, the Greek Warrior is shown on a Greek vase, a painting of which can be seen in Berlin Museum, studying the liver of a victim before he leaves for the Theban War.²²

Throughout much of recorded history, there was the belief that the liver was at the centre of things, which in truth, it is. The liver was chosen because it contains a great deal of blood and can skim off red cells or whole blood, holding either until needed. Since life and blood are synonymous, the liver was considered the seat of the soul. The theory of the four humours which ran through the teachings of Hippocrates, the father of medicine, Empedocles and Aristotle utilizes the concept of the liver being the seat of the soul when it states "blood is hot and moist like air, phlegm is cold and moist like water, yellow bile is hot and dry like fire and black bile cold and dry like earth." As one or other of these humours predominated in an individual, he was supposed to be of sanguine, phlegmatic, choleric or melancholic temperament. Examples of this concept taken from Shakespeare's Julius Caesar are Mark Antony (sanguine) Octavius (phlegmatic) or Cassius, (choleric or bilious) and Brutus (melancholic).

The belief in the immortality of the liver is enshrined in the legends of Tityos and Prometheus. Virgil's Aeneid describes Tityos' punishment as follows: "His body stretches over nine whole acres, and an enormous vulture crops with hooked beak his never-dying liver, tearing the entrails with their rich yield of pain, groping for food within and never leaving the deep wound in the breast and the tissues are ever reborn and never given repose".⁷² In the legend of Prometheus, he also suffers similar punishment. "Prometheus, the spot is out there waiting, and it is also your wound. It is the vulture of Zeus. When you return to this rock, the vulture will feast contentedly without pausing on you, and tear your flesh to ribbons, and dip his crooked, butter-yellow beak in your liver. Each morning, your liver and innards

will be as red and firm as the bald red head of the vulture; each evening, they will be as black and dead as mud. The vulture will never consume you—each night your slashed flesh will slowly and painfully heal, your liver will regain its natural colours".¹ These classic descriptions emphasize one peculiarity of the liver which is well known—the ability of regeneration.

The liver is a large visceral organ accounting for one-twentieth of the newborn's birth weight and at 1.5Kg in the adult, over one-fiftieth of the body weight. It is probably the most complex organ functionally in the body not excluding the brain. Although many misconceptions regarding its functions have been dispelled with the age of experimental medicine, it is still true to say that it is one of the least understood organs in man. The liver has many mysteries and unexplored aspects which continue to intrigue man. It consists of several millions of specialized glandular cells (the hepatocytes) packed into the meshes of a network of very fine subdivisions of blood vessels. Other small, flattened cells which line the fine subdivisions of blood vessels actively take up bacteria and foreign particulate matter from the blood. Each liver cell contains many different active components.

The liver is strategically placed so that the digested products of food and other substances that are taken by mouth and absorbed will pass through the liver before exerting their particular function in the body. This 'watchdog' function of the liver can be further illustrated by following what happens to the various groups of substances constituting a meal that is eaten.

Carbohydrates: The liver cell is very permeable to glucose, the end product of carbohydrate breakdown. Excess glucose is stored in the liver in a polymeric form called glycogen or burnt up by the tissues.

When a fall in blood glucose level occurs as during an overnight fast, glucose is secreted either from breakdown of liver glycogen or from the conversion of protein and fat to glucose. As glucose is the only substance that can be utilized by brain cells, this important function of the liver in maintaining adequate levels of blood glucose cannot be overemphasized.

Proteins: Ingested proteins are broken down to amino acids. By the ability of the liver to alter amino acids supplied in the blood, it ensures that optimal quantities, both quantitatively and qualitatively are made available to the tissues. In diseased states, even the normal breakdown products of proteins become poisonous to the individual and may produce coma.

Most plasma proteins except the immunoglobulins and anti-haemophilic factor are also synthesized in the liver.

Fats are absorbed mainly as fatty acids and triglycerides. About 5% by weight of the normal liver mass is lipid. Fatty acids (which may be an important source of fuel for the tissues) are transported bound to a fraction of plasma protein usually manufactured by the liver. Unbound fatty acids are toxic to the liver. The liver is also the only site of synthesis of arachidonic acid, an essential fatty acid, and precursor of prostaglandins. Fatty livers are found in chronic alcoholism, malnutrition and as a result of toxicity from various drugs or poisons.

