BLOOD IS HEALTH: OUR BLOOD MIRRORS OUR BEING

An Inaugural Lecture Delivered at Oduduwa Hall,

Obafemi Awolowo University, Ile-Ife, Nigeria

On Tuesday, 24th June 2025

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Inaugural Lecture Series 400

ISSN 0189-7848

Printed by:

Obafemi Awolowo University Press Limited,

Ile-Ife, Nigeria.

SALUTATIONS

The Vice-Chancellor, Sir.

The Deputy Vice-Chancellors of Academic, Administration, Research and Innovation,

The Registrar, The Librarian, and The Bursar,

The Provosts of the College of Health Sciences and the Postgraduate College,

Deans of Faculties, Directors of Units, and Heads of Departments,

Distinguished Members of the Senate,

Esteemed Ladies and Gentlemen

I express gratitude to the Almighty God for allowing me to stand before you all today to deliver this 400th Inaugural Lecture.

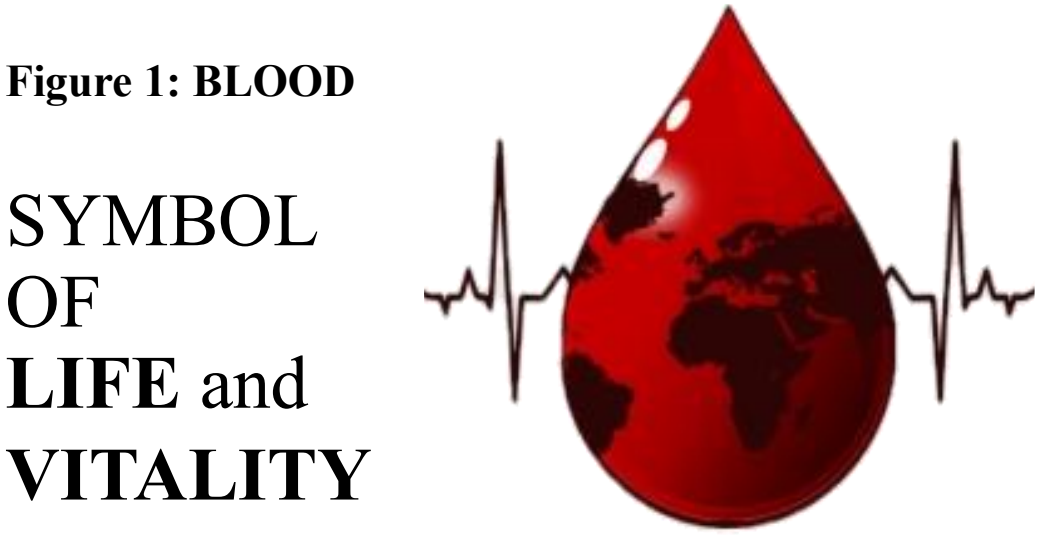
After my Secondary Modern School education in 1973, I never expected to have a university education. I intended to learn a craft at a Trade Centre. Though I obtained the admission Form, as fate would have it, my name was missing from the list of those to take the Aptitude Test for selection.

But here I am today, not only having had a university education but with an additional favour from the Almighty God to deliver this Inaugural Lecture, the fourth since the inception of the Department of Haematology and Immunology and the first from the newly established Faculty of Basic Clinical Sciences.

THE BLOOD: THE SYMBOL OF LIFE AND VITALITY

Blood symbolises life and vitality (**Figure 1**).

Figure 1: BLOOD



Biologically, it represents continuity as it carries genetic information across generations.

Culturally, blood often symbolises sacrifice, kinship, interconnectedness of life, and identity.

Physiologically, blood is a vital fluid that serves essential functions in the human body.

Blood signifies life and death simultaneously: life, through its circulation and nourishment of the body, and death, through its loss and spill.

It comprises the cellular elements (red blood cells, white blood cells and platelets) and the plasma (**Figure 2**).

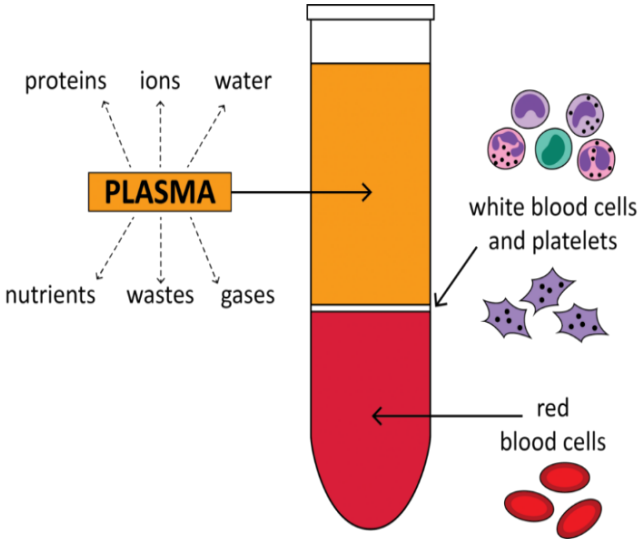
Figure 2:
Constituents of Blood

Cellular Elements

- ***Red Blood Cells***
- ***White Blood Cells***
- ***Platelets***

Plasma

- ***Nutrients***
- ***Proteins***
- ***Waste Products***



THE CELLULAR ELEMENTS

Red blood cells

The red blood cells (**Figure 3**) transport oxygen from the lungs to all the body's cells for essential metabolic processes and remove carbon dioxide, a byproduct of metabolism, from the cells back to the lungs.

Figure 3:
RED BLOOD CELL

- Transports O_2 and CO_2
- Surface antigens for
  - ✓ Blood grouping
  - ✓ Forensic investigations
  - ✓ Genetic studies

In addition to these physiologic functions,

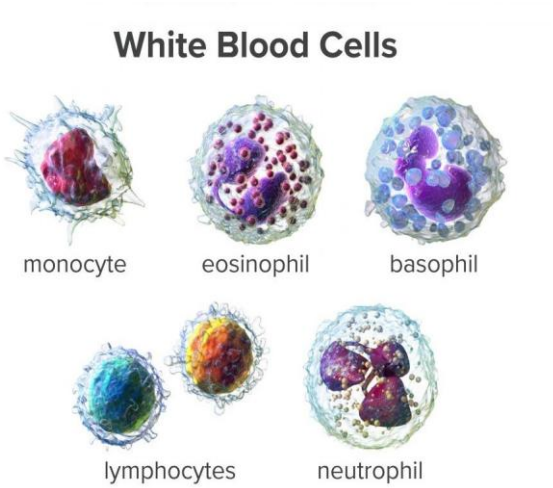
- The red blood cells also carry antigenic molecules on their surfaces that can be used to identify our "type of blood", which is also used in compatibility testing before blood is transfused.
- The red blood cell antigens are also useful in forensic investigations and genetic studies, including paternity testing and the investigation of human ancestry and migration patterns.

White blood cells (Leukocytes)

The white blood cells (**Figure 4**) protect the body from pathogenic organisms and other foreign substances by directly phagocytosing these substances and also producing antibodies and cytokines that can eliminate them.

Figure 4:
WHITE BLOOD CELLS
Protection from Infection and Foreign Substances

- HLA Antigens on their surfaces necessary for organ and tissue transplantation
- Genetic information in the nucleus necessary for:
- ✓ Instructions for cellular processes and functions of the body
- ✓ Medical and legal purposes: identity verification and biological relationships



- The leukocytes also carry genetic information in their nucleus, which contains the instructions necessary for all cellular processes and functions of the body.
- The genetic information in the nucleus can also be analysed for medical and legal purposes, particularly for identity verification and establishing biological relationships.

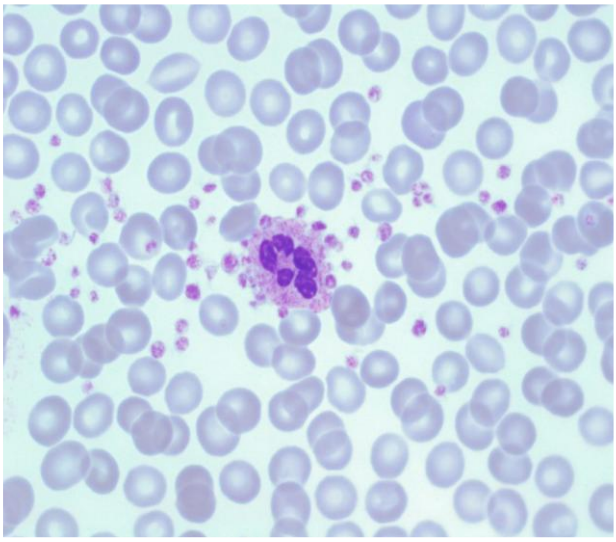
- The human leukocyte antigens (HLA) on the surfaces of white blood cells are vital for matching donors and recipients in organ and tissue transplantation to minimise the risk of rejection.
- Identifying specific HLA types linked to diseases can aid in early diagnosis, risk assessment, and effective treatment.
- The HLA is also instrumental in immune system regulation by differentiating between self and non-self, thus preventing autoimmune diseases and enabling immune responses against infections.
- Furthermore, the antigens influence how individuals react to vaccines and medications, impacting both effectiveness and side effects.

Platelets

The platelets (**Figure 5**), in conjunction with the coagulation proteins in the blood, prevent blood loss from both the intact blood vessels and when there is an injury by helping blood to form a clot and sealing any openings in severed blood vessels.

Figure 5:
PLATELETS

- Form clots to prevent bleeding
- Surface antigens are for
  - ✓ Identity verification
  - ✓ Organ and tissue transplantation to avoid rejection
  - ✓ Crossmatching of blood before transfusion



In addition to preventing blood loss, the antigens on their surfaces affect platelet transfusions, as mismatches can lead to immune reactions and the destruction of platelets.

- These antigens also assist the immune system in distinguishing between self and non-self, thereby preventing unwanted immune responses.
- Furthermore, platelet antigens can influence the outcome of organ and tissue transplantation by affecting immune compatibility between donors and recipients.

THE PLASMA

The plasma (**Figure 6**)

Figure 6: PLASMA

Transports:

- **Nutrients**
- **antibodies**
- **Coagulation proteins**
- **Hormones**
- **Enzymes**

- Contains coagulation proteins and antibodies that protect the body against infections.
- It also transports nutrients to cells and tissues to generate energy and removes metabolic waste products for excretion.
- Plasma albumin helps maintain blood volume and osmotic pressure
- The plasma also distributes hormones and enzymes that regulate metabolism, growth, and other vital bodily functions.
- It regulates the acid-base balance and carries essential electrolytes for nerve and muscle functions.

THE SPECIALITIES OF HAEMATOLOGY AND IMMUNOLOGY

Haematology

Figure 7: Haematology

Branch of Medicine and Biology that studies

- Blood and diseases of the blood and
- Blood-forming organs.

Haematology (**Figure 7**) is the branch of medicine and biology concerned with studying blood and diseases of the blood and blood-forming organs. It is a unique speciality that combines laboratory and clinical aspects of medicine. Haematologists are therefore involved in the laboratory investigation and management of patients with haematological disorders (**Figure 8**).

