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DEDICATION
This lecture is dedicated to the following that have made immense impact in my life as an individual from birth.

- The Almighty God
- My mother – Christiana Rosetta
- My wife – Akwaugo Nkechi
- My daughter – Ezinne Uchechi
- The one billion people worldwide living with the burden of high blood pressure

PREAMBLE

Mr. Vice Chancellor, I most sincerely thank you and the entire University administration for the opportunity to give this 73rd Inaugural Lecture of our great Institution. I also thank the current and the immediate past administrations for the re-awakening of academic and research activities in our University. This is reflected in the increasing number of professorial chairs in the entire University. Records show that this Inaugural lecture series became more regular from 2007. Professor Chinedu Nebo and Professor Batho Okolo are highly commended for this.

Going through records, it does appear that this lecture is the first inaugural lecture from my Department of Medicine. I give God the glory and wish my department, easily the most organized in the University, best of academic progress. I do sincerely hope this lecture would open up the flood gate for more lectures from the department, the College of Medicine, and the entire University academic community.
My previous intention had been to give this lecture in 2011 to mark my 35th year of graduating from this Citadel of Learning but this was cancelled by the University for official but unforeseen circumstances. A re-schedule for June 2012 also did not come to be for some other reasons.

I thank God for this historic event taking place today, and for putting me at the centre of it. It is obviously divine plan to place me as the 73rd Inaugural Lecturer as the figures ‘7’ and ‘3’ are biblically and culturally significant. This year also marks my 37th year of graduation!

An inaugural lecture is expected to be on a subject that the lecturer has, indeed, spent a significant part of his academic life participating actively in research and made a reasonable number of publications and general contributions. In my own case, this topic incidentally is not only of public interest but is, in fact, a condition that is expected to be ‘silently’ affecting approximately a third of the entire audience here today. Over half of those aged 60 years and above are ordinarily afflicted. This is, indeed, a subject I have been rather passionate about and have spent a significant part of my life in its management, control, prevention and rendering administrative service to concerned Organizations. The good news about this ‘silent killer’ is that if detected early and effectively controlled, morbidity (indisposition) and death could be prevented. In other words, it is reversible and its consequences avertable only if detected early before permanent pathophysiological processes take place.

INTRODUCTION

Blood Pressure

Blood pressure is the force that needs to be maintained to enable blood circulate to all parts of the human body. Blood is the medium by which nutrients and oxygen are sent to all parts of the body. The pressure is generated mostly by the pump action of the heart, a vital organ about the size of the clenched fist of a person. Since the blood flow needs to be maintained without any interruptions, the force is maintained during the relaxation phase of the heart by the elastic recoil of the major arteries thereby providing a continuous flow and supply of vital nutrients to all tissues of the body.

Blood pressure is recorded in two parts: systolic (the upper figure)– during the contractile phase of the heart, and diastolic (the lower figure)– during the relaxation stage. Blood pressure is said to be high when it exceeds an accepted normal level. High blood pressure is also termed hypertension, a less descriptive term that appears to be more popularly used. Both terms would be used inter-changeably in this text even though the later gives an impression of a terrible disease entity that sometimes frightens the sufferer. Normal blood pressure at rest is within the range of 100-140mmHg systolic (top reading) and 60-90mmHg diastolic (bottom reading). High blood pressure is said to be present if it is persistently at or above 140/90 mmHg.

High blood pressure is diagnosed on the basis of persistently raised blood pressure levels. This usually requires three separate measurements at one-monthly intervals using the instrument
called sphygmomanometer. Initial assessment of a hypertensive individual should include a complete history and physical examination. With the availability of 24-hour ambulatory blood pressure monitors and home blood pressure self-recording machines, the importance of not wrongly diagnosing those who have what is termed ‘white coat’ hypertension has led to a change in protocols. ‘White coat’ hypertension arises when fright and apprehension or both affect the blood pressure reading during a visit to a healthcare facility where the personnel traditionally wear white garments.

When an individual’s blood pressure is persistently high, it not only puts a strain on the heart but also damages the walls of the arteries, making them stiffer and more prone to clogging and haemorrhage (bleeding). This causes problems in the organs they supply and leads to potentially fatal conditions and incapacitating disorders, such as coronary heart disease and stroke.

Normal levels evolve from scientific evidence. Internationally, the World Health Organization (WHO) and the International Society of Hypertension (ISH) determine this level. These International bodies regulate the diagnosis and control of hypertension and other disease conditions globally. Regional and national organizations are usually given the responsibility of determining appropriate cut off points and guidelines bearing in mind the regional and national peculiarities and characteristics of the concerned population. It is now agreed that both systolic and diastolic pressures should be addressed in any determined cut-off point. Some of these regional organizations are: The American Society of Hypertension (ASH), the European Society of Hypertension (ESH), the International Forum for control and prevention of Hypertension in Africa (IFHA) and others. The national organizations include the Nigerian Hypertension Society (NHS), the South African Hypertension Society (SAHS), among others.

Blood pressure is classified by the WHO/ISH and the various regional and national organizations then adapt to suit their peculiarities based on available scientific evidence. The simplest and one of the latest is that of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) in its 7th Report (JNC7) reproduced below:

<table>
<thead>
<tr>
<th>Classification (JNC7)</th>
<th>Systolic pressure (mmHg)</th>
<th>Diastolic pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>90–119</td>
<td>60–79</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>80–89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>≥100</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>≥140</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>
The various hypertension organizations periodically produce evidence-based ‘guidelines’ for the management of hypertension to guide health-care personnel. These guidelines are not necessarily strict rules but provide evidence-provided recommendations to guide healthcare providers.

High blood pressure is a main factor responsible for premature death in the world and, therefore constitutes the major global burden of disease. It is a key risk factor for stroke, myocardial infarction (heart attacks), heart failure, aneurysms of the arteries (e.g. aortic aneurysm), and peripheral arterial disease. It is a significant cause of chronic kidney disease. Life expectancy of an individual could be considerably lowered even by moderate elevation of (arterial) blood pressure. It has become a major global health concern.

