# NIGER DELTA UNIVERSITY

WILBERFORCE ISLAND, BAYELSA STATE



# 23<sup>RD</sup> INAUGURAL LECTURE

# ASSOCIATES, ADVERSARIES AND ADJUTANTS: EXPLORING THE DIVERSE ROLES OF MICRO-ORGANISMS IN HUMAN HEALTH AND DISEASE

## BY

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# 15<sup>TH</sup> FEBRAURY 2016

# DEDICATION

This inaugural lecture is dedicated to all my teachers and students, and to all persons interested in the prevention and control of infectious diseases.

# PROTOCOL

The Pro-Chancellor, Sir

The Vice-Chancellor,

Members of the Governing Council,

Deputy Vice-Chancellors,

Other Principal Officers of the University,

Provost, College of Health Science

Dean of School of Postgraduate Studies,

Deans of Faculty,

Distinguished Professors and Scholars,

Heads of Department,

Staff and Students of NDU

Staff of NDUTH,

Distinguished Guests,

Ladies and Gentlemen.

# **PREAMBLE**

I give thanks to almighty God for the privilege to see this day. I must sincerely appreciate the University for this opportunity to present my inaugural lecture about 2years after my appointment as Professor in the Niger Delta University. Inaugural lecture is a tradition of all universities around the world and it is meant to showcase newly promoted or appointed professors of the university. The lecture provides a platform for new Professors to inform the university community and the public about their research career so far, as well as to highlight their intellectual activities and unveil current and future interests in scholarship, research and development. My goal in this lecture is to achieve all the above the objectives.

My VC Sir, my inaugural lecture is titled 'Associates, Adversaries and Adjutants: Exploring the diverse roles of micro-organisms in human health and disease. I have carefully selected this topic because I believe it roundly captures my past, current and future interests in scholarship, research and development. In the delivery of this lecture, I hope to take us through my journey in the field of infectious diseases and immunology, to discuss the concept of micro-organisms as man's 'Associates, Adversaries and Adjutants' and to highlight how the understanding of this concept could be exploited by man to promote health and prevent disease. As a physician with laboratory, clinical and public health experience, I also intend to emphasize how the intricate connections between the bench, bedside and the community is exemplified in the field of infectious diseases and immunology. Finally, as I make my submissions, I hope to highlight my contributions to research and scholarship as well as my future interests in research and development.

May I humbly welcome all of you to this inaugural lecture as I am confident that it shall be informative, stimulating and a worthwhile experience.

# MY JOURNEY IN THE FIELD OF INFECTIOUS DISEASES AND IMMUNOLOGY

#### **Medical school**

My VC Sir, I developed interest in the field of infectious disease and immunology during my 4<sup>th</sup> year in medical school, especially after inspiring lectures on microbes and immune system by Late Prof Laszlo G Egler (Professor of Medical Microbiology) and Prof Geoffrey C Onyemelukwe (Professor of Medicine and Immunology) respectively. Prof Egler was fond of starting his lectures with highlights on recent happenings in the field of Medical Microbiology and its implications for human health and disease. I developed so much interest in his lectures that I was the first among my classmates to volunteer to be part of a series of seminars initiated to introduce medical students to modern trends in Medical Microbiology. Prof Egler had assigned me to give a public lecture on 'microbial gene regulation'- a topic that was outside the scope of our curriculum at that time. This presentation opened my eyes to the world of microbial genetics and stimulated my interest in human genetics. It also led to my first scientific paper as a 4<sup>th</sup> year medical student titled 'Genetics, Medicine, and the Future' published in the 'Student Doctor' journal in 1997.<sup>1</sup>

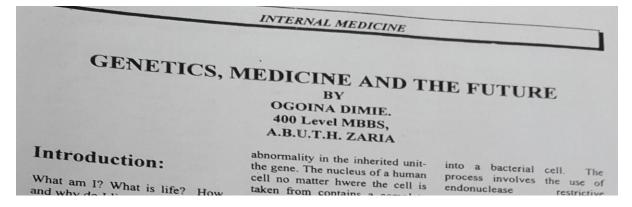


Figure 1: Caption of my first article as published in Student Doctor Journal in 1997

In 1998, I was selected by my classmates to deliver the guest lecture to students of Kaduna State Polytechnic to commemorate the World AIDS day as part of the medical student's health week. The topic was 'HIV/AIDS- The Scourge of Our Time'. This lecture turned out to be my first real experience of the social

aspects of the disease and it also made me to be recognised as an 'HIV/AIDSexpert' by my classmates and a few of my lecturers.

In my 6<sup>th</sup> year of medical school, I was appointed as the Editor-in Chief of the medical student journal named 'ABUMED'. In a bid to get excellent articles for publication in the journal, I approached Prof GC Onyemelukwe, the then Head of Department of Internal Medicine and Immunology, to summarise his inaugural lecture titled "Games Played by Infections and Nigerians -Immune Cells as Godfathers" as one of the scientific papers. I was stunned when he looked at me straight in the face and said- go and summarise it! You can do it! Although I was initially doubtful about my capacity to meet this challenge, I eventually accepted it and set out to read and understand the lecture of over 110 pages. This undertaking led to my second scientific paper titled "Re-Games Played by Nigerians and Infections: Immune System as Godfathers" published in ABUMED in 1999.<sup>2</sup> Reading his inaugural lecture and writing of this paper, enriched my knowledge in the field of immunology and strengthened my interest in the field of immunology of infectious diseases.

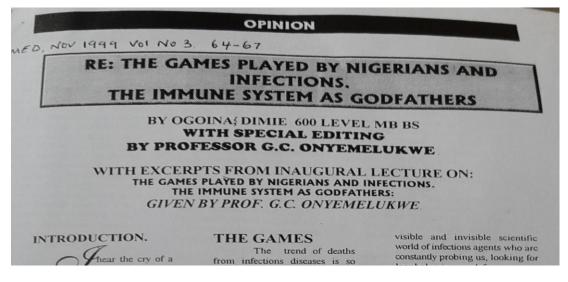


Figure 2: Caption of my 2<sup>nd</sup> scientific article published in ABUMED journal in 1999.

