UNIVERSITY OF PORT HARCOURT

Your Life; Your Blood

An Inaugural Lecture

By

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DEDICATION

This Inaugural Lecture is dedicated in memory of my Late Grandfather ***William Davenport Dapper*** [1880-1943] for encouraging his children into academic pursuits.

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OUTLINE OF INAUGURAL LECTURE

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1. INTRODUCTORY REMARKS

Physiology is basically the study of body function and it attempts to explain the physical and chemical factors that are responsible for the origin, development and progression of life [Guyton and Hall 2006]. Physiology is a vast subject that includes **Human Physiology** a branch that attempts to explain the cellular and molecular mechanism that ensures the maintenance of human life and our continued survival as individuals and evolution as a distinct modern species: *Homo sapiens sapiens*.

Vice-Chancellor Sir, I urge you to kindly note that the Nobel Prize in the field of the life sciences or medicine is actually in the subject of Physiology and is called the *Nobel Prize in Physiology or Medicine*. The subject of Physiology was indeed amongst the first five subjects to benefit from a Nobel Prize in 1901 [http://www.bbc.co.uk/news/magazine]; underscoring the importance of the subject to medicine and the medical and life sciences as a whole.

The topic for today's inaugural lecture centres on blood: the red fluid that flows in our veins, arteries and capillaries and gushes out ordinarily from our body only when we are wounded or injured. From a medical view point, blood is the fluid that essentially sustains our and indeed all of life. The Holy Bible in Leviticus 17:11 [NKJV] says that '*For the life of the flesh is in the blood'* affirming further the importance of blood in human life.

Humans attach a lot of import to this body fluid called blood. For instance, on the negative side we refer to individuals who do not speak the truth as *bloody liars*, we use abusive languages like *bloody fools* and *bloody civilians* and refer to unsavoury social relationship with terms like *bad blood*. The term *blood diamond* is a recently coined term referring to diamonds mined in a war zone and sold to finance an insurgency, an invading army's war efforts, or a warlord's activity indicating the negative effects for this trade. These diamonds are mined particularly in parts of Africa currently suffering from the

crisis of development and Russia [http://www.un.org/peaceafrica/Diamond.html/ Conflict Diamonds]. Vice-Chancellor Sir, may I add that I am a *blood physiologist* not a *bloody physiologist*.

On a positive side however, blood is used to indicate family relationships, ancestry or descendant [sanguinity]: *blood relations*, *blood lines*, *blood brothers* and of course the term *blood is thicker than water* are coinages in common use. Other terms also in common usage include *sweat blood* used to describe when a person makes great effort, to *spill blood* refers to wounding or killing people and by extension to *have blood on your hands* means to be responsible for somebody's death. The terms also extends to human emotions, for instance, in *cold blood* means in such a deliberate way that shows a complete lack of emotions, *make somebody's blood boil* describes making somebody extremely angry and to *make somebody's blood run cold* describes frightening or horrifying somebody. The term *blue blood* is used to distinguish nobility.

These terms and colloquial expressions are legion and have been coined and freely used. Once again, these terms show clearly the conscious and unconscious importance humans attach to this body fluid called blood.

2. BASIC PHYSIOLOGY OF HUMAN BLOOD

What is Blood?
Blood is the bright red body fluid that fills and flows in our heart and blood vessels. It is pumped by the heart and flows through our arteries, arterioles and capillaries to all peripheral tissues and returns back to the heart through the venules and veins.

In this process, blood ensures the supply of oxygen and nutrients to all tissues in the body and the removal of the waste products of metabolism from these same tissues to the organs of excretion mainly the kidneys and the lungs from where they are removed from the body.

This flow of blood from our heart through arteries, capillaries, veins and venules back to the heart was first discovered and described in the 18th century by the English physician and physiologist William Harvey [AD 1578-1657] working on fishes, eels and other lower animals [William 1628]. William Harvey had this to say about his discovery of blood: "And so I conclude that blood lives and is nourished of itself and in no way depends on any other part of the body as being prior to it or more excellent... So that from this we may perceive the causes not only of life in general... but also of longer or shorter life, of sleeping and waking, of skill, of strength and so forth.

In histological terms, blood is considered a specialized connective tissue since it arises from mesenchyme and contains a preponderance of molecular fibres called fibrinogen. Blood accounts for 8% of human weight; the average blood volume is 5litres in a 70kg male. On the average this consists of about 60% plasma and 40% red blood cells [Guyton and Hall 2006].

Using fairly simple physiological terms, I would attempt to present a brief review of blood physiology for the benefit of the audience.

Composition of Blood
Blood is composed basically of two parts: blood plasma and the formed elements. Blood is unlike a simple chemical solution: the formed elements in blood are not dissolved but are actually dispersed in the blood plasma. These formed elements are completely cellular in nature. However, like most solutions, blood plasma can be completely separated from these formed elements.

Blood Plasma: The Fluid Portion of Blood
Plasma refers to the liquid fraction of blood. Blood plasma is an extracellular fluid since it lies outside the formed elements [cells] found in the blood. Plasma makes up about 55% of the volume of blood and consists of mainly of water [90%] and a number of other chemicals in solution [Guyton and Hall 2006; Barret *et. al.,* 2010].

These chemicals include proteins [mainly as albumin, globulin and fibrinogen], hormones, mineral ions [mainly as electrolytes], glucose and carbon dioxide amongst other chemicals.

Blood Corpuscles: The Formed Elements of Blood
The formed elements refer to the cellular portion of blood. The blood cells consists of three types: red blood cells [erythrocytes], white blood cells [leucocytes] and platelets [thrombocytes].

The Erythrocytes: red blood cells
A mature red blood cell is called an erythrocyte. A typical erythrocyte has a biconcave or donut shape, lacks a nucleus and contains mainly haemoglobin. The nucleus is deliberately extruded during the process of red blood cell formation called erythropoiesis. Though it is shaped like a donut the red blood cell can indeed assume any shape because of an excess of cellular membrane. The haemoglobin is the red pigment that gives the red blood cell its characteristic red colour and functions majorly in the transport of oxygen and to some extent carbon dioxide. The erythrocyte transports oxygen from the lungs to the tissues and carbon dioxide in the reverse direction: from the tissues to the lungs. The typical erythrocyte count in adult males is between 4.5 and 6.2million cells per micro litre and between 4.2 and 5.4million cells per micro litre for adult females; although significant variations exist. A typical red blood cell is as shown in the Figures I and II below. Figure I also shows typical platelets and white blood cells:
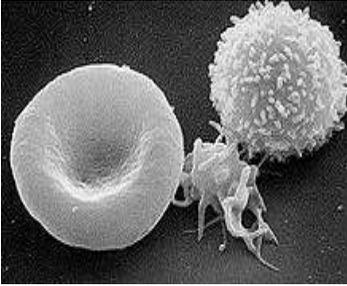
Figure I: *Scanning electron microscope of a typical red blood cell, platelet and white blood cell* [Source: en.wikipedia.org]

Fig. 1 - Erythrocytes

Figure II: *A typical Erythrocyte* [Source: funsci.com]

The red blood cell membranes also contain different glycoprotein types that determine the different types of blood groups; as would be described later in this Inaugural Lecture.

The Leucocytes: white blood cells

There are different types of white blood cells that collectively function with the immune system in protecting the body from invading organisms and foreign agents. The white blood cells have evolved in the multicellular organism as a need for survival in response to an environment populated by a diversity of micro-organisms many of which are intensely pathogenic [Auffray 2009]. The typical normal concentration in the blood is between 4000 to 10,800 cells per micro litre.

These white blood cells are classified into different types based on a number of criteria: reaction to dyes: basic, acidic or neutral, number of lobes in the nucleus and the presence and types of cytoplasmic granules [Gartner and Hiatt 2007]. For instance, based on the

presence or absence of granules in their cytoplasm, leucocytes are divided into those that have granules called granulocytes and those that have no visible granules called agranulocytes [non-granulocytes]. The agranulocytes are also called lymphoid cells.

The Granulocytes:
The granulocytes are further distinguished into Neutrophils, Eosinophils and Basophils based on their affinity for neutral, acidic and basic dyes respectively.

Neutrophils: these have multi-lobed nuclei and are intensely phagocytic in function. They help in destroying bacteria by phagocytosis and are mostly destroyed in the process. Figure III below shows a typical neutrophil
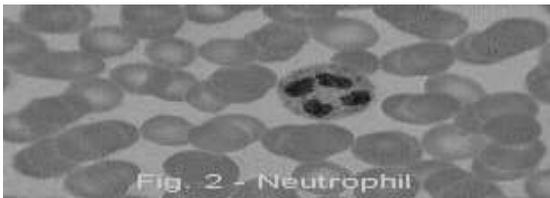
Figure III: A typical neutrophil [Source: en.wikipedia.org]

Eosinophils: attack parasites and ingest antigen-antibody complexes. Levels of eosinophils are thus elevated in parasitic infections and during various immune reactions. Figure IV below shows a typical eosinophil
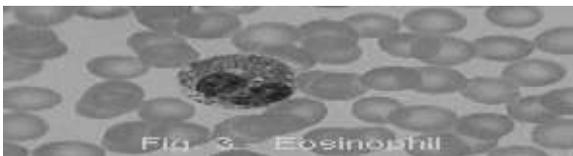
Figure IV: A typical eosinophil [Source: en.wikipedia.org]

Basophils: these cells typically secrete vasodilatory substances that mediate the hypersensitivity process. They are also phagocytic but to a lesser extent. Figure V shows a typical basophil
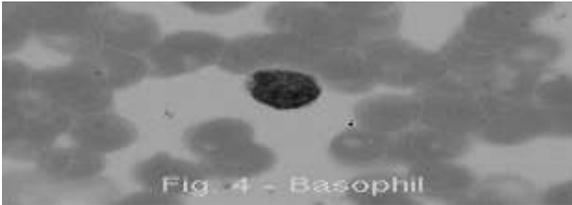
Figure V: A typical basophil [Source: en.wikipedia.org]

The Agranulocytes
The lymphoid cells or agranulocytes on the other hand are further distinguished to lymphocytes and monocytes.

Lymphocytes:
Lymphocytes though ordinarily indistinguishable under the light microscope can be further differentiated into two major types: T-lymphocytes and B-lymphocytes. Whereas, T-lymphocytes are developed in the thymus, B-lymphocytes are differentiated in the adult bone marrow and the foetal liver; the equivalents of the avian Bursa of Fabricus.

They are found mainly in lymph nodes, spleen and lymphatic tissue and function mainly in acquired immunity. Lymphocytes acquire the ability for recognising antigens through the development of specific surface receptors. T-lymphocytes are mainly responsible for cell-mediated immunity, while B-lymphocytes are responsible for humoral immunity via the formation of antibodies.

There are three major types of T lymphocytes: helper, cytotoxic and regulatory. T Helper cells are the most numerous and help in the production of several types of protein mediators called lymphokines. Lymphokines serve to enhance various parts of the immune process. Cytotoxic T cells [Killer cells] are able to attack and perforate the membranes of other infected cells thereby destroying them and the

regulatory T cells that essentially act to modulate the immune system.

Monocytes:

The monocytes are large circulating peripheral leucocytes that characteristically possess a single and well defined nucleus. They play important roles in the inflammatory response which is essential for the innate response to pathogens [Gartner and Hiatt 2007]. Once formed they circulate in the blood stream for 2 to 3 days and subsequently migrate to different tissues throughout the body. In the tissues, they mature and transform to tissue macrophages. They loose motile ability and are thus fixed in these tissues [tissue macrophages]; while others remain motile and are called motile macrophages. Kupffer cells, alveolar and tissue macrophages, Langerhans cells, microglia and osteoclasts are typical examples of fixed tissue macrophages. By phagocytosis of foreign substances, macrophages are important first line defence against harmful particles that have entered the body.