Vitamins: The liver takes part in converting some vitamins into their active state. To many lay people, the liver constitutes an item of delicacy in the diet. The therapeutic value of liver taken by mouth has been known for centuries. Yper's papyrus (1600 B.C.) contains a reference regarding the therapeutic value of the vitamin A content of the liver. "Treat night blindness with the roasted liver of a black cock. If no response, the case is not genuine night blindness". Minot observed that feeding large quantities of liver to patients with pernicious anaemia, a previously fatal disease, induced a remission in them.^{51a} This discovery won Minot a Nobel prize in Medicine. The substance in the liver, Castle's Extrinsic factor is now known to be Vitamin B₁₂. It is also now well established that Vitamin D is converted into its active form by the liver.

The liver in addition has many complex functions, one of which is the production of bile. Although about 1 litre of bile is produced almost continuously every day, release of bile into the duodenum only occurs during digestion. Bile contains bilirubin, bile salts cholesterol as well as other substances. Bilirubin is produced

mainly by the breakdown of the old red cells. This is insoluble but during its passage through the liver, it becomes water soluble and can thus be excreted. Water-insoluble bilirubin is toxic and at high levels in infants may produce severe brain damage.

Bile salts are totally synthesized in the liver from cholesterol. They play a very essential part in fat absorption. Liver disease may thus be accompanied by malabsorption of fat and other fat-soluble vitamins like Vitamin K which would result in tendency to excessive bleeding, Vitamin D (loss of bone mineral) and Vitamin A (nightblindness). If the flow of bile is obstructed, bile salts absorb to skin and may cause itching.

The liver also renders innocuous certain substances which normally are absorbed from the gastrointestinal tract such as ammonium and amines. Ammonium is produced during the breakdown of aminoacids and other nitrogenous substances in muscle, brain, kidney and the colon. Ammonium is toxic and rapidly converted into urea by the liver. No other organ is able to do this. Ammonium intoxication seen in liver failure leads from progressive brain damage to coma. Poisonous substances other than ammonia or amines may arise from bacterial action on proteins and amino acids in the colon. An example of how even the normal breakdown products of protein become poisonous to the individual is illustrated by the following case history.

Not too long ago, I was asked to see a very respectable member of the community because while he was in hospital for a minor complaint, he exhibited marked aberrant behaviour including the strong urge of pinching the nurses behind, poor memory and concentration and inappropriately micturating in public. He was a known chronic alcoholic but in hospital, he had been put on a high protein diet. He was obviously sick from his liver and his sickness was due to poisoning of his brain by normal substances absorbed from his gastro-intestinal tract which were not made innocuous by the liver.

The liver also plays a key role in drug metabolism since:

- (a) It may be the major site for storage, detoxification and excretion of drugs. These factors would thus regulate the circulating levels of drugs taken by mouth.

- (b) Liver disease may interfere with the metabolism of a drug and so cause undesired pharmacological effects, e.g., small doses of morphia or barbiturates may be harmful to a patient with advanced liver disease.
- (c) Some drugs which are used clinically occasionally cause liver damage either from a direct toxic effect or from a hypersensitivity reaction.
- (d) The use of a large number of otherwise valuable drugs must be restricted or prohibited because of their toxic effect on the liver.

Two other endogenously produced compounds—hormones like the thyroid, ovarian, testicular, adrenocortical are partially or completely altered, destroyed or excreted by the liver. Other hormones like insulin, gastrin and other vasoactive compounds also depend on an intact liver for metabolism, inactivation or excretion. The big group of physiologically active compound referred to as "kinins" have their precursors synthesized by the liver.

Other functions the liver performs include the probable synthesis of nucleic acids—the building blocks for proteins.

That brain function requires other substances manufactured by the liver is shown by experiments in which perfused cat brain functions better if the liver is in the circuit than if it is excluded. This factor or factors remain to be identified.

During foetal life, the liver is one of the most active sites of red blood formation. The liver is able to revive this activity in adult life when disease states make this necessary.

It is evident from the list of some of the functions I have outlined that the liver is essential for life. Thus sufficient disease or destruction of the liver is rapidly followed by death; but given a remnant, time and if life is kept going in the interim, regeneration of the liver occurs substantiating the myths of Tytyos and Prometheus.

Because of its strategic position, the liver is liable to suffer from a variety of insults. These include:

- (a) Trauma (Physical injury)
- (b) Infection
- (c) Nutritional

- (d) Toxic (Poison)
- (e) Immunological (Allergy)
- (f) Cancerous agents.

