



UNIVERSITY OF LAGOS, NIGERIA
Inaugural Lecture Series 2015

TOPIC:

HEART OF THE MATTER, MATTER
OF THE HEART: AUTONOMIC
CARDIOVASCULAR REGULATION IN
HEALTH AND DISEASE

By

PROFESSOR CHIKODI NNANYELU EZEGWUI ANIGBOGU

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HEART OF THE MATTER, MATTER OF THE HEART: AUTONOMIC CARDIOVASCULAR REGULATION IN HEALTH AND DISEASE

An Inaugural Lecture Delivered at the University of Lagos
Main Auditorium on Wednesday 7th October, 2015

By

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University of Lagos Press and Bookshop Ltd

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ISSN: 1119-4456

Published

By

University of Lagos Press and Bookshop Ltd
Works and Physical Planning Complex
University of Lagos
Akoka, Yaba-Lagos
Nigeria.
Unilag P.O. Bcx 132

Preamble

In the beginning was the WORD and the WORD was with GOD and the WORD was GOD and GOD said let there be LIGHT and there was LIGHT AND THE LIGHT WAS THE LIFE OF MEN.

The Vice-Chancellor, Professor Rahaman Adisa BELLO;
Deputy VC (A&R), Professor Babajide ALO;
DVC (MS), Professor Duro ONI;
Registrar and Secretary to Senate and Governing Council, Dr. Mrs. Taiwo Folashade IPAYE;
Provost of the College of Medicine, Professor Folashade Tolulope OGUNSOLA;
Dean, Faculty of Basic Medical Sciences, Professor Mrs. Olufunmilayo Olaide O. ADEYEMI
Deans of other Faculties;
Members of Senate;
Great Teachers, non – Academic Colleagues and Students;
My Lords Spiritual & Temporal;
Members of the Anigbogu-Okpaodukwe Family;
Gentlemen of the Press;
All invited Guests; Distinguished Ladies and Gentlemen.

Introduction

Physiology

Physiology - the science of life and the living process is the HEART of ALL HEALTH AND MEDICAL SCIENCES; a good knowledge of physiology is a sine-qua-non for all life sciences and health practitioners.

Physiology, the science of life and the living process is taught and studied in various subject components viz; General Physiology and Cellular Processes, Body fluids and Blood, Autonomic Nervous System, Cardiovascular or Circulatory System, Respiratory System, Renal System, Gastrointestinal System, Nutrition and Metabolism, Neuromuscular System, Sensory System, Motor System and Integrative Central

Nervous Systems, Endocrinology and Reproduction, Environmental Physiology, Sports and Exercise Physiology.

From the above it is clear that physiology is a vast and essential subject that covers all aspects of life. At the macro level physiology includes Plant physiology, Animal physiology, Microbial physiology and Molecular Physiology, and Human Physiology which encompasses Basic Physiology, Medical Physiology, Clinical Physiology and Applied Physiology. When physiological processes go wrong they via into Pathophysiology and when they are totally impaired or overtaken by disease they become Pathology.

In the beginning God moulded man from the earth (dust, sand, mud) to make the form – **Anatomy**. Then, he breathed life into the form and it became a **living person – PHYSIOLOGY**. Thus God is the first physiologist, (Genesis 1-3). God thereafter, performed many experiments with man and the animals. Physiology or physiological sciences gave birth to physiological chemistry (now Biochemistry) and medicinal physiology (now Pharmacology) and many other sub-specialties. It is also worthy to know that the Nobel Prize in all health sciences and medicine is awarded in physiology.

Professor Chikodi Nnanyelu Ezegwui Anigbogu

I was admitted to the University of Ibadan, Jos Campus then to read Biochemistry. After our prelim year, we moved down to Ibadan as Jos Campus became the new University of Jos. During our 1st year in the Faculty of Science, we were introduced to new subjects like physiology and pharmacology which were then subsumed under the Faculty of Science and located in Abadina area. After Youth Service in Ondo State where I taught Anatomy and Physiology at Schools of Nursing, Midwifery and Health Technology, I came down to Lagos and was employed as a Teacher in CMS Grammar School IV, Bariga. Thereafter, I was posted to teach Biology but the school had no Physics teacher so I started teaching Physics since there was already someone teaching Biology. Shortly, I was admitted to the University of Lagos for M.Sc. Physiology

and appointed as Graduate Assistant, under Prof. (Mrs.) Oyin Elebute, the then Head of Department of Physiology. I have since never looked back but continued to serve the University of Lagos in various capacities with the same zeal.

Some Historical Perspective

History of Human Physiology

One of the oldest records about human physiology is in the Bible where it is reported that God breathed His spirit into man (body of man – Anatomy) and it became a living being.

Aristotle (384 – 322 BC) also described blood vessels as a system with the heart at its centre. Herophilus (335 – 280 BC) - identified the brain as the seat of intelligence and also demonstrated that walls of arteries are thicker than those of the veins. He measured the pulse and showed that it varied in disease while Erasistratus (320-240 BC) believed that,

1. Blood was made in the liver from food.
2. Blood was delivered by ebb and flow in veins.
3. Arteries were the same as air vessels.
4. Air = Pneuma in Greek – the living force or vital spirit.

Galen (AD. 130-201) in his case demonstrated that blood, not air flowed in arteries by a simple experiment using a tube made from feather.

Also on this subject, Vesalius (1514 - 1564): made drawings from dissections of cadavers – Dead bodies to improve teaching and William Harvey (1578 – 1657) showed that blood flowed in one direction with the heart as pump and that back-flow in the veins were prevented by valves. He wrote the revolutionary book, “*De motu cordis et Sanguinis in Animalibus*” in latin i.e. (On the Motion of the Heart and of the blood in Animals).

The key features of Harvey's Theories of blood flow include:

1. The heart is a pump, worked by contracting to expel blood rather than expanding to fill with blood.

2. Blood moved from right ventricle of the heart to the lungs and not directly into the left ventricle.
3. Air stayed in the lungs, where it met the blood rather than coursing to the heart to meet the blood.
4. Blood moved in a circular path through the body rather than travelling both directions in the same vessels.

Harvey also introduced quantitative methods using the metric system for measurements in Physiology.

Marcello Malpighi (1628 – 1694) – discovered the blood capillaries following the invention of microscopes (In the lungs of a frog).

Modern Advances in Physiological Understanding

The following are the modern advancement in physiological understanding:

- Bodily Control Systems
- Genetic Processes
- Bioenergetics

The rate of modern discoveries has increased tremendously. Atrial Natriuretic Factor (ANF) was discovered in 1981 and within 3 years of its discovery, ANF was purified, its amino acid sequence was defined, assay methods were developed and synthesis by recombinant DNA technology was accomplished. The factors that contributed to this rapid development include:

- Rapid communications.
- International meetings/publications.
- Sophisticated research methods.
- Large no. of Scientists.

Joseph Priestley (1733 – 1804) – showed that something was removed from air during combustion and breathing and that the substance could be supplied by a plant. Antoine Lavoisier (1743 – 1794) later identified the essential substance as OXYGEN.

Cell Theory

ROBERT HOOKE (1635 – 1703) – detected “Cells” – compartments in cork using microscope. Two centuries later Schleiden and Schwann proposed that;

1. All organisms are made up of cells and their products.
2. New cells arise only from pre-existing cells.
3. All cells have same fundamental chemical makeup and metabolic processes.
4. Activities and processes of the organism as a whole result from the interdependent and cooperative working of groups of cells.

Scientific Method in Physiology

Scientific method involves posing questions and searching for answers.

Reasoning Process

The scientific method in physiology range thus:

- Deductive reasoning – General Rule \Rightarrow Specific Conclusion
- Inductive Reasoning - Specific Observation \Rightarrow General Conclusion
- Observation \rightarrow Hypothesis \rightarrow Experiment \rightarrow Conclusion: Retesting and Publication.

Examples

General Premises

All tissues are
composed of



Specific Conclusions

Muscle cells are
composed of cells

Nerve tissues are
composed of cells

Epithelial tissues are
composed of cells

DEDUCTIVE
REASONING

Figure 1: General Premises and Specific Conclusions (a)

Specific Observations

General Conclusions

INDUCTIVE
REASONING

Muscle cells have nuclei

Nerve cells have nuclei

Bone cells have nuclei

BUT

Red blood cells do not have nuclei

All human cells have nuclei

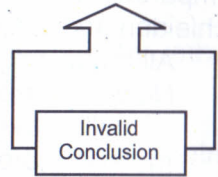


Figure 2: General premises and Specific Conclusions (b)

Medicine is an ever changing science. As new research and clinical experience broaden our knowledge; changes in treatment and drug therapy are required. Evidence based medicine requires that procedures, treatment and management must be based on verifiable scientific evidence.

The Heart and the Cardiovascular System

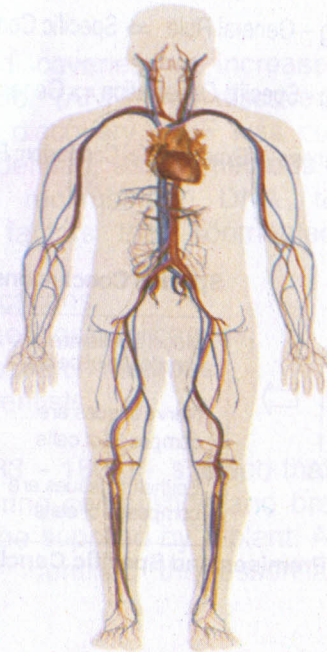


Figure 3: The Human Cardiovascular System

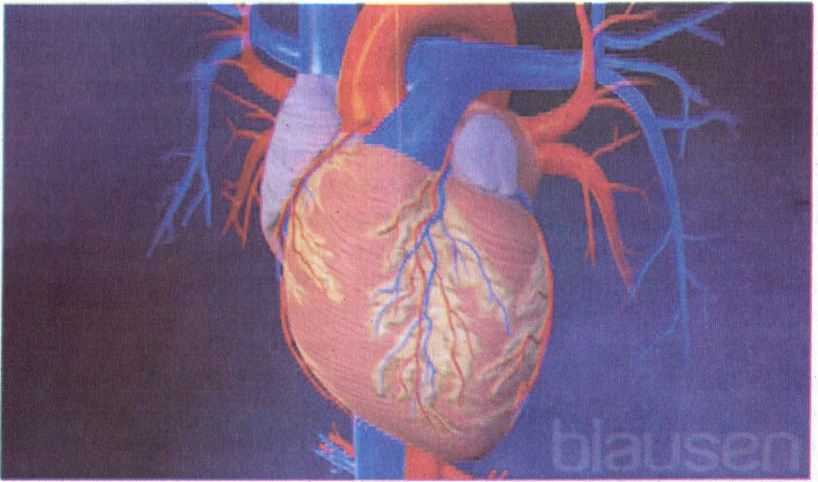


Figure 4: Model of the Human Heart

The heart is the centre of the cardiovascular system and is very important for life's functions. It is so important that various attributes and adjectives apply to the heart, some of these attributes are: **gentle heart, hard heart, soft heart, stony heart, sweet heart, faint heart, strong heart, weak heart, light heart, contrite heart, heavy heart, broken heart and loving heart**. Thus, the concept of the heart is important to life in all ramifications. Some of these concepts are physiological, philosophical, esoterical, spiritual, social, emotional, anatomical and even comical. Given the prevailing developmental conditions at the time in this country we decided to focus on research in areas directly relevant to the health and wellbeing of the populace.

