HUMAN UNIQUE BLOOD CELLS AND CONSEQUENCES

By

PROFESSOR MICHAEL O. KEHINDE
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AND CONSEQUENCES

An Inaugural Lecture Delivered at the University of Lagos
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By

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My Student: Past and Current;
The alumni of this centre of learning especially 72-77 set &
current Trainees;
The care givers;
My patients especially those with sickle disorder;
My Family and Friends;
Gentle Men of the Press;
Distinguished Ladies and Gentlemen

Ps 112
Bless the name of the lord both now and forever.
From sunrise to sunset let the name of the lord be praised.
The lord is high above all nations, his glory above the heavens
Who is like the lord our God who is enthroned on high, and
looks down on heaven and earth.
He raises the needy from the dust; he lifts up the poor man
from the dung hill.
To place him with princes, with the princes of his people.
He makes her who was barren to dwell in a home, the joyful
mother of children
INTRODUCTION
Mr Vice-Chancellor Sir, I welcome everybody to this Inaugural lecture being the Seventh from the department of Medicine, College of Medicine, University of Lagos. This is the first to be given by a physician who is also a Clinical Haematologist. Clinical Haematology is an important branch of Internal medicine and is highly regarded globally.

Haematology
Haematology is a varied and stimulating discipline, perhaps one of the broadest in the hospital, which includes both laboratory and clinical medicine specialties. There are multiple broad areas within haematology including haematology, genetic disorders (including haemoglobinopathies), sickle cell disease, thalassaemia, haemophilia, and storage disorders, and transfusion medicine. It’s a rapidly changing specialty mixing the best of laboratory and clinical medicine.

Clinical haematology
A physician is defined as a specialist in medical diagnosis and treatment, by the concise oxford dictionary of current English. Clinical haematologists are thus specialist physician who have further specialised in the area of clinical haematology.

Clinical Haematologist have direct responsibility for their own patients and are concerned with the management of medical, surgical, obstetric, and paediatric patients within the hospital. Patient care has now become the main focus of most haematologists' workload. Patients are of all ages and have a broad mix of life threatening, acute, chronic, and terminal disorders. Most patients are extremely worried about having to see a Haematologist and are grateful for the care we give them.

Specialist interests within haematology include the following:
Haemato-oncology:  
**Bone marrow transplantation**  
Coagulation and platelet disorders (including haemophilia, thrombophilia, thrombotic thrombocytopenic purpura)  
Red cell disorders (including sickle cell disease and thalassaemia)  
Transfusion medicine, Obstetric haematology, Liposomal storage disorders, Laboratory haematology (including diagnostic haemopathology), Paediatric haematology, and Bone marrow failure syndromes

Clinical haematologists also have considerable responsibility in the laboratory. A hospital always has a routine haematology laboratory, which provides basic haematological tests such as full blood counts, erythrocyte sedimentation rates, or plasma viscosity; coagulation screens; and blood cross matching. Most large hospitals also have specialist laboratories providing one or more of the following: haemoglobin electrophoresis, diagnostic bone marrow interpretation, specialist coagulation tests (thrombophilia screens and factor levels), specialist red cell tests (erythropoietin, red cell enzymes, and membrane tests), and specialist diagnostic haemato-oncology (immunophenotyping, cytogenetics).

Clinical haematologists must have an understanding of the principles and limits of the tests done as well as an understanding of the meaning of the results. The role of the haematologist is to provide interpretation of the tests within the clinical context and to give advice accordingly.

Because of the dual clinical and laboratory nature of haematology, Clinical haematologists often find themselves and their work split between two or more directorates in the hospital—usually Pathology and Medicine (or Paediatrics, or both).

Some haematologists rarely, if ever, have direct responsibility for patient care. These may include specialists
in transfusion medicine based in transfusion centres, and laboratory haemopathologists or academics who decide to work wholly in scientific research.

The Specialist Physician and Clinical Haematologist - My experience

My academic sojourn commenced in 1992, when I joined the Department of Medicine as a lecturer grade 1. I had completed both specialist training in Internal medicine (Part 1 FMCP) and undergone sub-specialty training in clinical haematology culminating in the Part II FMCP. At that time, I was fortunate enough to have on ground the retinue of moribund and obsolete facilities such as the Wild Heerbrugg microscope & accessory, Wild wet zlar microscope, Leitz video microscope, water bath (Grants Instruments), weighing balance (Sartorius) and small microscope (Olympus).

These facilities had been abandoned for over one half of a decade. They were the same equipment that had been fully functional and were in use during my medical student days and also during the residency training. When I started residency training, there were no clinical Haematologists except Prof. Olu Akinyanju who pioneered the Haematology Unit of the Department of Medicine in CMUL. Dr. C.C Okany and Dr. Chris Otigbo were also my senior colleagues and trainees in the programme.

The task of reviving the Unit fell on me; so I took the challenge very seriously. The work included the clearing and organisation of both the routine and specialised haematology laboratories. It also included teaching; conducting research and giving clinical service in internal medicine and haematology. I got the support of the Head of Department of Medicine, the Chairman, Research laboratories in the Department of Medicine. With a research grant, I was able to get some modern reagents and critically needed equipment for clinical practice and research.
Without being modest, these laboratories along with the clinical training in the wards and Out Patients were available to train Clinical Haematologists. Dr. Doris Amachree, Dr. Baba Fisher and Dr. A. Saidu successfully completed the essential laboratory posting and clinical rotation in internal medicine and clinical haematology. They also conducted relevant research and completed their dissertation projects. Dr. A. Saidu even obtained a special award for being the best that year. He is currently the CMD in Gombe Federal Medical Centre and also an examiner in Fellowship examinations at all levels in the Faculty of Internal Medicine of the National Postgraduate Medical College of Nigeria. Other specialists trained in the unit include Dr. A. Ajayi now in Federal Medical Centre, Ebute Metta, and Dr. P. Ereaga.

Through my effort, there is now an established Clinical Haematology Unit in the Department of Medicine, University of Kano Teaching Hospital. Many students have been trained in the Unit as they do their postings in medicine and surgery.

Mr Vice Chancellor Sir, at this time, this is the only centre for training now for Physicians with interest in Clinical Haematology in our country. The schedule of work in the Unit has been to teach whenever required; the undergraduate students-(Basic therapeutic skills (BTS) and Basic clinical (BCS), 400 and 600 level medical students), 500 level Dental students and pharmacy students in clinical posting in Medicine. Also, the postgraduate students are trained to provide the services to patients and to conduct clinical and laboratory research. To carry out these activities well, there must be adequate number of well-trained staff, adequate number of functioning equipment, reagents, audio-visuals, and microscopes. The clinical rotations include: management of patients on hospital admission, in out-patient clinics and in the accident and emergency wards. The services in the laboratories include: examination
of the bone marrow aspiration or trephine and blood film regularly with interpretation of results.

For over 20 years, I have been the sole member and head of the clinical haematology Unit and have devoted my time and talent to development and training. I am thankful for Dr. Ibidapo M.O.O. who was also on staff for about 4 years before she moved on to greener pastures in the United Kingdom. There was a challenge of maintaining the unit and various considerations in merging the clinical haematology unit with laboratory haematology in the Department of Pathology. Currently, these 2 branches of haematology serve different roles and maintain a strategic collaboration.