**The Silent Killer**

Uncomplicated high blood pressure is largely without symptoms. Most symptoms are usually those associated with the complications when they occur. This situation has given rise to the name ‘Silent-Killer’ frequently given to High Blood Pressure and making it a key priority for prevention, detection and control, and one of the most important challenges facing public health today globally. Sufferers who are ‘lucky’ to have symptoms could have headache, dizziness, tinnitus (ringing sensation in the ears), blurring of vision, palpitations, or symptoms of the specific complications. These individuals are deemed ‘lucky’ in the sense that they would have compelling need to see health care personnel that would check their blood pressures and possibly detect a significant rise for early intervention, unlike their asymptomatic counterparts.

**HISTORICAL PERSPECTIVES**

Hypertension was recognized by the early Chinese in the period 2600BC who palpated (felt) the peripheral pulses to determine the ‘pressure’ in the vessels and treated hard-to-palpate vessels by bleeding and leeches. High blood pressure was then called "hard pulse disease".

William Harvey (1578–1657), an English Physician is given the first position in the modern history of hypertension even though Dr Amatus had earlier given an insight into blood circulation. Harvey in his book, "De motu cordis" described completely and in detail the systemic circulation and properties of blood being pumped to the body by the heart. This was not an easy task as expressed by Harvey himself thus: "...I found the task so truly arduous... that I was almost tempted to think... that the movement of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place by reason of the rapidity of the movement...".
In 1733, Stephen Hales (1677 – 1761), an English clergyman and philanthropist first published measurement of blood pressure. He also made significant contributions to a range of scientific fields including botany, pneumatic chemistry and physiology and invented several devices, including a ventilator, a pneumatic trough and a surgical forceps for the removal of bladder stones\textsuperscript{7,8,10}.

Descriptions of hypertension as a disease came, among others, from Thomas Young in 1808 and Richard Bright in 1836\textsuperscript{7}.

Frederick Akbar Mahomed (1849–1884), an internationally known British Physician from Brighton, England was the first to report in 1874 a case of elevated blood pressure without evidence of renal disease\textsuperscript{11}.

A major revolution occurred in 1896 with the invention of sphygmomanometer by Scipione Riva-Rocci, an Italian Internist and Paediatrician. This enabled blood pressures to be measured and monitored in the clinics and wards\textsuperscript{12}.

In 1905, Nikolai Korotkoff improved the technique by describing the Korotkoff sounds that are heard when the artery is auscultated with a stethoscope while the sphygmomanometer cuff is deflated\textsuperscript{8}.

In 1925, Otto Frank, a German-born doctor and physiologist described the concept of essential hypertension ('hypertonie essential'). This is a common type of hypertension with no discernible cause\textsuperscript{13}.

In 1928, the term malignant hypertension was coined by physicians from the Mayo Clinic to describe a syndrome of very high blood pressure, severe retinopathy and adequate kidney function which usually resulted in death within a year from strokes, heart failure or kidney failure\textsuperscript{14}.

In 1931, John Hay, Professor of Medicine at Liverpool University who contributed immensely to the knowledge of hypertension, wrote that "there is some truth in the saying that the greatest
danger to a man with a high blood pressure lies in its discovery, because then some fool is certain to try and reduce it"\textsuperscript{15}.

**In 1937, Paul Dudley White**, prominent US Cardiologist reputed for cardiovascular care of many US Presidents, in his book titled “Heart Disease” suggested that "hypertension may be an important compensatory mechanism which should not be tampered with, even were it certain that we could control it"\textsuperscript{16}.

**Franklin Delano Roosevelt**, the 32\textsuperscript{nd} President of the USA was a prominent person in history known to have severe hypertension. On the afternoon of April 12, 1945 Roosevelt said, "I have a terrific pain in the back of my head." He then slumped forward in his chair, unconscious, and was carried into his bedroom. He died at 3.35 pm same day\textsuperscript{17}.

**In 1949, Charles Friedberg** in his classic textbook "Diseases of the Heart"\textsuperscript{18}, stated that "people with 'mild benign' hypertension ... [defined as blood pressures up to levels of 210/100 mm Hg] ... need not be treated"\textsuperscript{19}. This corroborated with White’s earlier view in 1937 that raised blood pressure needed not be treated\textsuperscript{16}.

In the 1950's and after, substantial evidence from landmark actuarial and longitudinal studies like the Framingham studies became available\textsuperscript{20,21}. The effect of cardiovascular risk factors (e.g., smoking, obesity, inactivity, diabetes mellitus, etc) in determining the management and outcome of hypertension became widely known. Risk factor identification then became part of routine assessment of the hypertensive subject. Risk factors also came to be recognized as important issues in determining the blood pressure level to initiate drug therapy and in fact the type of medication to be used. Life style modification also became a recommended management strategy for all hypertensive subjects with identified modifiable cardiovascular risks. The recommended cut-off for hypertension has also been lowered in the past fourteen years from 160/95 mm Hg to 140/90 mm Hg based on research-based evidence\textsuperscript{1}.

**Management of high blood pressure in history**

In ancient times, “hard pulse disease” was treated by blood-letting by the Chinese and use of leeches by the Greek and Indians\textsuperscript{2}. This was advocated by The Yellow Emperor of China, Cornelius Celsus, Galen, and Hipocrates\textsuperscript{2}.

During the 19th and 20th centuries, effective pharmacological treatment modalities for high blood pressure were yet unavailable, three treatment modalities with significant side-effects were used: strict sodium restriction\textsuperscript{3}, sympathectomy (surgical ablation of parts of the sympathetic nervous system), and pyrogen therapy (injection of substances that caused a fever, indirectly reducing blood pressure)\textsuperscript{22} All through the middle part of the 20th century, the treatment of hypertension was often ineffective. Even Roosevelt, reported to have BP levels greater than
250/150 mm Hg, was only treated with phenobarbital, a low-sodium diet, and rest at the time of his signing the Yalta treaty\textsuperscript{17}.

After the second world war, \textbf{hexamethonium, hydralazine} and \textbf{reserpine} (derived from the medicinal plant \textit{Rauwolfia serpentina}) became available.