Monocytes, macrophages and their progeny serve three main immune functions: phagocytosis, antigen presentation, and cytokine production. Monocytes perform phagocytosis by first coating [opsonization] the pathogenic organism with antibodies or complement proteins and by binding to the microbe directly. Monocytes are also capable of killing infected host cells via a cytotoxic effect. Monocytes by producing cytokines are important in immune functions [Ziegler-Heitbrock 2007]. These cells compose the Reticuloendothelial system also called macrophage system or mononuclear phagocyte system, and are part of the defense mechanism of the body. These cells can engulf and destroy worn-out or abnormal body cells by ingestion. Figure VI below shows both lymphocytes, monocytes and the various granulocytes.
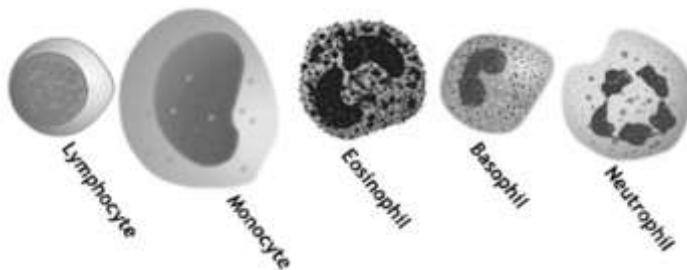
Figure VI: *Various types of white blood cells*
[Source: education-portal.com]

The proportion of each type of leucocyte present in the blood is extremely variable depending on the immunological challenge present in the ambient environment of the population under reference.

The Thrombocytes: platelets

The platelets, also called thrombocytes, are the least flamboyant of the formed [cellular] elements of blood. They are not very obvious like the erythrocyte that give the characteristic red colour to blood and they are generally not involved in fighting infectious agents like the white blood cells. However, thrombocytes perform very crucial homeostatic function of preventing blood loss during injury.

Within the innocuous and pale looking platelets are the machinery to perform diverse and important physiological functions. Platelets are formed in the bone marrow from megakaryocytes: extremely large haematopoietic cells located in the bone marrow. These cells fragment into minute platelets usually in the bone marrow. The normal concentration of platelets in the blood is between 150,000 and 300,000 per microliter. Like the erythrocyte, platelets lack a nucleus and therefore are unable to reproduce. Platelets are very active structures with several cellular enzyme systems. They possess actin and myosin molecules which confers on them contractile ability. This makes platelets usually the first line of defence against blood loss by formation of the platelet plug. The platelet plug is an aggregation of several platelets that seals off the site of a minor

vascular injury [Solum 1999]. A typical platelet is as shown in Figure I above.

Functions of Blood

The functions of blood can generally be divided into three: protective, regulatory and transport. These functions are interrelated and depend majorly on the circulation of blood in the blood vessels.

Protective functions: The protective functions of blood lies in the ability of the white blood cells [leucocytes] to seek out, neutralise and destroy invading agents and pathogenic organisms that are injurious to the body. The blood also bears antibodies called immunoglobulins, opsins and chemical agents of the complement system that also help to destroy and neutralise invading agents and pathogenic organisms [Auffray 2009]. Another protective function of blood lies in the ability of platelets and several clothing factors present in blood to form a clot and ensure hemostasis. In the final analysis, these processes function to help protect the human species from danger posed by pathogenic bacteria and from collapse or death due to an unstopped loss of blood.

Regulatory functions: The regulatory function of blood involves the ability of blood to ensure the regulation of several processes in the body. For instance, blood contains protein buffers, like haemoglobin, amongst others, that helps maintain the pH of the body fluids at about 7.4. The proteins in blood, especially albumin, help maintain fluid balance in the various body compartments by maintaining oncotic pressure. In warm-blooded [poikilothermic] animals, like humans, blood helps dissipate thermal heat generated from biochemical reactions in deeper tissues to the skin and also helps conserve heat loss from the skin in cold environments.

Transport functions: Blood functions as the major medium of transport of the body: blood transports oxygen from the lungs to the tissues where it is needed and transports carbon dioxide from the tissues to the lungs from where it is removed from the body. Blood transports nutrients, minerals and vitamins from the gut or body stores and ensures release of these substances to the cells where they

are needed; while transporting waste products of metabolism from the cells to the organs of excretion mainly the kidney and the liver. Blood also transports hormones, drugs and other chemical agents from the point of entry to the body or production to other areas of the body where they are needed.

These functions of the blood are intrinsically related to those of plasma and its other components, since blood as previously illustrated above consists of both formed cellular elements and a fluid or plasma component.

Basic rheological characteristics of blood
We all know that ***Blood is thicker than water***; that was the topic for the 17th inaugural lecture by late Professor Gabriel Ekeke of the Department of Biochemistry of this University [Ekeke 1997]. Blood is at least 3times, while plasma is at least 1.5times as viscous as water. Human blood is indeed thicker than water on account of its special rheological characteristics.

Rheology is the scientific field that deals with the flow and deformation behaviour of materials [Baskurt and Meiselman 1997]. Basically all physical matter can be classified as either solids or fluids. The term fluid includes both gasses and liquids. Haemorheology is the study of the flow and deformation behaviour of blood and its formed elements: erythrocytes, leucocytes and platelets. Haemorheology is a basic science of immense clinical interest as the flow behaviour of blood is a major determinant of proper tissue perfusion [Baskurt and Meiselman 1997]. Clinical Haemorheology refers to the study of haemorheological changes in various disease conditions.

We now know a lot about the rheological characteristics of human blood. These characteristics of blood confirm clearly its material nature. Solids and fluids have been found to exhibit fairly different rheological behaviour and characteristics. For instance, solids react to an applied force by deformation. Fluids on the other hand react to an applied force by flow. Flow can therefore be regarded as a

process of continuous deformation. Some materials, blood inclusive, exhibit both a solid and a liquid like behaviour to an applied force and are therefore described as viscoelastic [Baskurt and Meiselman 1997].

As stated earlier, the flow of blood is a major determinant of proper tissue perfusion and thus an important determinant of the ability of blood to service its function. Blood flow may be regarded as laminar or turbulent. Laminar flow is normal flow and occurs when the liquid particles moves in an organised and slowly manner in adjacent planes called laminae, usually parallel to the vessel wall. Turbulent flow occurs when the fluid particles moves in an irregular pattern with no organisation at all. Laminar flow is preferred normal flow while turbulent flow occurs commonly in disease.

From a rheological point of view, blood may be regarded as both a two-phase liquid with plasma and the erythrocytes [the most numerous formed elements in blood] behaving like different liquids under shear stress or as a solid-liquid suspension with plasma behaving like a liquid and the cellular elements behaving like solids [Merrill 1969; Baskurt and Meiselman 1997]. This is an intriguing rheological characteristic of blood.

On account of these differences, whereas plasma is a Newtonian fluid, whole blood on the other hand, is non-Newtonian [Merrill 1969; Baskurt and Meiselman 1997]. In other words, the non-Newtonian behaviour of blood is because of the ability of erythrocytes to aggregate or deform in response to shear rate and shear stress. The viscosity of blood is dependent on shear rate and shear stress.

The fluidity of blood is determined at a given shear rate and temperature by the rheological properties of plasma, the value of haematocrit and the behaviour of red blood cells. Each of these factors determine the fluidity of blood. Plasma being the suspension phase of the cellular elements of blood, therefore changes in plasma viscosity influences the viscosity of blood.

The rheological properties of plasma is also dependent on the concentration of fibrinogen, a protein found in plasma and formed in the liver. Haematocrit; the percent of blood that is cell [Guyton and Hall 2006] has an exponential relationship with the viscosity of blood [Chien 1975; Baskurt and Meiselman 1997; Guyton and Hall 2006]. The red blood cells exhibit special rheological characteristics that affect the rheology of blood [Schmid-Schönbein *et. al.,* 1971]. The behaviour of erythrocytes influences blood viscosity. For instance, red blood cells are highly deformable and exhibit special orientation ability. Rouleaux, a tendency of erythrocyte to aggregate into linear arrays by sticking to each another resulting in an arrangement like a stack of coins also influences blood viscosity [Rampling 1988].

Formation of Blood [Haematopoiesis]:
The overall process of formation of blood cells is called Haematopoiesis: Erythropoiesis refers to the formation of red blood cells, while Granulopoiesis refers to the formation of the granular white blood cells. The life span of red blood cells is approximately 120days while the life span of white blood cells ranges from a few hours to several days: 4 to 8 hours in the blood and 4 to 8 days in tissues. On account of the short life span of the cellular components of blood and the fact that these cell types are incapable of cellular division: new cells are therefore constantly required to replenish the ones lost to aging, senescence, blood loss, death or disease processes.

Haematopoiesis occurs almost exclusively in haemopoietic tissue which are specialized connective tissue type derived from embryonic mesenchyme. Embryologically, all blood cells are derived from yolk sac mesenchyme. The two type of haemopoietic tissue are myeloid tissue [red bone marrow] responsible for the formation red blood cells and lymphatic tissue [Thymus and others] responsible for the formation T-lymphocytes and proliferation of B-lymphocytes.

The most widely accepted theory of haematopoiesis is the Monophyletic theory that states essentially that all blood cell types arise from a single common stem cell called the haemocytoblast. According to this theory, the haemocytoblast, a pluripotent stem cell, gives rise to the erythrocyte [red blood cell], the various types of leucocytes [white blood cells] and the megakaryocyte [platelets]. It is estimated that we are born with about 20,000 stem cells and at any one time about 1000 [5%] are simultaneously active to replenish the cellular elements of blood [Coghlan 2014; Holstege *et. al.,* 2014]. A simple outline of the schema of haemopoiesis is as shown in Figure VII.
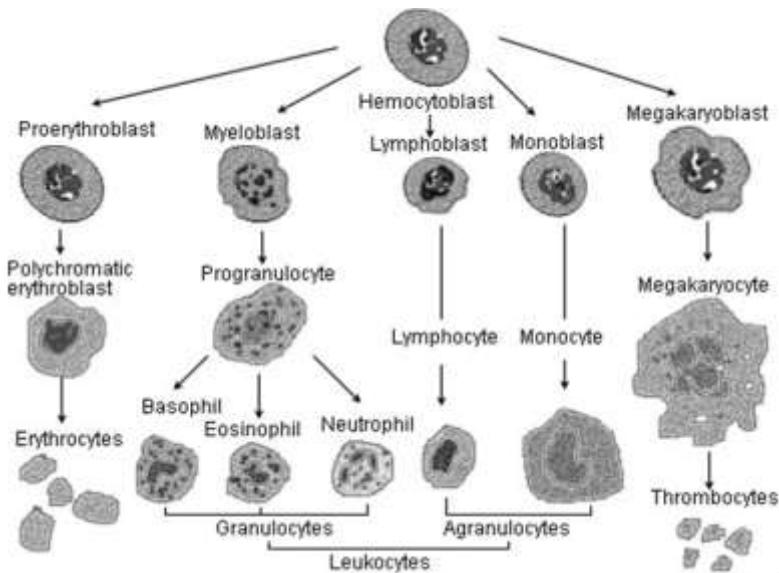
Figure VII: *A simplified schema of haematopoiesis.*
[Source: comed.uobaghdad.edu.iq]

Various factors have been identified as necessary for optimal erythropoiesis and haemopoiesis. These factors include: hypoxia; hormones: erythropoietin; cytokines; and an adequate dietary intake of several nutritional factors including proteins; vitamins: cobalamin; folic acid; pyridoxine; riboflavin; ascorbic acid; pantothenic acid; niacin; tocopherol; copper; and ferrous iron amongst other factors [van Dyke *et. al.,* 1954; Lewis *et. al.,* 2007]. A number of growth factors regulate and enhance the production and development of granulocytes [Barreda *et. al.,* 2004].

Blood groups and some inheritable characteristics in blood
There are characteristics present in the human blood that are inherited. Some of these characteristics cause problems and disease that are more common in specific ethnic or racial groups, while others do not. We shall take a look at some that are of relevance to us.

Blood Group: The blood group also called the blood type is an inherited characteristic. Blood grouping is a system used to classify blood into different types called blood groups. Classification is generally based on the presence of inherited antigens [agglutinogens] on the surface of the red blood cell. These antigens could induce the presence of antibodies [agglutinins] in the plasma of the individual determining the particular blood type. Based on the presence or absence of antigens and antibodies an individual is therefore classed into a particular blood type or blood group. A total of 33 major blood group systems are currently recognized internationally, however, two important blood group system are of clinical and medical import. These are the ABO and the Rhesus blood groups.