Although, I was fairly certain of my desire to become an academician and a researcher after my 4<sup>th</sup> year in medical school, I became fully convinced that I wanted to be a Professor of Internal Medicine with immunology or genetic engineering as a subspecialty. I even stated this as my professional aspiration in our final year medical student year book (Figure 3).



Figure 3: My page in our graduation year book.

# Residency training in infectious diseases and immunology

In pursuit of my residency training, I aspired to train in the Immunology Unit, Department of Internal Medicine, Ahmadu Bello University/Teaching Hospital, under the mentorship of Prof GC Onyemelukwe. I was fortunate that after working briefly as medical officer in FMC, Yenagoa in 2003, I was accepted into the residency training programme of Department of Internal Medicine, ABUTH, Zaria in November 2003. After passing my Part 1 Fellowship Examination in Internal Medicine in both the West African College of Physicians (WACP) and the National Postgraduate Medical College of Nigeria (NPMCN) in 2006, I approached Prof GC Onyemelukwe to inform him of my intention to specialise in Immunology and Infectious Diseases. He once again looked at me and said -Are you sure? Are you sure you can survive?! I was definite about my interest in the field regardless of the perceived obstacles- so my answer was an emphatic 'Yes Sir".

At the time I started my training there was no established curriculum in infectious and immunology in any of the Postgraduate Medical Colleges in Nigeria. Prof Onyemelukwe recognised the need for me to understand the bench, bedside and community aspects of Infectious Diseases and Immunology. I was co-opted as a member of the Immunology Department of the ABU, Zaria and beginning 2006 I was given the opportunity to teach Immunology to medical students as a junior resident doctor. For over two years, I participated in immunology bench work, learning theoretical and practical basis of immunological techniques in microbial diagnosis. I spent three months in the

Medical Microbiology in ABU learning bacteriology, parasitology and fungi. I travelled to Ibadan, Oyo state to spend 3 months in the WHO Poliomyelitis laboratory, Department of Virology UCH and Department of Medical Microbiology, University College Hospital learning viral diagnostic techniques such as viral culture, PCR, and hybridization techniques, as well as diagnosis and treatment of sexually transmitted infections. I also undertook a 2-week training on Infection Control at the UCH. Thereafter, I travelled to Awka, Anambra state, to undertake a 6month training on parasites and insects of medical importance in the Department of Parasitology and Entomology, Nnamdi Azikwe University, Anambra State. I was also opportune to have been selected to participate in a 2-week training on basic recombinant DNA technology in the Centre for Biotechnology, ABU, Zaria.

My VC Sir, as a physician, my training also included vast exposure to clinical infectious diseases. I undertook clinical postings and trainings on HIV/AIDS, tuberculosis and leprosy. I was actively engaged in the clinical management of infectious diseases patients including cases of malaria, tetanus, HIV, meningitis, sepsis, pneumonia, tuberculosis, cholera, rabies, among many others.

As part of the requirement of my training, I undertook two research projects on Clinical and Immunological aspects of Toxoplasmosis and Human Herpes Virus 8 infection. I am pleased to inform us that among my peers, I was fortunate to be amongst the few to conduct and successfully complete two research projects that led to the award two fellowships in Infectious Diseases and Immunology in both the WACP (FWACP) and NPMCN (FMCP) in 2009.

I would like to appreciate Prof GC Onyemelukwe for exposing me to research early in my training as a resident doctor. From him I learnt the rudiments of scientific writing -'be focused, use few words, make sense!'. I remember been given various assignments to bring up ideas for research, to critically appraise research topics and to write scientific manuscripts for publication. As a Senior Registrar in 2008, Prof Onyemelukwe challenged me to represent him to present a public lecture titled 'Guidance on public health management of cerebrospinal meningitis in Nigeria' at the Federal Ministry of Health-organised stakeholders meeting on Control of Epidemic Prone Infectious Diseases in Nigeria. I was presented with several other challenges to write papers, to present seminars and to teach students and my peers. At end of my residency training in 2009, I had completed two theses, undertaken more than 20 research works, published not fewer than 8 scientific papers and presented about 6 public lectures.

# **The Practice of Infectious Diseases**

On completion of my residency training at ABUTH, Zaria, my request for appointment as a lecturer/consultant physician in ABU/ABUTH was not granted. I left ABUTH in 2010 to Bingham University Teaching Hospital (BHUTH), Jos where I was employed as a lecturer/Consultant physician. In Jos, I worked at the HIV/AIDS clinic and managed all cases of Infectious Diseases. It was in Jos that I managed my first case of Lassa fever. Working with colleagues in Jos, we were able to describe and publish the burden of occupational exposures to body fluids and the status of hepatitis B vaccination among healthcare workers in the BHUTH.

About 10 months after my engagement in BHUTH, I left Jos for Bayelsa having been offered the position of Senior Lecturer, in NDU Bayelsa.

My VC Sir and distinguished ladies and gentlemen, as you must have learnt from my citation, since assuming duty as Niger Delta university, I have keenly pursued the path of expanding my knowledge and impact in the field of infectious diseases and immunology through scholarship, research and community service.

# **INTRODUCTION**

My Vice Chancellor Sir, in the following sections, I will take us through the concept of Microbes as Man's "Associates, Adversaries and Adjutants". Let me begin by providing some basic definitions.

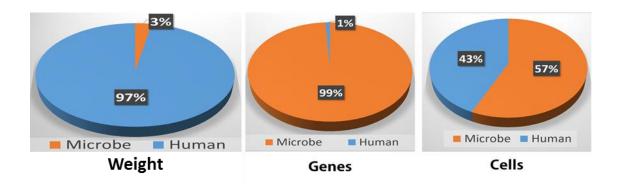
The term "Associate" is defined as someone who is closely connected to another person as a companion, friend, or business partner (Cambridge Dictionary). Adversary is defined as a person or group that is an opponent, enemy or foe to another person or group in a contest, conflict, or dispute. Adjutant is primarily used in the Military to describe a military officer who assists the superior officers. It is also used to describe one who helps, assist or supports.