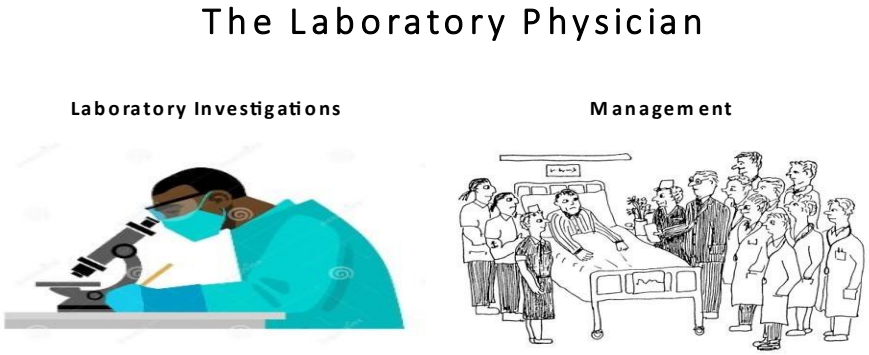


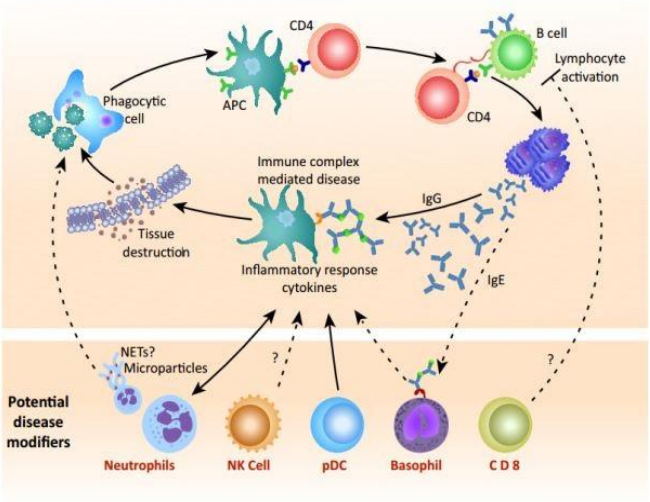
Figure 8: The Laboratory Physician
(dreanstime.com and open.edu respectively)

Immunology

Immunology (**Figure 9**), on the other hand, is the study of the immune system, a complex network of cells, tissues, and organs that defend the body against foreign invaders and diseases. Historically, immunology has been an important branch of medical and biological sciences. It emerged from the observation that individuals who had recovered from certain infectious diseases were not reinfected by the same disease, indicating that they had developed immunity.

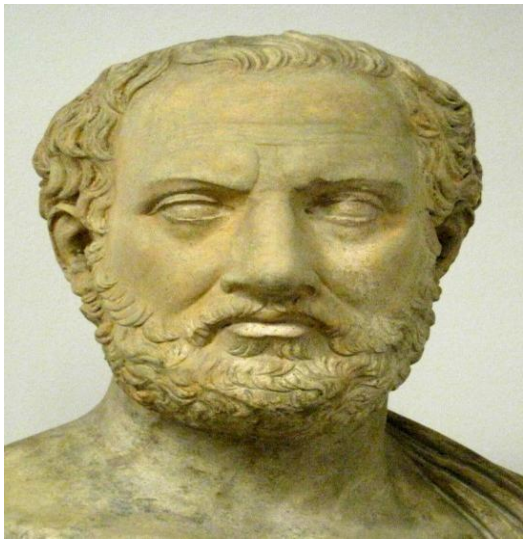
Figure 9: Immunology- Study of the Immune System

A complex network of
(i) Cells,
(ii)Tissues, and
(iii) Organs
that defend the body against foreign invaders and diseases.



However, the earliest written reference to immunity comes from Thucydides (**Figure 10**), an Athenian historian and military general, in 430 BC, who wrote that only individuals who had recovered from the disease would not be reinfected a second time and could nurse the patients (Tangye SG, 2015). In his observation, ***"the same man was never attacked twice—never at least fatally."*** He made this observation in his writings on the Peloponnesian War, during which the plague killed nearly one-third of the Athenian population. This can be considered an astute observation, recognising that after an individual is exposed to a pathogen, they may be protected from disease upon subsequent exposures without suffering the effects of infection.

Figure 10:
Thucydides
(en.m.eikipedis.org)



Immunity:

"the same man was never attacked twice- never at least fatally."

The term ***"immunity"*** is derived from the Latin word "*Immunitas*", which refers to the exemption of a community or an individual from obligations to the Roman state or a local community (**Figure 11**). However, in medicine, immunity means protection from disease, specifically infectious diseases (Zach and Greslehner, 2023).

Figure 11: *IMMUNITAS*

The exemption of a community or an individual from obligations to the Roman state or a local community

The study of immunity started with microbiologists (Kaufmann, 2019) who made several observations that linked the immunity of host animals to the entry of foreign substances.

MY CAREER DEVELOPMENT IN HAEMATOLOGY AND IMMUNOLOGY

Upon completing my specialist training in haematology at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, I was appointed as Lecturer I in the Department of Haematology and Immunology in 1999. At the time of my appointment to the department, there were three academic staff teaching haematology, but only one for immunology. Consequently, I was encouraged to consider including immunology alongside my primary training in haematology. The need became even more compelling as the department was unable to find a replacement for the retired Clinical Immunologist at that time. Through self-efforts, including

(i) Attending the Update Courses on the "*Molecular and Cellular Basis of Normal Immune Response*" given by Professor C. P. Muller from Luxembourg at the University College Hospital, Ibadan;

(ii) A Master's degree in Chemical Pathology from the University of Ibadan, with my thesis written on Immunology aspects; and

(iii) Short courses in Immunology organised at the

- ✓ Makerere/Uganda Virus Research Institute (UVRI) in Uganda, and
- ✓ The South African Immunology Society in South Africa, I acquired the

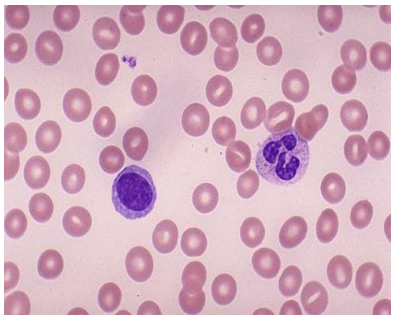
necessary knowledge in basic and clinical immunology to teach immunology to students. With my background in both specialities of Haematology and Immunology, my teaching activities and research interests shifted from pure haematology to ***Immuno-Haematology***. As I had earlier alluded to, haematology is the study of the physiology and disorders of blood constituents and blood-forming organs; Immunology, on the other hand, is the study of how the immune system works to defend the body from infectious diseases and harmful substances. The tools in both fields are essentially the same- blood and its related structures. Therefore,

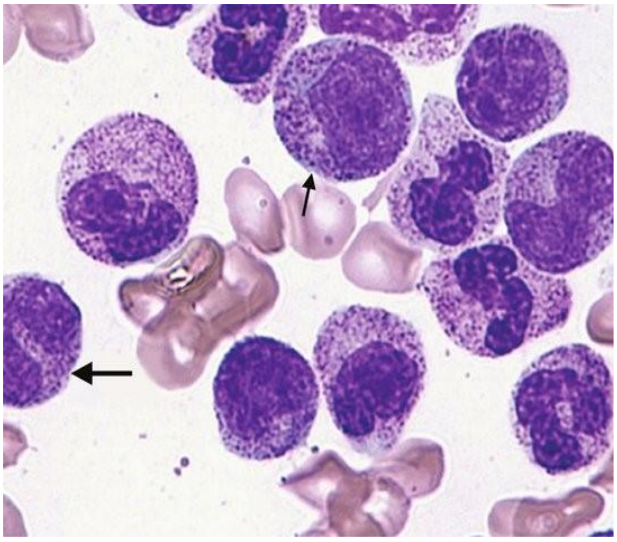
both specialities of Haematology and Immunology are interwoven, and as such, the research activities that I will be highlighting today will involve both.

MY CONTRIBUTIONS TO KNOWLEDGE

Blood is a unique connective tissue that links all organs, tissues, and cells within the body, facilitating their interaction (Poletaev, 2018). In addition to delivering oxygen and nutrients to the body's cells and removing carbon dioxide and other metabolic byproducts, it also serves as a medium for transmitting information between cells through chemical signals that govern all biological processes in the human body. Therefore, any changes in its composition will reflect alterations in the individual cells throughout the body. Thus, beyond its physiological function, blood contains a wealth of information regarding an individual's health status, making it an invaluable resource for understanding the causes of diseases, aiding in accurate diagnoses, guiding treatment decisions, and monitoring the effectiveness of treatment. For instance, detecting antibodies to the Human Immunodeficiency Virus (HIV) in the blood indicates the presence of an HIV infection in that individual. Similarly, alterations in the cellular composition of the blood may signify some pathological processes in the body. For example, complete blood count results indicating any of the cellular elements' counts outside the reference values or abnormal morphology in the cells may suggest an infection (**Figure 12**),

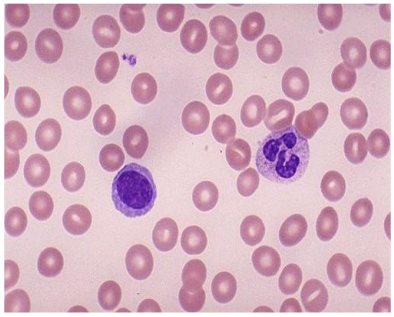
Figure 12:
Normal Blood Smear (L),
Blood smear in infection showing toxic granulation (R)

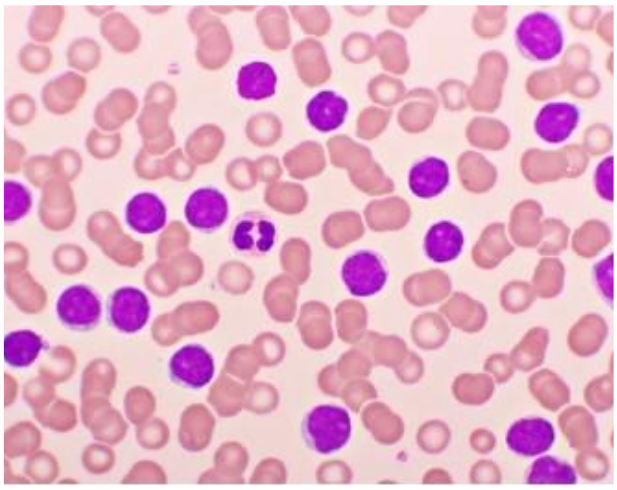




haematological disorder (**Figure 13**)

Figure 13:
Normal Blood Smear (L), Blood smear in Leukaemia showing many lymphocytes (R)





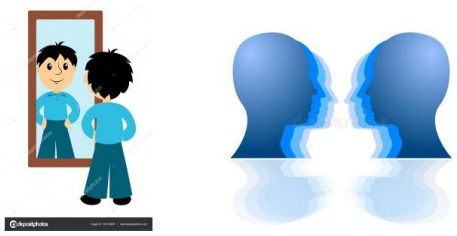
or other forms of pathological processes in the body.

Therefore, part of the ***Laboratory Physician's responsibilities*** **(Figure 14)** is to analyse the blood and provide an interpretation of the ongoing pathological processes.

Figure 14: Laboratory Physician

Because of this, blood can be likened to a ***"mirror"*** that reflects both normal and abnormal processes that are ongoing in the human body (**Figure 15**) or a ***"window"*** through which we can view our health status.

Figure 15: Our Blood Mirrors Our Being



Understanding how blood reflects our health status can empower us to take proactive steps toward preventive care and early diagnosis, as it provides a dynamic snapshot of our physiological state. Hence, this inaugural lecture is titled:

"**BLOOD IS HEALTH: OUR BLOOD MIRRORS OUR BEING**"

Mr Vice-Chancellor, Sir, with your kind permission, I will highlight some of my contributions to knowledge in the specialities of Haematology and Immunology, including Blood Transfusion Medicine, under the following sub-headings:

1. Autoimmunity,
2. Diagnostic Immunology,
3. Determinants of Survival in Haematologic Malignancies,
4. Immune Suppression and Anti-cancer Drugs, and
5. Modern Innovations in Blood Transfusion Safety in the last two and a half decades.

MY CONTRIBUTIONS TO IMMUNOLOGY

Immunology plays an essential role in disease diagnosis through:

- Serological testing to detect and measure antibodies or antigens,
- Identify and measure immune responses to antigens,
- Detect specific immune markers in tissues and cells,
- Determine immunity levels post-vaccination, and
- Identify autoantibodies attacking the body's cells.

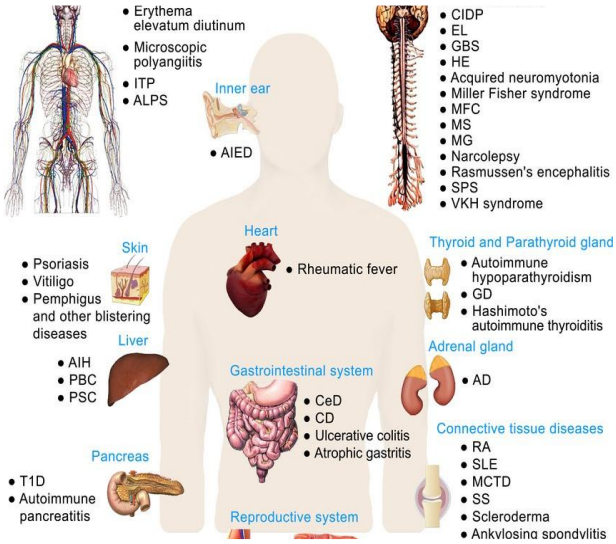
Because immunology enables the accurate and early detection of diseases, I conducted some studies on immune-mediated disorders.