A person could be of either blood group A, B, AB or O and each person with any of these groups could be either Rhesus negative or Rhesus positive. The antibodies that determine blood groups are generally inherited from both parents. The ABO blood group is controlled by a single gene and three alleles [Yazer *et. al.,* 2006]. There has been reported differences in the distribution of the ABO blood groups amongst various population groups with the O blood group been generally more frequent in people of African descent, and the A blood group occurs more frequent in Caucasians [Lewis *et. al.,* 2007]. Also recent studies has shown no significant association between the ABO blood groups and the presence of keloids [Mouhari-Toure *et. al.,* 2012]. Keloids are results of overgrowth of granulation tissue at the site of a healed skin injury which is then slowly replaced by collagen. It is a speculated hereditary skin condition more common to people of African, Indian and Hispanic descent as compared to Caucasians. The ABO blood group is also important in population genetic studies and assessment of the pattern of population migration. We have also studied the distribution of the ABO and the Rhesus genes amongst socio-economic classes in Port Harcourt, Nigeria [Korubo-Owiye and Igbigbi 1994].

The Rhesus blood group system is also usually inherited from both parents. However, unlike the ABO blood group where antibodies [agglutinins] develop spontaneously, agglutinins of the Rhesus system develops after only previous exposure of a Rhesus negative individual to Rhesus positive blood. The Rhesus antigen are designated C, D, E, c, d and e. The Rhesus D antigen is the most important and a person is regarded as Rhesus positive if he has the D antigen and Rhesus negative if he has the d antigen. The Rhesus blood group is important during blood transfusion and in the pathophysiology of Haemolytic disease of the new born.

Briefly, haemolytic disease of the new born occurs when a Rhesus negative woman marries a Rhesus positive man and gives birth to a Rhesus positive baby. Usually during the process of birth some of the new born baby's blood comes in contact with the mother's blood and subsequently causes the mother to develop antibodies against Rhesus positive blood. The mother and the first baby are usually unaffected. However, during subsequent pregnancies, the Rhesus positive antibodies developed by the mother may attack and destroy the red blood cells of the next baby if it is Rhesus positive. The incidence increases with each subsequent baby. This causes a wide range of pathophysiological effects on the baby called erythroblastosis fetalis or haemolytic disease of the new born. This may cause jaundice [yellow coloration of the eyes] in its mildest form or the intra-uterine death of the baby. For this condition, prevention is usually the best form of treatment as a drug called *Rhesus immunoglobulin globin* [an anti-D antibody] can be given to the affected mother.

Haemoglobin: Inheritance of variants of the haemoglobin structure are another example of these characteristics. These variations results in sickle cell disease and the sickle cell trait. Sickle cell disease refers to a group of conditions with clinical symptoms characterized by formation of sickle red cells. It is caused by the presence of Hb S; a variant of haemoglobin. It is a genetic disease caused by replacement of glutamic acid by valine on position 6 of the beta chain of haemoglobin. The resulting Hb S (sickle haemoglobin) is

insoluble in the deoxygenated state, causing the red cell to develop abnormal sickle shapes leading to severe haemolytic anaemia, vascular occlusion, acute crises and end organ damage in the affected person. In the Sickle cell trait, the heterozygous state causes no associated haematological abnormalities. Both Sickle cell disease and the sickle cell trait is common in people originating from Africa but also in people of Indian, Arabic and Greek descent. Other forms of structural haemoglobin variants common in people of African descent include Hb C disease that may occur in combination with Hb S.

The Thalassaemia syndromes are a heterogeneous group of inherited autosomal recessive disorders characterized by defects in the synthesis of the globin chains that form the haemoglobin molecule [Lewis *et. al.,* 2007]. Persons of Greek, Italian, African and south Asian descent are commonly affected. Persons with thalassaemia have less circulating red blood cells and make less haemoglobin.

Noteworthy, persons with both the sickle cell trait and thalassaemia are conferred with some measure of immunity against malaria which is endemic in the Mediterranean and African areas where both conditions occur. [Tassiopoulos *et. al.,* 2005].

Ethnic variations in various haematological parameters
Amongst apparently healthy subjects of various ethnic groups, are there any possible differences in the values of various haematological or rheological parameters? Are these differences genetic or induced by the environment? These are questions that has puzzled researchers on haematological parameters in their attempt to help establish population specific reference values for these parameters for several ambient populations. Several studies have attempted to document the nature, extent and determine the possible causes of these variability. Indeed locally determined reference values are of immense clinical importance because of intra- and inter-population variations [Kraemer *et. al.,* 1977].

It is fairly well established that hematological baseline values vary in different population groups and in different geographical areas [Gilles 1981]. Aside from analytical methods [Ernst *et. al.,* 1990], these variations are usually due to age [Guyton and Hall 2006], sex [Hawkins *et. al.,* 1954; Viteri *et. al.,* 1972], altitude [De Gruchy 1989; Sharper and Lewis 1971], environmental factors, social differences [Sharper and Lewis 1971; Woodliff *et. al.,* 1971], and the overall level of physical activity [Garn *et. al.,* 1975] amongst several other factors.

Racial differences have also been variously reported [Sharper and Lewis 1971; Garn *et. al.,* 1975; William 1981]. For instance, despite compensation for socioeconomic status, lifelong differences in haemoglobin and haematocrit values have been described between blacks and whites born and living in the United States [Garn *et. al.,* 1975]. Similar racial differences have been observed for other red cell indices for adults by other workers [Owen *et. al.,* 1973; Garn *et. al.,* 1974; William 1981]. Racial differences have also been described between children of Asian and European descent living in the United Kingdom [Harris *et. al.,* 1983; Isaacs *et. al.,* 1986]. Similarly, neutropenia a relative reduction in absolute neutrophil counts and a lower leucocytes counts have long been reported in the black African [Harris *et. al.,* 1983; O'Brien and Horton 1983; Adewuyi *et. al.,* 1994] living in either Africa or the United States [Broun *et. al.,* 1966; Zezulka *et. al.,* 1987]. Further, absolute lymphocyte counts and immunoglobulin levels have been found to be generally higher in the black African [Wassermann 1966; Zezulka *et. al.,* 1987]. The high eosinophil count seen in the black African has been attributed mainly to the effects parasitic infection [Broun *et. al.,* 1966].

Apparently, when compared to Caucasians, a lower hemoglobin and reduced total white blood cell, neutrophil and monocyte counts are a normal feature of apparently healthy black Africans. Disputes have arisen as to the exact cause of this finding; whether genetic [Kraemer *et. al.,* 1977] or non-genetic [Ezeilo 1972]. A clear explanation of these differences is uncertain however, both genetic and

environmental causes have been suggested. The argument that neutropenia may be found in black Africans whether or not they have been born in Africa, Europe or America supports a possible genetic hypothesis. Environmental factors are supported by an apparent lessening of these differences due to an improvement of socio-economic circumstances [Kraemer *et. al.,* 1977]. Dietary factors have however been long implicated as causative [Wassermann 1966; Karayalcin *et. al.,* 1972] and is currently the accepted possible thesis. It is indeed likely that environmental factors especially, diet may be responsible for these differences. The effect of a number of dietary factors including cholesterol has been implicated [Ogunranti 1994]. Though it may be argued that environmental factors may ultimately find genetic expression, the preponderance of scientific evidence and opinion is for a dietary causative factor. This is an arena that clearly warrants further investigation.

3. OUR MODEST EFFORTS AND CONTRIBUTIONS
Vice-Chancellor Sir, let me now review some contributions we have made to studies in the area of blood physiology.

The bulk of my researches over the years have been on blood physiology; though my research activities have spanned many arenas in the physiological and medical sciences.

A. Effects of cigarette smoking on blood rheology and modelling of simple haematological parameters
Cigarette smoking has been implicated in the pathogenesis of several diseases including: bronchial carcinoma, chronic bronchitis, peptic ulcer and ischemic heart –disease with an increased risk for cardiovascular and cerebro-vascular diseases amongst smokers [Mann and Marmot 1983; Boyu Teklu *et. al.,* 1984].

We determined the effect of cigarette smoking on some haemorheological parameters in apparently healthy Nigerian smokers [Korubo-Owiye *et. al.,* 1997]. Our results showed that smokers have higher values of haematocrit and whole blood relative

viscosity and significantly higher values of erythrocyte sedimentation rate compared to non-smokers; confirming suggestions that the combined effect of these changes were an enhanced susceptibility to intravascular thrombosis due to a possible enhancement of coagulation [Coull *et. al.,* 1986] with higher cardiovascular risk to Nigerian smokers. Results obtained from the study are as shown in Table 1.

Table 1: *Values of haematocrit, whole blood relative viscosity and erythrocyte sedimentation rate in non-smokers, mild to moderate smokers and heavy smokers. [Adapted from Korubo-Owiye et. al., 1997.]*

	GROUP A Non-Smokers (n = 60)	GROUP B1 Mild to Moderate Smokers (n = 131)	GROUP B2 Heavy Smokers (n = 29)	Significant Difference (Analysis of Variance)
Haematocrit (%)	44.1 ± 2.7 (40 – 50)	45.0 ± 3.0 (38 – 55)	44.9 ± 3.5 (39 – 55)	No (P > 0.05)
Whole Blood Relative Viscosity	5.48 ± 0.48 (4.73 – 6.40)	5.52 ± 0.45 (4.53 – 6.72)	5.62 ± 0.53 (4.53 – 6.72)	No (P > 0.05)
Erythrocyte Sedimentation Rate (mm/1 hr.)	9.24 ± 6.40 (1.0 – 23.0)	13.03 ± 10.73 (1.0 – 31.5)	13.34 ± 12.38 (2.0 – 48.0)	Yes (P < 0.001)

Values = Mean ± SD; Range in Parenthesis

Although not related to blood, we have in addition been able to describe the deleterious effects of cigarette smoking on semen parameters amongst reproductive aged males [Dapper *et. al.,* 2002]. Results obtained shows a significantly lower percentage of motile spermatocytes and a lower spermatocyte count among smokers compared to non-smokers; further validating the deleterious effect of cigarette smoking on reproductive health and especially semen quality [Dapper *et. al.,* 2002].

Our studies have contributed to knowledge by providing further scientific evidence and rationale for intensive campaign against smoking which appears to be on the increase amongst Africans especially Nigerians [Boyu Teklu *et. al.,* 1984]. We therefore join

the Federal Ministry of Health to warn that smokers are liable to die young and urge them to quit smoking.

We attempted to establish the possible mathematical relationship between some simple haematological parameters in apparently healthy adult Nigerians residing in Port Harcourt [Korubo-Owiye *et. al.,* 1998]. Using regression analysis, we were able to propose 3 mathematical equations to describe a possible linear relationship between some of these parameters.

The equations are:

a. **Haematocrit = 2.78xHaemoglobin concentration + 3.38**

b. **Specific gravity = 0.001170Haemoglobin concentration + 1.0348**

c. **Specific gravity = 1.0317 + 0.0004127Haematocrit + 0.001170 Haemoglobin concentration**

Our equations can be used to predict more accurately values of haemoglobin concentration from a simple routine and inexpensive determination of haematocrit or specific gravity of blood and conversely to predict values of specific gravity from determination of either or both of haematocrit and haemoglobin concentration.