## MICRO-ORGANISMS AS MAN'S ASSOCIATES

And God said, "Let the land produce living creatures according to their kinds: the livestock, the creatures that move along the ground, and the wild animals, each according to its kind." Genesis 1:24

Evidence of man's association with micro-organisms or microbes is as old as the history of man on Earth.<sup>3</sup> These micro-organisms may include bacteria, fungi, protozoa, algae and viruses, among others. Although, no specific mention of micro-organisms was stated in the Creation narration in the Bible, many Creation Microbiologists believe that micro-organisms where either created as separate entities or as part of the ecosystem of every living and nonliving entity that was created.<sup>4</sup> The Evolutionist's argue that micro-organisms have existed on earth for over 3.5billion years as the first living forms of life preceding the evolution of mankind.<sup>3</sup> Either way, microorganisms are ubiquitous in nature; they can be found in every part of the biosphere, including soil, water, air and space, as well as in the deepest, hottest and coldest parts of the planet.<sup>3</sup> It is estimated that there are about 5 X  $10^{30}$  microbial cells on earth, accounting for about 90% of the biomass of the entire biosphere.<sup>3</sup> Microorganisms are indispensable for the survival of life on earth and are necessary for the physical and chemical makeup of earth. They are responsible for cycling the chemical elements essential for life, including carbon, nitrogen, sulfur, hydrogen, and oxygen.<sup>3</sup>

Man is exposed to micro-organisms in-utero, at birth, throughout lifetime and at death. Indeed, as long as the earth remains, the exposure of man to micro-organisms shall never cease. While microorganisms remain closely associated with man's environment, they are also part and parcel of the human makeup. A recent study suggests that there are about 39 trillion bacterial cells in the human body compared to about 30 trillion human cells; a ratio of 1.3 bacteria to every one human cell.<sup>5</sup> Microorganisms constitute about 1-2kg of the weight of the average 70kg man.<sup>6</sup> Figure 4 illustrates the contributions of microbes to human cells, weight and genes.



**Figure 4**: Contributions of human microbiome to human weight, genes and cells. NB: Although the human tissues and cells account for about 97% of human weight, there are more microbial cells and genes in the human body than human cells and genes.

The first evidence of the presence of microbes in the human body was reported by Antonie van Leeuwenhoek in the 17<sup>th</sup> Century, when using a self-designed microscope, he identified microscopic living forms (then called animalcules) in his faeces and from the plaque scraped off from his own teeth.<sup>7</sup> Today, microorganisms are known to inhabit almost every part of the human body including the skin, gut, glands, placenta, uterus, and body fluids, as well as all mucous membranes.<sup>8</sup> Humans have even been shown to constantly emit microorganisms into their environment and these community of microorganism can be used to differentiate individuals. For instance, some studies have shown that the human fingertips can transfer microbes onto keyboards and it is possible to identify the person who touched the keys using their signature microbial communities.<sup>9</sup> Experimental studies also indicate that every person is surrounded by a personalised microbial cloud that is unique for that individual and may be used as an alternate fingerprint to determine if a person was in a room or in an environment at a point in time (Figure 5).<sup>10</sup>

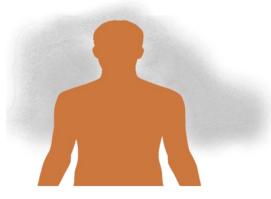


Figure 5: The human microbial cloud. Every human is surrounded by a unique community of micro-organisms that are distinct for that individual.

The human microbiota is the term used to describe the aggregate or community of microorganisms that live on and within the human body.<sup>11</sup> The human microbiome describes these microorganisms and their genomes. The human microbiome consists of more than 10,000 microbial species including bacteria, fungi, parasites and viruses.<sup>8</sup> It is estimated that 5-8% of the human genome is made of microorganisms.<sup>12</sup> These microorganisms are mainly endogenous retroviruses that represent traces of original viruses which had integrated with human genes millions of years ago. However, the human microbiome is dominated by bacteria organisms, consisting mainly of four groups or phyla of bacteria including Actinobacteria, Bacteroidetes, Firmicutes and Proteobacteria (Figure 6).<sup>8,11</sup>

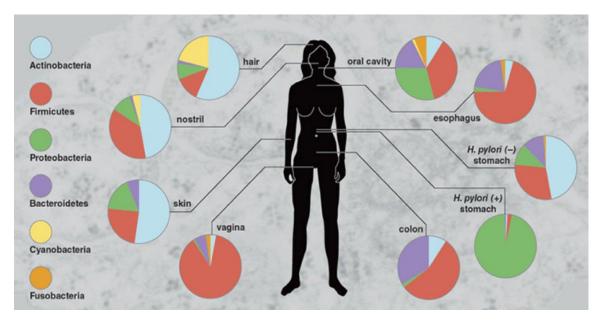


Figure 6: The human microbiome. The normal human body consists of various communities of micro-organisms that live in a symbiotic mutualistic relationship with human cells and tissues. Image Adapted from Nature Reviews Genetics 2012, 13:260.