Water-bath Grant Instrument

Wildwetzlarx1, Leiez Microscope, Wild Heerbrugg, Small
All the equipment for teaching and service that had broken down has been restored and are in good functioning state. I was able to get new microscopes, a coulter counter through the Department of Medicine grants and Unit research grants even a digital microscope and other equipment through the University grant.
- Coulter Machine (Swelab Alfax), with printer (EpsonLQ-300+II), Multifunctional Mixer and UPS (Bluegate)

Microscopes, Optika B-350, 33

Novel BM1600 Olympus 33
HP Deskjet 2050 printer & Scanner

Spectrophotometer Spectro V-16

Coagulation Analyzer Kayto RT-2204C
In the past 2 years, succour has come. My previous trainee and now colleague, Dr. Kalejaiye was employed as a Lecturer 1. At last, the Haematology Unit has a full complement staff comprising of two consultants and four senior residents. (One of whom has come for training from outside Lagos state). My thanks goes to the department of Medicine where all the staff members have been in support of the Unit and posting staff members as the need arose at all times.

When I started, there were no clinical Haematologists except the pioneer Prof. Olu, O. Akinyanju now there are Professors and Consultants in the field of clinical haematology including Professor C. C. Okany, Dr Chris Otigbo, Professor M. O. Kehinde, Dr. A. Saidu, Professor N. Akinola, (She also has a PhD), Dr. Baffa Guaram, Dr. A. Ajayi, Dr. P. Ereaga, Dr. AbdulSalam Dutse, and others.

HUMAN UNIQUE BLOOD CELLS AND CONSEQUENCES
Blood is a constantly circulating fluid providing the body with nutrition, oxygen, and removing waste. It is mostly liquid, with numerous cells and proteins suspended in it, making
blood "thicker" than pure water. The average person has about 5 litres (more than a gallon) of blood. A liquid called plasma makes up about half of the content of blood. Plasma contains proteins that help blood to clot, transport substances through the blood, and perform other functions. Blood plasma also contains glucose and other dissolved nutrients. Blood is conducted through blood vessels (arteries and veins). Blood is prevented from clotting in the blood vessels by their smoothness, and the finely tuned balance of clotting factors. But readily clots on leaving vessel.

**Figure 1: A blood vessel containing a variety of blood cells**

About half of blood volume is composed of blood cells: The 3 main blood cells are:

1) Red blood cells, which carry oxygen to the tissues
2) White blood cells, which fight infections
3) Platelets, smaller cells that help blood to clot, they prevent bleeding.
THE RED BLOOD CELLS
Normal red cells are disc shaped; they contain a pigment known as haemoglobin, which carries oxygen. This oxygen is circulated and supplied to every cell in the body.

Figure 2: The characteristic disc shaped red cells

THE WHITE BLOOD CELL-(Granulocytes and Lymphocyte and others)
White blood cells are roughly round in shape and each one contains a nucleus (unlike mature red cell that do not contain nucleus). The nucleus of some of the white cells contains two to five lobes. There are many types of white cells identified by characteristic colour uptake on special staining. Granulocytes are white blood cells that contain granules. Neutrophils are white cells that take a neutral colour on staining; Eosinophils and Basophils are reddish and bluish respectively on staining. Some white cells are devoid of granules are known as agranular cells. Some are non-granular in their cytoplasm and are known as lymphocytes.

Generally, white blood cells are concerned with various defensive and reparative functions of the body. They play important roles in the destruction of invading antigens. The major function of the white blood cells especially the
polymorphor nuclear leucocyte is to prevent or retard the intrusion of infectious agents and other foreign material into the host environment.

Figure 3: White blood cells
Platelets are smaller cells that help blood to clot and thus prevent bleeding.
White blood cell and AFRICAN NEGRO

Mr Vice Chancellor Sir, current evidence suggests that the white blood cell (WBC) count is lower in African Negro populations than in Caucasian populations. In pathological states, alteration in the total number of white blood cells (leucocytes) in the Negroes studies have shown that (Ebry-Roberts) there is a lower granulocyte count in the South African Bantu soldiers compared to the Caucasian. Similar lower total leucocyte counts with neutropenia have been reported in the American Negros (Forbes, Johnson and Consolazio 1941).

This pattern of leucocyte counts in the African Negros has been confirmed independently over quarters of a century in all parts of Africa. Most studies showed that mean leucocyte counts for African Negro is about $5.0 \times 10^9$ cells but a lower limit of about $2.0 \times 10^9$/cell/L.

Table I: Ethnic differences in white blood cells and platelets.

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<th>CAUCASIAN</th>
<th>AFRO ARRIBEAN</th>
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<tr>
<td><strong>MALE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>4.5 (2.8 - 7.2)</td>
<td>5.7 (2.8-9.5)</td>
<td>5.2(2.8-9.5)</td>
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<tr>
<td>Neutrophil Count</td>
<td>2.0 (0.9 - 4.2)</td>
<td>3.2(1.7-6.1)</td>
<td>2.5(1.0-5.8)</td>
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<td>Lymphocyte Count</td>
<td>1.8 (1.0 - 3.2)</td>
<td>1.7(1.0-2.1)</td>
<td>1.9(1.0-3.6)</td>
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<td>Monocyte Count</td>
<td>0.29 (0.15 - 0.58)</td>
<td>0.34(0.18-0.52)</td>
<td>0.33(0.18-0.52)</td>
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<tr>
<td>Eosinophil Count</td>
<td>0.12 (0.15 - 0.79)</td>
<td>0.12(0.03-0.48)</td>
<td>0.13(0.03-0.58)</td>
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<td>Platelet Count</td>
<td>183 (115 - 290)</td>
<td>218(143-332)</td>
<td>196(122-313)</td>
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<table>
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<th>CAUCASIAN</th>
<th>AFRICAN</th>
<th>AFROCARRIBEAN</th>
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</thead>
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<td>WBC</td>
<td>6.2 (3.5-10.8)</td>
<td>5.0 (3.2 - 7.8)</td>
<td>5.7(3.3-9.9)</td>
</tr>
<tr>
<td>Neutrophil Count</td>
<td>3.6 (1.7-7.5)</td>
<td>2.4 (1.3-4.2)</td>
<td>3.0(1.4-6.5)</td>
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</table>

**Contribution to Knowledge in Nigeria**

The function of white blood cells (WBC) is to protect the body from infection.

When there is an infection in the body, the WBC increases in its numbers to effectively control the infection. Other conditions like tissue injury, surgical trauma among others also causes an increase in WBC count. These have been well demonstrated in Caucasians. The physiological variations in the numbers of leucocytes had been shown to be related to the effect of stimulation of the adrenal cortex. It has been noted by some workers (Carrey and Byan, 1935) that the magnitude of the leucocytosis is a function of the intensity rather than of the duration of the infection or stress. The Leucocyte counts in African Negro even though lower than those of the Caucasian, do they function just as efficiently as in the Caucasian? This is an important issue that has clinical implication in the African.

Mr. Vice-Chancellor sir, we conducted a research study to observe the behaviour of WBCs undergoing severe stress during surgical operations in Nigeria.

The surgical operations were graded according to the degree of anticipated tissue trauma into minor, intermediate and major, in 66 patients (27 males and 39 females) who had elective surgical operations with no sign of infection.
The peripheral blood total and differential leucocyte counts were determined pre-operatively and at 2 hours, 24 hours and 7 days post-operatively.

We observed that a highly significant increase (P<0.001) in the total leucocyte, polymorphonuclear leucocyte (PMN) and stab cell count occurred 2 hours and 24 hours after major surgery. These changes persisted after major surgery and returned to the preoperative level by the 7th post-operative day. Mr Vice Chancellor Sir, in this study, we confirmed the low WBC counts in Nigerians. We also confirmed the robust increase in WBC count as a result of intermediate and major surgical trauma.