Cardiovascular Physiology

The cardiovascular system is a closed circuit consisting of a pump (**the heart**) and conduit pipes (**the blood vessels**) that circulates or conducts the life or living fluid (**the blood**) round the whole body. The heart is actually two pumps working in tandem; the right heart pumps blood through the pulmonary circulation of the lungs for oxygenation and removal of carbon dioxide while the left heart pumps blood through the high pressure systemic circulation to supply all parts of the body with oxygen and nutrients and remove by-products of

metabolism. The cardiovascular system also contributes to homeostatic mechanisms such as regulation of body temperature, humoral communication, adjustments of oxygen and nutrient supply in different physiological states.

The pulmonary circulation is a low pressure circulation with pressures ranging from 10mmHg at diastole to 25mmHg at systole. The systemic circulation is a high pressure circulation with pressures ranging from 80mmHg at diastole to 120mmHg at systole.

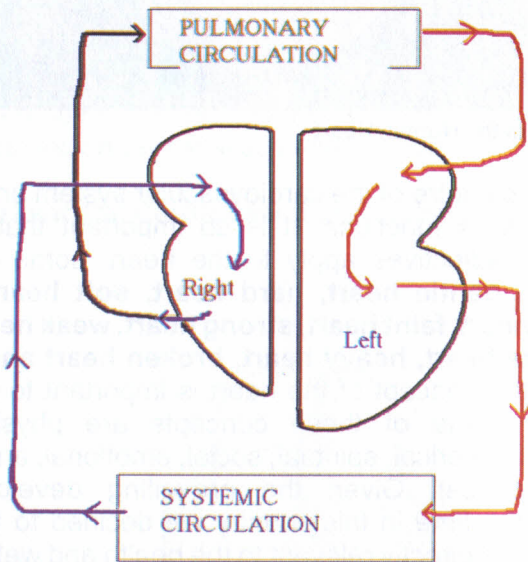


Figure 5: Schematic Two-pump/Two Circulation Diagram of the Cardiovascular System

What is Systole and Diastole?


Systole is the contraction phase of the heart and it lasts for about 0.3 seconds, while diastole is the relaxation phase of the heart which lasts about 0.5 seconds. The duration of systole and diastole put together is approximately 0.8 seconds and is called the heart period. The series of events that occur in the heart period make up the cardiac cycle.

The contraction and relaxation of the heart make one heart beat. The number of heart beats in one minute (60 seconds), make up the heart rate (beats/minute). The pulse or pulse pressure is the difference between the systolic and diastolic blood pressures which can be counted as the pulse rate (pulses per minute) this is coterminous with the heart rate as the pulse wave is rapidly transmitted and thus the arterial pulse rate is conventionally used as the heart rate.

Blood Pressure and Heart Rate

Blood pressure and heart rate are obviously the most common, frequently assessed and used parameters of the cardiovascular system. Other parameters also used include venous pressure, electrocardiogram (ECG), cardiac output, stroke volume, peripheral resistance, arterial compliance, venous return, and cardiac index and others.

Table 1: Blood Pressure Chart by Age

BLOOD PRESSURE CHART BY AGE			
 /DailyHealthGen			
Age	Min	Normal	Max
1 to 12 months	75/50	90/60	110/75
1 to 5 years	80/55	95/65	110/79
6 to 13 years	90/60	105/70	115/80
14 to 19 years	105/73	117/77	120/81
20 to 24 years	108/75	120/79	132/83
25 to 29 years	109/76	121/80	133/84
30 to 34 years	110/77	122/81	134/85
35 to 39 years	111/78	123/82	135/86
40 to 44 years	112/79	125/83	137/87
45 to 49 years	115/80	127/84	139/88
50 to 54 years	116/81	129/85	142/89
55 to 59 years	118/82	131/86	144/90
60 to 64 years	121/83	134/87	147/91
SHARE WITH EVERYONE			

Typically blood pressure is given as 120/80 mmHg, showing the systolic over the diastolic pressure. Your heart is older than you, so you must treat it with respect. The primordial heart cell – cardiomyocyte starts to beat at about 3 – 6 weeks after conception and over seven months before birth and it continues to beat throughout life. This is regulated with checks and balances by the autonomic nervous system.

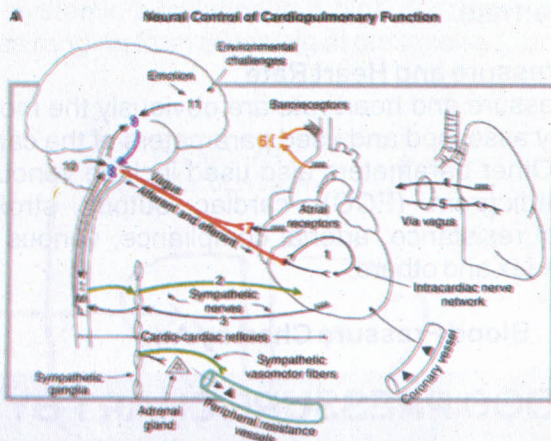


Figure 6: Schematic Diagram Illustrating the Autonomic and Neural Connections that Control the Heart and Blood Vessels

Circulatory Shock

The word shock is always confusing to many people because it connotes a difference, diversion or disruption and an interjection from normal or the expected natural course of things or condition. We often associate shock with sudden change, electrocution and surprise, however, in physiology shock may also be gradual or incipient.

Circulatory shock is a condition where the blood available in circulation is inadequate or the heart cannot pump blood adequately to supply the needs of the body or its various organs. This condition may result from inadequate amount of blood in the circulatory system or inadequate or reduced capacity of the heart to pump out blood, inadequate perfusion of tissue with pumped out blood or a combination of these factors. Sometimes there is a mismatch of available blood with

the volume of the vascular compartment such that the pressure of blood is not sufficient to supply blood adequately to the important tissues. Thus, we have various types of circulatory shock including haemorrhagic, cardiogenic, endotoxin/endotoxic, septic and, burn shock depending on the causative factors.

In the 1970s and early 80s expressways and new roads were built in Nigeria courtesy of the oil boom. Cars and vehicles were also affordable resulting in the upsurge in speed travel and its attendant accidents and fatalities. Many accident victims died on the spot but many survivors who eventually got to hospital or health facility died due to haemorrhagic shock resulting from the severe blood loss. This death may still occur even when the lost blood may have been replaced by blood transfusion – a condition termed irreversible shock.

We investigated the changes in cardiovascular function during haemorrhagic shock using experimental animals and the effects of various treatments on the outcome. Most drugs used then were geared to improve the pumping action of the heart and improve haemodynamics while ignoring the intense vasoconstriction, subcellular changes, metabolic alterations and acid-base imbalance.

We tested the effects of salbutamol a beta2-adrenoceptor stimulant and dopamine a sympathomimetic amine with alpha and beta adrenergic actions as well as dopaminergic actions, on haemodynamic alterations, blood chemistry and survival during haemorrhagic shock (36 – 40%). We found that both drugs improved cardiac output, mean arterial pressure and reduced total peripheral resistance. There was improvement also in blood chemistry. The two drugs reduced mortality and when combined; further improved survival. When administered together 15 minutes before or 1 hour after haemorrhage all the dogs survived (**Anigbogu** and Adigun, 1983, 1987).

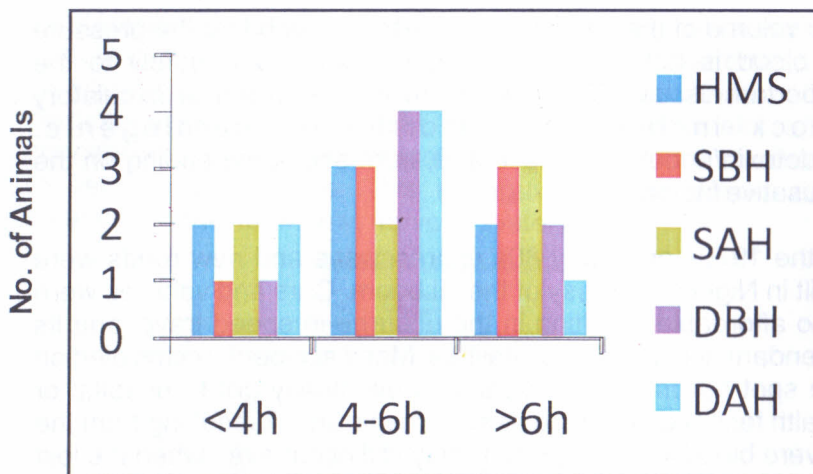


Figure 7: Effect of Salbutamol and Dopamine on Survival Period during Haemorrhagic Shock

E. coli Endotoxin Shock

Furthermore, we looked at the effect of the two agents (Salbutamol and Dopamine) on *Escherichia coli* induced shock and found out that there was improvement in haemodynamic and blood chemistry changes which increased survival, especially, salbutamol. In *E. coli* shock; management is aimed at improving the poor total peripheral conductance, low cardiac output, hypotension, central venous pressure level and associated metabolic changes (**Anigbogu** and Adigun 1986). Thus, we demonstrated that management of shock must be a balance between increasing cardiac contractility and reducing the workload of the heart which thereby reduces peripheral resistance and increase vascular conductance that enhances tissue perfusion.

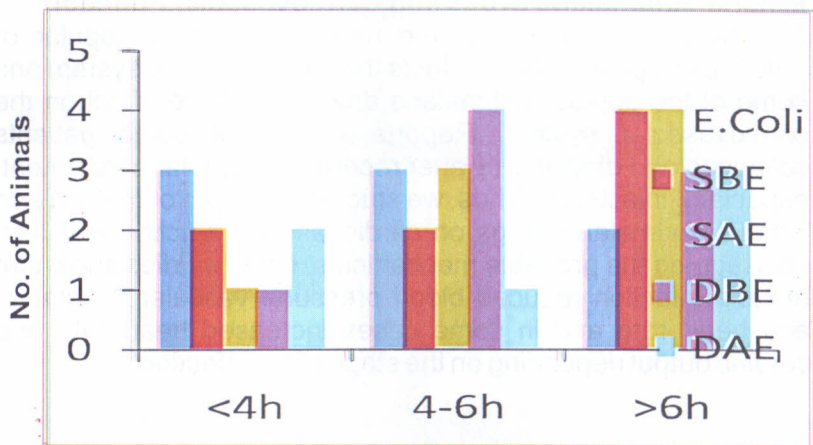


Figure 8: Effect of Salbutamol and Dopamine on Survival Period During E.coli Shock

We also investigated the effect of reserpinisation on the cardiovascular function during tetanus because tetanus toxicity was rampant in our filthy environment so we looked at the effect of reserpine on cardiovascular changes during tetanus toxicity. We found out that sympathetic overactivity resulted in raised plasma catecholamine, hypertension, and increased cardiac output and increased cardiac contractility. Reserpine depletes catecholamines thus, reducing the sympathetic overactivity. It was found also that reserpine may be useful in managing patients with symptoms of sympathetic overactivity (Sofola et al., 1981).

Table 2: Effects of Reserpinisation on BP and HR Responses to Tetanus Toxin

	NON-RESERPINISED RATS				RESERPINISED RATS			
	BP (mmHg)		HR (Beats/min)		BP (mmHg)		HR (Beats/min)	
	Control	Tetanus	Control	Tetanus	Control	Tetanus	Control	Tetanus
N/Group	111	143	332	393	106	108	306	305
SEM	33	77	77	100	33	44	100	144
pp	<0.0005		N/S		N/S		N/S	

Malaria, Antimalaria Drugs and Cardiovascular Function

Malaria which probably is the most common or popular or notorious tropical disease affects the cardiovascular system and some of the popular antimalaria drugs also have effect on the cardiovascular system. Reports show that some patients collapsed and died shortly after receiving antimalaria treatment, especially, injections. Thus, we studied the effect of malaria and various antimalaria drugs on cardiovascular function and also investigated the probable mechanisms. Other studies show that malaria infection reduced blood pressure, vascular resistance and heart rate and in some cases increased heart rate and cardiac output depending on the stage of the infection.