It was not until 1957 and 1958 that a major advance occurred with the development of the first thiazide diuretic, \textbf{Chlorothiazide} from the antibiotic sulfanilamide\textsuperscript{23,24}. A randomized controlled trial sponsored by the Veterans Administration in subjects with high blood pressure (diastolic BP 90–114 mm Hg) using hydrochlorothiazide, reserpine, and hydralazine versus placebo showed overwhelming benefit in reducing cardiovascular morbidity and mortality in the treated group\textsuperscript{25}. The study continued in people with lower blood pressures and showed that treatment even in people with mild hypertension more than halved the risk of cardiovascular death\textsuperscript{26}.

\textbf{Beta blockers} were developed in the early 1960s through the pioneering work of Scottish Physician and Pharmacologist, \textbf{James W Black} for which he received the 1976 Lasker Award and in 1988 the Nobel Prize in Physiology or Medicine\textsuperscript{22}.

\textbf{Calcium channel blockers} were the next to be discovered when Verapamil, initially thought to be a beta blocker and used for angina treatment was found to lower blood pressure significantly\textsuperscript{16}. This was later found to be effective in Blacks even as monotherapy\textsuperscript{27}.

\textbf{Angiotensin converting enzyme (ACE) inhibitors} the next group were developed through rational drug design with Captopril becoming available in 1977\textsuperscript{28} and other ACEIs later coming up and confirmed efficacious\textsuperscript{22,29}.

More recently \textbf{alpha adrenergic blockers} (AABs), \textbf{angiotensin receptor blockers} (ARBs) and \textbf{renin inhibitors} have also been introduced as antihypertensive agents.\textsuperscript{30-32}

Table 1 shows dates of discovery of antihypertensive drugs or drug classes\textsuperscript{33}.

Table 1: Dates of Discovery of Antihypertensive Drugs or Drug Classes

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Antihypertensive Agent(s)</th>
<th>Year(s)</th>
<th>Antihypertensive Agent(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>Sodium thiocyanate</td>
<td>1970s</td>
<td>$\alpha_2$ agonists (eg, clonidine)</td>
</tr>
<tr>
<td>1931</td>
<td>Reserpine</td>
<td>1973</td>
<td>$\beta$-Receptor blockers</td>
</tr>
<tr>
<td>1947 – 1950</td>
<td>Ganglion blockers</td>
<td>1975</td>
<td>$\alpha_1$ receptor blockers</td>
</tr>
<tr>
<td>1950s</td>
<td>Hydralazine</td>
<td>1977</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>1950s</td>
<td>Guanethidine</td>
<td>1977</td>
<td>Calcium channel blockers</td>
</tr>
</tbody>
</table>
### Table 2: Examples of Non-Pharmacologic Trials for the Prevention or Treatment of Hypertension

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary Intervention Study for Hypertension (DISH)</td>
<td>1985</td>
<td>Weight loss and salt restriction more than doubled success in withdrawal of drug therapy in patients with mild hypertension</td>
</tr>
<tr>
<td>Trial of Antihypertensive Intervention Management (TAIM)</td>
<td>1991</td>
<td>In the short term, drugs outperformed diet and weight loss in the treatment of mild hypertension</td>
</tr>
<tr>
<td>Trials of Hypertension Prevention (TOHP):</td>
<td>1992</td>
<td>In the short term, weight reduction and, to a lesser extent sodium reduction lowered blood pressure in persons with hypertension</td>
</tr>
</tbody>
</table>

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**Lifestyle and high blood pressure in history**

About **2600 BC** Huang Ti Nei Ching Su Wein made the earliest recorded comment on lifestyle when he wrote: “… therefore if large amounts of salt are taken, the pulse will stiffen or harden” \(^2\), as translated by Wan Ping in **AD 762**.

In **1904**, two French medical students, Ambard and Beaujard\(^34\), were the first to promote the concept that the cause of hypertension was salt in the diet, and they claimed some success in reducing blood pressure by restricting salt. They had incriminated chloride rather than sodium – a proposition later supported by Kotchen and Boegehold\(^35,36\).

In **1948**, Kempner\(^37\) renewed interest in salt restriction with his introduction of the rice-fruit diet, which contained 150 mg of sodium per day. Pickering\(^38\), in **1968**, condemned this, describing it thus: “**It is insipid, unappetizing and monotonous and demands great care in its preparation, for if the salt rises above 250 mg/d, the effect in most instances is lost.**”

In the past quarter of a century several controlled, clinical trials have documented the benefits of reduction of salt intake, other nutritional interventions, stress reduction, weight loss, and other lifestyle modifications on the prevention and treatment of hypertension\(^39–46\).

ACE indicates angiotensin-converting enzyme. Data derived from Freis\(^33\)

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1957</td>
<td>Spironolactone</td>
</tr>
<tr>
<td>1958</td>
<td>Thiazide-like diuretics</td>
</tr>
<tr>
<td>1960</td>
<td>Methyldopa</td>
</tr>
<tr>
<td>1993</td>
<td>Angio. II receptor blockers</td>
</tr>
<tr>
<td>2000</td>
<td>Renin inhibitors</td>
</tr>
</tbody>
</table>
Phase I

<table>
<thead>
<tr>
<th>Trial of Stress Reduction(^42)</th>
<th>1995</th>
<th>In the short term, transcendental meditation lowered blood pressure in older blacks with mild hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary Approaches to Stopping Hypertension (DASH)(^43)</td>
<td>1997</td>
<td>A diet rich in fruits, vegetables, and low-fat dairy products substantially reduced blood pressure in adults with high normal blood pressures or mild hypertension</td>
</tr>
<tr>
<td>Trial of Non-pharmacologic Interventions in the Elderly (TONE)(^44)</td>
<td>1998</td>
<td>Weight loss and reduced sodium intake each safely lowered blood pressure in older persons with hypertension</td>
</tr>
<tr>
<td>Trials of Hypertension Prevention (TOHP): Phase II(^45)</td>
<td>2001</td>
<td>Clinically significant long-term reductions of blood pressure were achieved with modest reductions of weight loss</td>
</tr>
<tr>
<td>PREMIER Trial(^46)</td>
<td>2003</td>
<td>Individuals with above-normal blood pressure, including stage 1 hypertension, can make multiple lifestyle changes that lower blood pressure and reduce cardiovascular disease risk.</td>
</tr>
</tbody>
</table>

### Sub-Saharan Africa

About a century ago, hypertension was known to have low incidence in most parts of Sub-Saharan Africa (SSA).