B. Cyclic changes in blood during the Menstrual cycle

The menstrual cycle (or more accurately the female sexual cycle) refers to the pattern of monthly rhythmic changes in the rates of secretion of the female sex hormones with corresponding changes in the ovaries (ovarian cycle), the endometrium (endometrial cycle), fallopian tubes and other accessory female sex organs [Guyton and Hall 2006]. Graphic illustration of these changes are as shown in Figure VIII and Figure IX below.
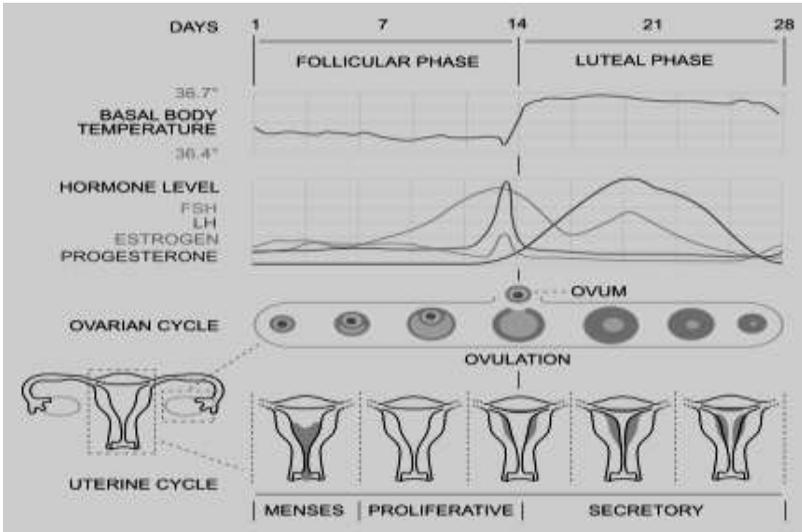
Figure VIII: *Graphic representation of events during the phases of the menstrual cycle.* [Source: bcmednet.com]
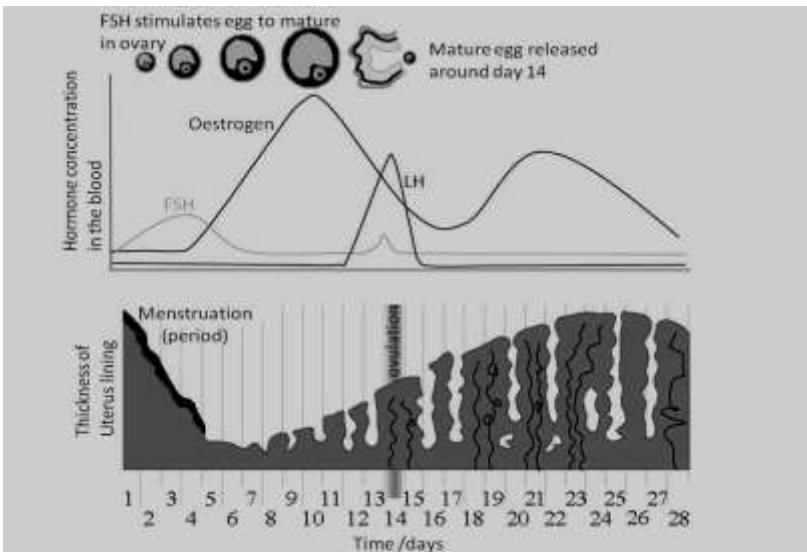
Figure IX*: Graphic illustration of the follicular and endometrial changes during the phases of the menstrual cycle*
[Source: bcmednet.com]

We were able to show that significant variations occurs in the values of haematocrit, whole blood relative viscosity [WBRV], erythrocyte sedimentation rate [ESR] and fibrinogen concentration during the phases of the normal menstrual cycle in apparently healthy undergraduate females of the University of Port Harcourt, Nigeria [Dapper and Didia 2002]. These changes are comparable to those that occur in Caucasians [Brooks and Easthope 1981]. Results are indicated in Table 2 below.

Table 2: *Values of the haemorheological parameters in the different phases of the menstrual cycle [Adapted from Dapper and Didia 2002.]*

	Menstrual phase (n=350)	Follicular phase (n=350)	Ovulatory phase (n=350)	Luteal phase (n=350)	F-value	Fcrit	Significance (ANOVA)
Haematocrit (Hct) (%)	38.09±1.54 (34-40)	39.26±1.98 (37-41)	40.86±0.91 (39-42)	39.82±0.82 (38-41)	40.96	2.67	Yes (P<0.05)
Whole blood relative viscosity (WBRV)	2.17±0.17 (2-2.1)	2.36±0.07 (2.3-2.5)	2.41±0.16 (2-2.6)	2.37±0.08 (2.2-2.5)	32.32	2.67	Yes (P<0.05)
Erythrocyte sedimentation rate (ESR) (mm/1 hr)	10.66±2.77 (7-15)	8.80±0.87 (7-10)	8.29±0.67 (5-9)	9.17±1.15 (7-12)	31.35	2.67	Yes (P<0.05)
Fibrinogen concentration (FC) (g/dL)	3.57±1.04 (3-6)	1.42±0.44 (1-2.5)	2.35±0.40 (2-3)	1.79±0.29 (1.5-2.5)	203.8	2.67	Yes (P<0.05)

The results of the study also suggest that blood viscosity apparently is highest during the ovulatory phase and lowest during the menstrual phase of the menstrual cycle. We are unable to posit on the clinical significance of these physiological and rheological findings.

Furthermore, possible cyclic changes in the total and differential white blood cell [WBC] counts, total lymphocyte count [TLC] and CD_4 cell count during the menstrual cycle in apparently healthy reproductive aged female undergraduate students were also assessed [Dapper *et. al.,* 2011].

We were able to confirm that aside from changes in the rheological characteristics, the immune competence of females also apparently undergoes significant cyclic variations during a normal menstrual cycle. However, we report significant differences only in the values of total WBC, and differential neutrophils, lymphocytes, and

eosinophil counts; while no significant differences were observed in the values of monocytes, basophils, TLC and CD_4 cell count during the phases of the menstrual cycle [Dapper *et. al.,* 2011]. The study confirms previous reports in Caucasians of significant physiological variations in the leukocyte counts during the phases of the normal menstrual cycle [Bain and England 1975; Tikare *et. al.,* 2008]. However, our results suggest that apparently TLC and CD_4 cell count do not undergo a similar physiological variation. These findings are as shown in Table 3.

Table 3*: Values of white blood cells and differentials, total lymphocyte and CD₄ cells counts in the different phases of the menstrual cycle [Adapted from Dapper et. al., 2011.]*

Parameters	Menstrual phase [n = 61]	Follicular phase [n = 61]	Ovulatory phase [n = 61]	Luteal phase [n = 61]	F value	F critic	Significant differences [ANOVA]
Total WBC count	4.97 ± 0.06	4.36 ± 0.05	4.80 ± 0.06	4.54 ± 0.08	6.80	2.64	Yes
[x10⁹ cell/l]	[3.9-8.4]	[3-6.2]	[3.4-9.5]	[11-34]			[p < 0.05]
Neutrophil count	49.26 ± 0.39	47.38 ± 0.38	49.82 ± 0.29	46.41 ± 0.44	7.67	2.64	Yes
[%]	[38-58]	[36-58]	[42-58]	[32-58]			[p < 0.05]
Lymphocyte count	35.15 ± 0.40	36.83 ± 0.41	33.87 ± 0.31	35.95 ± 0.43	3.10	2.64	Yes
[%]	[23-48]	[26-50]	[24-43]	[24-50]			[p < 0.05]
Eosinophil count	4.28 ± 0.20	4.92 ± 0.21	4.52 ± 0.17	5.59 ± 0.20	3.22	2.64	Yes
[%]	[0-12]	[9-13]	[1-9]	[0-11]			[p < 0.05]
Monocyte count	11.16 ± 0.18	10.18 ± 0.21	10.85 ± 0.26	11.36 ± 0.20	2.19	2.64	No
[%]	[7-18]	[5-17]	[3-17]	[5-18]			[p > 0.05]
Basophil count	0.41 ± 0.06	0.79 ± 0.07	0.89 ± 0.09	0.57 ± 0.06	2.82	2.64	No
[%]	[0-3]	[0-3]	[0-5]	[0-3]			[p > 0.05]
Total Lymphocyte Count [%cells/µl]	175.5 ± 3.01 [28.6-96.6]	160 ± 2.30 [108-240]	162.44 ± 2.6 [108-313.5]	162.3 ± 3.03 [108-341]	2.47	2.64	No [p > 0.05]
CD₄ cell count [cells/µl]	965.3 ± 23.73 [269-1826]	864.15 ± 17.58 [442-1328]	974.21 ± 21.11 [510-1824]	905.3 ± 18.55 [502-1596]	2.46	2.64	No [p > 0.05]

Values = mean ± SEM, range in parenthesis

Aside from the documentation of these cyclic changes, the combined significance and possible contribution to knowledge of these studies is the confirmation that rheological changes could possibly contribute to blood pressure changes even during the menstrual cycle [Chien 1977]. Furthermore, the results of our studies suggest that the Nigerian physician could interpret results of TLC and CD₄ cell counts in females with little regard to the menstrual cycle. However, on account of the possible significant physiological variations during the menstrual cycle of the values of total white blood cell and differential neutrophils, lymphocytes and eosinophil counts seen; the

interpretation of these particular parameters, for instance during single, serial and subsequent measurements may consider the phase in the menstrual cycle these parameters were assessed. Korubo-Owiye and Uzor 1999 have also described phase differences in normal blood pressure during the menstrual cycle in apparently healthy female undergraduate students.

Using animal models, we have been able to show that a hitherto commonly prescribed antimalarial drug Metakelfin a combination of pyrimethamine and sulphalene [sulfamethopyrazine] could cause interruption of the oestrus cycle in cylic rats with a persistent dioestrus vaginal cytology [Didia *et. al.,* 2000].

C. Studies on haematological values in various physiological states

Haematological parameters are of immense importance as they provide diverse and vital information about a population under investigation [Ernst *et. al.,* 1990]. Several factors determine the value of any particular haematological or haemorheological parameter under assessment [Ernst *et. al.,* 1990]; the importance of various population and gender specific reference values cannot therefore be over emphasized [Dirren *et. al.,* 1991; Mangwendeza *et. al.,* 2000].

In our contributions to this area, we determined and documented the values of various haematological and haemorheological parameters amongst Nigerians residing in Port Harcourt since such studies of subjects in various physiological states and ambient environments would continue to be relevant [Ernst *et. al.,* 1990; Dapper *et. al.,* 2006].

Adults: We attempted to document and establish haematological reference values for healthy adults residing in Port Harcourt, Nigeria [Korubo-Owiye *et. al.,* 1998; Dapper *et. al.,* 2006a]. Reference ranges for haematocrit, haemoglobin concentration, red and white blood cell counts, the basic corpuscular indices and erythrocyte sedimentation rates [Dapper *et. al.,* 2006a] and specific gravity of

whole blood [Korubo-Owiye *et. al.,* 1998] have been fairly documented and are as shown in Table 4. Like most other populations, significant gender variations were found: males had significantly higher values of most haematological parameters with exception of erythrocyte sedimentation rates which were predictably higher in females, likely due to the effects of menstruation and pregnancy; confirming previous reports [Reid 1984].

Table 4: Haematological reference ranges for healthy adults in Port Harcourt, Nigeria. [Adapted from Dapper et. al., 2006b.]

	Total population (n=250)	Male subjects (n=150)	Female subjects (n=100)	Significant differences (Z-test)
Haematocrit (%)	38.82±7.92 (28-48) *40	40.99±4.88 (32-48) *40	35.57±7.29 (28-42) *39	Yes (p< 0.05)
Haemoglobin concentration (g/dl)	12.99±2.51 (10-16) *13.5	13.56±2.10 (10.5-16) *13.5	12.12±2.08 (10-14.5) *12.5	Yes (p< 0.05)
RBC count (x 10¹²/L)	4.48±0.80 (1.80-5.50) *4.8	4.63±0.84 (1.80-5.50) *4.8	4.27±0.55 (3.6-5.0) *4.2	Yes (p< 0.05)
WBC count (x 10⁹/L)	7.80±3.21 (4.0-11.30) *7.5	8.12±3.08 (4.20-11.20) *7.5	.02±2.80 (4.6-11.0) *7.5	Yes (p< 0.05)
Mean Corpuscular Volume (MCV) (fl)	84.39±20.90 (10-97) *90	86.50±19.17 (11.0-97.0) *85	81.22±21.90 (10-97) *90	Yes (p< 0.05)
Mean Corpuscular Haemoglobin (MCH) (pg)	28.83±5.17 (13.6-45.3) *30	29.28±4.84 (24.3-45.3) *28.1	28.16±5.39 (13.6-37.6) *26.7	Yes (p< 0.05)
Mean Corpuscular Haemoglobin Concentration (MCHC) (g/dl)	33.47±4.47 (23.9-42.1) *33.*	33.10±3.68 (23.9-42.1) *33.7	34.04±5.27 (26.7-40.6) *33.7	Yes (p< 0.05)
Erythrocyte Sedimentation Rate (ESR) (mm/Hr)	6.80±3.65 (2-44) *5	4.93±3.15 (2-21) *4	11.02±3.19 (3-44) *11	Yes (p< 0.05)

*All values mean ± 1.96 standard deviation, range in parenthesis, *mode value*

Pregnancy: Our studies also explored values of various haematological parameters in the physiological state of pregnancy amongst Nigerians [Dapper *et. al.,* 2006b; Amah-Tariah *et. al.,* 2011]. We reported that except for haematocrit, significant changes apparently does not occur in the values of 'common' haematological parameters during the trimesters of pregnancy amongst our subject population [Dapper et. al., 2006b]. Significant changes observed for haematocrit were attributed mainly to the effects of haemo-dilution, due to volume changes in pregnancy [Guyton and Hall 2006]. These are as shown in Table 5.