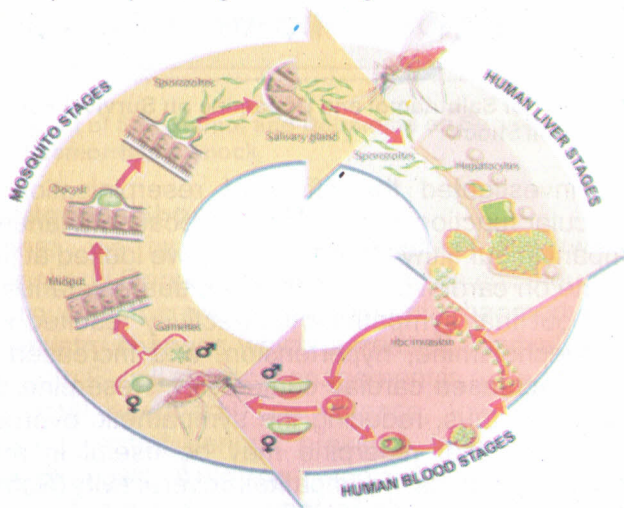


Figure 9: Malaria Parasite Lifecycle

In tests with dibenamine, bretylium tosylate and propranolol, malaria reduced the hypotensive effect of the alpha blocker and caused greater fall in blood pressure during sympathetic blockade. Malaria also potentiated the pressor effect of angiotensin II while the blockade of Rennin-angiotensin-aldosterone System (RAAS) with captopril, reduced the blood pressure in infected rats. These results suggest that sympathetic activation and activation of RAAS occur in malaria and may be part of a reflex response to the hypotension observed in malaria (**Anigbogu** and Adigun, 1996).

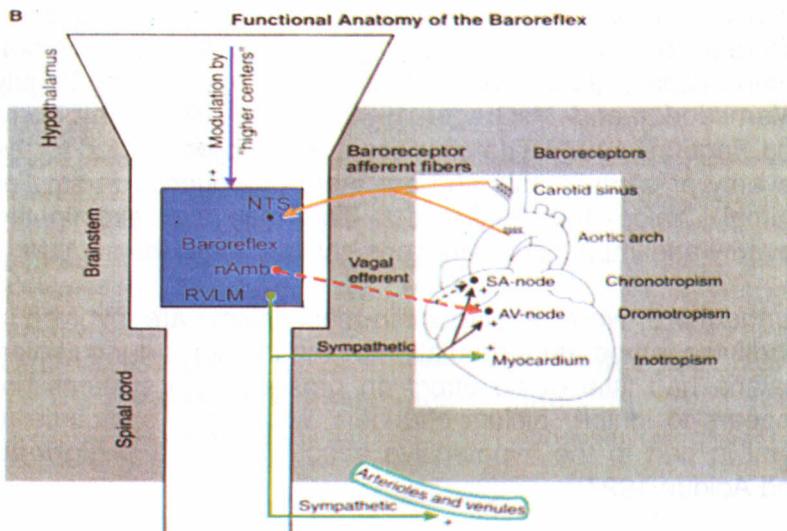


Figure 10: Schematic Diagram Showing the Autonomic Connections that Mediate the Baroreceptor Reflexes that Regulate Cardiovascular Function

Tests of the autonomic reflexes show that there is sympathetic activation and/or vagal inhibition which could be a reflex response to observed hypotension. **Anigbogu** and Olubowale (2002) showed that the rate of recovery and cardiovascular response to change in posture were reduced pointing to impairment of myocardial and neural mechanisms.

In man, our studies show that malaria lowered systolic, diastolic and mean blood pressures, which appeared a bit more pronounced in male subjects. It increased heart rate and decreased heart period (R-R intervals). Malaria also lowered the amplitude of QRS complex and T waves of the electrocardiogram (ECG) indicating changes in the ventricular depolarisation and repolarisation, thus, it is recommended that monitoring cardiovascular parameters will be beneficial especially in severe and complicated malaria (**Anigbogu** and Lawal 2000; **Anigbogu** and Olubowale 2002).

Malaria causes different pathophysiological changes in different organs, e.g. Splenomegaly, anaemia, cerebral complications, acute renal insufficiency and hepatomegaly (Wernsdorfer and McGregor 1988, Turner 1997, **Anigbogu** and Fagbure 1997). The changes appear to be related to the severity of parasitaemia and are more pronounced in smaller animal - mice than in the rats. This may also explain the severity and impact on infants and children more than adults.

Furthermore, while prostaglandin mechanisms are involved in modifying temperature regulation by the thalamus during fever, malaria had little or no effect on prostaglandin systems but appears to inhibit calcium channels, which may contribute at least in part to the hypotensive effect of malaria (**Anigbogu** and Adigun 1997).

Effects of Antimalaria Drugs

Chloroquine

Earlier reports show that most effective antimalaria drugs like quinine were toxic or had many toxic side effects like tinnitus, deafness, blindness and severe itching – urticaria. These medications were developed and manufactured in the western world with largely temperate climates, which did not have endemic malaria and only used them sparingly or for short periods, thus, they were focused largely on chemotherapy.

We decided to investigate the effects of these drugs on physiologic functions especially as we are unfortunately going to be exposed to and using some of these drugs for longer periods or for a lifetime. Chloroquine had been known to reduce blood pressure, heart rate and alter ECG (Sofola 1980, **Anigbogu** and Adigun, 1987) it also had a dual effect on isolated cardiac, vascular and gastrointestinal tissues (Ikhinmwin et al., 1981, Ebeigbe and Aloamaka, 1982, **Anigbogu**, 1987).

Chloroquine, a 4-aminoquinoline had replaced quinine as the drug of choice for treatment of malaria in the early 60s and

70s. While reports of alteration of cardiovascular function were made and occasional deaths reported, not much was reported about the mechanisms involved. Our studies show that chloroquine reduced blood pressure and increased Forearm Blood Flow (FBF) and had no effect on resting forearm vascular resistance. However, when the system was challenged by cold immersion, chloroquine reduced the increase in forearm vascular resistance, but had little effect on BF and FBF (Anigbogu et al., 1993).

Table 3: Effects of Chloroquine on Increases in Forearm Vascular Resistance Induced by Cold Stimulation

Δ forearm vascular resistance (arb. units)								
	During cold immersion				Recovery after cold immersion			
	30s	60s	90s	120s	30s	60s	90s	120s
Before chloroquine (BCQ)	8.3 ± 3.9	7.8 ± 2.2	6.3 ± 3.5	7.5 ± 4.5	3.8 ± 1.5	6.1 ± 3.7	30. ± 1.2	1.9 ± 0.81
One hour after chloroquine (CQ ₁)	3.9 ± 2.8	3.4 ± 1.1	2.0 ± 1.5	4.0 ± 5.3	1.7 ± 1.8	1.0 ± 1.9	-0.3 ± 0.9	1.2 ± 1.4
BCC cf CQ ₁	*	†	†		*	†	†	
Two hours after chloroquine (CQ ₂)	4.1 ± 2.4	5.1 ± 1.5	5.0 ± 0.4	2.0 ± 0.6	0.8 ± 0.4	1.7 ± 1.0	0.1 ± 0.2	1.1 ± 1.4
BCC cf CQ ₂	*	*		†	‡	†	†	
Three hours after BCQ cf CQ ₃	7.0 ± 2.3	8.0 ± 3.1	5.2 ± 1.5	4.4 ± 2.7	1.3 ± 0.7	2.2 ± 0.4	0.9 ± 0.2	1.2 ± 1.1
Twenty-four hours after chloroquine (CQ ₂₄)	8.2 ± 1.2	5.6 ± 1.6	4.7 ± 3.7	5.7 ± 0.9	5.4 ± 1.7	4.2 ± 0.7	1.8 ± 0.3	0.6 ± 0.9
BCQ cf CQ ₂₄								*

BCQ cf CQ₁, CQ₂, CQ₃ or CQ₂₄. **P*<0.05, †*P*<0.01, and ‡*P*<0.001.



Figure 11: An Original Plethysmographic Recording of Forearm Blood Flow (a) before Chloroquine Intake and (b) after Chloroquine Intake

Mr. Vice-Chancellor, Sir, this was the first reported demonstration of this phenomenon which may go to explain the orthostatic intolerance sometimes experienced during chloroquine therapy, when the subject feels dizzy upon standing or exertion because the vascular constriction and increase in vascular resistance which help to shore up blood pressure has been blunted such that the subject may collapse, as blood supply to the brain which is high above the heart may be inadequate. This may be further compounded in a malaria patient with fever where peripheral vasodilatation is already high due to temperature and heat dissipation.

Other studies we carried out showed that chloroquine had a dual effect on the contractility of the rabbit ileum. While the very low doses increased contractility; the normal and high doses reduced contractility. Atropine did not affect the response to chloroquine neither did chloroquine block the response to acetylcholine showing that the effect may not depend on neural mechanisms but may be direct. This may account for why some people feel constipated while others report diarrhoea following a course of chloroquine.

A relation once found out that each time he took chloroquine he was relieved of discomfort due to haemorrhoids, so he formed the habit of taking chloroquine, unfortunately over the years he lost his sight, due to chloroquine induced retinopathy, an oversight of a known side effect of chloroquine.

In the regulation of blood pressure four major mechanisms are involved, namely: neural, hormonal, renal and capillary fluid shift mechanisms. In order to have further insight into the activities of these antimalaria drugs their effects on renal function were studied. Using metabolic cages, we investigated the effect of chloroquine on renal function and we found that chloroquine increased urinary sodium excretion, creatinine clearance and pH but when administered for longer periods, it reduced creatinine clearance, thus showing that chloroquine affects glomerular and tubular functions of the kidney.

Mefloquine

Mefloquine, another anti-malaria drug that showed a lot of promise was investigated. The 4-quinoline methanol derivative was effective against chloroquine resistant malaria but was soon abandoned because parasite resistance to it developed so quickly. Mefloquine depressed cardiovascular function by reducing systolic and diastolic blood pressures in a dose dependent manner. This effect was not blocked by atropine showing that it is not mediated by cholinergic autonomic system (**Anigbogu**, Coker and Obaseki, 1990).

Mefloquine also increased urine output, sodium excretion, pH and ammonia estimation. Thus, suggesting that Mefloquine exerts effect on tubular function. The variable effect on creatinine clearance also shows that Mefloquine also affected glomerular filtration (**Anigbogu** and Nnagbogu, 1999).

Artemether and the Quinghaosu Derivatives

Just as parasite resistance to chloroquine and Mefloquine reared its ugly head, recourse was made to the old Chinese herbal remedy Quinghaosu (*Artemisia annua*) from which artemisinin was extracted. It was characterised and many new congeners were developed and tested. Artemether was found to be very effective and was increasingly being used. The derivatives were thought to be safe being of plant origin so we investigated the effects of Artemether on cardiovascular, renal and metabolic functions. Artemether, we discovered had little or no effect on resting blood pressure and heart rate but when the baroreflex was challenged by bilateral carotid occlusion (BCO) the maximal change in blood pressure and heart rate was reduced. This suggests that Artemether may interfere with ability of cardiovascular system to respond to challenges (**Anigbogu** and Osunmakinde, 1999).

Our studies showed further that Artemether increased urine output, pH, and creatinine clearance. It also reduced titratable acidity. This shows that Artemether affects glomerular filtration and tubular function (**Anigbogu** and Adebote 1999). When it was realised that parasite development of resistance was

easier to single drug usage than to combinations; the idea of multidrug or combination therapy was advocated. Before the idea became the norm we went further to investigate the effects of various combinations on cardiovascular and other functions. Thus, we compared the effect of Artemether and Mefloquine-sulphadoxine-pyrimethamine (MSP) combination on cardiovascular function and electrolyte metabolism. MSP we discovered caused a fall in blood pressure and heart rate. Plasma sodium and potassium concentrations were elevated in the treated rats. However, it was discovered that the two groups had no appreciable effect on baroreflex sensitivity (**Anigbogu** and Onwuchekwa 2000).