The reaction of the liver may take an acute, chronic or cancerous process. Examples of an acute reaction may be seen following acute infections like those of Infectious Hepatitis (wrongly referred to as Yellow Fever by the lay public) and true Yellow fever. In these conditions, there is an acute illness in which the patient feels very lethargic, loses his appetite, and becomes jaundiced. Anorexia and vomiting may be troublesome in the initial phases.

Chronic liver disease, an example of which is called cirrhosis is usually characterized by chronic ill health, loss of weight and accumulation of fluid in the legs and abdomen. An unfamiliar example is the executive who is a known hard drinker over many years who following an alcoholic binge at a party, returns home, vomits blood and dies soon afterwards. His obituary usually has the phrase "The wicked have done their worst" indicating that foul play at the recent party caused his death. It is probably not realized that death may have been due to complication of cirrhosis from his slowly poisoning his liver with alcohol.

Cancers in the liver may arise from the liver cells themselves (primary liver cancer) or come to the liver from other cancerous sites (secondary liver cancer). The latter are more common in many other countries while primary liver cancer is extremely common in Nigeria.

Liver disease in general is more frequent in the developing than the developed countries. Even in the developed countries, liver disease is commoner in the poorer socio-economic classes than in the upper classes. In the developing countries, this is no doubt related to the increased chances of exposure to infectious agents from poor environmental hygiene, prevalence of malnutrition in varying degrees in the population, the use of possible hepatotoxins in herbal infusions used as medicaments or which may be contaminants of food, freer use of cheaply-brewed alcohol such as ogogoro, alias 404, alias 'push me I push you'

as a solace, suppression of immunity in susceptible individuals by endemic parasites like malaria,^{37,78} delay in recognition and treatment during early stages of liver injury due to the absence of trained personnel.

Liver disease may be suspected in a patient who gives a history of previous jaundice, chronic alcoholism, dietary imbalance or exposure to known hepatotoxins or when diseases commonly accompanied by liver injury are present. Because of the lack of accurate data, it has been impossible to obtain any true appreciation of the magnitude of the problem of liver diseases in the country. In childhood, prolonged malnutrition as occurs in Kwashiokor produces a liver which is fatty. Although the bulk of evidence so far indicates that the fatty liver of Kwashiokor does not progress to cirrhosis, it is probably more susceptible to injury than the normal liver.

Some realization of the magnitude of the problem of liver disease in the life of a nation can be obtained from hospital records either as a primary or secondary cause of death, morbidity records in terms of hospital attendance with consequent loss of working time, disability claims, industrial or occupational absenteeism, non-effectiveness of certain important groups, for example, military personnel in times of war or on the amount of money and research devoted to it in the country. It is well known that communicable diseases, even those of considerable public health importance are consistently underreported in most developing countries. The lack of clinical expertise, finer diagnostic tools and autopsy confirmation make information of the more chronic or malignant forms of liver disease virtually non-existent.

I shall now consider in greater details some examples of liver diseases which illustrate acute, chronic and cancerous reactions of the liver.

Epidemics of jaundice have been recognized from the earliest times, the first reference of a major epidemic being ascribed to Hippocrates. The majority of reports of epidemic or sporadic jaundice is due to viral hepatitis. By definition, viral hepatitis, Iba aponju (Yoruba), akum (Ibo), Yellow fever (pidgin English) is acute inflammation of the liver by one or other of two types of

viruses. These two clinical forms are referred to as Infectious hepatitis and Serum hepatitis. The incidence of Infectious Hepatitis varies in different parts of the world, being endemic in many tropical and subtropical countries. It may be epidemic, this form being usually associated with disasters and overcrowding of populations as happens in wars including the Nigerian Civil War and the period immediately after it ceased.^{26,52} Sporadic cases of Infectious Hepatitis may also arise in a community spontaneously. In infectious hepatitis, contamination of food or water by the virus or intimate personal contact appear to be the primary sources of infection. Serum hepatitis has features which clinically resemble infectious hepatitis. Outbreaks of epidemics now recognized as due to serum hepatitis occurred in Bremen in 1885, during vaccination of workers⁵⁰ and following immunizations against yellow fever.^{25,43} Serum hepatitis is acquired by inoculating the virus into a susceptible subject through transfusion of blood and its products, vaccination, tattooing or unsterile injections.