Table 5: *Haematological values in the trimesters of pregnancy I. [Adapted from Dapper et. al., 2006b.]*

	First Trimester (n=46)	Second Trimester (n=36)	Third Trimester (n=48)	Significant differences
Haematocrit (%)	27.26±4.11 (20-32)	26.64±4.18 (21-32)	29.02±3.73 (21-35)	Yes (p<0.05)
Haemoglobin concentration (g/dl)	8.81±1.09 (7.2-10.5)	9.31±1.26 (7.0-11.3)	9.28±1.51 6.2-11.8	No (p>0.05)
RBC count (x 10^12/L)	5.69±2.23 (2.17-7.64)	4.58±1.63 (1.38-7.69)	4.82±1.50 (2.17-7.25)	No (p>0.05)
WBC count (x 10^9/L)	6.48±1.35 (4.0-9.4)	6.44±1.71 (4.0-9.6)	6.24±1.63 (4.0-9.6)	No (p>0.05)
Mean Corpuscular Volume (MCV) (fl)	63.94±2.72 (10.40-84.90)	67.79±3.25 (10.70-96.80)	67.27±2.59 (10.0-92.50)	No (p>0.05)
Mean Corpuscular Haemoglobin (MCH) (pg)	20.89±0.79 (10-39)	24.14±1.28 (10-73)	22.65±1.17 (9-72)	No (p>0.05)
Mean Corpuscular Haemoglobin Concentration (MCHC) (g/dl)	33.08±6.86 (26.9-46.2)	35.58±6.43 (24.1-53.3)	32.92±6.60 (19.4-46.2)	No (p>0.05)
Erythrocyte Sedimentation Rate (ESR) (mm/1hr)	38.07±22.8 (5.0-93)	45.61±25.86 (5.0-102)	44.06±25.31 (6.0-123)	No (p>0.05)

All values = mean ± standard deviation, range in parenthesis

Furthermore, we reported that the values of serum iron, unsaturated iron binding capacity, total iron binding capacity and serum transferrin concentrations showed significant variations in the various trimesters of pregnancy. While serum iron showed significant decreases during pregnancy; unsaturated iron binding capacity, total iron binding capacity and serum transferrin concentrations showed significant increases during pregnancy. By contrast the values of red cell distribution width, platelet count, mean platelet volume, platelet distribution width, plateletcrit and platelet larger cell ratio did not show any significant differences.

An important contribution is the confirmation, from our studies, that values of serum transferrin are perhaps a more useful screening tool for diagnosis of iron deficiency anaemia during pregnancy amongst Nigerian subjects. These findings are as shown in Table 6.

Table 6*: Haematological values in the trimesters of pregnancy II.
[Adapted from Amah-Tariah et. al., 2011.]*

Parameters	1st trimester (n=73)	2nd trimester (n=75)	3rd trimester (n=72)
Iron (µg/dl)	98.62±31.41* (15.79-151.02)	90.45±36.50* (15.25-221.79)	80.10±53.28* (25.73-316.32)
UIBC (µg/dl)	260.10±53.79* (134.38-405.72)	325.92±75.58*(116.30-654.92)	334.78±88.04* (43.15-625.00)
TIBC (µg/dl)	340.20±53.79* (221.75-449.77)	416.38±64.2* (258.38-702.96)	433.40±71.17* (287.72-699.68)
Transferrin mg/dl)	238.89±36.80* (155.00-315.00)	296.07±48.26* (180.00-492.00)	303.04±49.81* (201.00-489.00)
PTS (%)	23.72±9.09 (6.15-43.05)	22.27±9.93 (3.80-65.60)	23.19±13.35 (6.04-87.10)
RDW-SD (fl)	43.04±14.23 (29.7-78.1)	41.15±14.53 (26.00-95.70)	40.43±11.87 (29.70-81.30)
RDW-CV (%)	13.91±0.84 (11.7-16.5)	13.76±0.90 (12.00-16.90)	13.90±1.15 (11.30-18.20)
PLT (10³/µl)	289.40±21.68 (87.00-594.00)	259.93±98.96 (71.00-558.00)	279.63±107.97 (117.00-693.00)
MPV (fl)	8.45±0.79 (6.60-10.90)	8.65±0.76 (7.00-10.20)	8.69±0.75 (7.00-10.70)
PDW (%)	9.93±1.40 (6.90-14.4)	10.10±1.46 (6.90-13.40)	9.86±1.37 (7.70-14.90)
PCT (%)	0.26±0.14 (0.09-0.90)	0.24±0.18 (0.10-0.90)	0.25±0.11 (0.08-0.80)
P-LCR (%)	12.18±5.79 (3.00-36.1)	12.17±5.56 (14.00-29.00)	12.61±5.52 (4.20-34.00)

*Significant difference at P<0.05, UIBC=Unsaturated Iron Binding Capacity, TIBC= Total Iron Binding Capacity,
PTS= Percent transferrin saturation, RDW= Red Cell Distribution Width, PLT= Platelet count, MPV= Mean Platelet Volume,
PDW= Platelet Distribution Width, PCT= Plateletcrit, P-LCR= Platelet large cell ratio

Pre-primary and primary school children: Since published reports on the haematological reference values for pre-primary and primary school aged children in Port Harcourt, Nigeria are relatively scanty, we attempted to document these parameters for the population in a recent report [Dapper *et. al.,* 2009].

Expectedly, we reported no significant gender differences in the values of these parameters for both pre-primary and primary school aged children. Despite the apparently homogeneous nature of the population, significant differences were observed in the values of some of the haematological parameters determined: primary school children irrespective of sex were found to have significantly higher values of lymphocyte differential counts and erythrocyte sedimentation rates and significantly lower platelet counts and total white cell counts and differential neutrophils counts compared to their pre-primary school counterparts. Reasons for these distinctions were not immediately clear, but were attributed to the combined effects of age and surprisingly an apparently better response to acute infections amongst the pre-primary school subject population [Dapper *et. al.,* 2009]. However, a similar pattern has been described by workers from Uganda [Lugada *et. al.,* 2004]. The age and sex variations of these parameters is as shown in Table 7 below.

Table 7: *Age and Sex variations of haematological reference values for pre-primary school children in Port Harcourt, Nigeria. [Adapted from Dapper et. al., 2009.]*

Age in years	Sex	Haematocrit (%)	Total WBC count ($\times 10^9$/L)	Differential WBC counts (%)		Platelets ($\times 10^9$/L)	Erythrocyte Sedimentation Rate (mm/1hr)
				Neutrophils	Lymphocytes		
1-2 yrs	Males (n=34)	30.75±6.08 (24-38)	5.83±3.30 (3-12.1)	64.50±3.79 (59-70)	35.50±3.79 (30-41)	270.00±47.78 (200-305)	21.25±26.25 (2-60)
	Females (n=30)	31.71±3.90 (24-35)	8.80±3.03 (2.2-12.8)	36.57±3.05 (60-68)	3.57±3.05 (32-40)	217.14±62.31 (155-325)	11.86±7.10 (3-20)
>2- 3yrs	Males (n=26)	34.25±3.24 (32-38)	7.86±3.08 (3.2-9.6)	63.68±4.53 (57-67)	36.65±4.53 (30-41)	266.25±38.34 (200-300)	15.88±13.72 (2-30)
	Females (n=40)	30.60±4.90 (25-35)	8.18±4.66 (3.0-14.6)	62.70±7.32 (50-75)	37.30±7.32 (25-50)	226.50±47.96 (155-300)	16.10±19.34 (2-65)
>3-4yrs	Males (n=38)	31.43±6.78 (20-42)	7.71±3.98 (3-13.6)	65.43±5.35 (45-70)	34.57±5.35 (27-43)	212.86±90.36 (130-300)	31.00±21.15 (4-60)
	Females (n=36)	35.13±3.94 (25-35)	7.04±4.14 (3.6-15.9)	64.50±6.72 (52-66)	35.50±6.72 (20-42)	267.25±55.14 (175-320)	14.75±19.78 (2-62)
>4-5yrs	Males (n=26)	32.56±3.86 (20-42)	6.66±3.12 (5.2-12.1)	60.53±6.45 (45-73)	39.07±6.79 (31-55)	272.81±60.50 (155-375)	14.00±12.02 (2-50)
	Females (n=20)	32.36±3.96 (24-30)	5.86±1.88 (2.5-9.2)	61.27±4.22 (50-80)	38.73±4.22 (34-48)	253.18±66.53 (170-395)	16.64±15.04 (5-55)

New born and umbilical cord blood: Umbilical cord blood is blood retrieved from the umbilical cord following the birth of a new born. The umbilical cord is usually discarded with the placenta following successful birth. Umbilical cord blood is a potentially rich source of haematopoietic stem cells [Benito *et. al.,* 2004].

We attempted to document values of some haemorheological parameters of new born neonates using umbilical cord blood and correlated these parameters with corresponding parameters in maternal venous blood at the time of birth [Dapper and Didia 2006].

The parameters assessed were: haematocrit, haemoglobin concentration, red and white blood cell counts, erythrocyte sedimentation rates, whole blood relative and relative plasma viscosity, plasma fibrinogen concentration, and the various corpuscular indices. Expectedly, we reported that neonates have

significantly higher values of these parameters compared to maternal values, except for white blood cell counts, fibrinogen concentration and the corpuscular indices [Dapper and Didia 2006]. As contribution to knowledge, the study provides information on umbilical cord haemorheology for the Nigerian neonatologist since similar reports have been relatively scanty.

D. Haemorheology of health and disease: Hypertension.

Aside from establishing normative values for several haematological and haemorheological parameters, we also attempted to determine the effect of a number of disease conditions particularly, hypertension on these parameters [Dapper and Ighoroje 2002]. We reported significantly higher values of fibrinogen concentration, relative plasma viscosity and whole blood relative viscosity in hypertensives compared to normotensives. The study reports that the increased values of the various haemorheological parameters in Nigerian hypertensives are possibly attributable to the significantly elevated levels of fibrinogen concentration. This finding is consistent with earlier reports in this regard [Chien 1977; Lowe *et. al.,* 1988] and we confirmed previous suggestions that rheological factors may indeed play a potentially insidious role in the pathogenesis of hypertension [Lee 1977; Reid and Anah 1985].

Further, we have confirmed that the sex variations in the haemorheological parameters in healthy Nigerian subjects [Reid 1984; Reid and Anah 1985] apparently still persists in the hypertensive state [Ighoroje and Dapper 2005]. Additionally, the study reports significantly higher values of whole blood relative viscosity in both normotensive and hypertensive females compared to males [Ighoroje and Dapper 2005].

E. Physiology of Human Immunodeficiency Virus infection and Acquired Immunodeficiency syndrome

Since its identification in 1981, human immunodeficiency virus [HIV] infection and the associated acquired immunodeficiency syndrome [AIDS] remain a major health burden globally [Dapper *et. al.,* 2008]. Recent estimates indicate that over 35 million people are

affected worldwide with mortality counts of over 20 million; most of which have occurred in sub Saharan Africa where the burden of disease is high and poverty an importance accomplice [WHO UNAIDS Report 2004]. The national HIV sero-prevalence rate was estimated at 4.4%, with Rivers State predictably having a higher rate of 5.4% [FMH Nigeria 2006]. This is probably due to the recent urbanization of Port Harcourt due to influx of multinational concerns involved with petroleum exploration and exploitation [Dapper *et. al.,* 2006a]. We decided to study the basic physiology of immune cells and white blood cell populations and interactions to better understand the pathophysiology of HIV infection.