The pattern of leucocyte response to surgical trauma in the African NEGRO


Figure 5a
Pre – Operative and Post-Operative Leucocyte Counts Of Patients Who Had Minor Surgery

White cells were low pre operation confirming the previous studies that show low WBC due to low neutrophil count in
Africans. Mild trauma did not affect total WBC & Neutrophils counts.

**FIGURE 5b**: Pre-operative and post-operative leucocyte counts of patients who had intermediate surgery

![Graph showing leucocyte counts](image)

**Figure 5c**: Pre-operative and post-operative leucocyte counts of patients who had Major surgery

![Graph showing leucocyte counts](image)
Other diseases of White blood cells
Mr Vice Chancellor Sir, diseases of white blood cells include lymphomas, leukemia’s etc., many of which are common in Nigeria. They may begin with lymphadenopathy—swelling in the lymph nodes of different parts of the body. This is frequently found in lymphomas, but may also be found in conditions such as tuberculosis and even HIV. Diagnosis requires lymph node biopsy with histopathological evaluation.

Angio-immunoblastic Lymphadenopathy (AILD): We report the case of an 18-year old male food vendor who presented with four months history of fever, night sweats, weight loss and abdominal swelling. He has been treated with anti-tuberculosis drugs for about two months without response. Physical examination revealed a febrile, ill-looking asthenic young man with moderate pallor, lymphadenopathy, hepatosplenomegaly and ill-defined abdominal masses. All tests were not diagnostic except the lymph node biopsy, which showed numerous immunoblasts, plasma cells, eosinophils and arborizing blood vessels, diagnostic of angio-immunoblastic lymphadenopathy. The patient responded dramatically to a course of chemotherapy consisting of cyclophosphamide, vincristine and prednisolone.

AILD is rare but does occur in local practice. To avoid missing the diagnosis, a high index of suspicion and liberal policy of lymph node biopsy with histopathological report are required.

Angio-immunoblastic Lymphadenopathy in a young man: A case report

Figure 6: Patient with AILD

Before treatment

After treatment

After treatment (no operation)

RED BLOOD CELLS
Normal red cells are disc-like shape and they contain pigment haemoglobin. Haemoglobin is a protein pigment that delivers oxygen to cells throughout the body. This oxygen is circulated and supplied to every cell in the body and is used to produce energy. The red cell is able to
change its disc shape to manoeuvre through large and small blood vessel after supplying oxygen to tissues and cell after which it becomes deoxygenated (oxygen depleted). Restoration of oxygen to these cells is accomplished in lungs.

**Anaemia**

Is a condition in which the haemoglobin pigment in the red blood cell is less than expected for age, sex, race, state of hydration and altitude. This leads to decreased oxygen carriage of the red cell, and decreased supply to tissues and organs. It is a common clinical condition in Nigeria and an important cause of morbidity and mortality. It can be the first sign of many illnesses.

Acute anaemia is nearly always due to blood loss and haemolysis. If blood loss is mild, enhanced oxygen delivery is achieved through changes in the oxygen binding affinity with haemoglobin (Bohr Effect). However, with acute blood loss, hypovolaemia dominates the clinical picture. Signs of vascular instability appear with acute losses of 10 to 15% of the total blood volume. In such patients, the issue is not anaemia but hypotension and decreased organ perfusion with patients exhibiting postural hypotension and tachycardia. In severe cases, signs of hypotension, shock including confusion, dyspnoea, and diaphoresis occurs. Such patients have significant deficit in vital organ perfusion and require immediate volume replacement.

We have demonstrated the importance of a good history and a thorough clinical examination to detect the signs and symptoms of anaemia. The type of anaemia and finally the cause can be achieved from the consideration of both the clinical features and simple blood examination. In some cases, special investigations are necessary for the determination of the cause.

Sickle cell Anaemia

The normal RBC haemoglobin comprises of 2 proteins called alpha and beta chains made up of amino acids. These proteins maintain the structure of the haemoglobin. Although, there are over 400 types of abnormal haemoglobin, including Haemoglobin C, D, E, O etc. Haemoglobin S (HbS) is the most troublesome and prevalent.

In Sickle Cell Anaemia, there is a genetic abnormality of the beta chain of the haemoglobin which leads to abnormal function of the red blood cell. This genetic abnormality is one amino acid substitution of the beta globin gene. The abnormal haemoglobin crystallises and solidifies and forms a sickle shape, which is hard and sticky and rigid. The red blood cell thus becomes unable to manoeuvre through the blood vessels to supply oxygen to the cells and tissues. Multiple abnormal sickled cells clump together and impede blood flow in the vessel and lead to ischemia and sickle cell crises. In addition, the life spans of the red cells decrease from 120 days to about 30 days or less.

Figure 7: Sickle nucleotide substitution in codon 6 of the β-globin gene leads to an amino acid substitution (glu→val) that is responsible for the sickle mutation in β-globin (βs), which forms the abnormal HbS tetramer.
The term sickle cell disease includes a group of condition in which a pathological process results from the presence of HbS. The principal phenotypes include:

- Homozygous sickle cell disease SS
- Sickle cell-haemoglobin C disease SC
- Sickle cell-β-thalassaemia Sβthal.
- Sickle cell-β*thalassaemia type I Sβ*thal.type I
- Sickle cell-β*thalassaemia type II Sβ*thal.type II
- Sickle cell-β*thalassaemia type III Sβ*thal.type III

**Who has Sickle Cell Disease?**

A person born (inheritance) with two abnormal haemoglobin (Hb) one of which is HbS. In persons with sickle cell anaemia, this haemoglobin abnormality (HbS) occurring simultaneously in the 2 pairs of genetic material (homozygous). Occurrence of this mutation in only one of the 2 gene results in sickle cell trait.

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*Figure 8: Sickle cell disease is inherited and not acquired*
Inheritance of sickle cell genes

Question: How does a person get the type of haemoglobin he or she has?

Answer: From the parents (Every child inherits two haemoglobins, one from mother and one from father). Parents also got their own haemoglobin type from their grandparents.

Mr Vice Chancellor Sir, thus, if one child inherits HbS from one parent and from the other parent is also Hb S then the child has HbSS. This double inheritance is called SICKLE CELL ANAMIA.

People who inherit a sickle haemoglobin gene from one parent and a normal gene from the other parent have sickle cell trait. People who have sickle cell trait usually have few, if any, symptoms and live normal lives.

Figure 9a: Inheritance of sickle cell trait and disease
Sickle cell Disease (SCD) in Nigeria

People with SCD have abnormal haemoglobin, called haemoglobin S (HbS) or sickle haemoglobin, in their red blood cells. About 300,000 children are born with a form of sickle cell disease every year mostly, in sub-Saharan Africa, but in other parts of the world such as the West Indies and people of African Origin elsewhere in the world. Sickle cell disease occurs more commonly in tropical and sub-Saharan region where malaria is or was common. The prevalence of HbS carrier frequency decrease to 1-2% on the North African coast and <1% in South Africa (WHO sickle cell anaemia).

Nigeria being the most populous black nation in the world has the highest incidence of sickle cell disease (SCD). It is estimated that around 2% of new-borns in Nigeria are affected by sickle cell anaemia (HbSS) giving a total of at least 150,000 affected children born every year in Nigeria alone. Sickle Cell Disease causes approximately 8% of all
infant deaths per year. The mortality associated with sickle disease is well known to us all.

The carrier (HbS) frequency is between 10% to 40% with an average of 25% in Nigeria. That would mean a Sickle cell trait carrier population that is over 50 million. Thus, one person out of every four persons has haemoglobin S. Epidemiological evidence suggests that carrying a single sickle cell (trait) Hb AS confers selective advantage in malaria endemic areas. In other words, being a heterozyte is advantageous.