In 1929, Donnison\(^47\) in an article published in the Lancet wrote: “Over two years at a native hospital in the South of Kavirondo in Kenya, during which period approximately 1800 patients were admitted, no case of raised blood pressure was encountered, although abnormally low blood pressure was not uncommonly encountered. On no occasion was a diagnosis of arteriosclerosis or chronic interstitial nephritis made”. He further observed similar BP patterns in Europeans and Blacks until the age of 40 years after which BP rose in the African and not in the European\(^48\). The situation changed after decades with HBP noted from epidemiological studies to be a significant cardiovascular burden and increase of BP patterns noted with age\(^49,50\). Of note was the observed lower BP levels in rural than in urban dwellers. The prevalence of hypertension (BP≥160/95 mm Hg) in rural studies undertaken in the 1970s, 1980s, and 1990s has generally been low: 4.1% in Ghana,\(^51\) 5.9% in Nigeria,\(^52\) 7% in Lesotho,\(^53\) and 9.4% in the rural Zulu.\(^54\)

More recent data, such as those from Tanzania, Ghana, Nigeria, Egypt and South Africa, suggest that hypertension prevalence (using a partition value of 140/90 mm Hg) is on the rise in Africa and commonly exceeds 20%–25% in rural areas and is over 30% in urban and semi-urban areas\(^55\)–\(^60\). The changing pattern has been attributed to increasing urban – rural population drift and rapid urbanization as well as current preference for western-oriented lifestyle\(^55\). The rising prevalence of diabetes mellitus has also been shown to be highly contributory\(^48\).
To address the rising burden of high blood pressure in SSA, the International Forum for Hypertension prevention and control in Africa (IFHA) was formed in Brussels, Belgium, in 2003 with Nigeria playing a notable role. This resulted in the publication of the first guidelines for the management of hypertension in SSA in 200361.

Nigeria in history

A recent meta-analysis of hypertension in Nigeria62 revealed that probably, the first report of hypertension study in Nigeria was in 1953 by Callander63.

In 1955 and 1956, hypertension was reported as a cause of heart disease by Nwokolo et al64 and Beet et al65 respectively.

In 1960, the first recorded large scale epidemiological study was reported by Abraham et al66. Following this, Akinkugbe, generally regarded as the top-most opinion leader on hypertension in Nigeria, published extensively in the 1960s and 1970s67-76 working with collaborators. Among other findings, they documented that casual systolic and diastolic pressures did not significantly differ from those in Black populations in the Caribbean, but systolic and diastolic values were marginally higher in African Americans than in West Indian or West African Blacks.

Between 1961 and 1981, there were 36 recorded studies in Nigeria published by various researchers62. It is clear from the studies that age was the main determinant of presence of high blood pressure and there was significant increase in the observed prevalence from the first study by Abrahams et al66 in 1961 to the study by Ladipo in 198177. Increasing awareness in the populace might contribute significantly to the noted progressive prevalence rate increase over the years of study.

There was also an increasing trend in the prevalence rate of high blood pressure in Nigeria. Pooled prevalence rate of 8.9% was estimated from community-based study available from 1970 to1979. From 1990 to 1999, the pooled prevalence of hypertension was 15.0%; with a significant increase to 22.5% from 2000 to 200962. More recent studies even show higher rates. Onwubere et al59 in 2011 in a study carried out in rural Ezeagu Community, Enugu State found a prevalence rate of 46.4% in a population aged 40 – 70 years. Ulasi et al60 in a market survey in Enugu in 2011 had a rate of 42%.

An extensive literature search by Ogah et al62 documented 43 studies on prevalent rates of hypertension in Nigeria between 1960 and 2012. Six of these studies were carried out in Enugu State.

There are probably hundreds of publications on hypertension in Nigeria published in local journals that cannot be retrieved online.
The **Nigerian Hypertension Society** was inaugurated on April 27, **1993** at the first scientific meeting held in Lagos with the following objectives:

- To provide knowledge of the prevalence, causes, prevention and treatment of hypertension and its complications.
- To bring together all medical doctors, health professionals and scientists in Nigeria interested in the study and/or control of hypertension.
- To increase the awareness of the disease in the community.
- To establish contact and exchange information with similar organizations in other parts of the world.

The Society is affiliated to the World Hypertension League (WHL) and the International Society of Hypertension (ISH).

The following Presidents have served the Society since inauguration:

- 1993 –1997 - Emeritus Professor O.O.Akinkugbe
- 1997 – 2001 - Professor A.F.B.Mabadeje
- 2001 – 2005 - Professor B.J.C.Onwubere
- 2005 – 2010 – Professor A.O. Isah
- 2010 – till date – Professor A Arije

The NHS has published two guidelines for the management of Hypertension: first in **1996** and the second in **2005**

**PATHOPHYSIOLOGICAL CONSIDERATIONS**

The pathophysiology of hypertension is of prime research interest. Hypertension is classified as ‘Essential’ or Secondary. Essential hypertension where no medical cause is known constitutes 90 – 95 % of all cases of hypertension. Secondary hypertension (5 – 10%) is a situation where the cause of hypertension is known and usually from kidney, endocrine and vascular diseases.

The pathogenesis of essential hypertension is not only very complex but also involves multiple factors which include genetic predisposition, excessive salt intake, and adrenergic tone. Multiple factors that modulate the blood pressure (BP) to ensure adequate tissue perfusion include humoral mediators, vascular reactivity, circulating blood volume, vascular calibre, blood viscosity, cardiac output, blood vessel elasticity, and neural stimulation. A possible pathogenesis of essential hypertension has been proposed in which multiple factors, including genetic predisposition, excess dietary salt intake, and adrenergic tone, may interact to produce hypertension. Although genetic factors appear to contribute to essential hypertension, the exact mechanism is yet to be fully established.
The heritability of hypertension (genetic hypertension) is typically estimated from family and twin studies to be in the range of 30–70%, with multiple contributory genes and gene–gene interactions.\(^8\text{3-85}\).