The average duration of ill health of most people with a moderately severe attack of viral hepatitis is about 3–6 months and a small percentage of patients would die from the acute disease. Heavy manual workers and pregnant women, especially those in late pregnancy appear to be more susceptible to this fatal complication.^{53,55} As viral hepatitis is primarily a disease of children and young adults, the total economic loss caused from the prolonged nature of the illness and death are enormous.

It is well recognized that a great majority, probably up to 90% of people who are exposed to viral hepatitis have only minor symptoms unaccompanied by jaundice. This group are not only of epidemiological importance as possible carriers of the virus but also because clinico-pathological studies have shown the presence of severe chronic liver disease in a large proportion of these apparently healthy persons.^{19,21}

Due to inaccurate reporting, the incidence of infectious hepatitis in the country is unknown. Despite this, statistics from the Lagos State Medical Officer of Health's report (1971) shows that Infectious Hepatitis ranked eighth as the cause of death in persons over one year in 1971. When this group is added on to

the miscellaneous group who died from Hepatic failure, liver diseases rank as the sixth cause of death. This is a fact that many in this audience may not have thought possible.³

The number of cases of infectious hepatitis that occurred after the end of the Nigerian Civil War was reported as 31,103 from June 1970 to May 1971.⁵² This figure is probably an underestimate. It is well known that many Nigerians, especially those in rural areas, just seek herbal cures for jaundice and do not reach hospital at all. Looking at the figure of deaths, the table shows seventeen in August 1970. When I visited three hospitals in Aba and Onitsha over five days in August 1970, the total number of deaths from these alone was twelve.

Despite the tremendous amount of active research going on in the field of viral hepatitis, many problems have so far defied solution. Attempts at isolating the causative agent have ended like the fiasco of the South Sea Bubble—excitement, promise and then complete disappointment. Also no experimental animals except Marmosets and a few sub-human primates can be infected with the virus.²³ The search for a suitable vaccine which would enjoy universal utilization has therefore not been obtained. Recent studies have led us to hope that the development of a vaccine may not be too far away. Other unsolved problems in hepatitis research include factors that determine the duration of the carrier state, conditions under which chronic liver injury arises even in the apparently fit population who do not develop jaundice. The very high mortality for patients who develop the very severe form of hepatitis has called for drastic methods of treatment including pig-liver perfusion, chimpanzee liver perfusion and liver transplantation.

Attempts at developing specific diagnostic tests had been elusive until 1965 when Blumberg discovered a substance in the blood of an Australian aborigine out of several thousands tested which reacted immunologically with blood from a patient who had had numerous blood transfusions for a chronic blood disease.¹² All the evidence so far shows that this substance, Australia antigen is a marker for serum hepatitis.^{61,35,56} Australia antigen has been shown to be present in the blood of a very small percentage of patients with various diseases like leprosy

—12% in Nigerians²⁷ which normally do not have any primary liver involvement. Of greater importance is the finding that some apparently healthy people have this antigen in their blood, i.e., are carriers of Australia antigen. Several reports have shown that the prevalence of Australia antigen in the normal population is low in some countries like the United States of America and Scandinavia where it is about 0.1% but high in several tropical and subtropical countries where 4%–20% may be carriers.^{13,59} Our preliminary investigations showed that about 6% of apparently healthy adult Nigerians from Ibadan^{65,28,73} are carriers of this antigen. Using the same techniques, 20,471 apparently healthy Nigerians have had their blood examined for Australia antigen, between February 1971 and December 1972. Of these, 1,280 were positive, giving a prevalence rate of 6.26% (Table 1).²⁹ This is over sixty times the carrier rate in the United States of America. These carriers are present in each age group but are more in the 2nd and 3rd decades. When a random sample of 1,841 consecutive individuals seen over two months were analysed for age specific prevalence, the rate appears to be similar for each half decade (Table 2). In a sample of 423 school children aged 4 to 20, we found a prevalence rate of 6.7% for Australia antigen.³⁰ In another sample of 500 apparently well children aged from birth to 4 years, the overall prevalence rate was 2%.²⁹ This low figure was obtained because of the large numbers of children aged up to 2 years who did not have Australia antigen in their blood. Among 63 healthy Nigerian doctors, 4 (6.4%) were carriers of the antibody whereas only 2 of 128 healthy expatriates

TABLE 1

Age distribution of 1,280 Australia (Au (1) Hepatitis-B) Antigen Positive Donors (February 1971–December, 1972