We determined the normal values of CD_4, CD_8, CD_4 / CD_8 cell ratio, total WBC and differential counts, haematocrit and total lymphocyte count [TLC] in healthy HIV sero-negative and healthy HIV sero-positive subjects and assessed the prognostic significance of these parameters in these subjects compared to AIDS subjects [Dapper *et. al.,* 2008]. The study reported that in both sexes, these parameters were found to be highest in healthy HIV sero-negative subjects and lowest in AIDS subjects, with HIV sero-positive subjects having intermediate values. For male subjects, significant differences were found in CD_4 count, CD_4 / CD_8 cell count ratio, hematocrit, total WBC and TLC, whereas for female subjects, significant differences were found only in CD_4 and CD_4 / CD_8 cell count ratio in the three groups of subjects. The results confirm previous reports that the CD_4 count and CD_4 / CD_8 cell count ratio are fairly reliable indicators of the progression of HIV infection [Hoover *et. al.,* 1992].

Apparently, from our studies, the prognostic value of CD_8 count is limited and TLC possibly sex-dependent. TLC can only thus be interpreted with some caution in place of both CD_4 cell counts and CD_4 / CD_8 cell count ratio. Our study could assist in the management of persons infected with HIV [Dapper *et. al.,* 2008]. These results are presented in Table 8 and Table 9 for both male and female subjects respectively.

Table 8: *Haematological parameters, CD4 and CD8 counts and ratio in male HIV sero-negative and HIV sero-positive subjects and AIDS subjects [Adapted from Dapper et. al., 2008.]*

Parameter	Healthy HIV-negative subjects (Group A) [n=56]	Healthy HIV-positive subjects (Group B) [n=37]	AIDS subjects (Group C) [n=52]	Significant differences
Age (years)	36.98±0.99 (18-71)	35.68±0.87 (17-63)	41.23±0.99 (19.0-71.0)	No ($p>0.05$)
CD4 count (Cells/µl)	1019.0±33.74 (488.0-1609.0)	548.76±20.48 (58.0-2235.0)	99.04±4.36 (12.0-195.0)	Yes ($p<0.05$)
CD8 count (Cells/µl)	701.76±22.99 (197.0-1420.0)	806.30±36.5 (144.0-2561.0)	781.68±20.47 (290.0-1385.0)	No ($p>0.05$)
CD4/CD8 count ratio	1.71±0.07 (0.44-5.20)	0.79±0.07 (0.06-4.07)	0.13±0.01 (0.02-0.28)	Yes ($p<0.05$)
Hematocrit (%)	40.29±0.46 (30-58)	31.97±0.41 (22.0-42.0)	31.02±0.38 (21.0-38.0)	Yes ($p<0.05$)
Total WBC count (Cells/µl)	5.56±0.07 (3.90-7.30)	4.74±0.09 (2.80-8.30)	4.45±0.08 (2.60-7.10)	Yes ($p<0.05$)
Neutrophil count (%)	50.95±0.56 (45.0-73.0)	57.51±0.65 (34.0-72.0)	51.75±0.53 (50.0-78.0)	No ($p>0.05$)
Lymphocyte count (%)	39.43±0.55 (26.0-64.0)	40.73±0.60 (21.0-65.0)	37.35±0.56 (21.0-49.0)	No ($p>0.05$)
Monocyte count (%)	0.21±0.04 (0.0-2.0)	0.22±0.04 (0.0-2.0)	0.31±0.05 (0.0-2.0)	No ($p>0.05$)
Eosinophil count (%)	0.34±0.05 (0.0-3.0)	0.32±0.03 (0.0-2.0)	0.40±0.05 (0.0-2.0)	No ($p>0.05$)
Basophil count (%)	0.05±0.02 (0.0-1.0)	-	0.04±0.02 (0.0-2.0)	No ($p>0.05$)
Total lymphocyte count (%Cells/µl)	219.1±4.99 (116.8-340.8)	199.19±4.62 (98.1-302.0)	168.01±4.40 (72.6-302.4)	Yes ($p<0.05$)

Values=mean ± SEM, range in parenthesis

Table 9: *Haematological parameters, CD4 and CD8 counts and ratio in female HIV sero-negative and HIV sero-positive subjects and AIDS subjects [Adapted from Dapper et. al., 2008.]*

Parameter	Healthy HIV negative subjects (Group A) [n=42]	Healthy HIV positive subjects (Group B) [n=55]	AIDS subjects (Group C) [n=46]	Significant differences
Age (years)	30.00±1.19 [17-71]	30.96±0.90 [19-71]	31.78±0.12 [16-65]	Nil $p>0.05$
CD4 count (Cells/µl)	920.02±24.10 [588.00-1675.00]	451.48±20.23 [99.00-1377]	94.46±4.43 [14.00-190.00]	Yes $p=0.05$
CD8 count (Cells/µl)	834.60±24.54 [326.00-1452.00]	904.07±41.85 [399.00-3943.00]	900.10±54.86 [56.00-5600.00]	Nil $p<0.05$
CD4/CD8 count ratio	1.23±0.04 [0.48-2.41]	0.67±0.04 [0.16-2.51]	0.19±0.02 [0.02-1.76]	Yes $p>0.05$
Haematocrit (%)	33.76±0.31 [24.00-41.00]	30.49±0.44 [17.00-44.00]	30.38±0.41 [20.00-44.00]	Nil $p>0.05$
Total WBC count (Cells/µl)	5.07±0.10 [3.30-7.80]	4.85±0.11 [2.80-9.80]	4.82±0.11 [2.10-8.50]	No $p>0.05$
Neutrophil count (%)	64.74±0.54 [50.00-78.00]	61.48±0.71 [37.00-75.00]	61.77±0.82 [45.00-80.00]	Nil $p>0.05$
Lymphocyte count (%)	34.33±0.56 [21.00-48.00]	37.94±0.78 [22.00-73.00]	37.46±0.67 [20.00-57.00]	No $p>0.05$
Monocyte count (%)	0.24±0.04 [0.00-2.00]	0.17±0.04 [0.00-2.00]	0.21±0.05 [0.00-1.00]	No $p>0.00$
Eosinophil count (%)	0.02±0.07 [0.00-4.00]	0.57±0.07 [0.00-6.00]	0.66±0.06 [0.00-2.00]	Nil $p>0.05$
Basophil count (%)	0.12±0.03 [0.00-2.00]	0.02±0.01 [0.00-1.00]		No $p>0.05$
Total lymphocyte count (WBMxLC)	176.04±5.33 [84.0-338.0]	186.7±6.14 [66-409.1]	177.10±3.84 [90.9-277.9]	Nil $p>0.05$

Values=mean ± SEM, range in parenthesis

The possible sex variability of the value of TLC seen amongst female subjects in our studies informed the attempt to determine the pattern of physiological changes of these parameters during the phases of the menstrual cycle in apparently healthy female Nigerians [Dapper *et. al.,* 2011]. These findings were recently presented at *#Physiology 2014*, the annual scientific conference of The Physiological Society of the United Kingdom, along with the report on the prognostic value of these immune cells in HIV sero-negative and HIV sero-positive subjects [Dapper *et. al.,* 2014a; Dapper *et. al.,* 2014b].

Our Research Endeavours in Other Areas
Having given an overview of our research efforts over the years in the area of blood physiology, let me now briefly summarize our research endeavours in other areas.

A few studies of public health importance.

Malaria remains a major public health burden in sub Saharan Africa and indeed globally [Ebong 2011]. Studies attempting to determine and verify the anti-malarial potency of suspected herbal remedies and local agents would continue to be relevant. In collaboration with the Department of Pharmacology and Malaria Research Laboratory [now Centre for Malaria Research and Phytomedicine] we described two plants with potential anti-malarial activities. These plants have been previously described in an earlier inaugural lecture [Ebong 2011] include *Phyllantus amarus* Schumach and Thonn [Dapper *et. al.,* 2007a] and *Cymbopogon citrates* stapf commonly called lemon grass [Dapper *et. al.,* 2008].

Further, we reported for the first time on the incidence of lactose intolerance amongst an adult population in Port Harcourt, Nigeria [Korubo-Owiye and Dapper 1996], and the incidence of Joint Hypermobility Syndrome amongst an undergraduate student population in Nigeria [Didia *et. al.,* 2002].

We have described the adverse effects of a hitherto popularly consumed medication ''Melo's conquer mixture' on intestinal histology: inducing a dose dependent acute inflammatory response of the mucosa and sub-mucosa by inflammatory cells, reactive lymphoid hyperplasia and increased mucous secreting cells [Didia and Dapper 1999]. This report, amongst others perhaps contributed to the withdrawal of the medication from general consumption therefore enhancing the health of the general public.

Medical education.

In the area of medical education, we reported on the relevance of the Joint Admission and Matriculation Examination [UME] in Medical School admission [Didia *et. al.,* 2007] relating the performance of our preclinical students in the subjects of Anatomy, Physiology and Biochemistry to their scores at the UME over a 2year period. The study revealed no significant correlation between the performance of our students at the two examinations. The study suggested that the score of our students at the Joint Matriculation Examinations was

not an objective reflection of their ability, at least during their preclinical years of study. The report possibly provided further scientific rationale for the commencement of the post UME currently practiced by most public universities in Nigeria.

Other important physiologic studies…

We have reported on a number of important physiologic topics. For instance, we have described a significant left ward QRS axis deviation in the electrocardiographic pattern of pregnant women and a significant association between the incidence of left axis deviation in pregnant subjects [Iwobi and Dapper 2002]. We have further described the visual acuity pattern of school aged children [Dapper *et. al.,* 2002a] and the defects of colour vision amongst undergraduate students in Port Harcourt, Nigeria [Dapper *et. al.,* 2002b]. We have also shown that the gel of *Aloe vera* could impair blood clotting by actions on both the intrinsic and extrinsic pathways of blood clotting [Dapper *et. al.,* 2007b]. Changes in some markers of bone turnover amongst pre and post-menopausal female subjects in Nigeria and the relative effects of Body mass index and years since menopause on these biochemical parameters have also been reported [Chinko *et. al.,* 2012]. We have also investigated the effects of the methanolic extract of the rind of *Citrullus lanatus* on lead acetate induced toxicity on semen parameters, reproductive hormone assay and testicular histology in experimental animals [Kolawole *et. al.,* 2014].

One of our recent reports on serum immunoglobulins values in apparently healthy children and adults in Port Harcourt, Nigeria [Obiandu *et. al.,* 2013] clearly posits the future direction of our research endeavour. We described values of the immunoglobulin: IgG, IgA and IgM in apparently healthy children and adults in Port Harcourt, Nigeria and the significant gender differences for some immunoglobulin types: adult females had significantly higher values of IgG and significantly lower values of IgA compared to males. The results we described suggested that gender differences amongst adults were apparently a gradual build-up from childhood and that levels of some immunoglobulin types seen amongst African adults

may have possibly been attained during childhood [McFarlane *et. al.*, 1970].

4. OUR FUTURE PROSPECTS AND DIRECTION IN BLOOD RESEARCH:

Let me attempt to chart a sign post for our future attempts at research. This we hope will serve as our road map for the future especially in the Department and the Haemorhelogy and Immunology Research Group.

Briefly, we intend to explore further how the peculiar environment of the Niger Delta affects or influences the immune competence of the residents of the area. We also intend to determine the effect of various local nutritional and dietary agents on the immune cell populations. For instance on the short term, we have commenced studies on the effect of *Moringa oliefera* and *Discorea bulbifera* on the immune cell population. Further, we intend to determine the effect of various factors on the immune cell populations in various conditions and diseases associated with pregnancy amongst residents of the Niger Delta region of Nigeria.

We shall attempt to collaborate with other laboratories to explore the effect of various environmental, nutritional and local dietary agents on the genetic and biological variability of indigenes of the Niger Delta region of Nigeria especially as manifested in the blood and the various blood cells.

5. YOUR LIFE; YOUR BLOOD

Vice-Chancellor Sir, distinguished Ladies and Gentlemen the topic for today's Inaugural Lecture is Your Life; Your Blood. According to the Holy Bible, Blood is the life of the flesh. Blood is life. Your life is therefore your blood. This statement is a medical truism because the blood serves a lot of important and vital physiologic functions many of which have been described in the course of this Inaugural Lecture. That is why we have conducted our research on

parameters in blood to help enhance the life and wellbeing of Nigerians.