*If one can describe an inherited disorder as an epidemic, then sickle cell anaemia in Nigerian tropical sub-Saharan Africa would eminently qualify for that description. So it is an epidemic that has been over looked.*

**Sickle Cell Anaemia: Historical events**

Prior to the formal report in 1910, Dr. James Herrick of Chicago, the sickle cell disease was recognised, for generations based on characteristic clinical features. It was known in West Africa as “cold season rheumatism”.

- “Lakuegbe” in Yoruba
- A person that has this disease is an “Abiku”
- “Aranmoleku” in Yoruba
- “Ogbanje” Ibo
- “chweechcheechwe” in Ga
- “Antuotuo” in Twi
- “nwiinwii” in Fante.

The clinical presentation could also be used to identify a particular type of sickle cell disease for example, if a male patient of normal physical build presents with a history of cold-season rheumatism, sudden blindness in one eye; then he is more likely to be suffering from sickle haemoglobin C disease. I.e. he has HbSC.
While if a jaundiced female who appear much younger than her true age, with a chronic ulcer above the media malleolus, she is probably-suffering from sickle cell anaemia. She has (Hb SS); we see how this variation on the general background pattern of “cold-season rheumatism.

In 1922, Mason was the 1st person to use the term sickle cell anaemia.

Dr. Herrick first met them a rheumatic pain, anaemia and jaundice black student in Chicago (Rhoads 1982).

Apart from the clinical considerations, SCD is associated with multiple cultural and psychosocial challenges. Many stem from ignorance of the disease and mode of inheritance. It often can lead to breaking up of friendships, creating enmity, which leads to breaking up of family union, disharmony, sadness and regret in the family.

There are so many negative actions and publicity to the extent that some children with sickle cell disorder are not sent to school by many parents and guardians. Some are not properly cared for at home because they expect that the children will soon die anyway since they have sickle cell disorder or get married away early if girls.

These report in the newspaper depict these negative publicity.
Characteristics of red cells containing haemoglobin S (HbS)

All patients with sickle disease (SCD) have the abnormal haemoglobin (HbSS or HbSC) in their red cells instead of the normal adult HbAA. The red cells are characterised by shortened red cell life span, and predisposition to forming clumps of sickled red cells leading to acute vaso-occlusive events in blood vessels and tissue ischemia. RBCs are more fragile and more readily scavenged from the circulation, contributing to the chronic anaemia.
Recurrent ischemia-reperfusion injury results from high oxidative stress burden. There is also elevated cell free haemoglobin and higher auto-oxidation of sickle haemoglobin. Consequences of high oxidative burden in sickle cell disorder include:

- Haemolysis. Intravascular haemolysis is observed and the consequent release of Hb to circulate freely in plasma contributes to the vasculopathy
- Endothelial damage.
- Reduced nitric oxide metabolites activity,
- Decreased levels of antioxidant enzymes,
- Elevation of lipid per oxidation levels
- Resulting in vaso-occlusion

www.nhlbi.nih.gov/health/health-topics/topics/sca

Figure 10 Normal and sickled red cells and vascular consequences
BLOOD flow IS NORMAL HERE Flow of red cells is blocked by the sickle cells

Metabolic Abnormalities in sickled red cells
- Oxidative stress
- Vitamin E levels are reduced
- Decreased activities of Catalase and glutathione reductase
• Increase peroxide dismutase activities, superoxide (increased generation of free oxygen radicals).
• Increased activities of G6PD methaemoglobin reductase and levels of glutamine malondialdehyde (a secondary product of lipid peroxidation).
• HbS-containing red cells adhere more readily to endothelium from the microvasculature. Endothelial Adherence and micro-vascular endothelium express the marker CD 36

Clinical manifestation of sickle cell anaemia (SCA)
An important feature of SCD is that the clinical scenario is notably heterogeneous—patients may present with mild forms of the disease which rarely require medical intervention or alternatively with more severe complications warranting frequent hospitalisation and aggressive management.

The life journey of a person with sickle cell disease can be troublesome at times with occurrence of bone pains due to sickling and haemolysis so that the red cell lives only for about thirty days and less instead of living for about one hundred and twenty days (which is normal) as a result of prevailing unfavourable environment such as dehydration, infection, emotional stress, strenuous physical exercise, very cold weather. RBCs are more fragile and more readily scavenged from the circulation, contributing to the chronic anaemia.

Sometimes sickle cell crises occur spontaneously due to no identifiable risk factor. They have acute vaso-occlusion events chronic haemolytic anaemia and organ dysfunction due to repeated sickling episodes. Reduced flow and oxygen supply cause pain and lead to rapid destruction of blood cells.

Figure 11: Some clinical conditions in sickle cell anaemia
Acute and chronic trauma of painful crises

Hand foot Syndrome can be infected as this Sickle cell Leg ulcer

Some acute complications that have constituted major causes of morbidity and mortality in Sickle Cell Disease are:

- Overwhelming infection
- Acute chest syndrome
- STROKE (Cerebro-vascular accident) especially in children
- Aplastic crisis
- Hyperhaemolytic crisis (severe anaemia)
- Pain crisis and anaemia crisis
My Contribution to sickle cell research in Nigeria

Sickle cell pain crises

Mr Vice Chancellor Sir, sickle cell pain crisis is a medical emergency in Nigeria. The treatment approach to this common problem is known to vary amongst medical practitioners. **We have assessed the management of SCD pain crises in adults by medical practitioners in Nigeria.**

In a cross sectional survey of one hundred and seventy-four medical practitioners, we found that 70-80% of these doctors were giving appropriate strength of analgesics for appropriate severity in pain. 32 of 163 (18.4%) would however not prescribe narcotic analgesics even in severe pain crises, for various reasons. However, 38 of 174 (24.2%) would give inadequate quantity of fluid and 18 of 124 (14.6%) will not give antibiotic even in the presence of markedly elevated white blood cell count. 45 of 90 (50%) will give anti malaria drugs routinely. Others will give anti malaria drugs only if there is fever. None of the doctors will insist on a laboratory demonstration of malaria parasitaemia before giving anti-malaria drugs.

*(Kehinde M. O. Ibidapo M. O. O Nigerian journal of Clinical practice December 2002 Vo.5 (2) 100-114)*

**Figure 12a: Choice of Analgesics in mild pain crises among general medical practitioners**
Figure 12 b: Choice of Analgesic in Moderate Pain Crises

choice of analgesic in moderate pain crises

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<td>2.9</td>
</tr>
<tr>
<td>Novalgin</td>
<td>22.6</td>
<td>19</td>
</tr>
<tr>
<td>Tramadol</td>
<td>30.6</td>
<td>36.2</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>33.9</td>
<td>37.1</td>
</tr>
<tr>
<td>Narcotics</td>
<td>9.7</td>
<td>4.8</td>
</tr>
</tbody>
</table>

FIGURE 13: Reason For Non-Use of Narcotic Analgesics (In Severe Pain Crisis) By 32 Doctors

Reason for Non-Use of Narcotic Analgesics (in Severe Pain crisis) by 32 Doctors

- Cost: 18
- Non-Availability: 9
- Risk of Addiction: 5
**Conclusion**: Although, 70-80% of doctors manage pain crises appropriately, it would be desired that all doctors manage sickle cell pain crises appropriately. To achieve this, a pain management protocol may be introduced in order to ensure that every sickle cell pain is properly and constantly managed.

**Survival in Sickle Cell Anaemia**

We have examined our experience of sickle cell disease in the United Kingdom, London borough of Haringey over the past 20 years. There were 145 subjects (1980). Admission for painful crises in HB SS disease was more frequent in the UK than in Jamaica. But the acute chest syndrome appears to be less common in the United Kingdom than in Jamaica. Splenomegaly appeared less frequent in Hb SC patients in this country and there is also a lower incidence of leg ulceration in both Hb SS and Hb SC disease in the United Kingdom than in Jamaica.