Herbal and Traditional Antimalaria Preparations

Realising the increasing and pervasive use of traditional herbal preparations in the treatment of malaria and other ailments with little or no knowledge of the background effects of these herbs; we decided to investigate their effects on cardiovascular and other body functions. We found that *Ocimum gratissimum* (Nchuanwu, Efirin) increased cardiovascular function and urinary electrolyte reabsorption and reduced glomerular filtration rate (GFR). This suggests activation of sympathetic and rennin-angiotensin-aldosterone mechanisms. This increase in packed cell volume may indicate an increase in haematopoiesis probably due to activity of renal erythropoietic factor (**Anigbogu** and Uzoaga 2006).

The cardiovascular system in conjunction with intra-renal regulatory mechanisms ensures maintenance of a hydrostatic pressure gradient that provides the driving force for ultra filtration of blood in the kidney. This fundamental process contributes to the capacity of the kidney to perform excretory, regulatory, endocrine and metabolic functions.

An American based Nigerian professor was coming home with his American born daughters for the first time; all of them took prophylactic antimalaria except the Professor himself who believed he had immunity. Shortly after his return he fell seriously sick and being winter he thought it was the cold weather and was quarantined for two weeks.

In another report, a young pregnant Nigerian wife who had joined her US based husband fell ill and they carried out extensive and expensive tests. The husband who had no health insurance was paying out of pocket but the doctor could not treat her definitively as no one was sure of what was wrong. Before any test results could be obtained and the cause of her ailment known - she died, but calling home earlier, she had hinted that she must be suffering from malaria.

There was another story of a Nigerian patient who was hospitalised and had to call someone to smuggle in some chloroquine for him and was healed.

At lectures in Atlanta and in Kentucky, I proposed the '3 cans treatment' in addition to prophylaxis. I advised the Nigerian-Americans to do the following when visiting Nigeria:

1. Spray the entire house with a good insecticide immediately on arrival.
2. Spray the second can outside the house, in the surrounding bushes, flowers, plants, especially, banana, plantain and cocoyam stands and drains.
3. Spray the third can 2-3 days later. It will be discovered that mosquitoes and various other insect pests will almost vanish in the environment for nearly two weeks. This appeared to have worked as I can testify that in my hometown we have not had any such deaths again to my knowledge.

Salt, Water, Kidney and Hypertension

Hypertension is a condition where the blood pressure of a person is continuously maintained above normal dependent on age. Hypertension is a major health problem worldwide and

appears to be more so among the blacks. My hypothesis is that blacks who are tropical dwellers live in the hot sun and sweat a lot so are geared towards losing more salt in sweat and less in kidney urine, while Caucasians living in the temperate and cold environment hardly sweat, therefore, are geared to lose more salt in the urine. Now that blacks have migrated into temperate lands and we here no longer work in the sun especially with air-conditioning thus creating a temperate environment, we also no longer sweat and our kidney cannot excrete salt as Caucasians do, so salt and water accumulates, pushing up blood pressure. These factors, with other lifestyle changes may be contributory.

In this study, we investigated the role of Nitric Oxide (NO) in salt and water excretion in hypertension. Using a blocker of NO called L-NAME showed that salt and water excretion were reduced when NO was reduced. Thus, reduced kidney function may contribute to development of hypertension. (Mojiminiyi et al, 2007)

The endothelium also plays an important role in the maintenance of blood pressure as we have shown that the endothelium which produces nitric oxide, a relaxant, when altered or damaged cannot play its role properly, thus, making blood vessels less compliant and may contribute to higher blood pressures.

High-salt Diet, Cardiovascular Function, Hypertension and Androgens

High-salt diet has been associated with development/induction of hypertension through various mechanisms which include impairment of vascular functions. The higher incidence of salt-sensitive hypertension in males is believed to be linked to androgens (male hormones) while oestrogens (female hormones) are thought to confer protection on females. In spite of data supporting the effects of testosterone and other androgens in various normal arterial beds, not much is known about the role that exogenous androgens may play in vascular

reactivity of these arterial beds in disease states like hypogonadism and hypertension.

Our investigation in castrated (orchidectomised) rats showed that relaxation response to testosterone and dehydroepiandrosterone (DHEA) in protracted (0.1µmol/L Noradrenaline) vascular tissue were reduced while testosterone replacement restored the acute vasorelaxant effect of testosterone and DHEA in normal and salt-fed rats thus confirming, that gonadal status is important in the acute vasorelaxant effect of androgens (Oloyo et al 2013).

Table 4: Testosterone and Hypertension in Rats

Testosterone and hypertension in rats

Initial, final, and percentage difference of the mean arterial blood pressure of the rats across the groups.

Groups (n = 6)	Initial MABP (mmHg)	Final MABP (mmHg)	% Difference
INT + NS	99.5 ± 2.43	112.2 ± 3.71	15.23 ± 0.78
INT + HS	100.3 ± 2.33	134.3 ± 4.28 ^{***}	28.57 ± 1.23 ^{***}
ORCH + NS	100.0 ± 1.68	106.0 ± 3.02 ^{***}	7.55 ± 0.65 ^{***}
ORCH + HS	100.3 ± 1.95	124.2 ± 2.96 ^{***}	19.08 ± 1.01 ^{***}
ORCH + TES + NS	100.5 ± 1.56	112.5 ± 2.85	10.67 ± 0.74
ORCH + TES + HS	101.0 ± 1.68	132.7 ± 3.52 ^{***}	23.71 ± 1.65 ^{***}
SHAM + NS	99.67 ± 1.84	116.1 ± 3.01	14.23 ± 0.81
SHAM + HS	101.7 ± 2.49	134.7 ± 3.52 ^{***}	28.3 ± 1.62 ^{***}

Keys: INT = intact, ORCH = orchidectomy, NS = normal salt, HS = high salt, TES = testosterone, SHAM = sham orchidectomy. Data are presented as means ± S.E.M (n = 6) ^{***}significant increase (P < 0.05) when compared with corresponding control, ^{**}significant decrease (P < 0.01), when compared with intact plus high salt group. ^{***}significant decrease (P < 0.001) when compared with control.

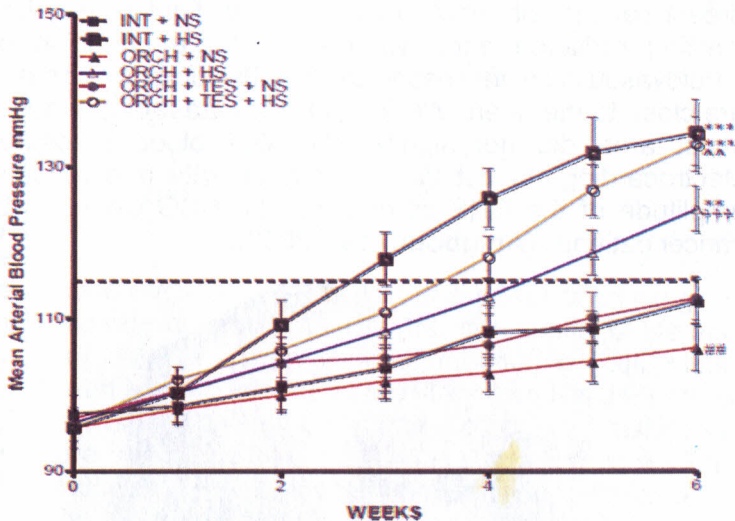


Figure 13: Mean arterial blood pressure of intact and sham-orchidectomised Sprague-Dawley rats fed a normal or high salt diet. ORCH = orchidectomy, NS = normal salt, HS = high salt, TES = testosterone. Data are presented as means \pm SEM (n = 6). ^^Significantly high (**P < 0.01, ***P < 0.001) when compared with Control. ^^Significantly high (**P < 0.01) when compared with orchidectomy plus high salt diet group. ##significantly less (P < 0.01) when compared with control plus testosterone replacement plus normal salt diet group. ***significantly less (P < 0.001) when compared with intact plus high salt group.

Changes in shear stress and geometric modifications of the blood vessels are also some of the pathways by which salt loading induces hypertension. Our studies show that high salt diet induced changes in histology of blood vessels and were ameliorated by orchidectomy via reduction in vascular smooth muscle proliferation and extracellular matrix protein deposition. Concomitant administration of testosterone it shows restored the increase in thickness of vessels (Oloyo et al 2013).

Cardiovascular Function, Breast Cancer and Radiotherapy

With increasing involvement of radiation and radiotherapy in the treatment and management of various conditions including

breast cancer and lung cancer, we investigated the effects of ionizing radiation and, we looked at the condition of the cardiovascular system especially as these organs and structures are close to the heart. We found that acute radiotherapy to the chest area did not significantly alter blood pressure and electrocardiogram but increased heart rate and reduced the amplitude of the QRS complex of the ECG waves in breast cancer patients, (Anigbogu et al., 2008).

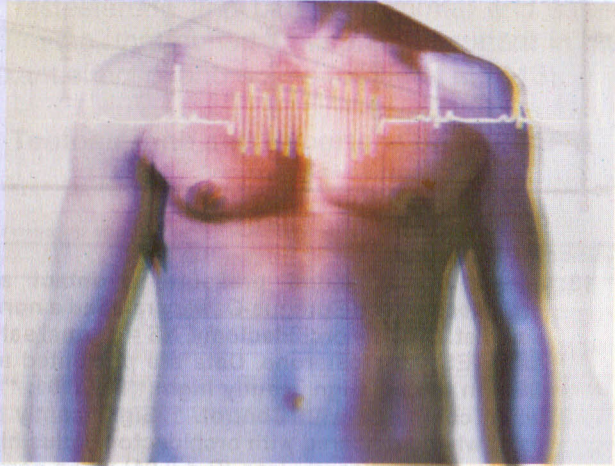


Figure 14: The Human Chest with Superimposed ECG Waves

Cardiovascular Rehabilitation and Exercise Physiology

Most countries in Africa have limited rehabilitation resources, so rehabilitation services often cease a few months after stroke and other incidents. It was therefore found necessary to evaluate different rehabilitation techniques and identify those that are available, safe and affordable which have a greater effect on locomotion recovery and aerobic abilities of the subjects.

Patients with stroke were put on controlled exercise training for 12 weeks and it was found that both Treadmill Walking Exercise Training (TWET) and Over ground Walking Exercise Training (OWET), produced significant improvement in walking function, however, OWET resulted in greater reduction in mean walking time (26.8%), over 10 metres than TWET and increased mean walking distance over 6 minutes than TWET.

Thus, these methods can be integrated into the traditional rehabilitation care given to adult patients with stroke, (Olawale, et al, 2011) since overground walking does not require any special equipment.

In Chronic Heart Failure (CHF) the hallmark symptoms are breathlessness and fatigue which impact negatively on the quality of life and capacities for Activities of Daily Living (ADLs). It was decided that subjects should be trained in combined aerobic and resistance exercise, to evaluate the effect of training on functional walking capacity, muscle strength, quality of life and activity level. All the same we kept monitoring their blood pressure, heart rate, six-minute walk distance and its derived six minute walk work. It was concluded that aerobic and resistance exercises are safe and have the potential to improve walking capacity, muscle strength, quality of life and activity level (Ajiboye et al., 2013).

We have also developed paradigms and prediction equations for 6-minute walk distance specifically for the Nigerian and tropical environment. These equations have been shown to have a higher fidelity than regression equations established for Caucasian populations who may have different physiognomy and anthropometric parameters (Ajiboye et al., 2014).