Mankind has always been fascinated by the desire to live long and live healthy. Recently, scientists have tried to identify the causes of longevity by studies of the blood of Hendrikje van Andel-Schipper [1890-2005]. Van Andel-Schipper was a Dutch woman who was in apparent relative good health and cognitive function till her death at 115years. It was discovered that about two-thirds of her white blood cells originate from only two stem-cells. Stem-cell give rise to all blood cells [indeed all cells] including white blood cells. It was discovered also that a number of harmless mutations occurred in her white blood cells; suggesting she may have 'a superior system for repairing or aborting cells with dangerous mutations' [Holstege *et. al*., 2014]. Stem-cells get exhausted and die, therefore there is a limit to human life. Is it a future possibility therefore so save stem cells from our youth, inject them to ourselves in old age to possibly enhance longevity? [Holstege *et. al*., 2014] The secret of long life may perhaps be in the blood and by extension the bone marrow, as our life may be ultimately limited by the capacity of stem cells to keep replenishing vital tissues especially blood day in day out. The picture of Van Andel-Schipper possibly taking a snack of ice cream is shown in Figure IX.

Figure X: Image of Hendrikje van Andel-Schipper [1890-2005]
[Source: en.wikipedia.org]

Your blood is also a very fair reflection of your health status and general well-being, this is because almost all toxic and non-toxic products of metabolic and absorptive processes must necessarily find their way into the blood prior to excretion by the kidneys, detoxification by the liver or transport to all parts of the body. Consider the fact that the average cardiac output at rest is approximately 5L/minute and the average blood volume of a 70kg male is approximately 5L. This physiological fact means that on entry into the blood stream a chemical substance is distributed all over the body in approximately 1minute and re-distributed again and again in each next subsequent minute. Our diet, our environment and

even the process of aging all produce substances that can be found in our blood. The blood is therefore a good reflection of a number of physiological indices that are a pointer to our health status. Health we say is wealth. Therefore, regular blood testing is an important way to not only protect and preserve our health but enhance our well-being and perhaps add more decades to our life [Baron 2006]. By regular blood testing I mean the conduct of specific laboratory tests on the blood in a scientific medical laboratory usually in a government recognized health care facility.

There are several tests that if done regularly, preferably at least annually, will be of immense assistance to your doctor to help you achieve optimum health and prevent any serious health problems. Preventive medicine we say is better than curative medicine; it is also much less expensive. These tests are recommended by medical experts and learned medical societies including the American Cancer Society, American Diabetic Association, American Thyroid Association and several others. I have deliberately selected and adapted a number of these tests as appropriate to our circumstance and environment from the report of Life Extension Magazine May 2006 [Baron 2006]. These selected tests are by no means exhaustive. They include:

1.   Complete Blood Count [CBC]
As the name implies this test gives a complete and overall picture of the various components of the blood; most have been described above. The CBC is a determination of the count, variety, percentage and overall quality of the various cellular components of the blood: platelets, erythrocytes and leucocytes. The CBC is relatively inexpensive and easy to determine. With the era of automated haematological analysers the CBC can be done rapidly with a minimal blood sample and effectively with fairly reliable results. The CBC screens for infections, anaemia and other simple blood abnormalities [Baron 2006]. It is also important to determine your ABO and Rhesus blood types during the determination of the CBC; although this only need be done once.

2. Blood Chemistry Tests

This includes a group of tests that assesses the normal chemical constituents of blood. Test of blood chemistry should include the determination of blood lipid profile, specifically: total cholesterol, high density lipoprotein [HDL], low density lipoprotein [LDL] and triglyceride concentrations. These simple indices give a fair reflection of your predisposition to cardiovascular diseases.

Test for blood sugar are also included here specifically: Random Blood Sugar [RBS] and more importantly, Fasting Blood Sugar [FBS]. The Fasting Blood Sugar is the blood sugar determined at least 8 hours after the last meal; while Random Blood Sugar is the blood sugar determined at any time of the day irrespective of meal schedule or pattern. Both tests are important for the diagnosis of diabetes mellitus as well as in the assessment of the cardiovascular status and the risk for developing metabolic syndrome and other heart diseases.

Also included here are test for the determination of blood levels of urea, creatinine and electrolytes: sodium, potassium, chloride and other electrolytes. Glomerular Filtration Rate can also be estimated from results of blood creatinine. These tests help to provide a basic assessment of kidney or renal function. It is noteworthy that more individuals are apparently being afflicted by kidney diseases. The determination of electrolytes, urea and creatinine concentrations would help in the early detection and prevention of diseases of the kidney.

3. Fibrinogen concentration

Fibrinogen is an acute phase protein and therefore elevated levels occur commonly in acute tissue inflammation [Dapper and Didia 2002]. Along with platelets, fibrinogen is also important in blood clotting [Guyton and Hall 2006]. Increased fibrinogen concentration are associated with an increased risk of heart disease, stroke and myocardial infarction [Lowe *et al.,* 1988]. High fibrinogen levels are also seen in inflammations of the kidney. Stopping smoking and participation in regular physical exercise to help reduce weight are

important and helpful in reducing fibrinogen concentration to optimal levels [Baron 2006]. There is an association between an increased fibrinogen concentration and the increased risk of venous thrombosis (blood clots) [Diez *et. al.,* 2006]. Fibrinogen concentration have been found to undergo significant variations during the menstrual cycle [Dapper and Didia 2002]; to be elevated amongst hypertensive Nigerians [Dapper and Ighoroje 2002] and smokers [Dapper *et. al.,* 2002]. Further our studies have revealed that the reported significant sex variations in fibrinogen concentration persist still in the hypertensive state [Ighoroje and Dapper 2005].

4. Prostatic-Specific Antigen [PSA]

This particular test is recommended exclusively for males. PSA helps to assess the absence or presence of diseases of the prostate gland. PSA is a protein synthesized by the prostate gland in males and released into the blood. Elevated levels may therefore indicate prostatic enlargement, inflammation or prostate cancer. The levels of PSA increases with age and it is therefore recommended by the American Cancer Society that tests for PSA be done for males annually beginning from age 50 [Baron 2006]. However, an elevated PSA level does not necessarily indicate the presence of prostate cancer and vice versa; prostatic cancer may not always be accompanied by an elevated PSA.

5. Thyroid Stimulating Hormone [TSH]

Thyroid Stimulating Hormone also called Thyrotropin is a glycoprotein hormone secreted by the anterior pituitary gland. It stimulates the secretion of the thyroid metabolic hormones: thyroxin and triiodothyronine by the Thyroid gland [Guyton and Hall 2006]. TSH levels are decreased in hyperthyroidism and elevated in hypothyroidism. TSH levels are the initial best test for the assessment of normal thyroid function; thyroxin and triiodothyronine levels can then be determined if TSH levels are found to be abnormal. This test is important for the early detection of thyroid diseases; as most go about undetected. Mild disorders of thyroid hormones may be associated with elevated cholesterol levels,

cognitive dysfunction, atrial fibrillation and heart palpitations [Baron 2006].

6. Glycated haemoglobin [Hb A$_{1C}$]

This is also called Haemoglobin A$_{1C}$. This is a test of the average blood glucose concentration over the past two to three months [Geberhiwot *et. al.,* 2005]. It is an independent predictor of heart disease with or without diabetes mellitus [Selvin *et. al.,* 2005]. It is also important if you are a diabetic to determine your glycated haemoglobin levels regularly preferably every 3 to 6 months to help prevent any possible diabetic complication [Nathan *et. al.,* 2005]. Normal levels of blood glucose produce normal levels of glycated haemoglobin. Long term elevation of blood sugar in the presence of diabetes mellitus is associated with an increased risk of heart disease and stroke [Baron 2006]. Glycated haemoglobin gives a more accurate picture of blood glucose control over a longer time frame, unlike both fasting and random blood sugar described above.

7. 'Free' testosterone concentration

Testosterone is the male sex hormone. It is a steroid hormone produced by the testes in the male, the ovary in females and the adrenal gland in both males and females [Guyton and Hall 2006]. Free testosterone is the active unbound form of the hormone that mediates most of its physiological effects. Testosterone plays different physiological roles in men and women including the regulation of fertility, libido and muscle mass. High levels of testosterone in females causes an excessive growth of hair and a disease of the ovary called polycystic ovarian syndrome. Reduced testosterone in women may indicate a reduced oestrogen levels [Baron 2006]. Reduced level of testosterone occurring with increased age in males are associated with several health complications [Barrett-Connor *et. al.,* 1999] including ischemic heart disease and atherosclerosis [Demirbag *et. al.,* 2005].

8. Estradiol concentration

β-estradiol is the primary circulating form of oestrogens in both males and females. β-estradiol is a steroid sex hormone, essentially

the female equivalent of testosterone. β-estradiol is secreted by the female ovaries and adrenal glands; levels may vary during the normal menstrual cycle [Guyton and Hall 2006] as illustrated in Figure VIII and Figure IX above. Levels become constantly low after menopause. β-estradiol levels therefore, evaluate sexual activity and menopausal status [Baron 2006]. In females, increased levels indicate increased risk for both breast cancer and endometrial cancer; while low levels increases the risk for osteoporosis making bones to more easily fracture [Baron 2006]. Significant positive correlations exist between β-estradiol concentrations and high cholesterol levels.

9. C-Reactive protein [CPR]

C-reactive protein is a sensitive marker of systemic inflammation that has emerged as a powerful predictor of coronary heart disease and other diseases of the cardiovascular system. Inflammation within the body can lead to a range of life-threatening degenerative diseases such as coronary heart disease, diabetes, macular degeneration, and cognitive decline. Measurement of C-reactive protein can help devise a strategy for diet, exercise and supplementation [Baron 2006]. Increased levels has been associated with increased risk of diabetes, loss of cognitive ability in seemingly healthy persons and depression in men [Pradham *et. al.,* 2001; Ford and Erlinger 2004]

These blood test if well-chosen and appropriately conducted can assess your state of health and help you better manage your health proactively [Baron 2006]. These tests are best done in consultation with your medical doctor or health care provider. You should urge your doctor on these tests; since most annual medical examination involves the determination of usually routine haematological and other blood tests. The consequences of failing to analyse blood for the markers of disease risk are indeed needless expenses, disability and perhaps death. That Prevention is better than Cure cannot therefore be overemphasized.

6. CRISIS OF DEVELOPMENT IN AFRICA

Vice-Chancellor Sir, the African plane is littered with what has been aptly referred to as a crisis of development. This crisis has arisen from a gross mismanagement of both the human and natural resources the continent has been endowed [Ikenna 2009]. This has led to a massive wastage of both human and material resources with dire socio-economic and psychological consequences on us all.

Vice-Chancellor Sir, one may want to ask why a medical scientist or indeed a medical doctor should be bothered with national or developmental issues. Several answers can be advanced in response to this question: Firstly, aside from the fact that the body of human knowledge coalesces to a fine point: the distinction therefore, between medicine and for example sociology is merely arbitrary. Indeed, there is symbiosis in the subject area of medical sociology. Secondly, however forlorn and apart they may both seem developmental studies and medicine are centred on improving the overall circumstance of the human condition. Thirdly, if our country Nigeria is developed, then our researchers and scientists would be able to more readily conduct high-impact research and compete with colleagues and peers the world over; in other words our researchers and scientists working on the continent, would be at the forefront of the advancement of the frontiers of human knowledge. We would be able to more easily find cures for diseases that afflict us and solve engineering challenges that confront us. It is therefore clear that the development of our country Nigeria (especially of our basic infrastructure) is intrinsically linked to the progression and ascendency of our careers as scientists. Therein lies the rationale for my seeming interest.

As we all know, Research is necessary for and eventually leads to Development; that is why Research and Development was coined. However, a society's development especially of its basic infrastructure is imperative for the proper conduct of research that could lead to any meaningful development. In Nigeria, this lack of basic infrastructure invariably compromises the quality of our research; a compromised research solves a problem slowly, if at all,

and eventually may result in no real development. This creates a scenario that we know in physiology as a vicious cycle. A vicious cycle of infrastructural deficiency leading to less effective research and persistence of identified problems obviously exists in Nigeria. However, for the purpose of this inaugural lecture the definition of development that I consider most appropriate is the one that defines development as the "systematic use of scientific and technical knowledge to meet specific objectives [challenges] or requirements" [http://m.businessdictionary.com/defination/development.html].