AUTOIMMUNITY:

A Paradox of Self-identity and Self-preservation (Figure 16)

Figure16: AUTOIMMUNITY

A Paradox of Self-identity and Self-preservation

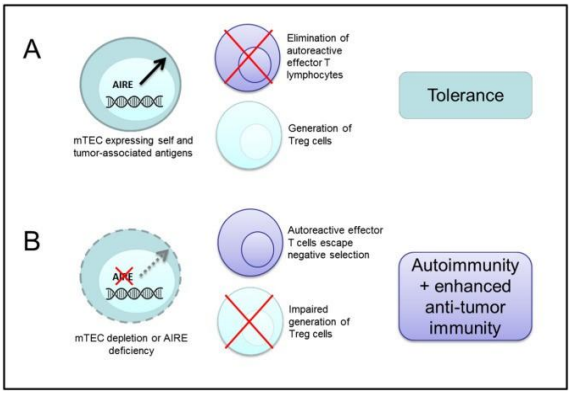


Under normal circumstances, an individual does not produce substances that can cause harm to their own body (autoimmunity) but to foreign substances. This is because, during the development and maturation of the cells of the immune system, the lymphocytes that will react against self-tissues are eliminated in the Thymus for failing thymic education (**Figure 17**);

Figure 17: Tolerance and Autoimmunity

A: Self-reactive T cells that bind strongly to self-antigen are eliminated through negative selection which induces tolerance

B: Self-reactive T cells that escape negative selection lead to the production of auto-reactive T cells and impaired generation of regulatory T cells and predispose to autoimmunity



hence, this provides an immune system that is tolerant to the host. This self-tolerance is maintained by a network of lymphocytes and their products.

The causes of autoimmune diseases are not fully known. However,

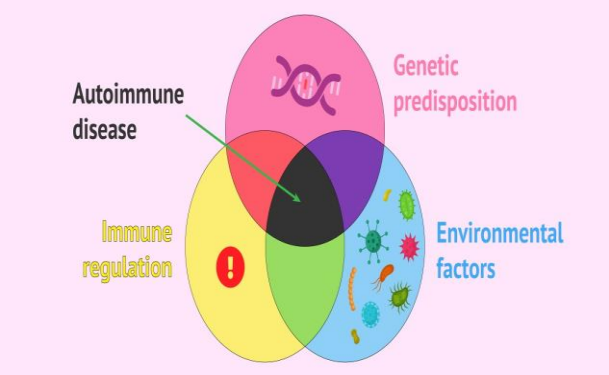
- A breakdown in the immune mechanisms to self-tolerance,
- Some hormonal and lifestyle factors,
- Molecular mimicry, and
- Interaction between genetic factors and environmental toxins (**Figure 18**), have all been

suggested to be responsible in many cases (Wang *et al*., 2015).

Immune system disorders are uncommon in indigenous African populations due to the high prevalence of infectious and parasitic diseases that impair the host's T-cell immunity (Dhingral *et al*., 2013). Because of this observation, I conducted some studies to ascertain the veracity of the assertion.

Figure 18: Causes of Autoimmune Diseases

- Genetic predisposition;
- Immune dysregulation;
- Environmental toxins;
- Hormonal; and
- Lifestyle factors



1. Immune Thrombocytopenic Purpura (ITP)

ITP is a bleeding disorder resulting from the destruction of platelets by autoantibodies produced in the affected person. Individuals suffering from ITP usually present with haemorrhagic manifestations such as gum bleeding, epistaxis (**Figure 19a)**, mucocutaneous bleeding, gastrointestinal tract bleeding, and heavy menstrual bleeding in women, all as a result of severe *platelet destruction by autoantibodies against the platelets antigens* (**Figure 19b**).

Figure 19a: Bleeding manifestations in ITP

(i) Gum Bleeding

(ii) Epistaxis (nose bleed)

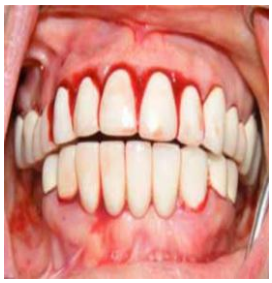
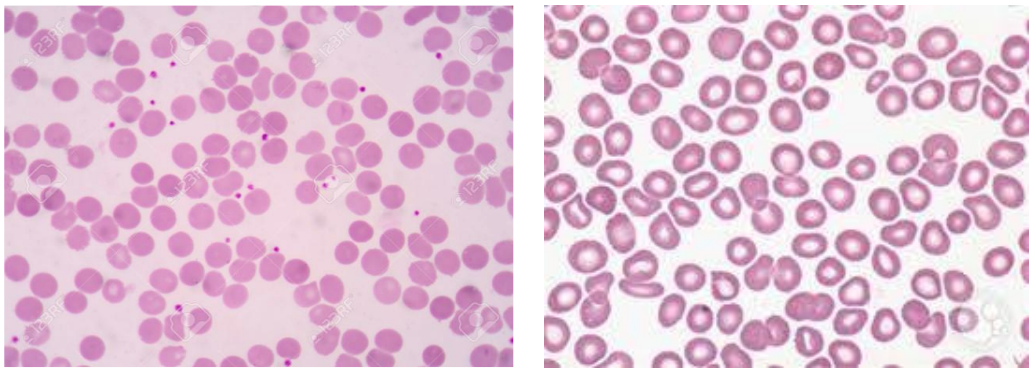


Figure 19b: Immune Thrombocytopenic Purpura: Peripheral Blood Smear

Normal Smear with Platelets Smear with Thrombocytopenia



Affected individuals may also bleed into the brain, and this may be fatal in some cases.

I investigated the pattern of presentation and the effectiveness of treatment available to patients presenting with ITP at the OAUTHC, Ile-Ife. The diagnosis was based on

- Mucocutaneous bleeding,
- Thrombocytopenia, and
- Examination of the bone marrow for quantitative and qualitative abnormalities of the megakaryocytes responsible for producing the platelets.

Twice as many females as males were recorded. More than 80% of them presented with gum bleeding, while others presented with purpura, haematuria, epistaxis, haematemesis and menorrhagia (**Table 1**).

Three of the affected patients also had a positive family history of a similar disorder. Moderate to severe anaemia occurred in more than 90% of them. Eighty (80%) per cent of the affected patients presented with severe thrombocytopenia. More than 80% of them required blood transfusions in addition to corticosteroid therapy, while one of them required immunosuppressive therapy to be in remission. Over eleven years, only eleven cases were

managed out of 217,422 clients seen in our facility during the same period, resulting in a period prevalence of 0.005% (Salawu *et al*., 2001).

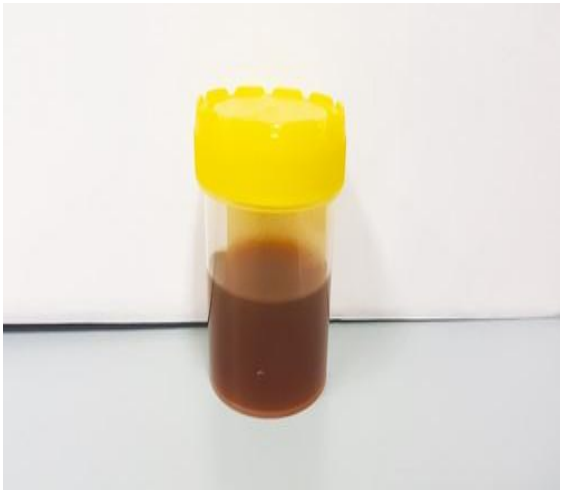
Table 1: Bleeding Sites in Patients with Immune Thrombocytopenic Purpura in Ile -Ife, Nigeria

Bleeding Manifestation	Number of Cases (%)
Gingival	9 (81.8)
Purpura	4 (36.4)
Haematuria	3 (27.3)
Epistaxis	3 (27.3)
Haematemesis	1 (9.1)
Menorrhagia	1 (9.1)

2. Autoimmune haemolytic anaemia (AIHA)

AIHA is another autoimmune disorder of man in which an individual produces antibodies against their red blood cells with consequent destruction of these red cells in the reticuloendothelial system, particularly in the spleen or within the blood vessels and may then be associated with the passage of red coloured urine (or haemoglobinuria) (**Figure 20**).

Figure 20: Haemoglobinuria
[Mohamed & Koay (Med J. Australia])



Passage of red-coloured urine due to the destruction of red blood cells by *autoantibodies*

This causes a shortened survival of the red blood cells. I reviewed the records of patients managed for AIHA over 10 years. The diagnosis was based on features of haemolytic anaemia and a *positive Coombs test* after excluding other causes of haemolysis. There were more females than males, with a median age of 42. Sixty per cent (60%) of cases were associated with secondary disorders such as haematological malignancies and collagen diseases, while the rest were the idiopathic type (**Table 2**).

Table 2: Aetiological Classification and Serological Findings in Autoimmune Haemolytic Anaemia Patients in Ile-Ife, Nigeria

Type of AIHA	Number of Coombs Positive Cases	Number of Coombs Negative Cases
1. Idiopathic	4	3
2. Secondary		
▪ Hodgkin lymphoma	2	-
▪ NHL	1	-
▪ Multiple myeloma	1	-
▪ Osteogenic sarcoma	1	-
3. Collagen Disease (SLE)	1	-

Investigations led to the identification of the autoantibody responsible for the destruction of red blood cells in approximately 77% of cases. All had moderate to severe anaemia that required blood transfusion in addition to corticosteroid therapy.

The study also confirmed the rarity of this immune-mediated disorder as only thirteen cases were managed over 10 years out of the 400,483 new clients seen within the same period in our facility, with a period prevalence of 0.003% **(**Salawu *et al*., 2002**)**.

3. Lupus Anticoagulants

Lupus anticoagulants are *acquired antibodies* first described in Systemic Lupus Erythematosus but have now been associated with other disorders. Interest in this group of antibodies resulted from the association of Lupus antibodies with:

- Venous and arterial thrombosis,
- Autoimmune haemolysis, and
- Thrombocytopenia.

HIV infection is known to cause polyclonal activation of B lymphocytes (Moir *et al*., 2010). Some of the resulting antibodies may have Lupus anticoagulant specificities and may be directed against self-antigens, which, therefore, explain some of the clinical and laboratory features of HIV/AIDS.

We studied 104 consecutive HAART-naïve adult patients with HIV/AIDS in an attempt to determine the prevalence of Lupus antibodies and their significance (Ndakotsu *et al*., 2009**).** Of the over 100 clients investigated, only three (2.9%) were positive for the lupus antibody (**Table 3**).

Table 3: Lupus Anticoagulant Status in HIV/AIDS Clients with Prolonged Kaolin Clotting Time

	KCT (% Test Plasma in Normal Plasma)						
Subject	**0/100**	**20/80**	**50/50**	**80/20**	**100/0**	**KCT Ratio**	**LAC Status**
Patient 1	86.5	117.0	191.5	198.0	204.0	2.16	Positive
Patient 2	66.0	129.0	137.0	140.0	162.0	1.95	Positive
Patient 3	72.0	138.0	157.0	165.0	169.0	1.92	Positive
Control	82.0	118.0	126.0	134.0	141.0	1.44	Positive

Legend: *KCT- Kaolin Clotting Time; LAC - Lupus Anticoagulant*

A similar study was also conducted in the paediatric age group. (Oyelese *et al.*, 2019). One hundred and sixteen (116) HIV-positive children and 61 healthy HIV-negative age- and sex-matched children were investigated for the prevalence of lupus antibody and its clinical and laboratory impact. Of the 116 subjects, only 7 (6.03%) were positive for lupus antibodies.

There was no significant effect on the patient's:

- Haematocrit level,
- Leukocytes or platelet counts (**Table 4**).
- There was also no correlation between the occurrence of lupus antibodies and opportunistic infections or thrombosis, similar to what was found in the adult study.