<i>Age in Years</i>	15–20	21–25	26–30	31–35	36–40	41–45	46–50	51–55
Number of Au(1) Positive Donors	232	432	292	128	90	34	40	7
Total Number of Donors								20,471
Total Number of Au(1) Positive Donors								1,280
Prevalence Rate of Au(1)								6.26%

TABLE 2

Age specific prevalence of Australia Au(1) antigen in a 2-month sample of 1,841 consecutive blood donors

Age in Years	15-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	Total
Total Number of Donors	179	510	470	223	199	75	68	14	3	1,841
Total Number of Au(1) Positive Donors	9	31	28	9	6	3	2	1	0	89
Age specific Prevalence	5%	6%	6%	4%	4%	3%	4%	3%	7%	5.1%

(1.6%) had Australia antigen in their blood.⁶⁶ These 2 expatriates were doctors and there is known increased risk of exposure to Australia antigen by doctors and medical laboratory personnel^{38,16}

As I stated earlier, there is very close association between the antigen and serum hepatitis. The significance however of the presence of this antigen in apparently healthy people with latent liver disease has not been very clear. Using other sensitive blood tests, the percentage of such individuals who show evidence of liver disease varies from 0%–100%^{69,41,58,46}.

From a 10% random sample of Australia antigen positive adult Nigerians, our studies show that nearly 70% of them have abnormalities in blood tests indicating liver disease and 100% of the carriers had livers which were very abnormal when examined under the microscope.⁶⁷ Williams and his associates in Ibadan have also found similar changes when the livers of children aged under 5 years who were carriers of Australia antigen were examined under the microscope.⁷⁴ The lives of these "normal" individuals would in many cases depend on how long their livers held out.

The difference in prevalence rates between the temperate countries with low values and tropical and sub-tropical countries with high values was initially thought to be genetically determined.¹⁴ However, other means of transmission by scarification especially inunction of traditional medicines or tribal marks, the indiscriminate and illegal use of injections with improperly sterilized needles by quacks in an injection-happy community like ours and vectors like insects may be more important.

Our pioneer work in Ibadan in 1971 demonstrated that under experimental conditions, *Culex* mosquitoes could act as biological vectors of Australia antigen.⁶⁸ The significance of this can be further assessed when it is realized that out of every 5 adult mosquitoes that are caught in any room overnight in Ibadan, 3 belong to the *Culex* species. Other workers have also confirmed our finding of mosquito transmission.^{77,60} We have further extended our original study to the field and have found Australia antigen in *Culex* and other species of mosquitoes.³⁴

Possible preventive measures will include wide scale screening of all "normal" persons in this environment to detect carriers. Such carriers are automatically excluded from being blood donors since transfusion of such blood may be followed by hepatitis in 65% or more of recipients.^{57, 36, 42} These persons should be advised as regards their personal hygiene so that they do not transmit the agent to others. After adequate tests of liver function, a small fraction of these carriers with established chronic active hepatitis may benefit from treatment with cortico-steroids which slow progression of the disease process. Health education regarding the dangers of indiscriminate injections, scarification practices with unsterilized equipment and eradication of possible insect vectors are long term projects which by protecting the liver of the individual from disease lengthens his life.

Yellow fever is an acute infectious disease caused by the yellow fever virus which is transmitted by *Aedes aegypti* mosquitoes. Epidemics of yellow fever were responsible for several deaths of American soldiers in the 1890s during the military campaign in Cuba and also several workers during the construction of the Panama Canal. It is said that there were not enough trees in Panama to make crosses for all those who died of Yellow fever at that time.

The discovery of the potential mineral wealth of West Africa in the opening years of the 20th century and the reported series of epidemics on the West African Coast in 1910 and 1911 resulted in the setting up in London of the Yellow Fever Commission. In 1925, the Rockefeller Foundation's Yellow Fever Commission sent out a team to West Africa whose headquarters was in Yaba. This team investigated the epidemic of 1926-27 in Ghana and as a result of their work reached epoch making strides in advancing

the study of yellow fever. They discovered that Africans as well as non-natives were susceptible to the disease. The previously held views were that the natives were immune to this disease. They confirmed the views of earlier workers like Walter Reed that the disease was caused by a virus and that transmission was by *Aedes aegypti* mosquitoes. Perhaps, their most important discovery was when they demonstrated that an experimental animal—the rhesus monkey—was susceptible to the infection. This led the way for isolation of the virus. Mr Asibi, then aged 27, a Ghanaian labourer from a town in the Volta Region has his name entered in the annals of history (even if his statue is not at Madam Tussauds) since it was from his blood that the virus was first isolated. A mutant non-virulent strain of the “Asibi” virus, now known as 17D provides an effective and safe vaccine.