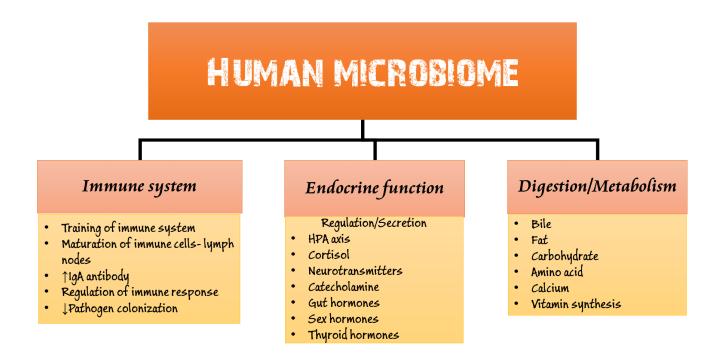
The human microbiome is very diverse and consist of a gene catalog of 3.3 million non-redundant genes as compared to the about 22,000 genes present in the entire human genome.<sup>11</sup> Furthermore, compared to the human genome that is 99% identical between individuals, the microbiome of two individuals may differ by 80 to 90%.<sup>11</sup> Consequently, the human microbiome might provide greater accuracy in distinguishing individuals that the human genome.

The microbiome of an individual begins to develop in-utero from exposure to placental microbiome, and continues at at birth from exposure to maternal microbiota (including breast milk and micro-organisms on the mother's skin and vagina) and environmental microorganisms.<sup>8</sup> The new-born's microbiome varies depending on mode of delivery, with predominance of vaginal microdelivery and organisms following vaginal predominance of skin microorganisms following delivery by caesarean section.<sup>13</sup> Through infancy to childhood, the microbiota continues to be shaped by human and environmental factors including diet, drugs, hygiene, lifestyle and behaviour, among other factors.<sup>8,13</sup> In most cases, before the 2<sup>nd</sup> year of life, the human microbiome is fully developed and comparable to that of adults.<sup>8</sup>

The healthy human microbiome (i.e. the microbiome identified in apparently healthy adults) consists of rich and resilient communities of microorganisms that live in equilibrium as a group and in a mutually beneficial or tolerant relationship with human cells.<sup>14,15</sup> Consequently, a normal healthy human body consists of 'good' and 'bad' microorganisms and human cells that live in equilibrium and in a mutually beneficial or tolerant relationship.

Healthy human microbiome is now known to contribute to human health through effects on the immune system, digestion, endocrine function and metabolism (Figure 7).<sup>8,15,16</sup> From the time of birth, the microbiome trains and educates the immune system through a very robust process.<sup>17</sup> It has been shown that the microbiome is required for normal and balanced development of immune system, including the regulation of immune responses.<sup>18</sup> The microbiome also prevents infection by resisting colonization by pathogenic microorganisms. They facilitate carbohydrate breakdown, regulation of pH of skin (via nitrate reduction and arginine deiminase), and regulation of pH of

vagina (via lactic acid production).<sup>15</sup> They also have a role in production of short-chain fatty acids via carbohydrate fermentation and glycosaminoglycan degradation in the gut, as well as in the synthesis of vitamins such as vitamin D, vitamins B12, thiamine, riboflavin and Vitamin K.<sup>15</sup> The gut microbiota exerts control over the hypothalamic pituitary-adrenal axis and may be directly or indirectly involved in the secretion and regulation of several hormones including cortisol, neurotransmitters, monoamines and other gastrointestinal hormones.<sup>16,19</sup>



**Figure 7:** The functions of the healthy human microbiome. The healthy human microbiome contributes to human health through effects on the immune system, digestion, endocrine system and metabolism.

Overall, in man's environment and on and within man's body, micro-organisms have co-evolved as man's associates, man's companion and man's friend. When, how and why did they become our adversaries?

# **MICRO-ORGANISMS AS MAN'S ADVERSARIES**

My VC Sir, microorganisms are man's greatest adversaries due to their ability to cause disease in man with consequent morbidity and mortality. Diseases caused by micro-organisms are referred to as Infectious diseases. They are also called communicable diseases due to their potential for direct or indirect person to person transmission. Infectious diseases are usually caused by pathogenic microorganisms or infectious agents which may include bacteria, viruses, parasites, fungi and prions, among others.

The evidence of the role of microorganisms in causing disease in man is as old as the history of man. Outbreaks of small pox, leprosy, tuberculosis and meningococcal meningitis, among others were reported in Ancient Greece and Egypt.<sup>7</sup> The plague of Athens (429-426BC) was reported to have killed up to half of the population of the people of Athens.<sup>20</sup> Between 165-180AD, the Antonine Plague killed about 30% of the population of Europe, Western Asia and Northern Africa. Bubonic plague (541-542; 1346–1350) ravaged Europe killing 30 to 70% of the population.<sup>20</sup> Flu pandemic (1889–1890; 1918–1920) killed more than 70 million people, causing more than deaths following World War 1.<sup>20</sup> Many other fatal outbreaks of small pox, cholera, measles, viral haemorrhagic fevers and yellow fever have been reported throughout history.<sup>20</sup> These infectious disease epidemics and pandemics greatly shaped human history, politics, commerce and culture. It led to collapse of Empires, stagnation of economic growth and civilization and annihilation of populations and cultures.<sup>7</sup>

Category	Examples	
Airborne diseases	Influenza (seasonal, pandemic, avian), severe acute respiratory syndrome (SARS), Middle East respiratory syndrome coronavirus (MERS-CoV)	
Vector-borne diseases	Yellow fever, chikungunya, Zika fever, West Nile fever	
Water-borne diseases	Cholera, shigellosis, typhoid fever	
Epidemic meningitis	Meningococcal Meningitis by Neisseria meningitidis	
Rodent-borne diseases	Plague, leptospirosis, hantavirus, Lassa fever, rickettsia (murine typhus)	

Table 1: List of common Epidemic and Pandemic diseases

Haemorrhagic fevers	Ebola virus disease, Lassa fever, Marburg virus disease, Crimean- Congo haemorrhagic fever, Rift Valley fever		
Other zoonotic diseases	Nipah virus infection, Hendra virus infection		
Smallpox (eradicated in 1979), monkeypox			
Any other emerging disease			

Unfortunately, at the time of these epidemics, disease causation was either attributed to supernatural causes or poisonous contaminated air (Miasma theory of disease).<sup>21</sup> The role of microorganism became widely accepted only after the relentless work of Louis Pasteur and Robert Koch who both described the germ theory of disease in the 19<sup>th</sup> century.<sup>7,21</sup>