Table 4: Antiphospholipid Antibody and Haematological Variables

Mean ± SD	aPLA positive	aPLA negative	t-test	p-value
PCV (%)	32.7 ± 4.1	33.7 ± 3.6	0.84	0.41
WBC (×109/L)	5,845 ± 2,541	5,635 ± 3,026	-0.23	0.82
PLT (× 109/L)	280,333 ± 85,970	265,913 ± 107423	-0.44	0.66
CD4 (/µl)	812 ± 557	885 ± 542	0.43	0.67
APTT (secs)	46.6 ± 3.9	38.4 ± 3.2	-8.45	0.0000

aPLA: Antiphospholipid antibodies; POS: Positive; NEG: Negative; PCV: Packed cell volume; WBC: White cell count; PLT: Platelet; CD4: Cluster of differentiation 4; APTT: Activated partial thromboplastin time

These studies confirmed the low prevalence of lupus antibodies in our patients but without thrombosis, opportunistic infections, anaemia, or thrombocytopenia. These studies support the observations that autoimmune disorders are not common in indigenous African populations and that females are more affected.

Although studies support the observation that autoimmune disorders are not common in Indigenous African populations, including Nigeria, total prevention of immune-mediated disorders would be ideal, because how can one explain a situation where the body's immune system mistakenly attacks its healthy cells, tissues, or organs, treating them as foreign invaders?

While there is no guaranteed way to prevent autoimmune diseases, strategies such as:

- Maintaining *a healthy gut* by eating a balanced, high-fibre diet with lots of fruits and vegetables will maintain a healthy gut microbiome, which is essential to immune function.
- *Avoidance of ultra-processed foods* that promote inflammation and disrupt the immune system.
- Smoking is a known factor for several autoimmune diseases and should be avoided.
- The use of personal protective equipment (PPE) in people working with heavy metals and pesticides will limit their exposure to these environmental toxins.
- Good hygiene practices, vaccination, and early infection management will help prevent autoimmune diseases, as some viruses and bacteria are linked to triggering autoimmunity.
- If there is a family history of autoimmune disorder, regular medical check-ups and symptom monitoring are advisable for early intervention.

DIAGNOSTIC IMMUNOLOGY:

The Role of Biomarkers in Disease Assessment (Figure 21)

Figure 21
DIAGNOSTIC IMMUNOLOGY:
The Role of Biomarkers in Disease Assessment

The assessment of serum immunoglobulins, antigens, cytokines, immunocytes, and other immunologic biomarkers plays a critical role in disease diagnosis, as they serve as biomarkers of the immune response to infections, autoimmune diseases, allergies, and immunodeficiency disorders. For instance,

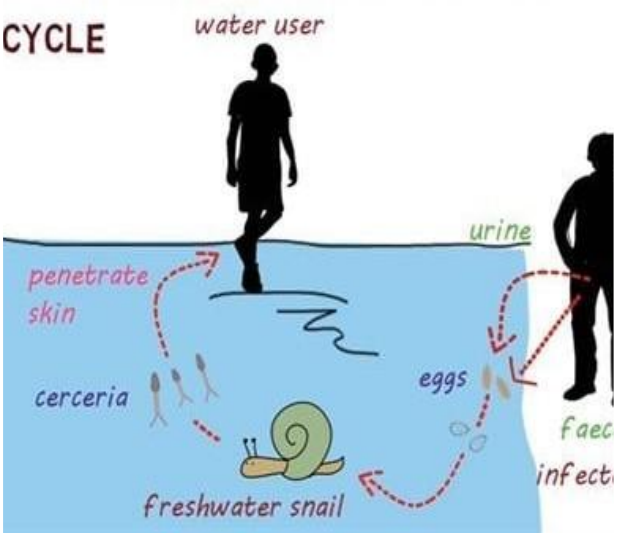
- CD4+ T cells are essential for immune function, and their decline in HIV/AIDS is a key indicator of disease progression,
- Changes in CD38 and CD56 expression on immune cells can be prognostic indicators of ITP,
- CD19 and CD20 are markers of lymphoid malignancies while CD13, CD15, CD33, CD34, CD36, CD117, CD64, CD45, and HLA-DR are markers of myeloid malignancies, and
- CD3, CD4, and CD8 are markers of T lymphocytes, while CD19 and CD20 are primary markers of B lymphocytes.
- High serum levels of IgM indicate recent or acute infection;
- High IgG indicates past infections or the individual has developed immunity; and
- High IgA indicates mucosal infection.
- Low levels of the notable immunoglobulins (IgM, IgG, and IgA) suggest primary immunodeficiency disorders, while
- Serum IgE levels are elevated in parasitic and allergic conditions.
- Monoclonal IgG or IgM may suggest haematological cancers such as Myeloma and Waldenstrom's macroglobulinemia.
- The immunoglobulins are also helpful in monitoring disease progression and response to treatment.

Because immunology-based diagnostic methods are precise, fast, and essential for the early diagnosis and management of diseases, I conducted studies to assess the role of some immunologic biomarkers in some disease conditions.

1. Schistosomiasis

Figure 22: *Schistosoma haematobium*

SCHISTOSOMIASIS
Infertility
Ectopic pregnancy
Low birth weight



Schistosoma haematobium (**Figure 22**) is a blood fluke that infects the urinary tract and is prevalent in Africa and the Middle East. It is the primary agent of schistosomiasis and one of the most widespread parasitic infections in developing countries, especially in rural communities where drinking water is contaminated by faecal matter and urine that harbour the parasite. The presence of its eggs or worms in the female genital tract is common and has been linked to infertility, ectopic pregnancy, and low birth weight. Most reproduction-related effects of female genital schistosomiasis have been largely attributed to the mechanical impact of the granuloma formed by schistosome eggs, with limited immunological evidence.

In my MSc research, I investigated several aspects of the humoral immune response to schistosomiasis by studying 108 pregnant women (Arinola *et al*., 2005) and measuring serum levels of some immunologic biomarkers. Significantly elevated serum IgG was observed in

pregnant women with urinary schistosomiasis compared to those without the infection (**Table 5**).

Table 5: IgG and IgA in Pregnant Women with and without Urinary Schistosomiasis

	P + USS (n = 30)	P – USS (n = 36)	t-value	p-value
IgG (mg/dL)	1546.70 ± 84.90	1311.80 ± 97.70	10.30	0.01
IgA (mg/dL)	598.70 ± 61.50	59.70 ± 29.20	41.50	0.01

Legend: P + USS = Pregnant women with urinary schistosomiasis; P – USS = Pregnant women without urinary schistosomiasis

IgG is the primary antibody in the blood responsible for guarding against blood-borne pathogens, which accounts for the high serum levels of IgG in women with schistosomiasis. Conversely, IgA is the main immunoglobulin responsible for protecting mucosal surfaces; thus, a significantly lower serum level of IgA is found in pregnant women without urinary schistosomiasis compared to those with the infection. These findings indicate that these serum proteins are valuable immunological diagnostic tools.

2. Sickle cell disease (SCD) is a genetic disorder resulting from the inheritance of a mutated form of haemoglobin referred to as haemoglobin S (HbS) either in the homozygous form (HbSS) or in combination with other forms of abnormal haemoglobins (e.g., HbSC). When deoxygenated, HbS becomes less soluble and more viscous and forms a polymer, thereby distorting the red cell membrane, eventually leading to the red cell assuming the characteristic sickled shape observable in peripheral blood smear (Figure 11A). However, the liquid state prevails in the presence of oxygen, and the red cell assumes its biconcave shape (**Figure 23**).

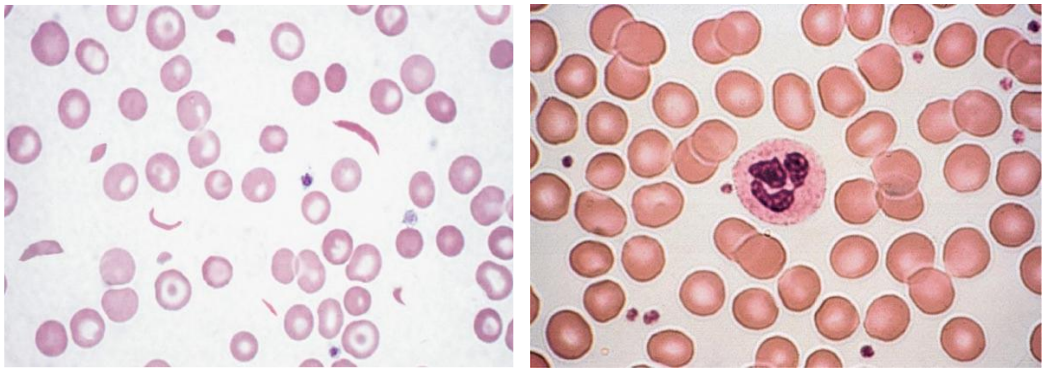


Fig. 23a. SCD Blood Film ***b. Normal Blood Film***

The effects of these abnormal haemoglobins are responsible for most of the pathology associated with SCD. Sickle cell disease causes significant morbidity and mortality with a high frequency of painful crises, which will need analgesia, anaemia that may require blood transfusions, infections that may require antibiotic treatment and organ damage in some cases. Some of the immunologic biomarkers of infections and painful crises were analysed in some studies on SCD.

2.1 ***Infection in Sickle Cell Disease***: Individuals who have sickle cell disease are susceptible to bacterial infections, particularly the encapsulated organisms (Ochocinski *et al.*, 2020), due to defective splenic functions, abnormalities of opsonisation, abnormalities in the alternative complement pathway, abnormalities in antibody production, and abnormalities in leukocyte functions and cell-mediated immunity. Infection of the bone (osteomyelitis) in sickle cell disease could result from haematogenous spread, direct injection of a pathogen from trauma, or complications from septic arthritis. Studies have shown that *Staphylococcus aureus*, the causative agent of osteomyelitis in SCD individuals, produces human-specific inhibitory proteins which prevent opsonisation, phagocytosis and killing of the pathogen (Pietrocola *et al.*, 2017).

We compared some immunological parameters in SCD individuals with osteomyelitis and those without osteomyelitis (Orimolade and Salawu, 2008). The serum levels of the C3 activator, C1 esterase inhibitor (C1INH), IgA, IgG, and IgM were determined using the Mancini technique. Our study found significantly high serum levels of C3 activator and reduced serum IgA levels in subjects with osteomyelitis (**Table 6**). The C3 activator is a regulatory protein that combines with unstable C3b to form a more stable C3bBb capable of activating more C3 complement proteins in the alternative complement pathway. Therefore, the activation of the alternative pathway of complement activation is expected to decrease the level of the C3 activator, contrary to our findings, suggesting a defective alternative complement pathway in SCD subjects with osteomyelitis. *Staphylococcus aureus*, which was cultured in 57.7% of wounds from subjects with osteomyelitis in our study, is known to produce a specific

Table 6: Laboratory Parameters of Sickle Cell Disease Patients with Osteomyelitis and those without Osteomyelitis

Parameters	SO (n = 30)	S (n = 30)	z = value	p = value
PCV (%)	22.7 ± 3.8	22.2 ± 4.7	0.416	0.678
WBC (/cmm)	13235 ± 6296	11716 ± 4594	0.745	0.451
Platelet (x10^9)	265 ±72	197 ± 827	3.69	0.0002
ESR (mm/hr)	70 ± 44	36 ± 34	3.20	0.0001
IgG (mg/dL)	700.6 ± 179.4	644.5 ± 171.2	1.042	0.297
IgA (mg/dL)	217.3 ± 78.3	249.0 ± 94.9	1.036	0.300
IgM (mg/dL)	123.1 ± 130.6	93.4 ± 100.7	-1.008	0.314
CI INH (mg/dL)	32.2 ± 23.8	27.0 ± 20.2	0.894	0.371
C3 act. (mg/dL)	25.7 ± 13.8	17.1 ± 7.4	1.984	0.015

Legends: *SO = sickle cell disease patient with osteomyelitis; S = sickle cell disease patient without osteomyelitis; PCV = packed cell volume; WBC = white blood cells; ESR = erythrocyte sedimentation rate; Ig = immunoglobulin; C1 INH = C1 inhibitor; C3 act = C3 activator*

Complement inhibitor that prevents efficient cleavage of C2 and C3 complement proteins and thus affects the formation of C4bC2a and C3bBb, resulting in a decrease in phagocytosis and killing of *Staphylococcus aureus* by neutrophils. This might be responsible for the high value recorded and probably explains the likely defect in subjects with osteomyelitis. C1INH

regulates many plasma mediator pathways, including the complement system. It inhibits the activities of factor B and the cleavage of C3 indirectly through C3b, and the removal of C1INH restores the activities of the pathway. Our study showed higher serum levels of C1INH in patients with osteomyelitis compared to the controls, suggesting a defective alternative complement pathway in SCD subjects with osteomyelitis. The serum levels of IgG and IgM were higher in individuals with osteomyelitis. IgG acts as an opsonin by aiding the phagocytosis of pathogens. On the other hand, IgM is an essential activator of the classical complement pathway that can lead to the generation of another opsonin (C3b) or the formation of a membrane attack complex, which can cause complement-mediated cytolysis of pathogens. The reduced serum levels of IgA could be due to the body's diversion of immunoglobulin production to more serum IgG to combat the haematogenous organisms responsible for the bone infection, as against IgA, which provides more mucosal immunity.