It is well recognized that most infections with yellow fever virus do not result in jaundice. It had been stated that prompt and complete recovery of the liver occurs in patients who survive an attack of yellow fever.⁷¹ The same results had also been found in experimentally infected monkeys killed from 16 to 72 days after the subsidence of the fever.⁴⁷ We studied this aspect during the 1970 Jos epidemic and found that changes of persisting liver cell damage are a feature even after 2 months of the onset of human infection. Thus microscopic studies of liver showing non-specific inflammatory changes in an endemic area of yellow fever could be due to this disease unless excluded by specific blood tests.³¹

The history of man's fight to conquer yellow fever is dotted with the names of many martyrs in medicine like Assistant Surgeon Lazeer, Noguchi, Stokes and Young. Their lives and their livers, all given up in search of the defeat of “yellow jack” further demonstrate the inter-relationship between life and the liver.

Yellow fever presents a continuing threat to the public health of Nigeria and indeed West Africa. The most recent outbreaks of Yellow fever in Nigeria have been mainly in the Jos Plateau area (1969),¹⁸ and Okwoga District of the Benue Plateau State 1970.^{51b} Had our major airports and harbours been declared yellow fever infected areas in the 1969 epidemic, the country's war efforts may have been very much affected. Because of other priorities and the shortage of vaccine, no programme of routine immunization has

been established in the country. Epidemiological surveillance must be our watchword in preventing further outbreaks of yellow fever.

The peculiar condition in which the liver became fibrous, nodular and of yellow colour had been recognized by many physicians from early days. This condition called cirrhosis is a chronic disease in which scar tissue which interferes with the blood supply is the predominant change. There is abundant evidence in the literature which shows that this condition is very common in Africans. Our studies in Ibadan show that the known causative factors are previous hepatitis (24%) and alcohol (7%).³² In 69% of our cases, the cause is unknown. In Lagos, alcoholism accounted for (20%), viral hepatitis (15%) and unknown factors 61%.²⁴

Alcohol has a number of remarkable characteristics including excellent solvent properties for many organic compounds as well as producing some of the most vexing human problems. Although the reasons for high consumption of alcohol have more to do with its effect on the brain, it is well known that chronic or excessive ingestion of alcohol is associated with derangement of liver function and development of liver disease. The social and economic seeds which breed alcoholism in any country are not too far away.

Considerable emphasis has been laid on malnutrition as a major factor in the development of liver disease in an alcoholic subject. It is well known that in many chronic alcoholics, there is an inverse relation between their alcohol consumption and the intake of food. In considering alcoholic liver disease, not only are impairment of nutrition or malutilization of proteins important but also the direct toxic effect on the liver.

Epidemiological studies showing the prevalence of cirrhosis in Nigeria are scanty. Femi-Pearse⁴ using a single sensitive blood test found that 30(15%) of 204 apparently normal male Nigerian soldiers, medical students, labourers and old people had evidence of chronic liver disease which could have been cirrhosis. There is therefore an urgent need in this environment to undertake studies of factors other than alcohol which may be related to cirrhosis. Some such factors which readily come to mind include nutritional deficiencies, hepatotoxic agents used as food or medicine, infections like malaria, schistosomiasis, chronic bowel infection

and genetically determined abnormalities like sickle cell disease, etc. Apart from the state of chronic ill health that cirrhosis causes, the risk of underlying cancerous growth in the liver is very high.

The incidence of primary liver cancer is known to vary in different parts of the world being uncommon in the United States (white and non-whites), Scandinavian countries, Europe and South America.³⁹ Primary liver cell cancer is common in Africa.^{10,40,63,54,33}

The overall incidence rates of primary liver cell cancer in males throughout the world is as shown in Table 3. In Ibadan, primary liver cell cancer is the fourth commonest tumour accounting for 7.2 per cent of all malignancies (Table 4). It is the commonest cancer in the male (Table 5) and eleventh in rank in females (Table 6). In males, it has its peak incidence between the ages of 20–45 years (Table 7). All classes of people including high ranking administrators, civil servants, athletes, professionals, may be victims of this dreadful condition. In fact, many important Nigerian persons (whom I cannot name) have died from this dreadful disease. The life expectancy is in most cases short and the tumour does not usually respond to conventional forms of treatment. Over 60 per cent of these cancers have an underlying cirrhosis.