Throughout history, man has engaged in unending battle against pathogenic microorganisms and infectious diseases. Vaccination, antisepsis, hand hygiene, hospital sanitation, environmental hygiene and antibiotics were pioneered at various times by various scientists. <sup>7</sup> (Table 2) By the late 1960's, the world witnessed improvements in health systems and standard of living resulting in remarkable decline in morbidity and mortality due to infectious diseases, particularly in the developed world.<sup>7,21</sup>

YEAR	INFECTIOUS DISEASE EVENT
1683	Anton van Leeuwenhoek identified micro-organisms using a self-made microscope
1796	Edward Jenner develops technique of vaccination against smallpox
1848	Ignaz Semmelweis introduces hand hygiene to prevent puerperal sepsis
1854	John Snow recognizes link between the spread of cholera and drinking water supplies
1860-64	Louis Pasteur concludes that infectious diseases are caused by living organisms called "germs."
1865	Joseph Lister's introduced surgical antisepsis by using carbolic acid to disinfect wounds
1876	Robert Koch validates germ theory of disease
1892	Dmitri Ivanowski discovers viruses
1918-1919	Epidemic of "Spanish" flu causes at least 50 million deaths
1929	Alexander Fleming discovers penicillin in mould
1941	Clinical applications of Penicillin
1953	James Watson and Francis Crick reveal the double helical structure of DNA
1979	The world is declared free of smallpox
1981	AIDS first identified as a new infectious disease by U.S. Centers for Disease Control and Prevention

 Table 2: Infectious disease history timeline

1982	Stanley Prusiner discovers prions as a cause of scrapie in sheep
1983	Luc Montagnier and Robert Gallo discover of the human immunodeficiency virus
1984	Barry Marshall discover Helicobacter pylori as a cause of peptic ulcer disease
2000s	Antibiotic-resistant pathogens spreading in many environments
2015	A global action plan on antimicrobial resistance was adopted by Member States at the 68 <sup>th</sup> World Health Assembly

The optimism of man's victory over microorganisms however, became dashed after the emergence of antibiotic resistance<sup>22</sup> and the emergence and reemergence epidemics and pandemics of various new and old infectious diseases.<sup>22</sup> Beginning with the HIV/AIDS pandemic of the early 80's, the world has witnessed various epidemics and pandemics of diseases such as Influenza, SARS, Viral Haemorrhagic fevers, and Zika, among others (Figure 8).<sup>20</sup> Now very worrisome is the global public health threat of antimicrobial resistance which is reversing the gains achieved in the treatment of infectious diseases such as HIV, tuberculosis and malaria and also fuelling emergence of healthcare-associated infections due to multi-resistance micro-organisms.<sup>22</sup>

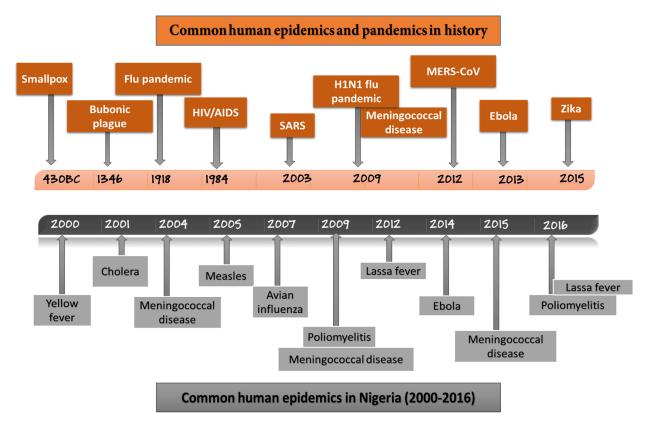


Figure 8: Timeline of common pandemics and epidemic in the world and in Nigeria (2000-2016).

Overall, the burden of infectious diseases is worst in developing countries due to weak health systems, poverty and poor environmental sanitation, among other factors.<sup>23</sup> While developed countries remain largely free of endemic infections, endemic and epidemic infectious diseases continue to ravage developing countries.<sup>24</sup> About 80% of the 19 million deaths caused by infectious diseases in 2015 occurred in developing countries. In Nigeria, infectious diseases such as respiratory tract infections, diarrhoea diseases, malaria, HIV/AIDS, and tuberculosis rank topmost as the most common cause of morbidity and mortality leading to for over 700,000 deaths annually.<sup>25</sup> (Figure 9)

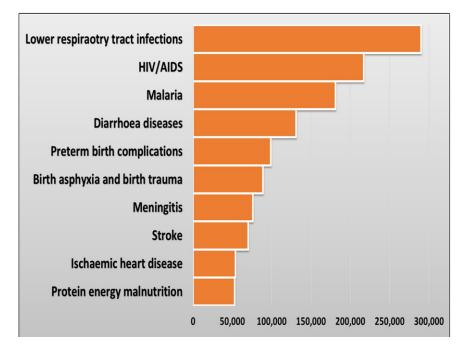


Figure 9: Common causes of disease mortality in Nigeria (2012)

#### Infection and Non-Communicable Diseases

My VC Sir, a growing body of evidence now suggest that acute, chronic or persistent exposures to pathogenic micro-organisms can also lead to non-communicable diseases (NCD).<sup>26</sup> It is also now well established that chronic asymptomatic infection may predispose or directly lead to various non-communicable diseases. Chronic asymptomatic malaria infection has, for

instance, being aetiological associated with growth retardation, growth stunting, chronic anaemia and neurocognitive impairment among children in malaria endemic countries.<sup>27</sup>

There are also incontrovertible evidences to suggest an aetiological link between infections and various NCDs including cancers, Peptic Ulcer Disease, and Sickle cell disease, to mention a few.<sup>26</sup> Micro-organisms have also been directly and indirectly linked to various other NCDs including Diabetes Mellitus, hypertension, stroke, heart disease, obesity, asthma and many other autoimmune and inflammatory disorders.<sup>26</sup>