2.2 ***Biomarkers of Painful Crises in Sickle Cell Disease***: A vaso-occlusive crisis is the most common and painful complication of sickle cell disease. It is the primary reason for seeking medical attention and accounts for most hospitalisations. This crisis occurs when blood vessels are obstructed by sickled red blood cells, which block blood flow and reduce oxygen delivery to tissues, resulting in acute pain, particularly in the joints, chest, and abdomen. Soluble E-selectin is a molecule released from activated endothelial cells during inflammation that facilitates the adhesion of leukocytes to the endothelium, thereby contributing to the obstruction of small blood vessels, and worsening the vaso-occlusive crisis. Elevated serum soluble E-selectin levels are also associated with increased inflammation, which may exacerbate sickling and microvascular obstruction. Given the roles of soluble E-selectin in endothelial cell activation and dysfunction during inflammatory processes, we investigated the relationship between soluble E-selectin and the severity of the disease, using the frequency of vaso-occlusive crises as a clinical manifestation in children with sickle cell anaemia and

various haematological parameters (Smith *et al*., 2021). The study found that children with sickle cell anaemia in vaso-occlusive crisis had significantly higher levels of soluble E- selectin (837. 9 ± 336. 9 ng/l) compared to those in a steady state (605.5 ± 257. 6 ng/l) ($t = 3.678$, $p < 0.001$). Soluble E-selectin also positively correlated with the frequency of vaso-occlusive crises ($r = 0.483$, $p = 0.001$), leukocyte counts ($r = 0.425$, $p = 0.004$), and platelet counts ($r = 0.455$, $p = 0.002$). Linear logistic regression indicated that soluble E-selectin is an independent predictor of the frequency of vaso-occlusive crises in children with sickle cell anaemia presenting with these crises (OR = 0.450, 95% CI = 0.001- 0.004, $p = 0.013$). Therefore, research on soluble E-selectin inhibitors to reduce the frequency of VOC in patients with SCA will be desirable.

The neuropeptide Substance P (SP) is another etiological factor associated with painful episodes of sickle cell disease. We compared serum levels of SP in subjects experiencing painful vaso-occlusive crises with those in a steady state (Olawuyi *et al*., 2024). We found significantly higher levels of SP ($t = 2.43$, $p = 0.02$) in SCD patients in vaso-occlusive crisis (375.78 ± 76.21 ng/l) compared to those in steady state (184.79 ± 18.67 ng/l). This finding suggests that soluble E-Selectin and Substance-P may be biomarkers for pain in sickle cell disease. Thus, estimating the serum levels of SP may help confirm or establish the resolution of VOC in patients with SCD with prior knowledge of the baseline level, especially those already addicted to analgesic use.

3. Immunisation against Infectious Diseases (Figure 24)

Figure 24: Immunisation in Infectious Diseases

Tetanus is an acute infectious disease characterised by tonic spasms of voluntary muscles, particularly those of the jaw, resulting from the exotoxin produced by the bacterium *Clostridium tetani*, which resides in soil, stool, or inanimate objects. It is a serious yet preventable disease. Skin lesions caused by either HIV infection or adverse drug reactions are known to lead to significant morbidity in patients with HIV/AIDS **(Figure 25).**

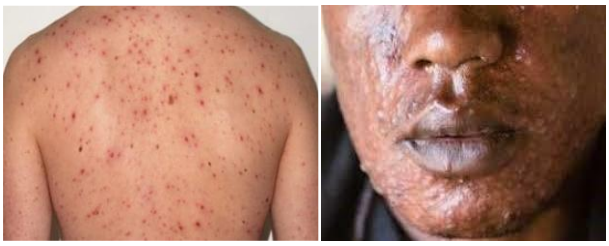


Figure 25: Skin lesions in HIV/AIDS (*Medscape*)

Because of the possible contamination of the skin lesions from the environment or autoinfection from diarrheal stool in HIV/AIDS patients, I investigated the need for routine anti-tetanus immunisation in patients living with HIV/AIDS (Salawu *et al*., 2010). Serum levels of IgG antibodies to tetanus organisms were quantified in 42 clients living with HIV/AIDS. I found no significant difference in the mean tetanus antibody levels in patients living with HIV/AIDS compared to those of the controls. Further analysis showed that the mean antibody levels to tetanus were not significantly different based on the patient's circulating CD4+ T lymphocyte count or age (**Table 7)**. By international standards (Bonetti *et al.,* 2004), 85.7% of our HIV/AIDS cohort had protective levels of antibodies to tetanus.

Table 7: Immunohaematological and Demographic Parameters in Nigerians with HIV/AIDS

	HIV/AIDS	Control	t-value	p-value
Mean Age (±SD) yrs	36.69 ± 9.29	43.00 ± 16.24	-1.18	0.11
PCV (%)	32.40 ± 5.64	39.49 ± 4.58	-3.64	0.001
WBC (/cmm)	4289.29 ± 2016.62	5380.00 ± 1250.60	-1.63	0.109
Platelets ($x10^9$)	191857.14 ± 93301.92	225200 ± 58537.38	-1.08	0.87
Tab (IU/mL)	0.50 ± 0.86	0.46 ± 0.65	0.04	0.89
CD4+ (/µL)	166.10 ± 102.94	708.00 ± 122.28	12.22	0.002
CD4+ < 200/mL	0.50 ± 0.98			
CD4+ > 200/mL	0.49 ± 0.53		0.04	0.97

Legends: PCV = packed cell volume; WBC = white blood cells; Tab = Tetanus antibody

In another study on the effectiveness of routine immunisation against tetanus post-injury, we conducted a prospective study in a cohort of adults with open wounds in the Emergency Room of the OAUTHC, Ile-Ife (Akinyoola *et al*., 2016). We determined the baseline serum levels of antibodies to tetanus organisms at the first contact and then immunised participants with anti-tetanus toxoid (**Table 8**).

Table 8: Serum Anti-tetanus IgG levels in Subjects Pre- and Post-Immunisation

	Subjects	Controls
Age (± SD) years	34.80 ± 16.05	29.08 ± 8.88
Sample Size	M = 114; F = 45	M = 78, F = 12
Mean Age (±SD)	M = 33.98 ± 14.34; F = 36.87 ± 19.77	M = 28.42 ± 8.03; F = 33.33 ± 12.82
BS Anti-Tetanus IgG (IU/mL)	1.13 ± 2.37	0.76 ± 1.39
	M = 1.12 ± 2.64; F = 1.15 ± 1.50	M = 0.59 ± 1.24; F = 1.96 ± 1.80
		t = -3.21, p < 0.001
PoI Anti-Tetanus IgG (IU/mL)	9.22 ± 11.25	NA
	M = 10.67 ± 12.11; F = 5.26 ± 7.81	
Past Immunization(IU/mL)		
Baseline (NI versus IM)(IU/ml)	1.02 ± 1.51 vs 1.19 ± 2.67	NA
Post-Immunisation (IU/mL)	9.40 ± 11.57 vs 8.69 ± 10.74	

Legends: M = Male, F = Female; BS = Baseline value of anti-tetanus IgG before immunisation; PoI= Post immunisation anti-tetanus IgG level; Past Immunisation = Previous history of anti-tetanus immunisation; NI = No history of anti-tetanus immunisation, IM = previous history of anti-tetanus immunisation; NA = Not Applicable

Four weeks after the immunisation, they were re-assessed for serum levels of antibodies to the tetanus organism. Our study showed a rise of more than eight-fold in antibody levels against the tetanus organism in our subjects. From the findings of this study, we confirmed the effectiveness of tetanus immunisation and the necessity to persist with these preventive measures in patients with an open wound due to the high mortality associated with the infection.

It is, therefore, important to note that assessment of disease is a form of warning system that:

- Helps detect health problems early before symptoms appear, so that steps can be taken to prevent the disease from developing or worsening and to avoid complications.
- Disease assessment also helps find risk factors even when there are no actual diseases yet. For example, exposure to radiation and chemicals can increase the risk of leukaemia. Therefore, regular assessment of complete blood count of individuals exposed to chemicals or radiation will be a good preemptive measure
- After diagnosis, the affected individual can receive specific advice or treatment to prevent the disease from progressing. For instance, a pap smear can detect abnormal

cells before they become cancerous, and with early treatment, cervical cancer can be prevented.

- Diagnosis also helps control outbreaks by tracking disease patterns, preventing the spread of diseases that are of public health interest, and enhancing medical research. For example, diagnosing latent tuberculosis infections allows for treatment before they progress to active tuberculosis, thereby preventing further spread and severe illness.

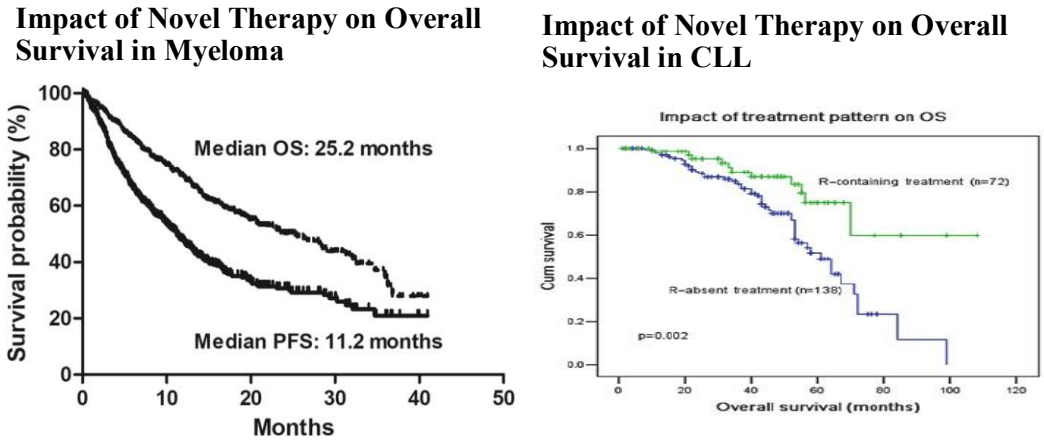
Therefore, diagnosis involves not only identifying the disease but also playing a crucial role in preventing its occurrence or progression.

MY CONTRIBUTIONS TO HAEMATOLOGY

Determinants of Survival in Haematologic Malignancies

Haematology not only plays a crucial role in the diagnosis, monitoring, and management of a wide range of blood-specific diseases, it also provides insight into systemic illnesses, infections, and organ function

Figure 26: Survival In Haematologic Malignancies



The survival of patients with haematologic malignancies (**Figure 26**)

is hinged on many variables including

- The type of malignancy,
- Some genetic and molecular features,
- Stage of presentation to the health care facility,
- Age at presentation,
- Presence or absence of other co-morbidities,
- Type and quality of treatment received,
- Access to specialised care,
- Patient's financial resources, and
- Psychosocial support received by the patient.

Collaborating with other researchers, I conducted some studies on haematologic malignancies and evaluated some factors affecting survival.

1. Multiple myeloma

Multiple myeloma is a haematologic cancer more commonly seen in Black populations (Michael *et al.*, 2023). The disease is characterised by the malignant proliferation of a clone of plasma cells in the bone marrow (**Figure 27a**) and the overproduction of abnormal monoclonal protein (*M-protein*) which is responsible for the characteristic rouleaux formation of red blood cells (**Figure 27b**) observable on the peripheral blood smear.