TABLE 3
*Overall Incidence Rates of Primary Liver Cancer in Males
throughout the World*

<i>Area</i>	<i>Rate per 100,000</i>
Lourenco Marques (Mozambique)	98.2
Johannesburg (South Africa)	14.2
Hawaii (Japanese Population)	7.2
Ibadan (Nigeria)	5.9
Singapore (Chinese Population)	5.5
Kampala (Uganda)	5.5
Hawaii (all races)	5.3
England	3.0
United States of America	1.8
Canada	0.8

From Doll: Payne and Waterham 1966.

TABLE 4

*Principal Neoplasms in order of relative frequency, Ibadan Residents
both Sexes*

<i>Type and side of Tumour</i>	<i>Percentage of all Tumours</i>
Ca cervix uteri	9.10
Burkitt Tumour	8.79
Ca breast	8.48
Primary Tumour Liver and G.B.	7.87
Ca stomach	6.32
Leukaemia	6.02
Adult Lymphosarcoma	4.93
Ca Prostate	2.77
Reticulum cell Sarcoma	2.62
Ca Thyroid	2.46
Ca bladder	2.31
Hodgkins Disease	2.31

Key Ca = Cancer

TABLE 5

Principal Neoplasms in order of relative frequency, Ibadan Males

<i>Type and site of Tumour</i>	<i>Percentage of all male Tumours</i>
Primary Ca Liver + Gall Bladder (Hepatoma alone = 12.57)	13.2
Burkitt Tumour	11.32
Ca Stomach	8.49
Leukaemia	7.55
Ca Prostate	5.66
Adult Lymphosarcoma	5.66
Hodgkins Disease	4.08
Ca Bladder	3.14

Key Ca = Cancer

TABLE 6

Principal Neoplasms in order of frequency, Ibadan females

<i>Type and site of Tumour</i>	<i>Percentage of all Female Tumours</i>
Ca Cervix uteri	17.87
Ca breast	16.66
Ovarian Tumour	9.39
Burkitt	6.36
Leukaemia	4.54
Adult Lymphosarcoma	4.24
Ca Stomach	4.24
Chorion Epithelioma	3.93
Reticulum cell Sarcoma	3.63
Ca Thyroid	2.72
Primary Ca Liver	2.72

Key Ca = Cancer

TABLE 7

Age/sex distribution of 144 patients with Hepatocellular Carcinoma, UCH Autopsies 1958-1968

<i>Age in Years</i>	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	<i>Total</i>
Male	3	-	3	3	5	14	13	21	19	8	11	8	6	3	117
Female	-	1	-	-	2	8	1	4	3	5	3	-	-	-	27
Total	3	1	3	3	7	22	14	25	22	13	14	8	6	3	144

Environmental factors have been shown to play a major part in the development of liver cancer. Poisonous substances which may induce cancer, i.e., carcinogens may be present in the diet or medications. These include the aflatoxins manufactured by a fungus (mould)—*Aspergillus flavus*; cycasin from cycad nuts, contamination of rice especially in Japan by fungi of some species of

penicillin, and pyrrolizidine alkaloids present in many senecio plants, e.g. *Senecio abyssinicus* (Sch. Bip. (compositae) ("Amunimuye" in the Yoruba language).

The Christmas of 1960 in the United Kingdom was memorable because outbreaks of disease in turkey poult, ducklings, pigs and calves caused a shortage of table birds and meat. The common factor linking these was the presence of contaminated Brazilian groundnut meal in the food.^{11, 4, 48, 49} Further work identified the group of toxic substances as aflatoxins produced by a commonly occurring mould. Contamination of other commonly occurring cereals and food like maize, beans, wheat, etc., have been demonstrated. The aflatoxins are the most potent liver carcinogens known. I must pay tribute to Professor Bassir and his colleagues in the Department of Biochemistry for their pioneer work in this area in Nigeria.^{5, 6, 7, 8, 9} There is strong circumstantial evidence to suggest that they may be one of the liver cancer inducing factors in Swaziland and Uganda.^{45, 2}

The various forms of liver diseases which could be caused by alkaloids of the *Senecio* group have been well recognized for at least 50 years.^{76, 64, 15} Williams and Schoental⁷⁵ demonstrated that when the dried ground stem of *S. abyssinicus* (*Amunimuye*) was added to make up 5% of the diet of laboratory rats for 9 months liver cancer developed in these rats later without their showing any obvious signs of toxicity. Thus some of the substances which go to the making of herbal remedies like "agbo" and "agunmu" may by their cumulative effect possibly cause serious liver disease in man. The relationship of liver cancer to viral hepatitis is still unresolved although it is known that Australia antigen may be associated with liver cancer.