#### Why and how did microbes become our adversaries

#### Why microbes are our adversaries

Man, microorganisms and every other living form on earth have a basic instinct of survival and perpetuation. For species to perpetuate themselves, they must take advantage of everything in the ecosystem that guarantee their reproduction, multiplication and preservation, as well as avoid or eliminate anything that hinders their survival. This concept of reproduction and multiplication of species to guarantee survival and preservation is supported by the Bible's account of God's creation (Genesis 1:20-31) as well as the scientific theory of evolution.<sup>28</sup>

The natural symbiotic interactions between man and microorganisms could be mutualism (both benefit), commensalism (microbes benefit, man not harmed), parasitism (microbes benefit, man harmed) or competitive (both harmed). Many microorganisms therefore exist as natural adversaries to man in a parasitic or competitive relationship so as to guarantee their own survival and perpetuation.

How microbes became our adversaries

Microbes have become our adversaries mainly due to ecological (defined as the interactions of species with one another and with their environment) and evolutionary (defined as the heritable characteristics of biological populations over successive generations) changes that lead to increased exposure of man to pathogenic microbes or increased susceptibility to these organisms.<sup>7</sup> The ecological and evolutionary changes may occur at the level of the host (man), the infectious agent (microbes) and the environment (Box 1).

The emergence of infectious diseases is influenced by an interplay between the host (man), the infectious agent (microorganisms) and the environment. Although, man and microbes have co-evolved as associates, microorganisms have become man's greatest adversaries due to imbalances or disruptions in the host, microbial and environmental interactions. The triad of host, infectious agent and environment are the active players in the chain of infection that leads to infectious diseases (Figure 10, Box 1).<sup>29</sup>

Box 1: Wh	y and How Microbes became man's adversaries

Nature/Make-up	Ecological changes	Evolutionary changes
<ul> <li>Parasitism</li> <li>Competition</li> </ul>	<ul> <li>Human related         <ul> <li>Human activity and behaviour</li> <li>Migration</li> <li>Technology and Industry</li> <li>Agriculture practises</li> <li>Animal husbandry</li> <li>Socioeconomic factors</li> <li>Public health services</li> <li>Host susceptibility</li> </ul> </li> <li>Environment-related         <ul> <li>Climate Change</li> <li>Sanitation, hygiene, crowding</li> <li>Food and water supply</li> </ul> </li> <li>Microbial/Animal Host related         <ul> <li>Microbial adaptation</li> </ul> </li> </ul>	<ul> <li>Microbial/Vector</li> <li>Genetic changes- Mutation, Gene transfer, recombination, reassortment</li> <li>Epigenetics</li> <li>Human</li> <li>HLA types and genetic polymorphisms</li> <li>Single and multiple genes variations and mutations</li> <li>Epigenetics</li> </ul>

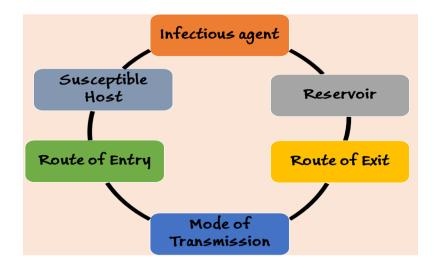


Figure 10: The Chain of Infection

#### **Host factors**

While there are many host factors that increase susceptibility to infectious diseases, the major players in the host are the immune system and the human genome.<sup>29</sup> The immune system exists to protect man against all invading foreign agents, including infections.<sup>30</sup> From birth the immune system is trained to recognise danger signals due to cell or tissue injury, and to tolerate and protect normal antigens and cells.<sup>30,31</sup> The training of the immune system includes the development of immunological memory and immune regulation to remember a previous exposure to a foreign antigen and to prevent excessive immune response to any antigen. Many infectious diseases occur, not necessarily due to the effects of the microorganisms themselves but due to the failure of the immune tolerance or excessive immune responses to the microbe.<sup>31</sup> Therefore, a disruption in the training of the immune system or a failure of immune protection, elimination and regulation functions could ultimately lead to disease.<sup>32</sup> It is for this reason that many infectious diseases have been attributed to primary or secondary defects in the immune system.<sup>33</sup> One typical example is HIV/AIDS in which HIV-induced secondary immunodeficiency leads to various types of opportunistic infections. Indeed, the major reason HIV/AIDS continues the define the field of infectious diseases is because of the ability of the virus to disrupt the immune system predisposing a wide range both infectious and noninfectious diseases.<sup>34–36</sup> Figure 11 outlines chronic non-communicable diseases

that have been causally associated with chronic HIV infection and or long term use of antiretroviral drugs.

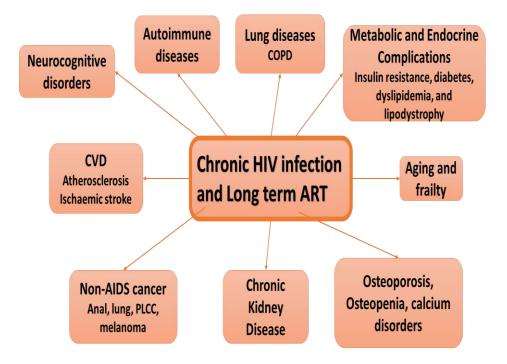


Figure 11: Clinical sequelae of chronic HIV infection and long term antiretroviral therapy (ART)