Figure 27a:
Bone Smear in Multiple myeloma

Malignant proliferation of **Plasma Cells** in the bone marrow

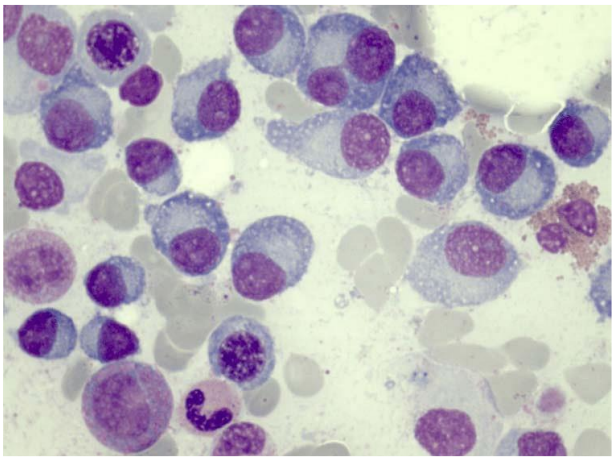
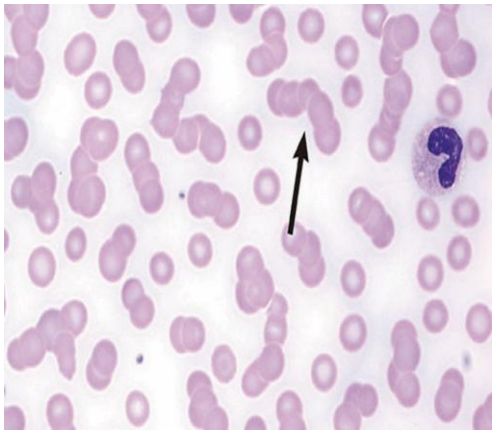


Figure 27b:
Blood Smear in Multiple myeloma

Rouleaux formation of the **Red Blood Cells** due to abnormal M-proteins



The monoclonal protein appears as a monoclonal band (M-band) on serum protein electrophoresis (**Figure 28**), and the light chains of the abnormal proteins can be detected in the urine as *Bence-Jones protein*.

Figure 28a: Normal Serum Protein Electrophoresis

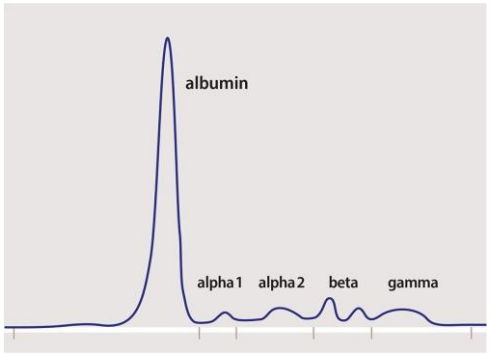
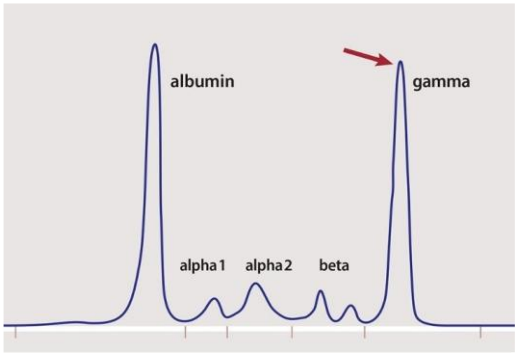


Figure 28b: Electrophoresis Pattern in Multiple Myeloma



It is an invariably fatal disease with a median survival of about six months when no treatment is given and about 3 years with drug treatment (Anderson *et al*., 1998).

Multiple myeloma has a progressive clinical course with increasing anaemia, weakness, bone pain, pathological fractures, hypercalcemia, renal insufficiency, bleeding diathesis, and neurological complications if treatment is not offered early.

To predict the survival of our patients at diagnosis by identifying adverse prognostic factors, I investigated 27 patients managed between 1986 and 2001 (Salawu *et al.,* 2005).

The study showed that:

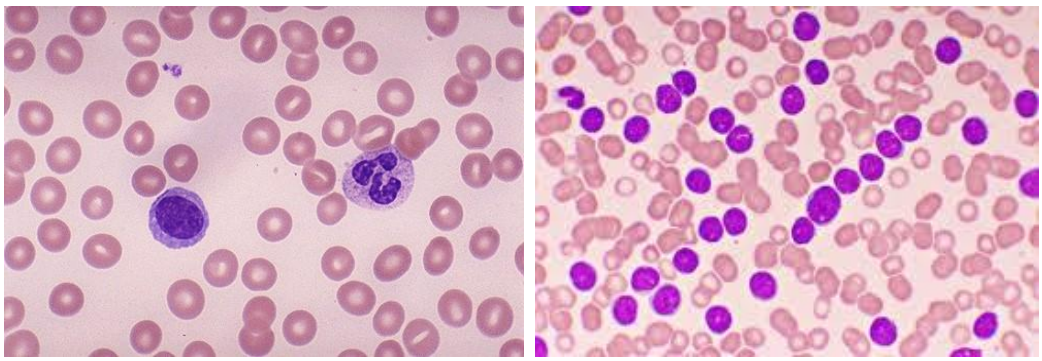
- Older age,
- Inability to afford the cost of treatment, and
- Complications such as anaemia, skeletal fractures, renal failure and neurological complications at presentation are important prognostic factors.

Of the 77.8% that received chemotherapy, it was inadequate in 85.7% due to inability to afford the cost of the drugs, and only three patients received up to 6 cycles of the drug combination before death or were lost to follow-up. The median period of their follow-up was 2.75 months, and the median survival was 1.2 months. Twelve (44.4%) of them were already dead at the time of analysis of our data as a result of renal failure (66.7%) and anaemia (33.3%).

2. Chronic lymphocytic leukaemia (CLL)

CLL is an indolent blood cancer that is less common in the Black population. It is characterised by the gradual accumulation of immunologically incompetent B lymphocytes in the blood, bone marrow, and lymphoid organs (**Figure 29**).

The clinical course of the cancer is variable, with some patients surviving for many years and sometimes dying of their cancer, while others may have a progressive disease and develop complications that may eventually lead to their death. Many studies have investigated factors associated with poor prognosis and those associated with more prolonged survival.



Normal Blood Film Appearance **CLL Blood Film Appearance**

Figure 29: Blood Film of Normal Film and that of Chronic lymphocytic leukaemia

Factors such as:

- Favourable genetic and molecular markers (mutated immunoglobulin heavy chain variable region genes),
- Favourable chromosomal abnormalities (deletion of the long arm of chromosome 13),
- Early clinical stage of the disease (Binet stage A/Rai stage 0),
- Lymphocyte doubling time of more than 12 months,
- Younger patients,
- Attainment of complete remission when treated, and
- Absence of co-morbidities is associated with much longer survival.

Because the facilities to carry out some of the molecular tests are not readily available in most Nigerian tertiary health facilities, I investigated the usefulness of some simple biological and laboratory parameters in assessing the prognosis and survival of CLL patients in Nigeria.

Table 9: Clinical and Laboratory features of CLL patients at diagnosis

Parameter	Mean (±SD)
Age (years)	59.00 ± 13.92
Haematocrit (%)	25.00 ± 7.52
White Blood Cell count (/µL)	111851.27 ± 122795.30
Absolute Lymphocyte count (/µL)	103954.91 ± 116897.97
Bone Marrow Lymphocyte count (%)	78.04 ± 16.99
Spleen size (cm)	13.32 ±8.14
Liver size (cm)	6.38 ± 5.00

I analysed 79 patients managed over 20 years whose diagnosis was based on clinical and laboratory features (**Table 9**) such as

- The presence of peripheral lymphadenopathy,
- Splenomegaly and hepatomegaly, and
- The presence of lymphocytosis in the peripheral blood and the bone marrow (Salawu *et al*., 2010).

More than 50% of the patients had no peripheral lymphadenopathy, while massive splenomegaly and hepatomegaly were recorded in 79% and 29.1%, respectively. However, the unavailability of other diagnostic modalities, such as flow cytometry or immunocytochemistry, to rule out other lymphoid malignancies creates diagnostic problems in our setting. More than 80% of them were older than 50 years at the time of diagnosis, 63% were in the advanced stage of the disease, and 74% presented with anaemia.

Assessing survival based on these simple and easily assessable and available clinical and laboratory parameters, the study found

- Splenomegaly,
- Younger age,
- Male sex,
- Moderate anaemia and thrombocytopenia and
- Fewer lymph node regions as good prognostic factors in our environment.

Assessing survival in patients with haematologic malignancies is very crucial because:

- Survival assesses the effectiveness of treatment and compares treatment modalities.
- The prolonged survival of patients underscores the success of medical research in drug discovery.
- Assessing survival aids in making informed decisions on approaches to treatment as to whether to be aggressive, offer palliative treatment, or explore clinical trials, i.e., the use experimental drugs.

- A longer survival means more time for the patient to live a quality life with family, work and pursue personal goals.
- Survival rates influence funding and healthcare planning. Diseases with poor survival often receive more research attention.
- The survival of a patient often has an emotional and social impact, as each additional month is significant for both the patient and their family.

Immunosuppression and Anti-cancer Drugs: The Paradox of Protection and Vulnerability

Nearly all patients receiving anti-cancer medications will undergo some degree of immune suppression. This presents a paradox, as the drug is intended to eliminate cancer cells without harming normal ones. However, anti-cancer drugs target rapidly dividing cells and do not discriminate between cancer and normal cells. Since blood cells are among the rapidly dividing cells, they are also prone to being affected by anti-cancer drugs. As anti-cancer drugs damage the bone marrow, the bone marrow cannot produce enough blood cells. Typically, the main impact is on the white blood cells, that is responsible for protecting the body against pathogens; hence, the body is more vulnerable to various infections, particularly opportunistic infections. In addition, their weakened immune system may also lead to:

- Reactivation of latent infections and autoimmune disorders,
- Life-threatening sepsis,
- Delayed wound healing,
- Increased risk of secondary malignancies, and
- Vaccine ineffectiveness.

Because of these serious consequences, I assessed some immunological parameters of chronic myeloid leukaemia (CML) patients receiving the anti-cancer drug, Imatinib mesylate (Glivec), in OAUTHC.

1. Glivec and Immune Suppression

Based on knowledge of the effects of anti-cancer drugs on blood cells, I carried out a study on the impact of Glivec, a targeted therapy, on patients with CML (Salawu *et al.*, 2010). Baseline complete blood counts and circulating CD4+ T lymphocyte counts were assessed in these patients before commencing Glivec at a standard dose of 400mg daily and 6 months on the drug. There was a significant reduction in the CD4+ T lymphocytes and absolute lymphocyte counts after 6 months of therapy (**Table 10**).

Table 10: Laboratory Parameters Before and After Imatinib mesylate Therapy

Mean (±SD)	Baseline	After Imatinib mesylate	t-value	p-value	95% C I
PCV (%)	30.1 ± 4.067	37.60 ± 4.949	3.78	0.002	3.24 - 11.76
WBC (/µL)	449000 ± 910600	6016 ± 4045	3.28	0.004	62257 -283710
ALC (/µL)	20071.20±17267.99	2696.60±1587.69	3.17	0.005	5882 -28924
CD4+ (/µL)	1774.60 ± 1044	841.80 ± 373.57	7.90	0.001	684 -1180
Platelet (/µL)	274000 ± 305400	212000 ± 1587	0.58	0.57	161396 -285396

CI: Confidence Interval; PCV: packed cell volume; WBC: white blood cell; ALC: absolute lymphocyte count.

The CD4+ T lymphocytes are central to the function of the immune system in the control of adaptive immunity against pathogens and cancer cells by activating the other effector immunocytes. Although several workers have reported severe microbial infections in patients using Glivec (Senn *et al*., 2005**)**, none of the patients in our study developed any infection. However, the short period of observation, the fact that the mean absolute number of circulating CD4+ T lymphocytes and granulocytes counts were within reference values might have a mitigating effect on the reduction in the absolute lymphocyte count. The study, however, confirmed that Glivec can cause lymphopenia.