Table 5: Comparison of Measured Distance in Nigerian participants with Predicted Distance from Foreign Regression Equations

Participants	6MWD in this study, mean ± SD	6MWD (m) Predicted from foreign equations, mean ± SD	6MWDmean difference (m)	t value	p
Combined participants (m) n = 422	5,17.6 ± 72.0 (364-741 m)	647.3 ± 91.0 ^a 648.2 ± 90.4 ^b 616.6 ± 23.1 ^c 830.4 ± 84.2 ^d 472.3 ± 21.1 ^e	-129.7 ± 88.9 -130.6 ± 90.1 -99.0 ± 67.0 - 312.8 ± 82.6 - 45.3 ± 62.7	-29.9 -29.9 -30.3 77.6 -6.6	<0.001* <0.001* <0.001* <0.001* <0.001*
Male participants n = 224	548.9 ± 67.9 (403-741 m)	658.4 ± 82.2 ^a 655.8 ± 79.5 ^b 617.1 ± 23.1 ^c 844.1 ± 75.5 ^d 483.3 ± 18.8 ^e	- 109.5 ± 83.8 - 106.9 ± 85.4 - 68.2 ± 62.1 - 295.2 ± 79.1 - 65.6 ± 61.6	-18.5 -16.4 -55.6 -8.2 1.6	<0.001* <0.001* <0.001* <0.001* <0.016*
Female participants n = 198	482.5 ± 59.9 (364-608 m)	582.4 ± 91.5 ^a 641.0 ± 99.4 ^b 554.6 ± 24.3 ^c 625.5 ± 84.0 ^d 459.6 ± 15.7 ^e	- 99.9 ± 82.3 - 158.5 ± 89.7 - 72.1 ± 54.4 - 143.0 ± 81.4 23.3 ± 57.8	-15.5 -24.9 -19.7 - 21.4 -1.0	<0.001* <0.001* <0.001* <0.001* 0.118

**p* < 0.0001.
^{a, b} Enright and Sherrill (1998) [25].
^c Iwana et al 92009) [26].
^d Ben Saad et al (2009) [27].
^e Alameri et al (2009) [28].

Table 6: Stepwise Multiple Regression Equation to predict 6MWD in a Nigerian Population

$$6MWD_{combined} = [419.834 \times Height_{(m)}] - [1.021 \times Age_{(years)}] - [1.031 \times Weight_{(kg)}] - 79.023$$

$$(SEE = 58.050, R = 0.550) \tag{1}$$

$$6MWD_{male} = [153.142 \times Height_{(m)}] - [1.595 \times Age_{(years)}] + 336.585$$

$$(SEE = 61.713, R = 0.367) \tag{2}$$

$$6MWD_{Female} = 1253.862 - [406.447 \times Height(m)] - [1.010 \times Age_{(years)}] - [7.890 \times Weight_{(kg)}] - (23.551 \times BMI)$$

$$(SEE = 50.856, R = 0.542) \tag{3}$$

Mr. Vice-Chancellor, Sir, the presentation of this study won the award for the Best Presentation from Africa at the recently concluded World Congress of Physical Therapists in Singapore.

Sickle Cell Anaemia and Cardiovascular Function

In our focus on relevant and applied research, we have studied cardiovascular function and nitric oxide (NO) activity in sickle cell subjects because NO in the endothelium is a vasodilator and plays a role in the patency and vasomotion which with the sickled cells contributes to the pain of sickle crisis. It was found that low dose, chronic oral supplementation with l-arginine increased the NO availability and attenuated pressor and heart rate responses to change in posture. This attenuation is thought to be an improvement and thus a protective cardiovascular response to change in posture especially to sickle cell sufferers who possess abnormal autonomic cardiovascular function.

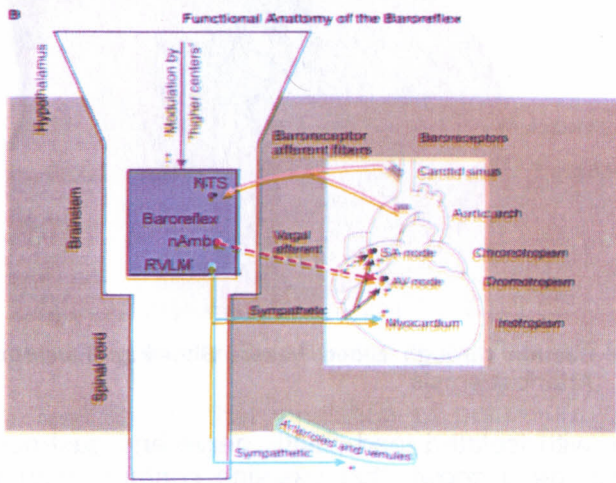


Figure15: Schematic Diagram Showing the Central Autonomic and Cardiovascular Systems Mediating Baroreflex Functions

Petroleum Contamination, Neuromuscular, Autonomic and Cardiovascular Functions

Petroleum, its products and derivatives have become part and parcel of our lives, economically, politically, socially, culturally and invariably medically. Petroleum products are being

increasingly used among the populace and thus environmental contamination is on the increase. This may be due to oil exploration, exploitation, distribution and even criminal vandalisation. Thus, there is increased contact and exposure to these products. Indiscriminate use and abuse of petrol is not limited to mechanics that suck it with their mouth and wash hands and legs with it, it also extends to those who use it as solvents, sniff it for 'pleasure,' or use it as insect repellent. Some people find it in their drinking water not to talk of bioaccumulation from soil and marine animals and the food chain. We have therefore investigated various aspects of the effects of various petroleum fractions on bodily functions.

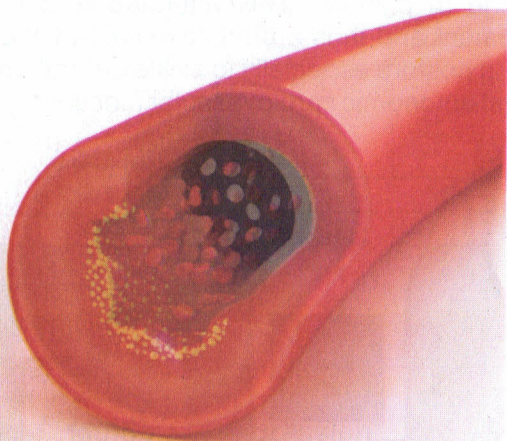


Figure 16: Section through Blood Vessel Showing Development of Arteriosclerosis

In studies with isolated toad sciatic nerve and gastrocnemius muscle, we have shown that gasoline contamination altered contractility, lower concentrations of petrol increased motor activity, with little or no effect on threshold or maximal voltages absolute refractory and relaxation period. Higher concentrations were also found to reduce activity and at 4% all neuromuscular activity ceased. Histology revealed tissue damage, disruption of membranes, infiltration and tissue oedema. This confirms the toxic effect of petrol on neuromuscular structure and function (Anigbogu, Idowu and Anunobi 2011).

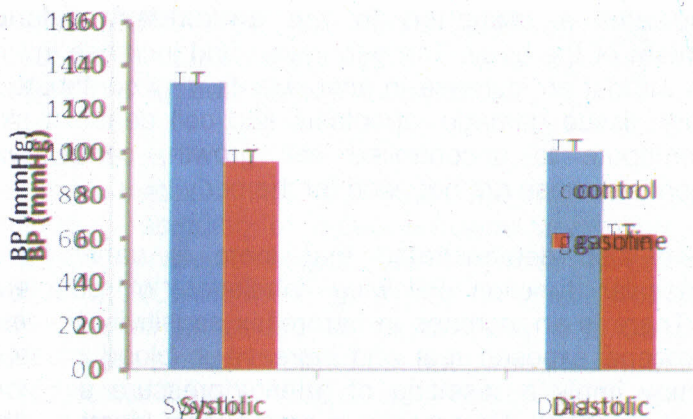


Figure 17: Comparison of Blood Pressures in Control and Gasoline Treated Rats * $p < 0.05$

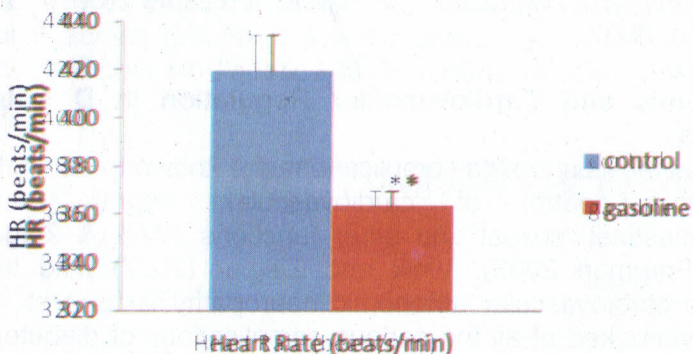


Figure 18: Heart Rate in Control and Gasoline Treated Rats * $p < 0.05$

We have also shown that inhalation of petroleum products resulted in variability of cardiovascular functions especially resetting of baroreflex sensitivity and arterial pressures (Azeez et al., 2012). In studies with petrol, diesel and kerosene we found that lipid peroxidation was increased with rise in malondialdehyde (MDA) and decrease in superoxide dismutase (SOD) and catalase (CAT) activities and glutathione (GSH) levels. Thus indicating pulmonary dysfunction associated with oxidative stress (Azeez et al., 2012b) and similarly renal dysfunction in the kidney with rise in serum urea and creatinine and fall in urinary values (Azeez et al., 2013).

This indicates a **reduction in the antioxidant defence mechanism** of the body. The generation and increase in free radicals without an increase in antioxidants may contribute to cell injury, tissue damage, apoptosis and cell death. It may also contribute to uncontrolled cell growth, cancer and tumorigenesis; these are not good for the body.

We have also demonstrated that there is variability of cardiovascular function following inhalation of petroleum fumes. There is an increase in baroreflex sensitivity in diesel and kerosene exposed rats and increase in blood pressure which may imply a resetting of arterial pressure set point (Azeez et al., 2012). Baroreceptors are sensors located within the vascular compartment which act as part of the cardiovascular baroreflex negative feedback mechanisms in the short term regulation of blood pressure (Levy and Pappano, 2007).

Autonomic and Cardiovascular Regulation in Diabetes Mellitus

Diabetes mellitus and its complications are known to affect the autonomic control of cardiovascular, neural, renal, gastrointestinal, sexual and other functions (Vinik & Ziegler 2007, Freeman 2005). Vinik and Ziegler (2007) said that diabetic cardiovascular autonomic neuropathy is “one of the most overlooked of all the serious complications of diabetes.” Diabetes mellitus is one of the diseases that are on the increase in both developed and developing populations of the world. The disease may damage small and large fibres of both the sympathetic and parasympathetic nervous system.

In a study over nine years ago, Gerritsen et al., in 2001, showed that individuals with diabetes and low autonomic function had approximately doubled risk of mortality and hypertension which was common in diabetic patients (Czupryniak et al., 2006). Because it is difficult to demonstrate from observations in human any causal relationships between diabetes and associated cardiovascular co-morbidities, we have used a newly developed experimental rat model of

diabetes, (BBDP/Wor rat) which develops spontaneous diabetes without injection of alloxan or streptozotocin to kill the insulin-secreting beta cells of the pancreas.

Procedure

We anaesthetised the rats and instrumented them for continuous recording of blood pressure and heart rate in conscious, unanaesthetised rats for over 6months. The diabetic rats (DIAB) were maintained on insulin from the day blood glucose exceeded 250mg/dl ("Day 0"). Control rats (CONT) were similarly treated but not given insulin. Monitoring started before Day 0. Weights were similar in the two groups until about 3 weeks before Day 0 when weight in diabetic rats lagged behind the controls; this difference persisted throughout the study. Plasma glucose reached up to 371+109 mg/dl by day 1 in diabetic rats. Mean blood pressure was similar across groups in 4 – 6 months. Heart rate in control exceeded that of diabetics (341+13bpm vs 325+_25bpm) at day 1.