Evolutionary changes in the human genome can also predispose to the emergence of infectious diseases. Various single gene and multiple gene variations, and epigenetic changes (defined as changes in gene expression due to processes that arise independent of changes in the underlying DNA sequence), as well as specific human leucocyte antigen (HLA) types could increase or decrease susceptibility to various infectious diseases (Table 3).<sup>37,38</sup> Although the evidence is yet conclusive, some geneticists are now proposing a genetic theory of infectious diseases; suggesting that all infectious diseases occur due to genetic defects that render the host incapable of controlling or eliminating the infection.<sup>39</sup> There is also evidence to suggest that both old and new infectious diseases exerted and continue to exert significant selective pressure on human genes leading to either increase susceptibility or increase resistance to various infectious and non-infectious diseases. For instance, Sickle cell disease- a red cell genetic defect, is believed to have emerged and persisted in Africa due to selective pressure exerted by endemic malaria infection on red cell genes that led to increase frequency of HbAS – a variant of the disease that protects against severe malaria.<sup>26</sup> Similarly, mutation of the CCR5 chemokine

receptor that leads to HIV resistance among Europeans is believed to have been caused by selective pressure exerted by the plaque outbreak that occurred in Europe in the 14<sup>th</sup> century. <sup>40</sup>

Gene	Variant	Disease	Effect
a-Globin	Thalassaemias	Malaria (Pf)	Resistance
p-Globin	Sickle, thalassaemias	Malaria (Pf)	Resistance
Erythrocyte band 3	27 bp deletion	Malaria (Pf, Pv)	Resistance
G6PD	Deficiency variants	Malaria (Pf)	Resistance
HLA-B	HLA-B53	Malaria (Pf)	Resistance
HLA-DR	HLA-DRB1*1302	Malaria (Pf)	Resistance
HLA-DR	HLA-DRB1M302	HBV persistence	Resistance
HLA-DR	HLA-DRB1*11	HCV persistence	Resistance
CCR5	32 bp deletion	HIV infection/progression	Resistance
CCR2	codon 64	HIV progression	Resistance
Duffy receptor	Promoter variant	Malaria (Pv)	Resistance
ABO	Blood group 0	Cholera	Susceptibility
HLA-DR	HLA-DR2	Tuberculosis	Susceptibility
HLA-DR	HLA-DR2	Leprosy	Susceptibility
TNF	Promoter 308	Malaria (Pf)	Susceptibility
FUT2	Non-secretors	UTI	Susceptibility
NRAMP1	5' and 3' variants	Tuberculosis	Susceptibility
Interferon-i' receptor	Various mutations	Disseminated BCG	Susceptibility
IL-12 receptor	Various mutations	Intracellular bacteria	Susceptibility
PRP	Codon 129	Creutzfeldt-Jakob Disease	Susceptibility

Table 3: Some infectious diseases with genetic associations

NB: This table highlights gene variants, gene defects and HLA types that increase or decrease susceptibility to various infectious diseases. Key: PRP-prion protein, Pf-Plasmodium falciparum; Pv Plasmodium vivax, FUT2-fucosyltransferase 2, NRAMP-natural resistance-associated macrophage protein. Adapted from British Medical Bulletin 1999;55 2: 401-413

#### **Microbial factors**

Of the many drivers of microbial pathogenesis, microbial evolution and changes in the microbial ecology represent the most common reasons for infectious disease emergence and re-emergence.<sup>7</sup> Microorganisms are constantly and rapidly evolving in their interactions with humans, other hosts and the environment. This dynamic process of microbial evolution could turn a 'good' microbe to a 'bad' disease-causing microbe. Microbial evolution is for instance largely responsible for widespread emergence of antimicrobial resistance microbes.<sup>22</sup> Furthermore, the ability of micro-organisms to continually evolve accounts for their ability to adapt to new hosts, new vectors and new environments.<sup>7</sup> The HIV is for instance believed to have originated from a simian immunodeficiency virus that later evolved and adapted to the human host. <sup>41</sup>

Changes in microbial ecology are related to disruptions in the interactions microorganisms have with one another, as well as with their environment and hosts.<sup>42</sup> These disruptions could place humans at increased contact with a previously unfamiliar microbe or its natural host or promote spread of microbes that cause disease.<sup>42</sup> In Lassa fever outbreaks for instance, infection is spread when human activity such as bush burning leads to migration of Lassa virus-infected rats to human settlements.<sup>43</sup> The infection is later propagated by human to human transmission leading to an outbreak of the disease.

In view of the diverse roles of the human microbiome in promotion of human health, a disruption in the ecology, including the composition, number and location, of the human microbiome could predispose to metabolic, immunological, and developmental disorders, as well as increase the susceptibility to development of infectious disease.<sup>8,44</sup> Human microbiome dysbiosis may occur at any time from birth to adulthood, and may be induced by inappropriate exposure to micro-organisms at birth, inappropriate antibiotic use, inappropriate diet and excessive alcohol intake, among other factors.<sup>8,15</sup> Studies indicate that caesarean delivery and lack of breast feeding could lead to an imbalance in the human microbiome due to inadequate colonization of the baby's organs from maternal microbiome (Figure 12).8,13 This disruption is thought to increase the risk for autoimmune and allergic diseases in later life and has been implicated as one of the reasons for the increase prevalence of autoimmune and allergic diseases in some developed countries where caesarean delivery and infant bottle feeding is widely practiced.<sup>45</sup> Similarly, inappropriate antibiotic use could also lead to immediate and long term disruption of the human microbiome; decreasing colonization by commensal microbes and promoting growth and persistent of resistant microbial strains. Consequently, the wide spread use of antibiotics has the potential of not only fuelling emergence of infectious diseases but also facilitating the emergence of various autoimmune and allergic diseases which have been described by some as modern plagues of 21st century.46,47

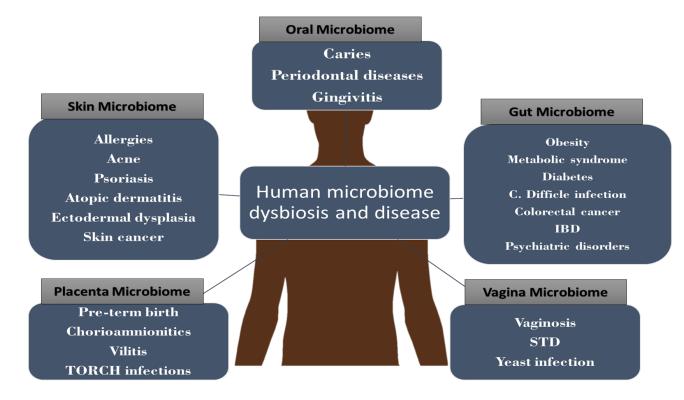


Figure 12: The role of human microbiome dysbiosis in disease causation. A disruption in the human microbiome could predispose to several infectious and non-infectious diseases.