In 1965, Tatarinov⁷⁰ demonstrated the presence of a foetal protein in the blood of some patients with primary cancer of the liver. The positivity rate varies from less than 50 per cent of liver cancers in Europe and America to between 70–80 per cent in some parts of Africa including Nigeria. This test makes the diagnosis of primary liver cancer much easier and can be used for screening susceptible populations as early diagnosis is the keynote to treatment of all cancers.

Because of the very high incidence of liver cancer in our adult males, the poor results from treatment with inevitable loss of manpower, the role of environmental factors in its development, preventive measures are the only reasonable methods for attacking this condition. Mass screening for breakdown products of aflatoxins, alpha foeto-protein are necessary but expensive. General health education of the community, emphasizing the possible damage toxins in food and herbs could do to the liver is the task of every educated man.

From the examples given earlier, it is clear that in Nigeria, life very much depends on the liver. There is however a great shortage in manpower of all types. There is also much ignorance regarding the importance of liver disease in the community. Financial support for research and training in liver diseases from the University or other Agencies is virtually nil and priorities in medicine now appear to be in the direction of population control or the other popular (to the layman) and favoured specialities in medicine. The size of the problem of liver disease in Nigeria is enormous. The need for further study and control of these conditions are urgent and compelling. Clinical training programmes both at the undergraduate and postgraduate level and research cost money. An urgent plea to funding Agencies, Government or voluntary, is that they make substantial funds available for training and research in liver diseases.

The future as regards the control of established liver disease is very exciting. With newer investigative techniques, using blood, immunological, radiographic, microscopic (light and electron microscopic) ultrasonics, the type and extent of liver disease can be accurately assessed. Our better knowledge of the derangements in some previously rapidly fatal diseases has resulted in improved methods of treatment with resultant increased life expectancy in some of these cases. In cases of fulminant hepatic failure, the combined use of steroids and exchange blood transfusion probably with blood containing Australia antibody may improve survival. Temporary liver support may also be obtained by extracorporeal liver perfusion. The commonest procedure in use is the connection of the patient to an isolated but functioning animal liver like that of a pig or baboon.

Cross-circulation between an individual with severe liver disease and a subject with normal liver has been undertaken with success. Such individuals with normal livers may be volunteers or patients dying of an irreversible brain lesion or cancer elsewhere which has not affected the liver. The problems of choosing a donor as well as ethical implications have not made this method of treatment as popular as it could be.

Liver transplantation is the one area in which given the technological know how, a lot of our young patients with hepatoma may benefit from this radical form of treatment. This involves the complete removal of the diseased liver and its replacement by a donor liver. There are reports of several successful transplants with the longest recorded survivor enjoying over 3 years of a happy, useful and active life. Unsung and lacking the spectacular headlines of cardiac transplantation, old livers are being replaced by new ones.

Professor Marc Sankale, Dean of the Medical School in Dakar remarked "Hasn't it been said that if in Europe, one has "the age of one's arteries, in Africa one has "the age of one's liver".⁶²

I will spend the dying minutes of this lecture in considering several claims of importance made by other organs in the body. The heart is a pump and is also commonly thought of as the seat of emotion: hypertension is the physician's biggest headache in this environment. The kidneys excrete waste products from the body and although there are still a number of unresolved problems regarding renal disease, their main function as excretory organs can be taken over by machines. The lungs are just bellows and when pulmonary tuberculosis is eradicated in the country, there will be little left of lung diseases. All of these organs can be removed and their functions taken over by machines. As of now, there is no known mechanical device that would successfully take over all liver functions. Although the current definition of death is not cessation of respiration or heart beat but brain activity, everyday examples of "brainless" persons in the country would tend to support the view that the brain is not essential for life.

Mr Vice-Chancellor, ladies and gentlemen, we sometimes ask ourselves the question "Is life worth living"? I am confident that following this lecture, you will not hesitate in the answering "Yes, it depends on the liver"

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