Page, in 1949, had introduced the concept of a “mosaic theory” to explain the aetiology of hypertension. By this he meant that “… most of the known and probably many unknown control factors could be accommodated as long as they were in equilibrium, maintain blood pressure and tissue perfusion at relative constancy, but still adapting to tissue needs.” Essential hypertension was designated a disease of control or regulation, and no constant dominant cause could be expected except in the secondary hypertensions.\(^86, 87\).

**Figure 1:** Page’s Mosaic theory of hypertension\(^86\)

Guyton in 1967 described a “hierarchy of pressure control systems” that provided both short-term damping and long-term control of arterial pressure.\(^88\) This was followed in 1972 by Brunner et al.\(^89\) who emphasized that hypertension was not a single disease but a heterogeneous group of disorders with discrete aetiologies. They observed that over 30% of hypertensive subjects had low renin while 20% had high renin.

Blood pressure is determined by cardiac output and peripheral resistance. Most patients with essential hypertension have a normal cardiac output but a raised peripheral resistance. Peripheral resistance is determined not by large arteries or the capillaries but by small arterioles, the walls of which contain smooth muscle cells.\(^82\).

Certain mechanisms have been proposed to account for the increase in peripheral resistance in hypertension. Greatest evidence implicates either disturbances in renal salt and water handling, especially abnormalities in the intra-renal renin-angiotensin system\(^90\) as well as abnormalities of the sympathetic nervous system.\(^91\) Additionally, it is strongly believed that endothelial dysfunction and vascular inflammation may also contribute to increased peripheral resistance and vascular damage in hypertension.\(^92, 93\).

**Pathological consequences (Complications)**
I. The Cardiovascular System
• Sustained increased vascular resistance leads to left ventricular hypertrophy (LVH). A concomitant ischaemic heart disease would make this worse. LVH is an independent risk factor of cardiovascular disease and leads to relative myocardial ischaemia from reduced supply of blood from the coronary arteries. In addition to angina pectoris, dysrhythmias (abnormalities with heart rhythm are common in this situation. Diastolic dysfunction, atrial fibrillation and significant ventricular extrasystoles are fairly common. Eventually, left ventricular failure may ensue, consequently leading to congestive heart failure\(^1\). \(^{94\,-\,97}\).
• Hypertension enhances coronary atheroma predisposing the individual to myocardial infarction. Heart disease is in fact, the commonest cause of death in hypertensive subjects\(^94,\,95,\,98\,-\,100\). 
• Atherogenesis in the arteries predisposes to dissecting aneurysm of the aorta, peripheral artery disease, and increased stroke incidence.
Cardiovascular complications are the greatest cause of hospital admissions for hypertensive subjects in Nigeria\(^101\,-\,105\).

II. Cerebrovascular disease
• The prevalence of both major and minor stroke is higher in individuals with Charcot-Bouchard aneurysms. Hypertensive subjects have greater predisposition to sub-arachnoid haemorrhage if they have Berry aneurysms on the circle of Willis.
• It is recognized that hypertension is the most prevalent risk factor for stroke. Transient ischaemic attacks occur several-fold more in hypertensive subjects than in normotensive persons\(^106\,-\,108\).

III. The Kidneys
• Hypertensive nephro-sclerosis is the major lesion in the kidneys and affects the afferent arteries more than the others. This leads to progressive reduction in renal function.
• Arteriolar fibrinoid necrosis is found in most individuals with malignant and accelerated hypertension.
• Large renal artery branches are prone to atheromatous degeneration causing renal ischaemia.
• Significant renal ischaemia especially at the juxtaglomerular apparatus stimulates the Renin-angiotensin system and further increases the blood pressure\(^109,\,110\).

IV. The Eyes
• Atheromatous involvement of the retinal arteries leads to retinal artery thrombosis. The affected individual presents with partial or total field defect (blindness).
• As mentioned earlier, fibrinoid necrosis of the retinal arterioles causes haemorrhages and exudates.
• Papilloedema is the extreme form of hypertensive retinopathy\(^111\).
A GLOBAL BURDEN – THE KILLER INDEED

High blood pressure constitutes an important public health burden globally\textsuperscript{112}. Various observational data attributed BP elevation with systolic values above 115mmHg to be responsible for a total of 7.6 million deaths (13.5\% of total global mortality) and 92 million (6\% of total) of the sum of deaths and disability adjusted life years (DALYs). It is disturbing that 80\% of worldwide cardiovascular-related deaths occur in low-to-middle income countries, and, in comparison with high-income countries, these deaths (and events such as stroke and acute myocardial infarction) occur at a younger age, exerting a profound impact on the family unit and the workforce. It is predicted that non-communicable forms of cardiovascular diseases will become the leading cause of death and disability globally, by 2020\textsuperscript{5, 113-117}.

The prevalence rates of hypertension vary around world-wide with the lowest prevalence in rural India (3.4\% in men and 6.8\% in women) and the highest prevalence in Poland (68.9\% in men and 72.5\% in women). The overall prevalence of raised blood pressure in adults aged 25 years and over was around 40\% in 2008. Even though the proportion of the world’s population with high blood pressure, or uncontrolled hypertension, fell modestly between 1980 and 2008, because of population growth and ageing, the number of people with uncontrolled hypertension rose from 600 million in 1980 to nearly 1 billion in 2008\textsuperscript{118}.

There is, therefore clear evidence that \textbf{global prevalence of hypertension has been increasing}. In 2000, 972 million people had hypertension with a prevalence rate of 26.4\%, 333 million in economically developed countries and 639 million in economically developing countries. It is
projected that by 2025 a total of 1.54 billion people accounting for 30% of the World population would be hypertensive with 75% of these from the developing countries and regions5,112,118.

Regarding attributable deaths, the leading behavioural and physiological risk factors globally are raised blood pressure (to which 13.5% of global deaths are attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%) and being overweight or obese (5%)119.