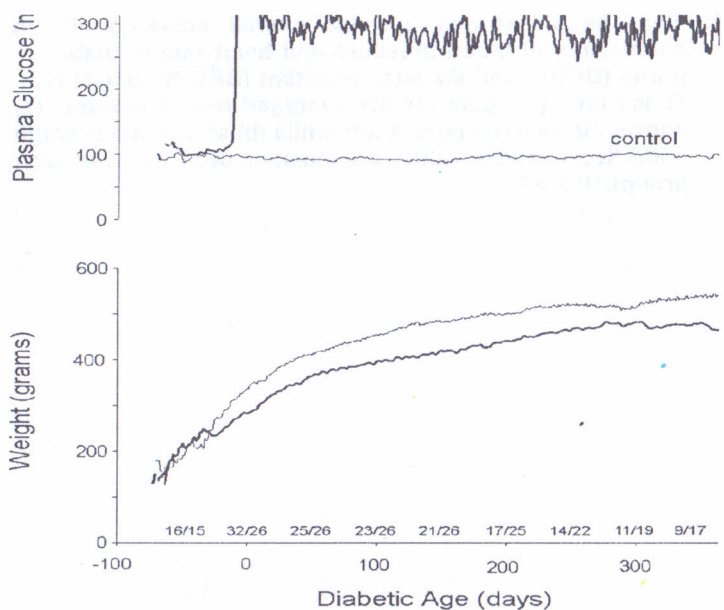


Figure 19 & 20: Diabetes Duration (days)

Plasma glucose measured in the morning for control (thin line) and diabetic rats (thick line). The numbers immediately above the abscissa scale give the number of diabetic animals/number of control at 50 day intervals, excepting the pre-conversion data are for 40 days before conversion. Starting on day 0, which designates the onset of diabetes (blood glucose >250 mg/dl), insulin was administered to diabetic rats after blood glucose measurement; glucose value given here, therefore, is at or near daily peak value (top panel). Body weight of diabetic and resistant rats. Measurements commenced one week after receipt from vendor. Note between-group divergence in weights prior to conversion which was sustained over ensuing – year (bottom panel.)

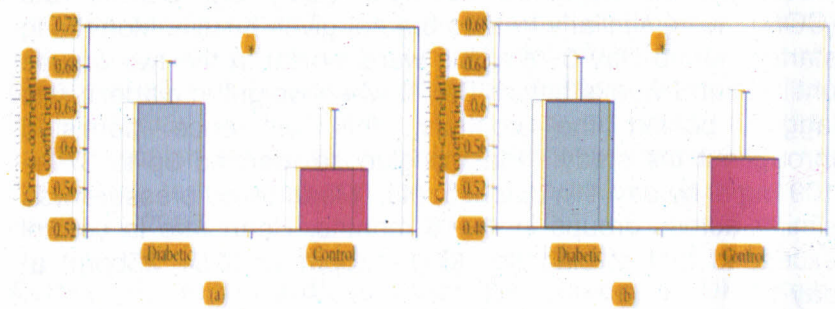


Figure 21: Bar charts showing average overall cross-correlation coefficients of blood pressure and heart rate in diabetes-prone (BBDP) and diabetes-resistant (BBDR) control rats. These are aggregate results averaged over 9 months. (a) shows the average peak Xcorr while (b) shows the average nadir Xcorr values. Values are means \pm SEM. (n = 8 in each group). *P < .05.

Table 7: Baseline Pressure and Heart Rate (\pm SD) at Designated Times Pre- and post-Conversion for Diabetic and Age-matched Control Rats

	<i>Control</i>		<i>Diabetic</i>	
	<i>mBP</i>	<i>HR</i>	<i>mBP</i>	<i>HR</i>
	(mm Hg)	(bpm)	(mm Hg)	(bpm)
	<u>Cadre1</u>			
Mo 1	120 \pm 8	383 \pm 15	114 \pm 12	382 \pm 41
Mo 2	123 \pm 9	382 \pm 12*	117 \pm 9	339 \pm 28
Mo 3	118 \pm 12	373 \pm 15	114 \pm 6	334 \pm 28
	<u>Cadre 2</u>			
Mo 4	119 \pm 9	368 \pm 32	112 \pm 8	353 \pm 31
Mo 5	115 \pm 11	383 \pm 27	111 \pm 13	356 \pm 30
Mo 6	114 \pm 16	399 \pm 18*	108 \pm 8	352 \pm 28
Mo 7	112 \pm 13	385 \pm 22*	110 \pm 10	354 \pm 27
Mo 8	112 \pm 6	368 \pm 22	109 \pm 8	349 \pm 20
Mo 9	111 \pm 9	380 \pm 21*	105 \pm 4	330 \pm 44
	<u>Cadre 3</u>			
Mo 10	112 \pm 10	395 \pm 26*	104 \pm 8	334 \pm 20
Mo 11	105 \pm 9	372 \pm 36	106 \pm 3	328 \pm 32
Mo 12	103 \pm 14	354 \pm 27	100 \pm 7	338 \pm 35

* = p < 0.05, diabetic vs. control HR

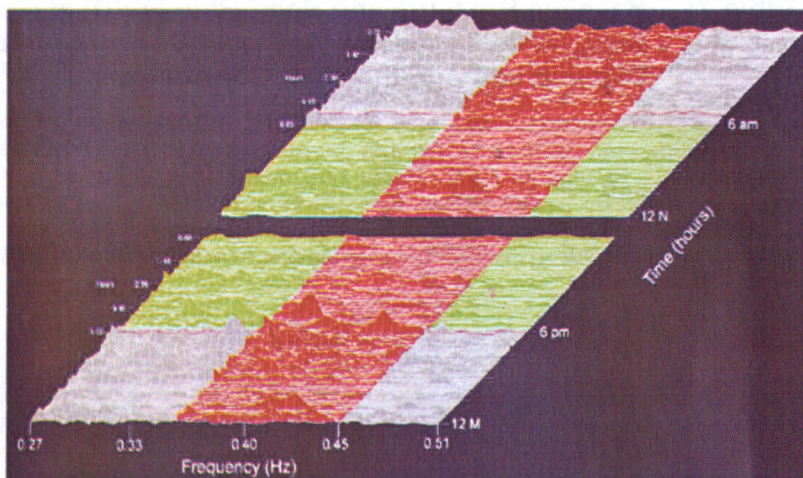


Figure 22: Panel A – Mean Arterial Blood Pressure Power Spectra

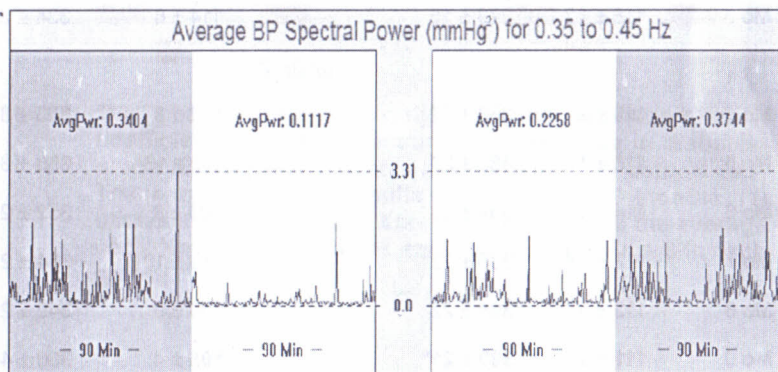


Figure 23: Panel B – Average BP Spectral Power

Panel A. Mean arterial blood pressure power spectra centred upon 0.4 Hz (i.e., red tone, extending from 0.35 to 0.45 Hz) for a single 24 hour day for a single control rat during the Month 1. Successive, juxtapositioned spectra, each computed from 248 second long intervals, were chained to yield this 24 hour plot. The earliest spectrum starts at midnight (rear-most' portion of plot in back panel); individual spectra extend progressively forward to noon (N; bordering on the blue area in middle). The front panel extends from noon to last panel at (next) midnight (M). Dark period is shown in gray shading, while lights-on period is given in green. In this animal spectral power decreased noticeably as soon as the lights turn on 6 a.m., though there were individual spectra showing transient increases in 0.4 Hz power.

'anticipation' of lights-on, and was clearly increased during the first 90 min of dark. Panel B. Left half: average spectral power from 0.35-0.45 Hz in a rat over last 90 min of dark (gray shading, left-most panel) immediately prior to lights-on (i.e., at '6 a.m.'). and for first 90 min after lights were turned on (left-most non-shaded panel). Right half: Average spectral power during final 90 min of lights-on (non-shaded panel) immediately prior to lights-off (i.e., at '6 p.m.'). and during first 90 min of dark (right-most shaded panel). The individual spectra were computed from a 51 second long interval such that the power shown in the plot 'marches' from left towards right at successive 51 s intervals. Numerical values in each panel are average power over the respective 90 minute intervals. Spectral power centred on 0.4 Hz was dynamic: higher during periods of dark than periods of light. Power appears to increase prior to lights-out, perhaps as rats 'anticipate' the coming 'night'.

We carried out power spectral analysis of the moment to moment changes in blood pressure. The BP power within the 0.35- 0.45 Hz changed 90 minutes before vs 90 minutes after transition from dark to light and light to dark but there was no difference between groups in the 6 months. The slope of the log-log linear portion of the BP power spectrum was similar across groups and increased with similar profiles thus showing that the regulatory mechanisms maintain similar activities at least in the first six months on insulin treatment. In similar experiments when diabetes was left untreated the patterns changed and animals died within a few weeks (Anigbogu et al., 2012).

The diabetic rats showed cardiovascular instability as indicated by high heart rate variability.

Cardiovascular Reflexes in Hypertension

Our studies have shown that among Nigerian subjects, hypertension results in the alteration of electrocardiographic waves and cardiovascular reflexes. In the tests with change in posture from supine to standing, it showed that there was a reduction in the blood pressure and heart rate response to change in posture (Anigbogu, Isichei and Ajuluchukwu 2012).

MAP in Control and Hypertensive

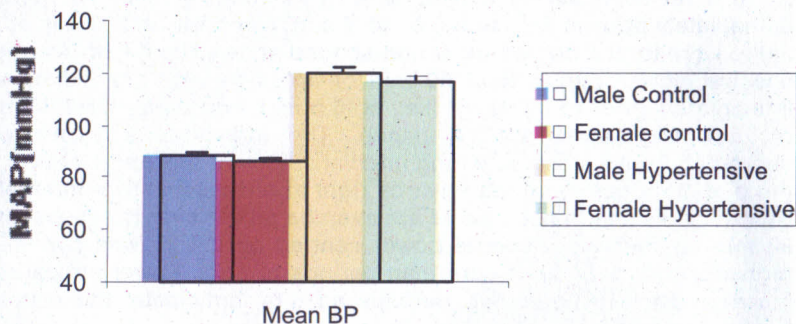


Figure 24: Mean Arterial Blood Pressure (MAP) in Control and Hypertensive Subjects. Values are Means \pm SEM

HR in Control & Hypertension

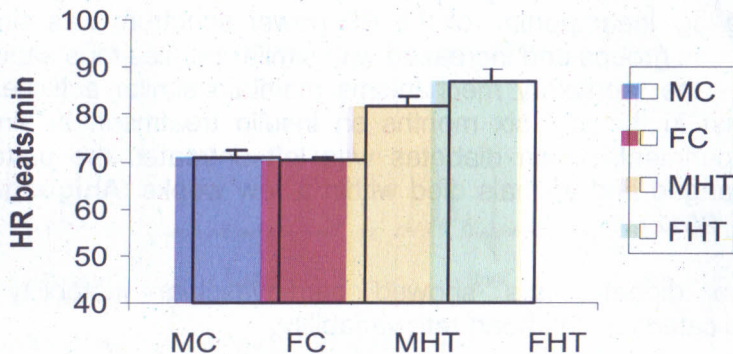


Figure 25: Bar Chart Showing Heart Rate Obtained from Control and High Blood Pressure Subjects