Cold weather is often postulated to increase the risk of SCA complications. I undertook a research in North London, United Kingdom to evaluate the effect of seasonal variation on the incidence of sickle cell pain crises. (Figure 14)

![Figure 14: seasonal variation in frequency of sickle cell hospital admission in North London, UK](image-url)
Examination of the effect of seasonal variation on the incidence of hospital admissions for painful crises reveals no signification clustering of cases in a particular month or season of the year.

**Survival in Nigeria: Our hospital outpatient experience**

Mr Vice Chancellor Sir, when we look at the patients in our sickle cell out patient record in 1984, there were no patients older than 30 years of age. (1984). 20 years later, in 2004, 30% of patients with sickle cell disease were over 30 years. This effect has been consistent and shown even up to 2015. The oldest patient was over 60 years. This is as a result of the increased medical care and support instituted in our haematology unit.

The main cause of poor survival of children with sickle disorder is the lack of consistent coordinated care and follow up. Whereas when people have bothered to care for them like children should be cared for, the results have been very good. Persons with sickle cell anaemia have been able to do all things getting good results and even being in charge of thriving successful companies, live full healthy life with their offspring. In addition to medical care, modifier genes and/or environmental factors are significant in patient survival. The genetic aspect related to longer survival remains poorly understood but is now receiving considerable research attention.

Subjects with SCA can live old with full normal life. With proper appropriate care many do very well.
Figure 15 A- Survival of subjects with SCA in clinic cohort 1984, Total No=516 patients

1984 SCD survival analytical graph

Figure 15 B- Survival of subjects with SCA in clinic cohort 2014, Total No=570 patients

2004 SCD Survival Analytical Graph
Figure 15: Survival of subjects with SCA in clinic cohort 2015-2015, Total No = 247 patients

Figure 16: SEPTUAGENARIAN patient with SCA

DIED AFTER EIGHTY YEARS
Over eighty years alive, well and hearty

Longevity in Sickle cell Disease
We report a case of unusually long life in a Nigerian with sickle cell anaemia. The patient, a 77 year-old Nigeria woman and a retired primary school teacher with sickle cell anaemia, was diagnosed at a relatively late age of 37 years. She had been hospitalised for only three occasions for bone pain crises since diagnosis. She has never had jaundice, leg ulceration, or blood transfusion and has led an active life. Her steady state haematocrit was 0.27/l. Her foetal haemoglobin and haemoglobin A2 measured 23.6% and 2.7% respectively.


CONCLUSION
Benign course of sickle cell anaemia is related to a normal life span. This benign course appears to be associated with the presence of high foetal haemoglobin and a relatedly moderated level of normal haemoglobin.
Sexual dysfunction Affecting Men with Sickle Cell Disease

Mr Vice Chancellor Sir, priapism is a urological emergency, which occurs frequently amongst SCD patients, and can be associated with erectile dysfunction (ED) and priapism. We conducted a cross section survey of 120 male patients with SCD to evaluate erectile dysfunction. The patients were aged 16-44 years with a mean of 25.42 ± 6.34. 21(48.8%) had a satisfactory erectile function (EF) while erectile dysfunction occurred in 22 (51.2%) patients. 15 (34.9%) had mild ED, 2 (4.7%) had moderate ED and 5 (11.6%) had severe ED. Erectile dysfunction reduced with increasing age, having occurred in 85.7% (6 of 7) in ages 16 – 20 years.

PRIAPISM

Figure 19: Stuttering priapism in a male sickler
Priapism in Sickle Cell Anaemia Patients at a Lagos Tertiary Hospital
Priapism is defined as painful persistence prolonged penile erection in the absence of penile stimulus. It is commonly recurrent or stuttering and a well-recognised complication of sickle cell disease. The acute complications of priapism include pain, dysuria, and psychological stress.

Priapism can also precede or follow some acute bone pain crisis, long term sequel of priapism were also psychologically and physically damaging. These include varying degrees erectile dysfunction, frank impotence, and sexual dissatisfaction including a fear of engaging in sexual activity.

Mr Vice Chancellor Sir, priapism in sickle cell person's exhibits considerable heterogeneity in frequency and severity of attack. We studied 315 patients in steady state, between ages of 10 to 42 years. We found that 104 (33 %) had had priapism. The time of occurrence of priapism did not conform to any pattern and was describe as irregular in 65 (62.5%) patients. In others, it occurs daily in 14 (13.5%), weekly in 11 (10.6%), monthly in 9 (8.7%) and yearly in 5 (4.8%). Priapism was of moderate severity on 51 (49.0%) patients. It was of mild severity in 35 (33.7%), and severe in 18 (17.3%) patients. The occurrence of priapism was spontaneous in 80 (76.9%) patients. The duration of an attack of priapism was about 1 hour or less in 76 (73.1%). In 69 (66.3%) patients, priapism occurred at night and in daytime in 23 (22.3%). It was associated with sleep disturbance in 26 (53.1%), dysuria in 13 (26.5%), acute urinary retention in 7 (14%), penile oedema in 2 (4%) and scrotal oedema in 1 (2%) patient.

**Treatment of Priapism**

Various conservative measures have been tried to abort attacks of recurrent or stuttering priapism. These include: hydration, simple and compound analgesia, exercise, tranquillizers, blood transfusion, vasodilators, anticoagulants and lately Hydroxyurea. There is a lack of consensus on the
best treatment for this condition. The conventional surgical treatment is intra-carvenosal injection of alpha agonist first recommended by the United States Urological Association. It has lots of complications including bleeding. From previous works, it seems that prevention of recurrent attacks of stuttering priapism may prevent an acute major attack with its catastrophic consequences.

Oral medication is required to prevent stuttering priapism from going to ischaemia and resulting complications. The drug found useful orally is Etilefrine, a French drug not readily available and expensive.

In an International randomised controlled trial, we studied the usefulness of ephedrine in the prophylactic management of priapism and compared various doses of ephedrine (30mg and 15mg) and Etilefrine (50mg) and placebo. Its aim is to compare documented treatment modality with a more easily available alternative in terms of tolerability and efficacy.

We found ephedrine to be safe and efficacious at 30mg daily and as good as etilefrine (50mg).

This work was made possible through the indefatigable Dr. Ade Olujohungbe, Consultant Haematologist and a SCD patient himself in England. The fund was from UK sources in collaboration with Professor Akinyanju, Professor Akenova and others. May his gentle soul rest in peace Amen.

A Prospective Dairy Study of Stuttering Priapism in Adolescents and Young Men with Sickle Cell Anaemia: Report of an International Randomized Control Trail-The Priapism in Sickle Cell Study.
Problems Affecting Women with Sickle Cell Disease

Mr Vice Chancellor Sir, the onset of puberty is usually delayed in women with sickle cell anaemia. Washburn noted a delay of menarche at age 18 years and Mason recorded a slender build, absence of auxiliary hair and scant beard and pubic hair in a 21-year-old male. Recently, a Jamaican cohort study showed mean age at menarche was 2.4 years later in homozygous sickle cell disease. An early pathological review noted a tendency for adult to be tall and slender with long extremities and with poorly developed sexual characteristics. The first anthropometric studies reported long thin extremities; narrow pelvic and pectoral girdles, a hood-shaped chest with increased antero-posterior diameter and low body weight. The mean weight of children and adults with SS disease patients is subnormal (Sergeant et al. 2001). The finding from this study suggests that weight was the principal determinant of age at menarche. The height of HbSS patients catches up and overtakes that of AA controls during adolescence resulting in a greater mean height in adult patients. Timinez et al (1966) noted a mean age at menarche of 13.6 yrs. in Washington DC compared to 12.2 yrs in normal black controls.