Evidence shows that raised blood pressure causes 51% of stroke deaths and 45% of coronary heart disease deaths119. It is worthy to observe that mean blood pressure has decreased dramatically in nearly all high-income countries. A recent worldwide study from 199 countries and territories involving 5.4 million participants showed that on average, global population SBP decreased slightly since 1980, but trends varied significantly across regions and countries. SBP is currently highest in low-income and middle-income countries. The mean age-standardized male systolic blood pressure (SBP) in the United States decreased from 131 mm Hg (95% uncertainty interval 127–135) in 1980 to 123 mm Hg (120–127) in 2008, while mean age-standardized female SBP decreased from 125 mm Hg (121–130) to 118 mm Hg (115–122) mm Hg120. On the other hand, mean blood pressure has been stable or increasing in most African countries. Currently, mean blood pressure remains very high in many African and only few European countries120 - 122.

According to the 2012 World Health Organization Health statistics for 2012 for Nigeria, the mean SBP was 132 mm Hg in 1980; fell to 128 mm Hg in 1990; and rose steadily to 132 mm Hg in 2008 for Men. For Nigerian women it rose steadily from 129 mm Hg in 1980 to 133 mm Hg in 2008122.

The silent killer is, indeed, on the prowl!

Ironically, this scourge targets economically weakened and unwary populations that are of course ill-prepared to combat it.

**COMBATING THE ALBATROSS**

Available data show that lowering blood pressure in people with hypertension is associated with a reduction in cardiovascular disease risk. A large-scale meta-analysis of observational, prospective studies123 among hypertensive patients aged 40-69 years showed that a 20 mmHg lower SBP is associated with:

- Less than half the risk of dying from a stroke, and
- Half the risk of dying from coronary heart disease.
The decision to treat a hypertensive individual should be based on the blood pressure level as well as the total cardiovascular risk and not on the blood pressure level alone\textsuperscript{124 - 126}.

Risk factors, target organ damage and associated clinical conditions

Studies have demonstrated the effects of a number of risk factors for heart disease divided into non-modifiable and modifiable\textsuperscript{127 - 129}:

1. Non-Modifiable: age, gender, family history, and ethnicity.

2. Modifiable: High blood pressure, high serum cholesterol levels, tobacco smoking, excessive alcohol consumption, obesity, lack of physical activity, psychosocial factors, diabetes mellitus, and air pollution\textsuperscript{130}. While the individual contribution of each risk factor varies between different communities or ethnic groups the consistency of the overall contribution of these risk factors to epidemiological studies is remarkably strong. Some of these risk factors, such as age, gender or family history, are immutable; however, many important cardiovascular risk factors are modifiable by lifestyle change, drug treatment or social change\textsuperscript{131}.

The major risk factors, target organ damage, and associated clinical conditions are shown in Table 3

Table 3: Major risk factors, TOD and ACC (Adapted from ESC/ESH Guidelines\textsuperscript{132})

<table>
<thead>
<tr>
<th>MAJOR RISK FACTORS.</th>
<th>TOD</th>
<th>ACC.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Levels of systolic and diastolic BP.</td>
<td>• LVH: based on ECG [Sokolow-Lyons &gt; 38 mm; Cornel &gt; 2440 mm.ms)</td>
<td>• Coronary heart disease.</td>
</tr>
<tr>
<td>• Smoking.</td>
<td>• Microalbuminuria: albumin creatine ratio 3-30 mg/mmol.</td>
<td>• Heart failure.</td>
</tr>
</tbody>
</table>
| • Dyslipidaemia:  
  o total cholesterol > 5.1 mmol/L, OR | • Slightly elevated creatinine:  
  o men 115-133 µmol/L;  
  o women 107-124 µmol/L | • Chronic kidney disease:  
  o albuminuria > 30mg/mmol OR  
  o creatinine men > 133 µmol/L  
  o creatinine women >124 µmol/L |
|  
  o LDL > 3 mmol/L, OR | | • Stroke or TIA. |
|  
  o HDL men < 1 and women < 1.2 mmol/L. | | • Peripheral arterial disease. |
| • Diabetes mellitus. | | • Advanced retinopathy:  
  o haemorrhages OR;  
  o exudates;  
  o papilloedema. |
| • Men > 55 years. | | |
| • Women > 65 years. | | |
| • Family history of early onset of CVD:  
  o Men aged <55 years;  
  o Women aged <65 years. | | |
| • Waist circumference- abdominal obesity:  
  o Men ≥ 94 cm;  
  o Women ≥ 80 cm.  
The exceptions are South Asians and Chinese: Men: >90 cm and Women: >80 cm. | | |
The decision to initiate therapy and the mode of treatment are influenced by the number of risk factors present, the target organ damage identified at evaluation and the associated clinical conditions present. Various regional and national Guidelines provide details in form of Risk stratification.\(^\text{132}\)

The new WHO guidelines for primary prevention of CVD recommend total cardiovascular risk assessment before making decisions on drug treatment including lipid-lowering therapy.\(^\text{133,134}\)

**Effect of lifestyle modifications**

Table 4 shows the effect of lifestyle modifications on the systolic blood pressure.

Table 4: Effect of Lifestyle modification on SBP as recommended by JNC7\(^4\)

<table>
<thead>
<tr>
<th>Modifications*</th>
<th>Recommendation</th>
<th>Approximate SBP reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce weight</td>
<td>Maintain normal body weight (BMI of 18.5 - 24.9 kg/m(^2))</td>
<td>3-20 mm Hg</td>
</tr>
<tr>
<td>Adopt DASH diet(^\text{130})</td>
<td>Rich in fruit, vegetables, and low-fat dairy; reduced saturated and total fat content</td>
<td>8–14 mm Hg</td>
</tr>
<tr>
<td>Reduce dietary sodium</td>
<td>&lt;100 mmol (2.4 g)/day</td>
<td>2–8 mm Hg</td>
</tr>
<tr>
<td>Increase physical activity</td>
<td>Aerobic activity &gt;30 min/day most days of the week</td>
<td>4 – 9 mmHg</td>
</tr>
<tr>
<td>Moderate alcohol consumption</td>
<td>Men: ≤ 2 drinks/day; Women: ≤ 1 drink/day</td>
<td>2 – 4 mm Hg</td>
</tr>
</tbody>
</table>

*Combining 2 or more of these modifications may or may not have an additive effect on blood pressure reduction.