Several factors have been advanced to explain this crisis of development in Africa. Nigeria particularly, represents a pathetic instance. For despite earning about US$500 billion in oil revenues since the 1970's, it remains immersed in poverty, unemployment, a burgeoning domestic debt, infrastructural squalor, abysmal health and educational services and attendant social frustration and unrest [Suberu 2007]. These factors responsible for the crisis of development in Africa can be summarised as:

a. *The combined after effects of slave trade, colonialism, neo-colonialism and continued dependency of Africans.*
    Indeed the Atlantic slave trade and the subsequent colonisation of the African continent wrought a deep damage to the African psyche [Frantz 2008]. The genetic material [DNA] of these abducted Africans are perhaps forever lost and unavailable for development efforts of the African continent [Salas *et. al.,* 2004].

b. *The effects of the current globalisation.*
    Despite the inherent immense opportunities offered, the process of globalization has not been to the advantage of Africa and Africans [Nsibambi 2001]. Indeed, one of the major consequences of globalisation is the "brain-drain" phenomena.

c. *The role of the African ruling elite and perhaps the ordinary African.*
    The adverse contributions of systemic corruption to the developmental crisis facing the African continent and indeed Nigeria in particular, cannot be overemphasized [Okowa 2005].

Noteworthy is the thesis that malaria with the associated high morbidity and mortality amongst Africans is another possible cause of our current state of underdevelopment [Akyeampong 2006]. This thesis has been disputed using a statistically-based approach showing little evidence of any relationship between malaria ecology, population density and other measures of development [Depetris-Chauvin and Weil 2013].

Vice-Chancellor Sir, it is clear that our problem is mostly with the enemy within and this is the cabal-like African leadership. An African proverb says: *When there is no enemy within, the enemy outside cannot harm us*. In other words, we need to ensure we enthrone a responsible and responsive leadership all over the continent of Africa, especially in our country Nigeria. The surest way this can be done is for us to participate and continuously ensure a transparently free and fair electoral process. We need to remove the current cabal-like leadership in Africa through entirely peaceful means. However, I must confess that this would be a rather difficult task considering the orientation of the average Nigerian [Okowa 2005]. However, it is noted that the present Federal Government of Nigeria has done a lot in this direction; not only to build physical infrastructure, but attempting to dethrone the cabal-like leadership and also ensuring a transparent, free and fair electoral process. Although, it is clear that we have not yet arrived at the Promised Land; however, if we continue on this present course I see a brighter horizon for Nigeria and indeed the continent of Africa. Our recent handling of the Ebola disease outbreak in Nigeria is a clear indication of our abilities if well harnessed [Fashina *et. al.,* 2014].

For us to essentially jump start the African continent towards the path of sustainable development and take a step closer toward the much talked about African renaissance, we need to amongst others:
a. Aggressively build the human capital resources of the continent and bring human capital development into the centre stage of our developmental efforts.

b. Focus on the development of certain critical areas of our economy important to the development of our human resource capital these are the educational and health sectors.
c. Formulate an educational policy and operate an educational sector that not only re-orientates and produces individuals that would be competent enough to drive the desired development efforts on the African continent but are confident enough to lead us into the next millennium.
d. Develop a health sector that enhances and ensures the maintenance of the optimum health of our people. We need a healthy human capital base to undertake the research aimed at the development of the African continent. Medicine if properly harnessed can be an asset that can assist in the development of our human capital resources.
e. Develop the basic infrastructural facilities that is necessary for the conduct of appropriate research needed for development of the continent and perhaps more importantly to keep the human resources capital we have created comfortably back at home.

Clearly, Universities and tertiary institutions have an important role to play in this direction. The Motto of the University of Port Harcourt: 'For Enlightenment and Self-Reliance' immediately comes to focus and fairly captures this need. Vice-Chancellor Sir, we need to deepen this further.

7. RECOMMENDATIONS:

Establishment of a Centre for Blood Research [CBR]
This centre is to pursue the health of Nigerians, especially those of the Niger Delta through research in blood and blood related processes. A similar Centre exist at the Faculty of Medicine of the University of British Colombia, Vancouver, Canada and other centres.

Postdoctoral scheme for junior academics
We need to entrench a Postdoctoral scheme for young academic staff of the University who have recently completed their PhD's or their

medical fellowships. This scheme will provide our younger academics the desired opportunity to spend a couple of months outside the country and acquire skills, expertise and experience that would help them in their careers when they return. A similar scheme was established at the premier University of Ibadan, Nigeria and is currently be actively managed by the University. This scheme would further deepen our research culture and improve the ranking of the University.

Before I conclude this Inaugural Lecture, I wish to leave members of the audience with a few words of advice:

1. Intake of a balanced diet is important to ensure that your blood is able to perform its various functions optimally; necessary for the maintenance of life and good health. Drink plenty of water as the blood plasma is more than 90% water and adequate hydration ensures adequate blood flow to the liver and kidney enhancing better health. Watch carefully your diet as previously advised by Professor Anele Ihekwaba and Professor Iyeopu Siminialayi at the 80th and 109th Inaugural Lectures respectively [Ihekwaba 2011; Siminialayi 2014].

2. Regular exercise schedule is important. This ensures an adequate blood flow to all organs of the body to enable them perform their various functions. Regular physical activity enhances blood flow and decreases the risk of cardiovascular diseases.

3. Reduce alcohol and salt intake and avoid smoking in whatever form or guise especially passive smoking. Cigarette smoking exerts a deleterious effect on blood and most health indices [Korubo-Owiye *et. al.,* 1997; Dapper *et. al.,* 2002].

4. Monitor your blood pressure, weight and Body Mass Index regularly. Take time for rest and leisure.

5. And not to forget, the regular conduct of the blood tests described above is important.

8. CONCLUSION:

Vice-Chancellor Sir, before I conclude this Inaugural Lecture I want to seek your permission to announce that I wish to endow a prize for

the best graduating medical student in the subject of Human Physiology in this University. The prize is to be called the *William Davenport Dapper Memorial Prize* **for the Best Graduating Medical Student in Human Physiology.** My reasons for endowing the Prize are not only to encourage excellence, scholarship and hardwork amongst medical students of this University, but to also provide a framework to harvest our best medical doctors and encourage them to pursue careers in the basic medical sciences. It is also to give back to the younger generation of medical doctors the recognition and encouragement they need to continue to excel in their careers.

I would like to say "*A 'very' big thank you very much indeed*" to everyone who has sacrificed the time and made the effort to attend this Inaugural Lecture today. I hope you all have gained in some way from this lecture and that I have, at the least, stimulated your thoughts towards the possibility of a renaissance of Africa.

Finally, I will like to end this Inaugural Lecture by leaving you with the words of the late German writer and statesman Johann Wolfgang von Goethe [1749-1832]. He said and I quote "Blood is a very special juice." Distinguished Ladies and Gentlemen, we cannot but all agree with Johann Wolfgang von Goethe, Blood is indeed a very special juice, which is equally very important for the sustenance of life

Thank you all so very much also for your kind attention.

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PROFESSOR DATONYE VICTOR DAPPER
B Med Sc [Physiology] *UPH*; MB; BS *UPH*; MSc [Human
Physiology] *Benin*; MD [Physiology] *UPH*; MSB

Vice-Chancellor Sir, the Lecturer for the 113th Inaugural Lecture of
the University is Professor Datonye Victor Dapper [MSB]. Professor
Dapper was born on the 26th of November, 1966 to Alabo and Mrs
CU Dapper in Bakana Town, Degema Local Government Area of
Rivers State, Nigeria.

Professor Dapper had his primary education at the Mushin Town
Council School, Mushin, Oshodi, Lagos State, Nigeria from 1972 to
1977. He had his secondary education firstly at Ikeja Grammar
School, Oshodi, also in Lagos State, Nigeria from 1977 to 1980 and
later at Baptist High School, Port Harcourt where he completed in
1982. He was admitted to study Medicine at the University of Port
Harcourt in 1984. Professor Dapper is one of the products of the
Bachelor of Medical Science degree program of the University of
Port Harcourt. He graduated Bachelor of Medical Science [B. Med.
Sc] degree in Physiology Second Class Honours Upper Division in
1988 and a Bachelor of Medicine; Bachelor Surgery [MB; BS]
degree in 1991. He has a Master of Science [MSc] degree in Human

Physiology from the University of Benin, Nigeria obtained in 2002 and a Doctor of Medicine degree in Physiology of the University of Port Harcourt, Nigeria obtained in 2007.

Professor Dapper has always been a very cerebral scholar even during his days as an undergraduate student of this University. He was both the Best Graduating Student in the Department of Physiology, Bachelor of Medical Science Graduating Class and Best Graduating Student of the College of Health Sciences, Bachelor of Medical Science Graduating Class of the University in the 1987/88 academic session. In addition, he won the Subject Prize in Preventive and Social Medicine in the Bachelor of Medicine; Bachelor of Surgery Graduating Class in the 1990/1991 academic session. On graduation in 1991, the young medical doctor was promptly encouraged by Chief [Dr] Tonye Korubo-Owiye the then Head, Department of Human Physiology to pursue an academic career in Human Physiology. This was based on his outstanding academic performance. His first position in an academic career was thus as a part-time Demonstrator in the Department of Human Physiology of this University; this position he combined with his internship training at the University of Port Harcourt Teaching Hospital, Port Harcourt between 1991 and 1992. On completion of the mandatory National Youth Service in 1993, Professor Dapper promptly joined the services of the University as a Lecturer Grade II. He rose through the ranks and was promoted to the rank of Senior Lecturer in 2002 and Professor of Human Physiology in 2009. Professor Dapper has recently endowed a prize for the Best Graduating Medical Student in Physiology not only to encourage excellence, scholarship and hard-work amongst Medical Students' of the University, but to also help provide a framework to harvest our best medical doctors; encourage and build them as medical researchers of the future.

Professor Dapper has served the University in various capacities. He was appointed Acting Head, Department of Human Physiology between 2004 and 2006 and was elected Dean of the Faculty of Basic Medical Sciences of the University in 2009. He has served as

Hall Warden, Medical Students Hostel, Member [representing Congregation] on the Search Team for the Selection of the 7th Vice Chancellor of the University, Member of the Board of School of Basic Studies and Member of the Editorial Board of the *Port Harcourt Medical Journal*; the international medical journal of the College of Health Sciences of this University. He was Member, College of Health Sciences Research Day Committee. He has served the College and University in several other capacities.

Professor Dapper is member of a number professional and learned societies including the Physiological Society of Nigeria [PSN]; the Society of Biology of the United Kingdom; the Physiological Society of the United Kingdom [*PhySoc*]; The American Physiological Society [The APS] and the International Society on Thrombosis and Haemostasis [ISTH]. He is the society representative of the Physiological Society of the United Kingdom in this University. He has attended several local and international conferences and workshops where he has presented his research findings. The most recent being Physiology2014 the annual scientific conference of the Physiological Society of the United Kingdom at The Queen Elizabeth II Conference Centre, London, United Kingdom July 2014.

Professor Dapper has supervised several undergraduate and MSc students in Physiology. He is currently supervising a number of PhD candidates. He is author of a number of chapters in books and over 56 published articles and abstracts in various local and international scientific journals. His area of research interest is blood physiology; specifically the effect of various physiological factors on the immune cell population and haemorheology. He has at various times served as external examiner in the subject of Physiology and professorial assessor to several Universities across the Country, including the Universities of Ibadan, Benin, Maiduguri, Uyo, Calabar, Nnamdi Azikiwe University, Awka and Niger Delta University, Bayelsa State.

On a personal note, Professor Dapper is a very unassuming and friendly person [don't let his occasional frown deceive you], who is meticulous in all he does. He is the first in a family of six. He is happily married to Idongesit and together they have a daughter Stephanie. He enjoys photography, reading, travelling especially on adventures and listening to classical and jazz music.

Mr. Vice Chancellor Sir, I present to you my classmate, colleague and friend of many years; a distinguished Professor of Blood and Body Fluids Physiology; the first alumnus of the College of Health Sciences to be elected Dean of the Faculty of Basic Medical Sciences of this University; a loving husband and a caring father; a mentor and inspiring role model; a natural leader and trailblazer: Professor Datonye Victor Dapper [MSB] to deliver the 113th Inaugural Lecture of the University,

Professor Iyeopu M. Siminialayi
Thursday, 13 November, 2014.