In our recent report, poor nutritional status and socioeconomic background were shown to have adverse effect on the age at menarche.

Neurological complication of SCA

Sickle cell anaemia (SCA) has widespread clinical manifestation that involves nearly all the system of the body including the central nervous system.
neurological complications in patients with sickle cell disease was known for decades but the explanations for clinical variability were not well known. Sickle cell anaemia results in recurrent vascular thrombosis and ischemia causing vasculopathy of large and small vessels. Intravascular haemolysis is observed and the consequent release of Hb to circulate freely in plasma contributes to the vasculopathy, probably by scavenging nitric oxide (NO) and causing a functional deficiency of that molecule. There is also evidence of small vessel slugging and relative deficiency of nitric oxide in the vessels further reducing compensatory vasodilations. This results in both ischaemia and infacts and association with motor and cognitive cerebral functions. No specific studies have addressed the neurological complications of sickle cell anaemia and its contribution to morbidity.

NEUROLOGICAL COMPLICATIONS OF SICKLE CELL ANEMIA IN NIGERIA AFRICAN – A CASE-CONTROL STUDY

We determined the neurological complications associated with sickle cell anaemia (SCA) in Nigerians in order to evaluate the relative frequencies. Six hundred and thirteen patients (613) with SCA attending the outpatient's clinics of Lagos University Teaching hospital and 616 control subjects were evaluated using a uniform structured questionnaire to determine the occurrence of neurological complications. The relative frequencies of neurological abnormalities in patients and control were compared.

Mr Vice Chancellor Sir, we found neurological abnormalities occurred in a significantly higher proportion of SCD patients (76%) compared to control (32.1%). Among children these abnormalities included stroke, febrile seizure and headache. Among adolescent and adult, the abnormalities included paraplegia, epileptic seizures and localised sensory neuropathy. Headache occurred in a significantly higher
Treatment of Sickle Cell Anaemia

Background

Sickle haemoglobin molecules suffer repeated polymerisation/depolymerisation generating great amounts of reactive oxygen species leading to chronic and systemic oxidative stress. This can lead to a cyclic cascade characterised by blood cell adhesion, hemolysis, vaso-occlusion, and ischemia–reperfusion injury. Control of symptoms and prevention of disease complications are important in SCA. Management during the steady state includes: counselling of patient and family, clinical monitoring, nutrition and hydration and lifestyle counselling. Various analgesics are used for pain management. Blood transfusions are used to treat severe anaemia. Prevention of infection is important and Pneumovax vaccine is...
recommended every five years. Nutritional supplementation with Folic acid daily 5mg is recommended.

**Hydroxyurea** is a potent inducer of foetal haemoglobin and evidence over the past 30 years has documented its laboratory clinical efficacy for both adults and children with SCA.

Hydroxyurea reduces the morbidity and mortality of both adults and children with sickle cell anaemia.

Hydroxyurea is well tolerated in adults and children with SCA without significant short-term toxicities or long-term safety concerns.

Mr Vice Chancellor Sir, with a large body of evidence demonstrating its safety and marked efficacy for SCA, hydroxyurea should now be considered as a disease-modifying therapy for all patients with SCA, regardless of age or clinical severity.

The extension of hydroxyurea treatment into economically and resource-poor countries could provide substantial benefits to the global sickle cell population.

Therapeutic agents that can target oxidative stress constitute a valuable means for preventing or delaying the development of organ complications.

**Vitamin C (Ascorbic acid)**
Various studies have shown that vitamin C is one of the most efficient antioxidant in human plasma (Froi et al 1989).

**Vitamin C in SCA**
Vitamin C is a water-soluble vitamin and is reported to possess anti-oxidant properties. We undertook a study to assess the effect of vitamin C on blood pressure, osmotic fragility of red blood cells, haemoglobin concentration [Hb],
packed cell volume (PCV), mean corpuscular haemoglobin concentration (MCHC) and percent irreversibly sickle cell count (%ISC) of sickle cell anaemia subjects. Twelve (12) male sickle cell anaemia subjects whose ages ranged between 16.0 years and 25.0 years were studied. Each subject received three hundred milligrams (300mg) of vitamin C (Mopson Pharmaceuticals, Lagos, Nigeria) in addition to his normal medication. The study was carried out over a period of 6 weeks. Vitamin C loading significantly reduced systolic blood pressure (SBP) diastolic blood pressure (DBP) and mean arterial pressure (MAP) but had little or no effect on pulse pressure.

Vitamin C also significantly increased [Hb]) and PCV but reduced MCHC (p<0.05) and % ISC (p<0.001). Vitamin C reduced the concentration of NaCl that caused initial lysis of red cells from 0.87 ± 0.01% to 0.39 ± 0.01% NaCl (p<0.001) but had little or no effect on the concentration at which complete analysis occurred.

Mr Vice Chancellor Sir, through our research, we have found ascorbic acid useful in sickle cell disease at a dose of 300 mg. We have therefore incorporated it into our recommended treatment daily for the patients.

EFFECT OF VITAMIN C ON ARTERIAL BLOOD PRESSURE, IRREVERSIBLY SICKLED CELLS AND OSMOTIC FRAGILITY IN SICKLE CELL ANEMIA SUBJECTS. S. I. JAJA, M. O. KEHINDE, S. GBENEBITSE, F. B. O. MOJIMINIIYI AND A. I. OGUNGBEMI
Figure 21: Effect of Vitamin C Supplementation on haematological and osmotic fragility parameters

**NaCl CONCERNTRATION (%)**

Effect of vitamin C supplementation on osmotic fragility of red cells in sickle cell subject.

**%HAEMOLYSIS**

Fig. 21 shows the osmotic fragile gram before and after vitamin C supplementation. Vitamin C supplementation significantly decreases the concentration of NaCl ($p<0.001$)
but did not affect the concentration at which the complete lysis occurred.

**Arginine in SCD**

Arginine is one of the essential amino acid that the body needs. We showed that oral, low-dose l-arginine supplementation (1 g/day for 6 weeks) enhances antioxidant activity and erythrocyte integrity in patients with sickle cell anaemia.

**Figure 22 Effect of l-arginine supplementation on measured parameter**

![Bar chart showing the effect of l-arginine supplementation on erythrocyte osmotic fragility](chart)

Fig 22 shows the effect of supplementation with l-arginine on the erythrocyte osmotic fragility gram of the SCA subjects. Supplementation shifted the curve to the right. Concentration of buffered NaCl at which initial lyses of erythrocytes occurred fell from $0.86 \pm 0.01 \text{ g}\%$ to $0.57 \pm 0.02 \text{ g}\%$ ($p < 0.001$). Supplementation also decreased the concentration of NaCl at which complete lyses occurred ($0.21 \pm 0.002 \text{ g}\%$ vs $0.11 \pm 0.02 \text{ g}\%; p < 0.001$).
Twenty eight sickle cell anaemia subjects were recruited for the study. Five millilitres of blood was withdrawn from an antecubital vein for the estimation of plasma arginine concentration ([R]), total anti-oxidants enzymes (TAE) Activity, malondialdehyde concentration ([MDA]), RBC count, [Hb], PCV, MCHC, MCV, MCH, percent irreversibly sickled cells (%ISC) and osmotic fragility of red blood cells in the subjects. Supplementation shifted the osmotic fragile gram to the right and reduced the concentrations of NaCl at which initial and complete lyses of erythrocytes occurred. Study showed that low-dose, oral L-arginine increased antioxidant activity, red blood cell resistance to osmotic lysis but reduced red cell density in SCD.