SBP = systolic blood pressure; BMI = body mass index; DASH = Dietary Approaches to Stop Hypertension

**Drug Treatment**

Hypertension is reversible, and several lines of evidence show that reducing BP affords cardiovascular protection, regardless of which antihypertensive drug is used. The BP Lowering Treatment Trialists’ Collaboration performed a series of prospective overviews of numerous randomized trials that investigated the effects of different BP-lowering regimens on serious cardiovascular morbid and fatal events. These BP reductions were accompanied by significant reductions in primary outcomes, which included cardiovascular disease (18–22%), coronary heart disease (16–22%), and stroke (28–39%).\(^\text{125 - 127}\)

The therapeutic goal should be to reduce blood pressure to less than 140/90 mmHg for most individuals, and lower for those with diabetes or kidney disease (usual recommendation is to achieve levels below 120/80 mmHg).\(^\text{135}\) Guidelines on the choice of agents and how best to step up treatment for various subgroups have changed over time and differ between countries. No
consensus first line is agreed. While the Cochrane collaboration, World Health Organization and the United States guidelines support low dose thiazide-based diuretic as first line treatment\textsuperscript{136–138}, the UK guidelines emphasize calcium channel blockers (CCB) in preference for people over the age of 55 years or if of African or Caribbean family origin, with angiotensin converting enzyme inhibitors (ACE-I) used first line for younger people\textsuperscript{139}.

The majority of people require more than one drug to control their hypertension. JNC7\textsuperscript{4} and ESH-ESC guidelines\textsuperscript{132} advocate starting treatment with two drugs when blood pressure is >20 mmHg above systolic or >10 mmHg above diastolic targets. Most common combinations are renin–angiotensin system inhibitors and calcium channel blockers, or renin–angiotensin system inhibitors and diuretics\textsuperscript{139}. Other combinations include calcium channel blockers and diuretics, beta-blockers and diuretics, dihydropyridine calcium channel blockers and beta-blockers, or dihydropyridine calcium channel blockers with either verapamil or diltiazem.

\textit{In spite of global improvement in the management of high blood pressure, control rates still remain significantly low due to certain impediments}

\textbf{Strategies for surmounting impediments to effective control}

\textbf{Table 5: Impediments and possible interventions} (Source: Siegel D: Vasc Health Risk Manag. 2005 March; 1(1): 9–14)

<table>
<thead>
<tr>
<th>Impediments</th>
<th>Possible interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Patient-based}</td>
<td></td>
</tr>
<tr>
<td>Attitudes about hypertension</td>
<td>Education at the community and individual level concerning consequences of hypertension</td>
</tr>
<tr>
<td>Medication side effects</td>
<td>Use of medications with fewer side effects</td>
</tr>
<tr>
<td>Medication cost</td>
<td>Use of diuretics and other generically available medication</td>
</tr>
<tr>
<td>Medication adherence</td>
<td>Less frequent dosing of medications, promotion of pillboxes, combination medications</td>
</tr>
<tr>
<td></td>
<td>Methods to increase ease of medication renewal (ie, telephone or computer-linked)</td>
</tr>
<tr>
<td></td>
<td>Rewards for higher adherence and lower blood pressure</td>
</tr>
<tr>
<td>\textit{Provider-based}</td>
<td></td>
</tr>
<tr>
<td>Knowledge</td>
<td>Conferences, academic detailing, computer-based algorithms, publication of clinical trials</td>
</tr>
<tr>
<td>Access</td>
<td>Use of physician extenders, group visits, work site care, expansion of health coverage</td>
</tr>
<tr>
<td>Awareness</td>
<td>Computer based reminders</td>
</tr>
<tr>
<td>Motivation</td>
<td>Incentives for health providers and managers</td>
</tr>
<tr>
<td>\textit{Societal-based}</td>
<td></td>
</tr>
<tr>
<td>Awareness</td>
<td>Public education campaigns</td>
</tr>
<tr>
<td></td>
<td>Community-screening programs</td>
</tr>
<tr>
<td></td>
<td>Work-based programs</td>
</tr>
<tr>
<td>Access to care</td>
<td>Expansion of health coverage (private and government financed)</td>
</tr>
</tbody>
</table>
Preventive strategies

The rising prevalence of hypertension worldwide calls for intensification of preventive measures. This is highly recommended for populations in the low- and medium income communities due to a looming explosion of cardiovascular morbidity and mortality. Important issues in hypertension prevention are:

- Patient education
- Screening for hypertension
- Primordial prevention
- Primary Prevention, and
- Secondary prevention.
- Improving Awareness

**Primordial Prevention**

- Primordial prevention of hypertension deals with addressing socio-cultural and socio-economic factors in the community that encourage the development of hypertension. Health policy makers and professionals should all be involved. Success would also be enhanced if community leaders and local chiefs are committed.
- Primordial prevention programmes should be part of local health policies for it to be sustained.

**Primary Prevention**

- Primary prevention of hypertension addresses the risk factors that favour the development of hypertension. Examples are: obesity, physical inactivity, excessive salt consumption etc. Community based programmes aimed at encouraging healthy lifestyles should be organized. Target groups e.g. school children; market women should be identified and used as focal points for the programmes. Individuals should be advised to maintain healthy lifestyles. Healthy eating with foods rich in fruits and vegetables should be recommended to the populace.

**Secondary Prevention**

- Secondary prevention of hypertension refers to the management of the complications. It is necessary to intensify both primordial and primary prevention of hypertension in low- and medium economy settings. This is because the cost of managing the complications of hypertension in such environment could be enormous and beyond the reach of a majority of individuals. Adequate follow-up is advocated and this should be life-long even when blood pressures have been adequately controlled. At each visit, physical examination should be done and at least once yearly, detailed investigations to assess complications should be carried out. Any identified complication should be appropriately managed.