Key

MC = Male Control

FC = Female Control

MHT = Male Hypertensive

FHT = Female Hypertensive

Resting BP in Hypertensive Subjects

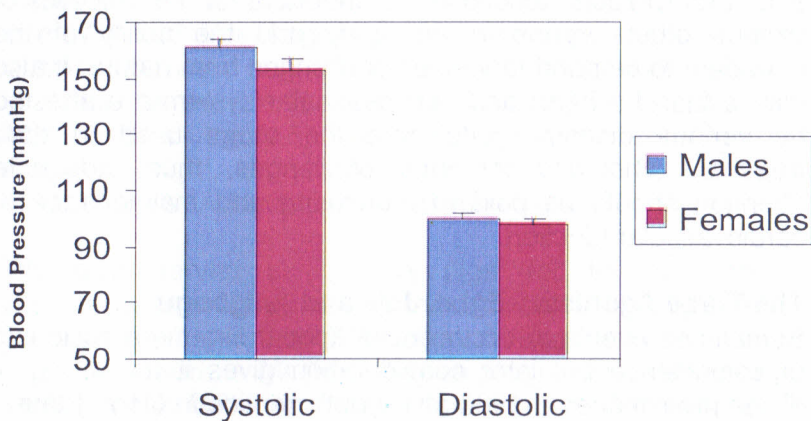


Figure 26: Resting Blood Pressure in Hypertensive Subjects. Values are means \pm SEM

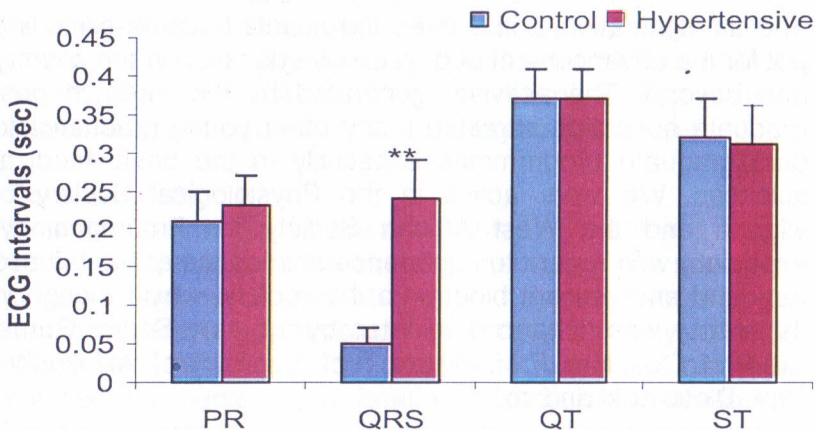


Figure 27: ECG Intervals and Duration in Control and Hypertensive Subjects. Values are means \pm SEM

Mr. Vice-Chancellor, Sir, these studies have shown that heart and cardiovascular functions are important for the functions of various other organs in the body and the ability of the individual to respond to various challenges from nature. It also shows that the heart and cardiovascular system are affected by various disease conditions; the drugs used in their treatment and environmental challenges, thus, adequate attention should be paid to monitoring and maintenance of cardiovascular function.

The Three Agonists - Egbe, Jaja and Anigbogu

Sometimes events or occurrences appear like mere accidents or coincidence but later consideration gives it an inkling of divine providence. In 1980 after youth service in Ondo State, I arrived Lagos for commencement of an M.Sc. programme in Physiology at the College of Medicine, University of Lagos. I later ran into two other young men; one had also come back from youth service, while the second, a Cameroonian 'Nigerian' had been in the department as a Graduate Assistant since he could not serve.

The amalgamation of the three individuals became a melting pot for the advancement of physiology education in the country and beyond. The activism generated by the three in post graduate education attracted many other young graduates to post graduate programmes especially in the basic medical sciences. We were active in the Physiological Society of Nigeria and the West African Society for Pharmacology, especially with regard to conference attendance as we infused new and effervescent blood into the society, which though in its infancy was hitherto dominated by the very Senior Gurus' like Prof. Dosekun, Prof. Amure, Prof. Ezeilo, Prof. Akinkugbe, Prof. Diete-Koki and co.

Our presence, participation and social activities livened up the formerly staid conferences and attracted more participants both young and old and also increased interest in the study of physiology either as adjunct to medical practice or as stand-alone applied and medical science. No conference was

complete without the Lagos group because as other delegates arrive at conference venues they will all inquire, 'Have they come? Who? The Lagos group of course, was always the answer. We were now trailed by a young group of graduates, who saw us as role models, mentors and vibrant scientists. Many of these today have come of age and become gurus in their own right, e. g., Mojiminiyi, Olatunji-Bello, Obiefuna, Onwuchekwa, Adegunloye, Nwachukwu et al.

We also served as 'guinea pigs' for the evolution of postgraduate programmes in the University of Lagos and in the advancement of the PG School. We started with research and coursework; a Masters Degree programme said to be the equivalent of MPhil which was open-ended. Our experiences and feedback led to the institution of a new curriculum with a clear-cut one to one and half calendar year (12 to 18 months) programme for the straight M.Sc. and other professional Masters degrees. This increased the attraction of many graduates to pursue postgraduate studies especially in Unilag, the University of First Choice and the nation's pride. I was nominated the leader of postgraduate students as we articulated our views with the authorities, then, led by Professor S.O.A. Bamgbose, Dean School of Basic Medical Sciences and Prof. A. Okusanya and Prof. F. Fajemirokun - erstwhile Deans of the School of Postgraduate Studies.

Contributions

Vice-Chancellor, Sir, I have contributed to medical education these past years through teaching, mentoring and supervising of all categories of students in the following programmes - medicine, dentistry, physiology, pharmacology, physiotherapy, med lab science, radiography, nursing, biomedical engineering, nurse tutors, health and physical education and residency programmes. I also have trained about 5000 medical doctors, 2000 dentists, 3000 pharmacists, 2500 physiotherapists, 2000 physiologists, pharmacologists, nurse tutors, radiographers, and others.

Mr. Vice-Chancellor Sir, I have continued to serve with zeal since I was first appointed and this year I was rewarded by the fact that my department recorded 24 Distinctions in the 2nd MB, 4 distinctions in BDS, 3 First Class in B.Sc. Physiology, 3 PhDs, Best Ph.D. Thesis in Medicine and Pharmacy, also, my Department was the first department to earn a 2nd Emeritus Professorship in the College and Pharmacy, after being the first in the University to earn that through Prof. Dosekun about 30 years ago. These, my Vice Chancellor are not mere coincidences but the product of hard work, perseverance, ingenuity and long-suffering, dedication to duty by the Faculty, staff and students of the Department of Physiology, who believe that they are the heart and lifeblood of a system which must not fail at all costs; (with a little help from our friends).

Mr. Vice-Chancellor, Sir, I have made modest contributions to the University and my country and the world of learning as a whole. As President of Lagos University Medical Society – LUMS by bringing together all academics and professionals in the College of Medicine and Lagos University Teaching Hospital, through the organisation of the highest number of international seminars in the history of the society.

I facilitated and processed for indexing in the Index Medicus and Pubmed - the Quarterly Journal of Hospital Medicine and ensured its unbroken and regular publication. Under my watch, we earned the first \$30 for hits at the AJOL listing. We have since reached up to \$200.

I also had earlier facilitated the indexing of the Nigerian Journal of Physiological Sciences during my IUPS fellowship in the University of Kentucky.

I facilitated 11 travel scholarships for Nigerian Physiologists to the 33rd IUPS Congress in San Diego, USA and 4 of these came to University of Lagos staff.

As Secretary and Treasurer of PSN and International Liaison, I sustained our membership affiliation and this has been unbroken even in the most difficult of times for nearly 25 years now.

Having contributed to training of over 10,000 doctors, dentists, pharmacists, physiologists, pharmacologists, physiotherapists, med lab scientists, nurses, radiographers, nurse-tutors and biomedical engineers who are some of the best in the world, as attested to by their ubiquity and spread, I cannot but rejoice. If each medical scientist earns about \$50, 000 annually as in the global index, then, gross earnings of about five hundred million dollars are generated by our products worldwide. Furthermore, the value of the human lives they have touched will definitely be unquantifiable.

Conclusion

Basic medical and clinical research findings and publications may not always be applicable to direct human use and patient care but will always contribute to the body of knowledge and shape developments in many areas and skills that ultimately impact the general wellbeing of people and sometimes foster breakthroughs that result in improvement of patient care, disease reduction, performance enhancement and disease prevention. Research findings also revolutionise the thinking about body functions, processes and activities leading to phenomenal changes in the way and manner the world is viewed.

Recommendations

1. I recommend that the monitoring of cardiovascular function be increased and taken seriously in health and disease as this will promote healthier life and also improve health care delivery because cardiovascular malfunction or failure is a major contributor to morbidity and mortality in most disease states.
2. The university should institute Marshall Plan in the physiological sciences because of the inadequate infrastructure and equipment. The Department of Physiology is servicing four faculties now as against one faculty for which it was established.
3. Recruitment and training of academic and technical manpower to redress the shortage of manpower in the subject area should be increased.

4. There is the need to establish a West African Faculty of Basic Medical Sciences. This will enable the West African Sub-region tackle the acute shortage of qualified manpower by pooling resources together, so that maximum and efficient deployment of available manpower will reduce the gap in service provision and skills acquisition in the resource challenged areas.
5. The basic medical sciences are often more time consuming, more stressful but less lucrative than the clinical sciences, this contributes to the continuous attrition and migration of manpower. Therefore, I recommend the full and faithful implementation of the basic medical science teachers allowance; this will help bolster morale of the scientists.
6. The establishment of Cardiovascular Monitoring Centres by government, corporate bodies and private individuals.

ACKNOWLEDGEMENTS

I wish to acknowledge the work of God in my life and my world that has brought me thus far. If I can list all the Lord has done, then, I will not be here giving this lecture. My thanksgiving will never cease and my praises will never end, to the GLORY of GOD the Father. May the Lord's Name be PRAISED!

I will appreciate the earliest known contributors to my success - my grandfather; Nwokafor 'Kalajine' Anigbogu, "Akwukwo du ndu n'enwuoku" who asserted that, "He - CHIKODI NNANYELU EZEGWUI ANIGBOGU, will attain and surpass the white man's learning or wisdom." It is also worthy of note to know that I was given a name before I was born as he informed my mum and dad before I was born. I acknowledge the sacrifices of my late parents Mazi Godwin Nwankwo Okafor and Janet Ngozi Anigbogu who ensured that all their children and wards were educated. In fact my father said that anyone who lived in his house has gone to university. Then, we lived opposite a University Campus.

I will acknowledge the known roots of my academic career and influences; my teachers - Nnanyiukwu Nwafor, Mr. Iruene, Miss. Edet, Madam Kaodiechi and Headmaster Oguejiofor. Also, my secondary school teachers and mentors at Government Secondary School, Owerri; Mr. Robert Nwuzor, N. Orji, Bassey, Tikili, B. Aguta and Mr. Agbo who inspired and encouraged me. I also acknowledge my undergraduate teachers and supervisor, Professor, Prof. D.D.O. Oyebola, Prof. A. Bolarinwa, Prof. R. Elegbe, Prof. V. Subbarao and Prof. B. Amure. I am also not forgetting, my postgraduate teachers; Late Prof. S.A. Adigun, Emeritus Prof. O.A. Sofola, Prof. G. Ojo, Prof. (Mrs.) Oyin Elebute, Prof. Ronald Evans, Dr. Aneja and Dr. S. Jain.