Other Pharmacodynamics therapy in SCD
Pharmacodynamics approach includes the use of prospective anti-sickling agents which modulate the sickling phenomenon by interacting with various macromolecular targets. These have no curative effects but offer more prospects than common palliatives.
- Gene modifier like clotrimazole.
The RBC membrane modification involves Na/K+ATPase modulation.
- Anticipideme and antigelling agents.
- Natural products comparing plant based formulae marine based spacies, animal parts.
- Some herbs have been claimed to useful in sickle cell disease like Sicklavit, (Xanthoxylum Xantholoides) Fagara, Niprisan, Celloid S, Solamin (honey herbal products comprising of three plant materials) and more have been used with varying results.

Mr Vice Chancellor Sir, we have evaluated some of these local herbs for palliative therapy in SCA including Carica Papaya leaf extract, celloid-S and Solamin with variable results.


Bone marrow transplantation in SCD

Bone marrow transplant is also known as a stem cell transplant. It is the only cure for sickle cell anaemia. It involves replacing the affected bone marrow with bone marrow
donated by someone without sickle cell anaemia. After the transplant, the new bone marrow will produce healthy blood cells.

Curative prospects include – Bone Marrow transplant (90-95%) success reported. Limitations includes cost implications, strict type-matching requirements associated high risks posing deterring factors.

Other contribution to haematology in Nigeria
Glucose 6 Phosphate Dehydrogenase Deficiency
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common inherited metabolic disorder of red blood cells. It is a hereditary abnormality in which the activity or stability of the enzyme Glucose-6-phosphate dehydrogenase is significantly diminished leading to haemolysis during oxidative stress. Erythrocytes are most severely affected and may haemolyse and result in anaemia chronically or during certain stressful situations. A high frequency of G6PD deficiency coincides with the present or historical distribution of plasmodium falciparum malaria. This accounts for the persistence of the allele in certain populations in that it confers a selective advantage.

A conservative estimate of 100 million people is affected worldwide but the greatest frequency occurs in the tropical and subtropical zones of the eastern hemisphere which include Nigeria. The inheritance is sex linked and incompletely dominant. Of the many isoenzymes with varying activities, type GdA- with diminished enzymes is the variant responsible for clinical disorder in Nigerians. Twenty two percent of the male population has GdA- in Nigeria. The main goals for the control of the disease are the ability to make diagnosis, treat appropriately and prevent recurrent episode of illness in affected individuals.

Strategies for achieving these goals should include appropriate education of health care provider and members
of the public and installation of adequate diagnostic facilities and a monitoring system within the health service. A community based natural history research project should provide better information to guide the development of appropriate control measures.


2. **MO Kehinde.** Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency. Nigeria Medical journal No.1 January-February 1997

**MALARIA**

Mr Vice Chancellor Sir, Malaria affects over 200 million people worldwide and kills more than two million people annually well over 80% of malaria case and death occurs in Africa. Malaria is an important cause of morbidity and mortality in Nigeria.

The effects of malaria infection are wide spread. Anaemia often occurs as a result of non-sequestration erythrophagosisisis and dyserythropoiisises. Thrombocytopenia is a less often recognised haematological change in spite of being a common occurrence. It has been observed in about 70% plasmodium falciparum infections. The malaria related with thrombocytopenia has a multifactorial aetiology which includes auto immune mechanisms, splenic sequestration, disseminated intravascular coagulopathy and platelet activation and consumption from the effects of ADP release from damaged cells.

Complicated malaria has received much attention possibly because of its rapid fatal end if appropriate management is not provided. However, uncomplicated malaria that occurs more commonly requires continuing study. Platelet counts are really
determined routinely when requesting for blood counts by attending physician who manage patients with acute uncomplicated malaria infection, yet thrombocytopenia is a recognised feature of malaria. We have reported changes in platelet counts in semi-immune adult with uncomplicated malaria in urban Nigeria setting.

**Thrombocytopenia in Malaria**

We researched the effect of uncomplicated malaria in platelet count in adult Nigeria residing in Lagos metropolis that was diagnosed of having uncomplicated malaria were treated with a standard regime of chloroquine. Platelet counts were obtained before treatment, at onset of treatment and again on day 14 when parasitaemia had been cleared in the patient. There were 40 (21 male 19 female) patient enrolled for the study. Their ages ranged from 15 years to 56 years with a mean ±SEM of 27.4 ± 1.8 years. 28 (14 males 14 Females).

**Results:** the malaria parasite count ranged from 1020/mm$^3$ to 72,000/mm$^3$ at day 0 with a mean ± SEM 15,638.0 ± 3,727.0/mm$^3$ and Zero on 14. The mean platelet count prior to therapy was 137.0±58.4x 10$^9$/L while the day 14 mean platelet count was 234.0±96.9x 10$^9$/L. We found that comparison of mean platelet counts on day 0 with those on day 14 showed a highly statistically significant difference (p<0.001). The degree of malaria parasitaemia was not significantly related to the level of platelet counts. Transient thrombocytopenia is very common in uncomplicated malaria in semi immune adults. The mechanism, aetiology and clinical relevance of the phenomenon deserve further studies.

Effect of Acute Uncomplicated Malaria on Platelet Counts
Human Immunodeficiency Virus/ Adult Immunodeficiency Syndrome (HIV/AIDS)

United Nation AIDS estimates that currently 33.6 million people are living with HIV/AIDS globally, since the beginning of the epidemic another 17 million cases have died. African south of the Saharan continues to bear the brunt of the disease accounting for 70% of the global cases even though it is home for only 10% of the world population. Nigeria ranked currently 2nd in the world with a national sero prevalence of 3.4% and with 2.6 million infected cases as a major focus of HIV infection. Every zone in the country is affected and it is estimated that the figure will rise sharply in the coming years as the epidemic is still growing and there is a large population of sexually active young people.

In recent days, powerful and effective anti-retroviral (ARV) treatment regimens have become available. In a proportion of patient's triple combination of ARV especially regimes containing Protease Inhibitors have been found to reduce viral loads to indictable plasma levels and have a beneficial clinical effect. HIV symptoms were observed to disappear. The incidence of opportunistic infection reduced and the quality of life improved.

Nelfinavir (Viracet), a potent PI that inhibits HIV protease has been demonstrate to have a potent antiretroviral activity against a broad range of laboratory and clinical isolates of HIV-1 and HIV-2 strains.

Previous studies from industrialised countries have shown that Nelfinavir with 2RTIS was very effective in HIV infection with good tolerability. This study was therefore undertaken to determine the efficacy and tolerability of PI containing ARV triple regimen.
Contribution to knowledge
A MULTI-CENTRE STUDY TO DETERMINE THE EFFICACY AND TOLERABILITY OF A COMBINATION OF NELFINAVIR (VIRACEPT), ZALCITABINE (HIVID) AND ZIDOVUDINE IN THE TREATMENT OF HIV INFECTED NIGERIA PATIENTS


We conducted an open, non-comparative study of a triple ARV combination regimen containing the protease inhibitor (PI), Nelfinarvir and two reverse transcriptase inhibitors (RTIs), Zalcitabine (HIVID) and Zidovudine for a period of 24 weeks. Forty (40) HIV positive patients with CD4 cells counts between 100-500 cell/mm³ were recruited from 8 different centres in Nigeria including a research Centre and specialist and teaching hospitals. Thirty-one (31) patients completed the study. 9 patients withdraw from the study. Two of these patients withdraw because of the Adverse Events (AE), 2 others because they developed tuberculosis and had to withdraw because of rifampicin therapy. The remaining 5 withdrew voluntarily.