**Role of International, Regional and National Organizations and Societies**

International Organizations like the World Health Organization (WHO) and World Hypertension League (WHL) as well as Societies like the ISH collaborate in prevention of hypertension through encouraging research, organizing scientific meetings, workshops and arts competitions. The WHL in 2005 declared a ‘World Hypertension Day’ – an annual event to improve awareness
Our contributions in the control of the scourge.

Our interest in hypertension stems for the desire to make our modest contributions to the control of a preventable scourge that is causing significant mortality and morbidity globally. The contributions have been in the areas of research and administration. Our research activities started with hospital based studies dating back to 1999 and continuing ever since mostly aimed at generating much needed data from our local institutions.

Drug trials for anti-hypertensive drugs were also carried out in collaboration with colleagues and associates. In 2005, we published a book on the management of hypertension which is undergoing revision now.

The need to have hypertension management guidelines to take care of national and regional peculiarities stimulated our interest in being part of the publication of guidelines for hypertension in Sub-Saharan Africa (2003) and Nigeria (2005).

Recently, our interest shifted to epidemiological studies in search of the much needed local data on hypertension. This involved a market survey and community-based studies.

Apart from dedicated participation in hypertension research, we have been actively involved in local, national, and international hypertension society activities regularly attending annual scientific conferences with over 40 abstract presentations. We have also been at leadership positions in these Societies.

It should be pointed out that these contributions would not have been possible without the highly appreciated roles of my mentors, teachers, and friends who are appropriately acknowledged later during this lecture.

CONCLUSIONS

I would conclude this lecture by a quote from the United Nation’s Secretary-General, Ban Ki-moon in response to a question by the Global International on his vision for the new year 2013.

“We stand at a critical crossroads in history when our actions – or inaction – can shape the future of life on Earth as we know it………..

….. This is a global challenge, one requiring global cooperation among all sectors of society. In the coming year, my hope is that governments, working with the business community, civic organizations, foundations, academic and faith based groups, will continue to work with the United Nations to help forge a more sustainable path to the future. Working together, we can bring hope and opportunity to all. The future is truly in our hands.”

This statement can aptly be applied to the hypertension scourge which is indeed a global challenge that needs all of us and all Nations to Unite in combating the albatross.
ACKNOWLEDGEMENT

I thank the Almighty God who created man and bestowed him with knowledge and wisdom to surmount challenges strewn along the pathway of his life’s journey, among other reasons, to lessen boredom.

I thank the Vice Chancellor, Professor Batho Okolo and the University administration for ensuring the success of today’s event. I specially thank Professor Chinedu Nebo, immediate past Vice Chancellor for touching lives of staff and students and providing the firm academic framework maintained and upgraded infra-structurally and internationally by the current administration. I appreciate the dedication to duties of the Chairman, Senate Ceremonials Committee, Professor Obi Njoku and the members of that Committee.

My family members, nuclear and extended – the entire Onwubere family, the Aguta and Onyekuru families, and all friends and associates for being there for me all the time. My immediate family members who continue to cope with my periodic absence from home attending conferences or attending to clients sometimes into late hours are highly appreciated.

I wish to pay tribute to my mentors who stimulated and sustained my interest in Hypertension notably Professor Emeritus Oladipo Akinkugbe, the Father of Hypertension in Africa and Nigeria whom I have learnt a lot from over the years. I have also trailed behind him (at a safe distance) in the hypertension story nationally and internationally. Professor Emeritus Yackoob Seedat, another Father of Hypertension in Africa who has also been a father to me at the international arena. YK ensured my nomination to sit on the Scientific Council of the International Society of Hypertension after his two-term tenure four years ago. I appreciate my colleagues and collaborators in cardiovascular medicine within the Country – Professors Solo Kadiri, Austin Obasohan, James Odia, Clement Odigwe, Basil Okeahialam and a host of others.

Without the tutelage and special care of my Teachers at various stages of my education, I would not be giving this lecture today. I would just mention one per education stage as point of contact to represent the rest – Mr Goddy Kamalu (my Standard 6 Teacher), Mr J A Garrod (my Principal at Government Secondary School, Owerri), and Professor Chukwuemeka Nwokolo (representing my University Teachers). I remain grateful to them for shaping my future.

The Department of Medicine has been a source of inspiration to me. Among those who at one time or the other guided me on the path of my career path include Professors Johnny Oli, Dede Iheanacho, Vincent Ikeh, Eddy Okoroma and others. Professor Sam Ike (Venerable of the Anglican Church) deserves special mention. A relationship that started with me as his academic/professional supervisor has grown into a situation of mutual trust and confidence. He did proof-read not only this script but also a book publication I made 8 years ago. I thank him and his wife who also participated actively in the logistics of this Lecture. Dr. Emmanuel Ejim has been and remains my professional son right from his days as a medical student. He has been
highly reliable and ever there for me in both official, private and family capacities. The recent passing on of his dear spouse at a time finishing touches were being put on this Inaugural Lecture pained me immensely. (May Chinelo’s soul rest in perfect peace. Amen). I love all staff of my department – academic and administrative for the cohesion and friendship that exists in that family.

I learnt a great deal from and remain appreciative of late Professor John Goodwin, Dr. Celia Oakley and others at the Royal Postgraduate Medical College/ Hammersmith Hospital, London where I had part of my postgraduate programme between January, 1981 and May, 1983.

I appreciate in a special way, the entire College of Medicine staff for their un-alloyed support these past few years. The College academic community have consistently reposed great confidence in my administrative capacity in spite of obvious challenges while the administrative staff, especially Principal Officers of the College of Medicine have not quivered in their co-operation.

I thank all who are here today, Your Lordships, Your Excellencies, and distinguished ladies and gentleman for giving me this honour today. May God bless you all abundantly and grant you safe journey back home.

Finally, the Inaugural Committee members contributed tremendously to the successful event today and deserve mention - Profs. Ifeoma Ulasi and Sam Ike; Drs. Chuba Ijoma, Ben Anisiuba, Sylvester, Nwokediuko, Emma Ejim, Chinwe Onyekonwu, Raph Anakwue, Oluchi Ekenze, Ekene Young, and Esther Ekwe; Mrs. Ngozi Uzoagba, and Mrs. Becky Anyanwu. God bless you all.

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