I acknowledge the invaluable support and camaraderie of my colleagues in the department, Prof. S.I. Jaja, Prof. P.E. Egbe, Prof. (Mrs.) O.A. Adegoke, Dr. B.O. Iranloye, Prof. I.I. Olatunji-

Bello, and Dr. G.O. Onokpite, Dr. E.T. Larmie, and late Dr. P.I Odigie, Dr. S. Gbenebitse-Daniels and Dr. A. Osinupebi.

The immense support of my younger colleagues and "running mates" Dr. Adegunloye, Dr. Obiefuna, Dr. Mojiminiyi, Dr. Iyare, Dr. Nwachukwu, Dr. Onwuchekwa, Dr. Raji and Dr. Ladipo among those who migrated and the in house crew Dr. F. Awobajo, Dr. A.K. Oloyo, Dr. O. Morakinyo, Dr. P. Arikawe, Dr. S. Ogungbemi, Dr. Kemi Oyelowo, Dr. G. Oludare, O. Medubi, Mr. Bawa-Allah is also highly appreciated. My Graduate Assistants and Demonstrators Mr. K. Dada, A. Adejare, Dr. F. Agbaraolorunpo (Akinwolere), J. Uweru, have been of very tremendous help.

I must acknowledge the technical support of my technologists from the early days Messers Adejayan, M. Adewusi, Mrs. Balogun, Mrs. Ayeni, Mr. Soyemi, Rev. A, Ogunjimi, Mr. O Fagbure, Mr. Igwe, Aliade Adejayan and the current team Pastor S. Adesina, Mrs. Olubumuyi, Mr. Olowe, Mr. Dike, Duncan Ota, David Erhabor, Deji Jegede and others, I say, thank you.

My fantastic and efficient secretariat and administrators; Messrs Celestine Owunna, Amusat, Oderinde, Mrs. Lawal, Mrs. Mojume, Mrs. Adepoju, Mrs. Ofili, Mr. Umoh, Mr. Bassey, Mr. Akinmuda, Messrs Nwoke, Akinlaja, Osho, Rolfe-Olumide, Felix Uzoyare and Ayeni are highly appreciated. God bless you all.

The Bishop Crowther group of colleagues who started the journey with us; Profs A. Oyekan, A. Laniyonu, Dr. Paul Eke, Prof. D. Agbonlahor (former VC AAU), Steve Aigbogun, Dr. Beatrice Jaji, Late Dan Edemeka, Busola and Cynthia Nwakibu, and Pharm. Abass; you are also highly appreciated

My immense gratitude goes to Provosts of the College of Medicine, past and present Professors; Ade Elebute who recruited me, Prof. D. Femi-Pearse, Prof. A. Akinkugbe, Prof. J. Akinosi, Prof. G. Sowemimo, Prof. O.A. Sofola, Prof. O.

Abudu, Prof. S. Elesha, Prof. Tolu Odugbemi, Prof. Wole Atoyebi and Prof. (Mrs.) Sade Ogunsola for their support and encouragement.

My profound gratitude also goes to Deputy Provosts, Late Prof. R. Abidoye, Late Prof. (Mrs.) A. Fagbenro-Beyioku and currently, Prof. Abayomi Okanlawon; they all have been very supportive and kind.

I wish also to acknowledge the role of some elder mentors who have supported me morally and intellectually Prof. S.N.N Nnatu, Prof. D. Osegbe, Emeritus Prof. DaRocha-Afodu, Prof. Thomas Johnson, and Prof. J.K Renner, Prof. MC Isiekwe. Also the invaluable support of my Deans, Prof. S.O Bamgbose, Prof. O. Ashiru, Prof. O. Sofola, Prof. S. Adigun, Prof. J. P. Oyerinde, Prof. S. Omilabu, and Prof. (Mrs.) O. Adeyemi will not go unmentioned as it is highly valued.

I am also indebted to Deans of Pharmacy past and present, Prof. F. Ifudu, Prof. Fola Tayo, Prof. H.A.B. Coker, Prof. Udoma Mendie, Prof. Kemi Odukoya and Prof. B. Silva for their support. Other colleagues, Prof. Toyin Ogundipe (Director of Academic Planning), Dr. and Dr. (Mrs.) Nwanna, Dr. C. P. Nnorom, Dr. G. Ajayi, Dr. S. Ogbonnia, Dr. E. Anyika, Dr. T. Egwuatu; they all have been very supportive.

I am indebted to many members of the Physiological Society of Nigeria for their unflinching support and loyalty, especially, when I held the positions of Secretary and Treasurer, Prof. L.F.O Obika, Prof. A.B. Ebeigbe, Prof. Arthur Nwafor, Prof. Sir. AC Ugwu, Prof. P. Aloamaka (Ag. VC, DELSU, Abraka), Prof. V.I Iyawe (Provost, UNIBEN), Prof. A.R. Alada, Prof. Fasanmade, Prof. Raji, Prof. E. Soladoye, Dr. S.B Olaleye, Prof. E. E. Osim, Prof. Atim Antai, Prof. D.V. Dapper, Prof A. Adelaiye, Prof. Kola Olorunshola who have all contributed to my success. Dr. I. Ajayi, Dr. Oge Uche, Dr. Dan Nwachukwu and Dr. E. Iyare have all been helpful and so I say a big thank you.

To my former PhD. students, Prof. Frank Mojiminiyi, Dr. A. K. Oloyo, Prof. O. Olawale, Dr. (Mrs.) A. Azeez, Dr. (Mrs.) O. Ajiboye, and Dr. S.I. Ogungbemi, I say a big thank you; you have been my backbone and you have done me proud by winning so many laurels. Also, to my current students, Mr. A. Adejare, Dr. Francis Agbaraolorunpo, Mr. Akinbosola, Mr. Ojo Olumide; please keep the flag flying. To my other postgraduate and undergraduate students/mentees, I say thank you, the road may be rough at times but the tough keep going till they reach the Golden Prize. Dr. Seun Ogunbona, Odemona Glory, A. Alade, A. Idowu, O. Ogundana , K. Oji and Toyin Omodele I am proud of you as you struggle to be the best.

The Chapel of the Healing Cross (The Protestant Chapel of CMUL and LUTH) Idi-Araba has been my spiritual base. I pay special tribute to the ministers who worked but have gone to be with the Lord, Venerable (Prof.) S.A. Olaitan, Rev. Dr. Tola Roberts and Rev. Dr. Efunkoya.

I also acknowledge the support and guidance of Rt. Rev. George and Mrs. Jumoke Bako, Retired Bishop of Lokoja Diocese and Chairman Board of trustees of the Chapel, Chief Resident Ministers, Very Rev. M. Euler-Ajayi, and Ven. Arc. Tunde Osho and all other Resident Ministers of the Chapel. I also thank all past and present Leaders and members of the Fellowship of Love, Bible Study and Prayer Project (BISAPP) Leaders and DCM and Choir of the Chapel of the Healing Cross. May your labour of Love not be in vain. Amen.

I also thank the Old Boys Association of Government Secondary School, Owerri for their immense support and love – Dr. Dan Onwujekwe, Dr. Eto Osuji and Mr. Lucky Abara.

I must express my appreciation and deepest gratitude to my international benefactors, mentors and colleagues, Prof. Heinz Valtin of Dartmouth College, New Hampshire who initiated the process of the International Fellowship for the Promotion of Teaching of Physiology in the Developing World, this

cascaded to Prof. George Somjen of Duke University, Durham, North Carolina, then, to Prof. Dan Richardson, Prof. Don Frazier, and finally ended up in the laboratory of Professor "Nwannedinamba" Dave and Mrs. Lea Randall where the Lord had prepared a place for me, at the University of Kentucky. Other members and Chairmen of the department; Prof. LuYuan Lee, Prof. Michael Reid, Prof. Dexter Speck and Prof. Phyllis Wyse of the University of Kentucky Lexington, Prof. David Kosistreva of Dayton Ohio, Prof. Simon Malpas of University of Auckland New Zealand, some have even become second family.

By divine providence the Randall family bonded with me and soon with my family as Professor Walt Randall the father of Prof. Dave Randall who was also a physiologist and a former President of American Physiological Society and still active in semi retirement often joined in the laboratory in the experiments in search of the elusive 'heart brain' which he suspected was embedded in the atrial fat pad. I joined the whole family in their spring, summer and Christmas vacations at the family log cabin in Upstate New York, or at sister Merylin's place in Glenview, Chicago or Dave's Farmstead Home at Versailles, Jefferson County, Kentucky, where we rode horses Fifi, Babe and Pryse. This extended to my children and my brothers family in Chicago. My profound appreciation goes to them all.

Members of the Anigbogu-Okpa Odukwe family of Nibo deserve special commendation for their support, endurance and perseverance which helped me through thick and thin to this glorious pedestal. Justice C.E.K. Anigbogu, Surv. Engr Kalajine Ejike Anigbogu, Hon. Emeka Kalajine Anigbogu, Arch Uche Anigbogu, Dozie Anigbogu, Umeadi Anigbogu, and Dr. Okwudili Anigbogu; to all I owe a lot of gratitude. I also thank my sisters Mrs. Oby Ugwualor, Mrs. Udo Obidiegwu and Barr. (Mrs.) Ngozi Nwankwo has always provided solid material, spiritual and emotional support.

Also, the families of Joseph Nweke Anigbogu, Josiah Nwanna Anigbogu and James Nwafor Anigbogu; I am grateful to you all. Mbadugha, Orji, Nwakaji, Okelekwe and Nwachukwu families, Rev. Canon and Mrs. Igboasoiiyi, Rev. Canon Anosike, Onyeka (Bobo) Nwanna, Chibuikem & KC Obika Ogonna & Obi Aguegboh, all our In-Laws, cousins and grand cousins, the Nwadiogbu Family, Nnake's, Nwankwo and Obidiegwu Family are appreciated for their support. I wish to appreciate members of Nibo Union Lagos, Umuanum Village and Umunono Family Union Lagos for their love and support all these years. I also thank Princess Uche Mokeme and Mrs. Gloria Ujor for their love and support.

Likewise, The Anigbogu wives have been superlative in love, care and moral and material support. I acknowledge the love, support, understanding and sacrifices of my children Weluchukwu Chukwunweike Anigbogu and Kodichinma Chinonyelum Anigbogu. I wish also to acknowledge the Love and support of my other 'God children,' Chinedu, Chibuzo, Uchechi, Aanu, Tochukwu, Ikechukwu, Ifeatu, Toyin and Dr. Chidiogo. God bless you all.

Mr. Vice-Chancellor, Sir, on a sad note, in the run-up to this lecture the cruel hands of death took away my cousin, brother and playmate; Surveyor-Engr. Chukwudi Emmanuel Nwadiogbu, (an alumnus), may the Lord grant his soul eternal rest in Jesus name. Amen!

Vice-Chancellor, Sir, I must acknowledge the role and support of some local and international organisations especially earlier in my career development. I appreciate Wellcome Nigeria Fund-For a research award that was given to me, International Union of Physiological Sciences (IUPS) also awarded me the First Fellowship for the Promotion of Teaching Physiology in the Developing World. May and Baker Plc, - Travel Fellowship, American Physiological Society-Perkins Memorial Fellowship, also were in succession. I wish to acknowledge University of Kentucky, Lexington for the International Fellowship Award. I

also thank IUPS/EB2005 for the Congress Travel Award and PhySOC UK for the 2013 Congress Grant.

“The heart is deceitful and desperately sick who can understand it?” Jer. 17-9.

Mr. Vice-Chancellor, Sir, we have delved into various aspects of cardiovascular function, to study the heart and its function and regulation, so that with increased knowledge hopefully we will prevent, minimise and manage better any challenges that may arise.

Mr. Vice-Chancellor, Sir, distinguished audience, may God give us hearts of flesh and preserve our hearts in Jesus name, Amen!

Thank you for your attention.

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