Efficacy of the PI containing triple regimen was evaluated using viral load and absolute CD4 changes. Weight gained and clinical response during the course of the trial. Twenty-two (22) patients had plasma viral load measured at the beginning and at the end of the trial (24 weeks). Seventeen out of the 22 patients (77%), experienced a significant reduction in their plasma viral load (p<0.05). There was 1 log reduction in viral load in 6 patients (25%), 2 logs in 4 patients (17%). In 2 patients (8%), plasma viral load was reduced below the level of detection. The viral load increased over the treatment period in five patients (21%). Similarly, 22 out of the 26 patients (85%) experienced increase in the level of their CD4 lymphocytes counts at the end of the study. The average CD4 counts of all 26 patients
rose from 272.94±137.71/dl to 414±243.71/ul over 24 weeks (p<0.05). There was monthly rise of 27 CD4 cells/ul. Four (4) patients (15%) had a fall in their CD4 lymphocyte counts. Twenty (20) out of the 26 patients (77%), who completed the study was observed to have weight gains ranging from 1.5 to 31 kilograms over the 24 weeks study period. In 4 patients, there was no weight gain during the study period.

The study demonstrated the significant efficacy and tolerability of (Nelfinavir/Zalcitabinel Zidovudine combination in suppressing viral replication, increasing the CD4 cell counts and improving the quality of the Nigeria patients with HIV.

**SUMMARY**

1. Our evidence confirms that the white blood cell (WBC) count is lower in African population than in Caucasian population. We also confirmed the robust increase in WBC count as a result of intermediate and major stress such as surgical trauma.

2. We have demonstrated the importance of a good history and a thorough clinical examination to detect the signs and symptoms of anaemia. The type of anaemia and finally the cause can be achieved from the consideration of both the clinical features and simple blood examination. In some cases special investigations are necessary for the determination of the cause.

3. Sickle cell anaemia causes significant morbidity and mortality in Nigeria. We have evaluated the treatment of pain crises by general practitioners and record satisfactory pain control except in severe pain where the use of narcotic analgesics is insufficient.


5. The effects of Priapism in male subjects with SCD have been characterised however, effective therapy
remains obscure. Ephedrine actions were comparable to Etilefrine for prophylactics of priapism. In girls, menarche was delayed by over 2 years was shown.

6. Patients with sickle disorder can live full productive lives, command great respect and accomplish high ideals. With proper appropriate care many do very well and enjoy a full and productive life. Therapy with antioxidants such as vitamin C, arginine and various herbal preparations like Solamin, Carica papaya, Celloid-S have been demonstrated preclinical to be effective in patient care. Bone marrow transplant however remains the only cure for SCA.

7. G6PD deficiency remains a challenge in Nigeria. Strategies for achieving these goals include appropriate education of health care provider and members of the public and installation of adequate diagnostic facilities and a monitoring system within the health service.

8. The scourge of HIV/AIDS is gradually being controlled with the widespread reach of government and global support and treatment programs. Powerful and effective anti-retroviral therapy remains an important pillar in the success of these programs.

Success is not measured by what a man accomplishes, but by the opposition he has encountered, and the courage with which he has maintained the struggle against overwhelming odds.

By Winston spencer Churchill, The former prime minister of Great Britain and the man that defiled Adolf Hitler's might said,

"Never, never, never, never in nothing great or small, large or petty never give in except to conviction of honour and good sense. Never yield to force; never yield to apparently overwhelming might of the enemy."
RECOMMENDATIONS
Effective management and palliative care of sickle cell disease continues to be a clinical and research priority.

- Even though sickle cell anaemia is among the world's most common inherited haemolytic anaemia affecting three quarter of sickle cell disease cases occur in Africa where Nigeria has the largest population of the people.
- Patient education is critical and cannot be left to pressure groups or Non-Governmental organisations alone. There is need for Government effort in dissemination disseminating appropriate information. Means of identification should be readily available without stigma to the patient.
- Care of those with the disorder - how to prevent the disorder- Information should be available right from primary school. All school children should know their haemoglobin (genotype and blood group).
- Although, 70-80% of doctors manage pain crisis appropriately; it would be desired that all doctors manage sickle cell pain crises appropriately. To achieve this, a pain management protocol should be introduced in order to ensure that every sickle cell pain is properly and constantly managed.
- Nutrition is critical: Adequate water at least three litters in 24 hours Ascorbic acid 300mg daily -Tocopherol (vitamin E) - L-Arginine 1gm, oral control of water (H2O) to prevent dehydration.
- Anti-oxidant medications from locally relevant herbal supplements -Orinata, Jubelyn Niprisan

Recommendation to improve care of persons with SCA
Persons with sickle cell anaemia
A call for setting up a day care centre
Nigeria our country has the largest number of persons with sickle cell disorder in the world since it has largest number of black people.
Seeing sickle cell disorder person should not be a surprise but we should have a clear unambiguous arrangement to care for the person. To find the correct diagnosis of the various types should be everywhere and have the means of caring for them when they are identified. All hospitals should have a day room for short stay admission and care specifically for sickle cell disorder patient with access to proper hydration (Fluid 4.3% dextrose in 0.18 saline) and effective drugs – including Hydroxyurea. Most patients with SCD will be all right within 18-24 hrs only a few will need admission and blood transfusion but with the day room care, it will provide fast access and aid prompt recovery. They don't need to be going to where other emergencies are seen like Diabetic emergencies, hypertensive emergencies in stroke, cardiac failure, kidney failure and respiratory emergencies. Occasionally, hospital admission is required. With prompt attention, symptoms will resolve within 24 hours. Blood can be given in the day room. The delay or lack of attention (having not known what diagnosis is right or wrong) is the cause of prolonged hospitalisation and or could lead to death. Basic guidelines for management should be provided. Laboratory diagnosis has to be improved by suitably qualified person using effective tests - solubility test. There should be no room for wrong diagnosis. The type of haemoglobin of a person should be determined for all Nigerians. Earl testing should be done in primary school or secondary school. Education and counselling (should be provided at National, State, Local government area, Institutions). Accurate Information on inheritance pattern of SCD should also be made widely available. This will help prevent stigmatisation.
• Appropriate health care personnel education and availability: Nurses and Doctors.
• SURGICAL care must be available: orthopaedics to care for chronic osteomyelitis and avascular bone necrosis.
• Obstetric: care of the pregnant women with sickle cell anaemia.
• Care of the child: every child with sickle cell disorder should have transcranial Doppler (about stroke).
• Neonatal Screening for Major haemoglobinopathies to identify all homozygotes for sickle cell anaemia and thalassemia major and many other heterozygotes.

Recommendations for G6PD deficiency
• More research for patients with G6PD deficiency: A community based natural history research project should provide better information to guide the development of appropriate control measures.
ACKNOWLEDGMENTS

Mr. Vice-Chancellor Sir, I sincerely wish to thank God for making it possible for me to deliver this inaugural lecture today. To God be the glory. He is of YESTERDAY AND TODAY, THE BEGINNING AND THE END, ALPHA AND OMEGA; ALL TIME BELONGS TO HIM AND ALL THE AGES, TO HIM BE GLORY AND POWER THROUGH EVERY AGE AND FOR EVER. AMEN

One former Provost of the College of Medicine of the University of Lagos; Professor Dosekun used to be called Prof Doh, to the present Professor Folashade Ogunsola whose record is in superlative, the first female Provost. Also an outstanding acknowledgment to Professor Elesha and Professor Wole Atoyebi.

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