In another study, I assessed the humoral arm of the immune system (Salawu *et al*., 2015). This study determined the serum levels of IgG, IgA, IgM, albumin, and globulin before initiating Glivec treatment and six months into the treatment (**Table 11**).

TABLE 11. Humoral Parameters of CML Patients Pre- and 6 months Post-Imatinib mesylate

Parameter	Mean (±SD) Pre-treatment	Mean (±SD) Post-treatment	t	p
ToP (g/L)	75.52	72.40	1.79	0.080
Alb (g/L)	36.80	35.82	1.38	0.174
Glo (g/L)	38.68	36.78	1.10	0.277
IgA (mg/dL)	236.92	120.62	4.64	0.000
IgG (mg/dL)	1984.60	2067.72	-0.36	0.718
IgM (mg/dL)	234.88	276.66	-1.86	0.068

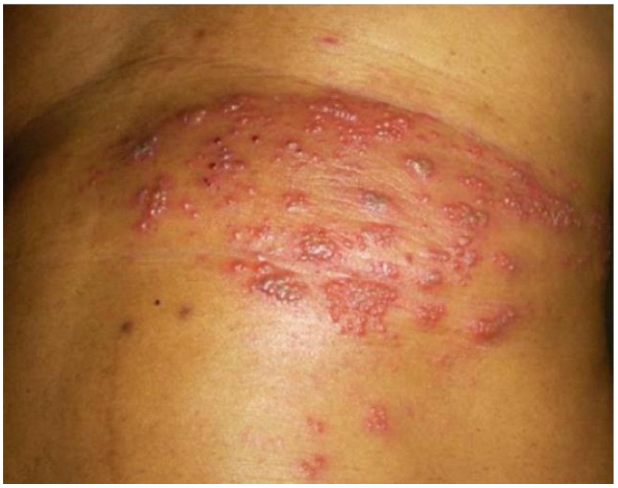
I noted a significant reduction in IgA concentration but a non-significant increase in IgG and IgM six months into treatment. The reduced IgA may lead to mucosal infections, particularly respiratory tract infections, indicating that this should be monitored while patients are taking this medication. On the other hand, the mechanism by which the production of both IgG and IgM, which are crucial in combating blood-borne infections, is preferentially stimulated and becomes more abundant while using Glivec is unknown. These studies on the effects of Glivec suggest that the drug has some deleterious effects on some aspects of immunity.

2. Glivec and Reactivation of Latent Viral Infection

The administration of Glivec in gastrointestinal stromal tumours (GISTs) has been very effective as neoadjuvant and/or adjuvant therapy. Most Glivec-related skin reactions include self-limiting dermatitis rashes, maculopapular eruptions with or without pruritus, erythematous eruptions, skin desquamation, periorbital oedema, psoriasis, mycosis, dermatofibromas, pityriasis rosea-like eruptions, and hypopigmentation (Paolino et al. 2016).

Although unusual presentations of GISTs are not uncommon, *de novo* immunosuppression is not a typical presentation. About two years into the use of Glivec therapy for GISTs, we reported the case of a 56-year-old man who developed multiple, painful, and tender blisters with distinctly dermatomal distribution over the left side of the trunk (**Figure 30**).

Figure 30: Skin blisters secondary to the ***reactivation of Herpes zoster*** in a patient with GISTs treated with Imatinib mesylate



Serial neutrophil, lymphocyte and CD4+ T-lymphocyte counts were within normal limits. The dermatomal presentation of a vesicular rash associated with severe pain is characteristic of herpes zoster infection. He was treated with Acyclovir and showed significant improvement in symptoms within one week. Considering that the absolute lymphocyte and CD4+ T-lymphocyte counts were adequate, a functional defect in cell-mediated immune mechanisms leading to the reactivation of latent varicella-zoster virus is the only plausible explanation for this presentation. Since the infection responded well to antiviral therapy, we concluded that reactivation of latent herpes infections is possible in patients with GISTs on Glivec therapy and that Glivec may interfere with cell-mediated immunity.

Aside from the increased risk of infection and reactivation of latent infection noted in the above studies;

- Immunosuppression can delay and interrupt cancer treatment and cause complications that may directly increase mortality independent of the cancer progression itself.
- Immunosuppression can cause vaccines to be less effective or ineffective because the immune system cannot mount a strong enough response.
- Long-term immunosuppression can increase the risk of secondary malignancies.
- Long-term immunosuppression can also negatively impact the quality of life for patients, as prolonged hospital stays can significantly affect their physical, emotional, and social well-being.

Therefore, patients can achieve better overall health and functionality by physicians balancing the need for immunosuppression with protection from the disease in the management of malignancies.

MY CONTRIBUTION TO BLOOD TRANSFUSION SAFETY AND MODERN INNOVATIONS

Transfusing blood is no doubt a life-saving procedure (**Figure 31**).

Figure 31: BLOOD TRANSFUSION SAFETY & MODERN INNOVATIONS

However, it may be associated with some hazards if safety measures are not implemented, particularly the transmission of transfusion-transmissible infections (TTIs) and allogeneic transfusion reactions. The essence of screening intending blood donors (**Figure 32**) is to ensure that the donation is not harmful to the donor and that the donated blood does not constitute a potential vehicle for transmitting infectious diseases or pose any hazardous effects to the recipients.

Figure 32: Blood Donor Screening

Screening of Blood to ensure that:

- The amount donated does not harm the donor
- The donated blood does not:
  - ✓ Constitute a potential vehicle for transmitting infectious diseases or
  - ✓ Pose any hazardous effects to the recipients

The safety of patients receiving blood transfusions has improved over the years due to enhancements in donor screening, eligibility criteria, and laboratory testing methods (**Figure 33**).

Figure 33: The Blood Donor (***Vanguard News; December 15 2023***)

1. Antibody Screening Method for Infectious Disease Agents in Blood Donors

A large pool of blood donors is not easy to obtain in most blood donor centres in Nigeria; donors arrive in trickles, primarily during urgent needs. The practice, at the time, was to pool donated blood and screen the units for infectious disease agents before transfusion. However, the increase in the incidence of HIV and other TTIs prompted the recommendation for pre-

donation screening to reduce laboratory staff's exposure to TTIs. This will also decrease waste in screening materials and reagents and allow for counselling blood donors who test positive for TTIs on the need for appropriate treatment. Consequently, I conducted a study to determine the effectiveness of pre-donation screening for intending blood donors. (Salawu *et al*., 2006). One thousand two hundred and fifty-nine (1259) intending blood donors were screened pre-donation. One hundred and fifty-one (151 or 12%) of the donors were rejected due to:

- Positivity for antibodies to HBV, HCV and HIV,
- Microfilaria infections, and
- Anaemia.

This study showed that:

- 151 blood bags were conserved by the pre-donation screening method.
- Disposing of the infected blood also involves using disinfectant, thereby increasing the financial loss to the blood bank.

Since our blood bank relied more on commercial (paid) donors, the pre-donation screening method:

- Reduced the number of high-risk donors who may want to conceal their high-risk behaviour during pre-screening counselling for fear of rejection.
- The method also reduces the risk of exposure of blood bank workers to TTIs,
- While it affords the opportunity of counselling those found positive for infectious disease agents on the treatment options available and the preventive methods to adopt to avoid the spread of the disease to their spouses, loved ones or caregivers.

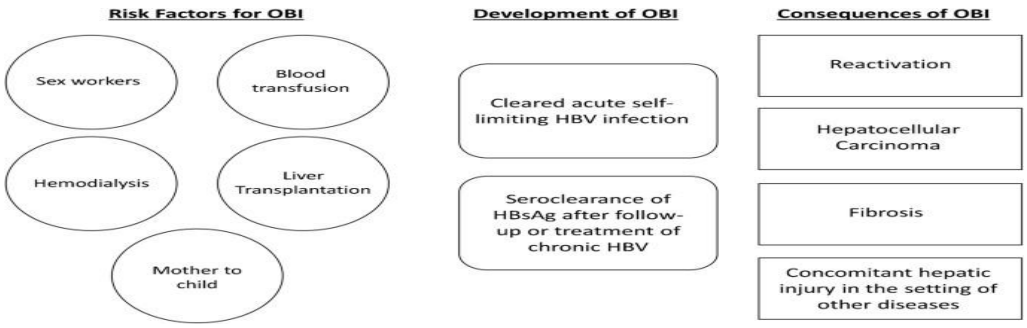
This study informed the current practice of screening all potential blood donors at the OAUTHC, Ile-Ife, before being bled.

2. Occult Hepatitis: An Indication of Failure of Antibody Screening Method (Figure 34)

Figure 34: Occult Hepatitis: Failure of Antibody Screening Method

Advances in the genomic amplification of viral DNA have shown that it is possible to be infected with the hepatitis B virus but be negative for HBsAg, which is one of the criteria used to exclude donors. This has shown that reliance on antibody testing in screening for transfusion-transmissible infectious disease (TTIs) agents, as commonly done in most blood banks in resource-limited economies like Nigeria, may be fraught with false-negative results. Studies have shown that occult hepatitis B infection increases hepatocellular carcinogenesis by eight times (Ikeda *et al.,* 2009). (**Figure 35**).

Figure 35: Occult Hepatitis B Virus Infection and Hepatocellular Carcinoma



Because of this observation, I conducted a prospective study on the burden of occult hepatitis B virus infection in our pool of predominantly commercial blood donors (Salawu *et al*., 2011). Four hundred and fifty-seven (457) prospective donors who were negative for antibodies to HBsAg, HCV and HIV were recruited.

Their serum samples were tested for

- antibodies to hepatitis B core antigen (anti-HBc), which is a marker of past or current exposure to HBV infection,
- antibodies to hepatitis B surface antigen (anti-HBs),
- antibodies to hepatitis B envelope antigen (anti-HBe), and
- hepatitis B envelope antigen (HBeAg).

Eighty (80 or 17.5%) of the prospective blood donors who were initially considered fit to donate blood based on HBsAg negativity were found to be positive for various other markers of hepatitis B infection. Of these markers of previous HBV infection,

- ✓ 20 (25%) were anti-HBc positive, and
- ✓ 58 (72.5%) were anti-HBs positive.

While some investigators found HBV-DNA in subjects positive for anti-HBc (Panigrahi *et al*., 2010), others did not (Ramezani *et al*., 2010). However, despite the non-detection of HBV-DNA in blood samples positive for anti-HBc core antigen, there were reports of post-transfusion HBV infection in recipients of blood positive for anti-HBc alone (Uemoto *et al*., 2009). Similarly, serum from patients with anti-HBsAg, evidence of recovery from HBV infection and a sign of protective immunity, has been shown to contain HBV DNA (Manzini *et al*., 2007). Studies have also shown that lymphoma and HIV-positive patients with positive anti-HBs have detectable HBV DNA in their serum (Koo *et al*. 2007). It could be inferred from these reports that serum-containing anti-HBs and anti-HBc can transmit HBV infection, emphasising their importance as significant markers of occult HBV infection, which can reduce

post-transfusion HBV infection when screened for. Therefore, this study has shown that we might have been under-assessing the prevalence of HBV infection in our blood donors by simply using HBsAg negativity alone as an exclusion criterion because this study showed that 17.5% or approximately one in every six of the donors investigated, is a potential carrier of HBV that can transmit the infection to recipients of their blood. There is, therefore, a need to include other markers of HBV infection to reduce the prevalence in our environment.

3. Improving the Screening Protocol for TTIs: The Nucleic Acid Testing Option

Since the screening protocol in Nigeria for HBV infection does not include the detection of occult hepatitis B infection (OBI), we sought to determine the prevalence of OBI at the OAUTHC, Ile-Ife **(**Olotu *et al*., 2016) using the presence of HBV DNA marker, to enable us to make an informed recommendation for effective HBV screening to prevent the transmission of the virus from blood donors to our patients. This study recruited 502 intending blood donors who were initially negative for HBsAg, out of which 345 (68.7%) were found positive for antibodies to HBV core antigen.

The detection and quantitation of HBV DNA in the anti-HBc positive samples were done at the Human Virology Laboratory of the Nigerian Institute of Medical Research (NIMR), Lagos. However, out of the 345 donors positive for anti-HBc, 19 (5.5%) had HBV DNA in their serum, signifying occult hepatitis B virus infection. In some earlier studies, 8.0%, 8.7%, and 11.2% were the reported prevalences of occult hepatitis B virus infection in Nigerian blood donors (Nna *et al.,* 2014; Akintule *et al.,* 2018; Opaleye *et al.,* 2014). These studies showed that occult hepatitis B virus infection exists in our blood donors and that the use of HBsAg alone for screening prospective donors, as presently being done in our blood banks, will not eliminate the risk of HBV transmission in Nigeria.

This calls for adopting NAT methods for testing blood donors in our various hospital blood banks and the National Blood Transfusion Centres in Nigeria to halt the spread of TTIs.

However, aside from preventing bloodborne infections,

- Blood screening maintains healthcare trust, encouraging blood donations and their use for medical treatment.
- Blood screening can detect the early spread of infectious disease in a population and allows prompt public health responses.
- The screening of blood will also protect vulnerable groups, such as surgical patients, cancer patients, or those with blood disorders who often require blood transfusions.
- Blood screening will also meet legal and international organisation standards, such as those set by the WHO, which establishes strict guidelines to ensure that donated blood is safe.

MY SERVICE TO THE UNIVERSITY, OTHER INSTITUTIONS AND ORGANISATIONS

1. Obafemi Awolowo University

- Mr Vice-Chancellor, Sir, I have taught undergraduate medical and dental students haematology and immunology since 1999. I have also taught several postgraduate students and supervised four MSc and two PhD students in Immunology.
- I was appointed as the acting Head of the Department of Haematology and Immunology in February 2007 and continued in this position till July 2011, during which I was able to resuscitate the Postgraduate Programme in Immunology and later became the coordinator.
- In October 2015, I was appointed the Chairman of the Faculty Postgraduate Committee and a member of the Board of the Postgraduate College and Academic Research Committee until August 2021.
- I was appointed the substantive Head of the Department of Haematology and Immunology in August 2020, serving until July 2021.
- I also served as the Dean of the Faculty of Basic Medical Sciences from August 2021 to July 2023.

In addition, I have served the University in other capacities, including

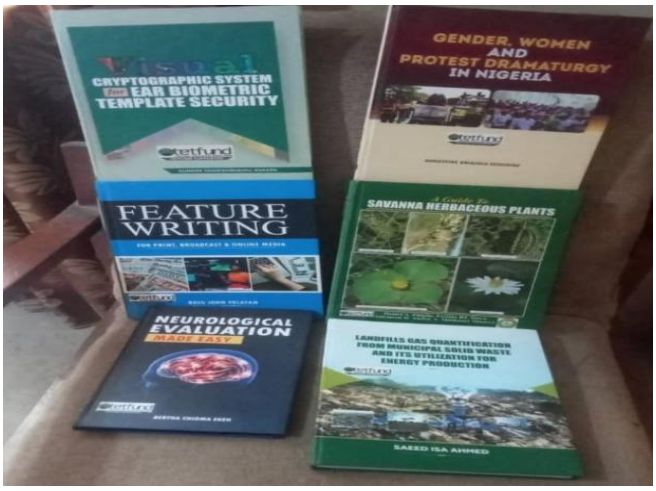
- The Dean's Representative to the Faculty Boards of the Institute of Public Health and the Institute of Ecology,
- Faculty Representative to the Faculty Board, Selection Panel and Review of the Faculty of Science.
- I have also served the University as an Examiner to the Postgraduate College and
- Senate Representative to the University Development Committee and Finance Sub-Committee.

2. Tertiary Education Trust Fund (TETFund)

- I served in the Tertiary Education Trust Fund's Technical Advisory Group (TAG) between August 2019 and November 2023. During this period, I promoted the writing of a pathology textbook for medical and dental undergraduate students to be published by the TETFund.
- In collaboration with Professor A. A. Abegunde of the Faculty of Environmental Design and Management, we convinced the TETFund TAG to patronise Obafemi Awolowo University Press Limited in book publication. The first set of 10 basic textbooks for students in tertiary institutions was delivered to TETFund by OAU Press Limited in April 2024 (**Figure 36**).

Figure 36:
OAU Press, Ile-Ife

First set of Basic Textbooks for Students in Tertiary Institutions in Nigeria published by Obafemi Awolowo University Press



3. Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife

Mr Vice-Chancellor, Sir, in addition to serving the Obafemi Awolowo University, I equally served the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) in various capacities.

- I was appointed the Head of the Department of Haematology and Blood Transfusion and a member of the Postgraduate Training Committee in August 2007. I served in this position till July 2011 and also between August 2020, and July 2021.
- I served as a member of the OAUTHC Committee on Anti-Retroviral Therapy and Prevention of Mother-to-Child Transmission.
- I was the Chairman of the Laboratory Revolving Fund Committee between 2010 and 2011, and
- I had the rare privilege of serving as the hospital's Acting Chief Medical Director between July 5th and September 20th, 2023.
- I have contributed to training many resident doctors at the OAUTHC and supervised the fellowship dissertations of 34 resident doctors.
- Aside from OAUTHC residents, I have also contributed to the training of many resident doctors in haematology in other teaching hospitals in Nigeria, including Ladoke Akintola University of Technology, Osogbo, Jos University Teaching Hospital, Jos, Federal Teaching Hospital, Ido-Ekiti, Ekiti State and Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State. Many are now consultants in various institutions both within and outside Nigeria.

4. Other Universities

- I have served as the External Examiner to several medical schools, including the universities of Ibadan, Ilorin, Jos, Maiduguri, Lagos, ABU Zaria, Usumanu Danfodiyo University, Sokoto, Ladoke Akintola University of Technology, Osogbo, University of Medical Sciences, Ondo, Ondo State and Ebonyi State University, Abakaliki. I have also served as an External Reviewer for professorial cases of these universities and others, including Lead City University, Ibadan; Lagos State University, Ikeja; Gombe

State University, Gombe; Nnamdi Azikiwe University, Nnewi; and Kaduna State University, Kaduna.

5. Professional Bodies

I am a member of several national and international professional bodies, including:

- The National Postgraduate Medical College of Nigeria (NPMCN) and the
- West African College of Physicians (WACP) for which I have served as an examiner, Sub-Chief Examiner (Haematology), assessor, educational resource person and member of the accreditation team to several teaching hospitals on behalf of these professional bodies.
- I was the Training Coordinator and a member of the Education and Research Committee of the Faculty of Laboratory Medicine of the WACP between 2015 and 2018.
- I am a member of the committee on the Doctor of Medicine (MD) programme of the Faculty of Pathology of the National Postgraduate Medical College of Nigeria.

CONCLUSIONS AND RECOMMENDATIONS

Mr Vice-Chancellor, Sir, Pathology is often called **"*the science behind the cure*"** because it plays a central role in understanding diseases, their causes, and their mechanisms, which are essential for developing treatment and cure. To haematologists,

- Blood serves as a tool that aids in unravelling the nature of diseases,
- It is useful in screening for those yet to be clinically diagnosed,
- It is a means of predicting the risk of an individual being affected by a particular disease.
- The decision on treatment modalities that can be chosen or necessary treatment modifications can be suggested from the results of blood tests.
- The results of blood tests can also be used to monitor treatment compliance or its effectiveness.
- In addition to making specific diagnoses through blood tests, screening for diseases is a cost-effective measure to detect diseases and initiate treatment much earlier for a better outcome.
- Blood transfusion is much safer today because tests are done to determine the compatibility between the donor and the recipient and to exclude donors with transfusion-transmissible infectious diseases.

Sickle cell disease is the most common inherited genetic disorder in sub-Saharan Africa, with Nigeria having the highest affected population. In addition to the debilitating complications associated with the disease,

- Affected individuals are also faced with some psychosocial problems in society, such as negative societal attitudes and perceptions,
- Discrimination by employers and colleagues at work,
- Teasing and bullying by schoolmates,

- Anxiety and depressive feelings and sometimes self-hate.

Therefore, early diagnosis in babies whose parents are carriers of the sickle gene can prompt early management and prevention of many complications associated with the disease by instituting measures that will lessen the clinical presentation, hence, affected individuals can live a completely healthy life.

Mr Vice-Chancellor, Sir, and distinguished audience, recent advances in diagnostic technologies in haematology, such as

- Advanced flow cytometry has made it possible to detect and characterise blood cells with high precision and aid diagnosis,
- Artificial Intelligence-enhanced blood smear analysis allows the detection of abnormal cells,
- Next-generation sequencing Technology identifies genetic mutations linked to blood disorders, opening doors for personalised medicine, and
- Lab-on-a-chip technology allows for rapid analysis of blood samples.

Therefore, we should not wait for occasions, such as when we wish to travel abroad or take up employment, to make carrying out medical test mandatory. It is advisable to detect a potentially life-threatening disease well before it escalates into an irreversible health crisis that is difficult to manage.

- A regular medical check-up can help identify diseases that can be nipped in the bud,
- A medical check-up can establish whether our vital organs are functioning well,
- A medical check-up can establish if we have markers for diseases or cancers, or if we are susceptible to certain genetic conditions.

As diagnostic technology advances, blood tests are becoming increasingly precise, further enhancing our ability to detect and treat diseases at earlier stages, as well as to monitor and plan effective treatments.

I, therefore, encourage everyone to undergo medical tests at least once a year, even when they are healthy because ***blood is more than just a life-sustaining fluid circulating through our bodies***.

In blood:

- We find the script of our DNA,
- The chemical whisperer of our health, and
- The silent warnings of disease.
- Our blood is a testament to the lineage we carry.
- Like a mirror, blood reflects the state of our body and mind: inflammation, infection, stress, and love, all leave their mark on its flow.

Blood is, therefore, ***Nature's powerful "mirror"*** reflecting our internal health.

APPRECIATION

Mr Vice-Chancellor, Sir, I sincerely thank all my teachers starting from my primary school at the

- Roman Catholic Mission School, Sokoto,
- Local Authority Primary School, Isale Oyo, Oyo, and
- Saint Luke's Primary School, Idode, along Oyo-Ogbomoso Road.

I appreciate all my teachers at

- Ansar-Ud-Deen Secondary Modern School (now Ansar-Ud-Deen Grammar School), Opapa, Oyo, and
- Oranyan Grammar School, Oyo, as well as my teachers at the
- Federal School of Arts and Science, Ondo.

They all have contributed in one way or another to my success in life. My profound appreciation also goes to my teachers in the

- Faculty of Science of this great university and the then
- Faculty of Health Sciences. May the Lord Almighty reward them abundantly.

I acknowledged, with gratitude, my trainer, Prof M. A. Durosinmi, for his contribution to my success. I appreciate the contributions of Professor N. O. Akinola, Professor R. A. Togun, Professor R. A. Bolarinwa, and Dr T. O. Owojuyigbe. I also appreciate the contributions of my other colleagues in OAUTHC, Dr O. J. Olarewaju, Dr O. A. Omoyiola, Dr (Mrs) O.O. Oguns, and Dr I. O. Ahmed. May the Almighty God reward every one of you.

I want to express my heartfelt appreciation to the laboratory technologists in the Department of Haematology and Immunology, Obafemi Awolowo University, Ile-Ife and the laboratory scientists of the Department of Haematology and Blood Transfusion, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife for the cooperation I enjoyed working with them.

I am eternally grateful to my late parents, Alhaji Salawu Akande and Alhaja Sifawu Abebi, for their enormous sacrifices and contributions to my success in life.

I also appreciate my wife, Fausat Olatundun, and my children, AbdulRahman, Ridhwanullah, AbdulHameed, and Habeebllah, for their unwavering love and support.

In the *Holy Qur'an*, Chapter 55 (*Suratul-al-Rahman* or "The Most Gracious"), Almighty Allah brings to our remembrance the many favours He bestowed on mankind and asks, ***"Then which of the favours of your Lord will you deny?*** Indeed, none of the favours of the Almighty Allah is deniable. Therefore, my unquantifiable gratitude goes to the Almighty Allah for His innumerable favours to me, including the favour of this inaugural lecture.

Therefore,

"Glory to thy Lord, the Lord of Honour and Power!

(He is free) from what they ascribe (to Him)!

And Peace on the Messengers!

And Praise to Allah, the Lord and Cherisher of the Worlds. **(**Q37 verses 180-182)

Mr Vice Chancellor, Sir, distinguished audience, I am highly honoured by your presence here today and sincerely grateful. May God Almighty bless you all! Amen. Thank you all, and God bless.

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