#### **Environmental factors**

These refer to factors that facilitate increased exposure of the host to the microorganisms. They may include physical factors such as geology and climate, biologic factors such as vectors or other biological reservoirs that transmit the infectious agent, and socioeconomic factors such as crowding, hygiene, sanitation, food and water supply, as well as the availability of health services, among other factors. <sup>48,49</sup>

Environmental factors have been implicated in the emergence of various infectious disease outbreaks.<sup>49</sup> From the time of John Snow in 1854, who established a relationship between cholera outbreak and water contamination, to present day outbreaks of Zika virus facilitated by global warming, travelling and human-made mosquito habitats, environmental factors are known to alter the natural ecosystem of pathogenic microorganisms promoting transmission of microbes from animate and inanimate sources to humans or increase the susceptibility of the host (humans) to infectious diseases.<sup>49</sup> Perhaps the most important biological factor driving emergence of infectious diseases in humans is animal reservoirs (Table 4). About 75% of new infectious diseases in humans

are attributed to animal reservoirs and up to 70% of emerging and re-emerging infectious diseases in humans have origins in animals as vectors or reservoirs.<sup>50</sup>

Disease	Main reservoirs	Usual mode of transmission to humans	
African sleeping sickness	Range of wild animals and domestic livestock	transmitted by the bite of the tsetse fly	
Anthrax	livestock, wild animals, direct contact, ingestion environment		
Avian influenza	poultry, ducks	direct contact	
Bovine tuberculosis	cattle	milk	
Brucellosis	cattle, goats, sheep, pigs	dairy products, milk	
Cat scratch fever	cats	bite, scratch	
Chagas disease	armadillos, Triatominae (kissing bug)	bite	
Cryptococcosis	commonly – birds like pigeons	inhaling fungi	
Cryptosporidiosis	cattle, sheep, pets	water, direct contact	
Cysticercosis & Taeniasus	commonly – pigs and cattle	meat	
Ebola virus disease	chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines	through body fluids, organs	
Crimean-Congo HF, Lassa and	rodents, ticks, livestock, primates,	direct contact, inoculation, ticks	
Marburg viruses	bats		
Echinococcosis	commonly – dogs, foxes, wolves, sheep, and rodents	Ingestion of infective eggs animal faeces	
Foodborne illnesses (commonly diarrheal diseases)	animals domesticated for food production (cattle, poultry)	raw and/or undercooked food made from animals	
Giardiasis	humans, wildlife	waterborne, person to person	
Hantavirus syndromes	rodents	aerosol	
Histoplasmosis	birds, bats	inhaling fungi	
Hydatid disease	dogs, sheep	ingestion of eggs excreted by dog	
Influenza	wild birds, horses, pigs, domestic and wild aquatic mammals	droplets transmitted through air	
Leprosy	mainly armadillos	any contact with armadillos	
Leptospirosis	rats, mice, dogs	direct or indirect contact with urine of infected animals	
Listeriosis	cattle, sheep, soil	dairy produce, meat products	
Lyme disease	ticks, rodents, sheep, deer, small tick bite mammals		
Lymphocytic choriomeningitis	rodents	direct contact	
Pasteurellosis	dogs, cats, many mammals	bite/scratch, direct contact	
Plague	rats and their fleas	flea bite	
		1.1.	
Psittacosis	birds, poultry, ducks	aerosol, direct contact	

Table 4: List of Zoonotic diseases of humans and their main reservoirs and mode of transmission.

Rabies	dogs, foxes, bats, cats, other animals	bite or scratch	
Rat bite fever (Haverhill fever)	rats	bite/scratch, milk, water	
Rift Valley fever	cattle, goats, sheep	direct contact, mosquito bite	
Ringworm	cats, dogs, cattle, many animal species	direct contact	
Tick-borne encephalitis	rodents, small mammals, livestock	Tick bite, unpasteurised milk products	
Toxocariasis	dogs, cats	exposure to faeces	
Toxoplasmosis	cats, livestock, poultry	ingestion of faecal oocysts, meat	
Trichinellosis	pigs, wild boar	pork products	
Trichinosis	rodents, pigs, horses, bears, walruses	eating infected meat	
Tularaemia	rabbits, wild animals, environment, ticks	direct contact, aerosol, ticks, inoculation	
Variant Creutzfeldt–Jakob disease	cattle	eating meat from animals with bovine spongiform encephalopathy (BSE)	
West Nile fever	wild birds, mosquitoes	mosquito bite	
Zoonotic diphtheria	cattle, farm animals, dogs	direct contact, milk	
Relapsing fever	ticks, lice	Bite, blood transfusion	
Visceral Larval Migrans	Dogs, cats	Ingestion of eggs through direct contact with faeces or contaminated materials	
Strongyloidiasis	Dogs, cats, monkeys	Careless handling of contaminated fecal materials	
MiddleEastRespiratorySyndromeCoronavirus(MERS-CoV)	Bats, dromedary camels	direct contact	
Severe acute respiratory syndrome (SARS)	bats, palm civets, raccoon dogs, ferret badger	direct contact, meat	
Rocky Mountain spotted fever	ticks	bite	

# MICRO-ORGANISMS AS MAN'S ADJUTANTS

My VC Sir, while microorganisms are established as man's associates and adversaries, they could also serve as aids, assistants or adjutants to man in promoting health and preventing disease. In the following section, I outline the various ways microorganisms can be used to aid human health and disease prevention.

# Modifying the human microbiome

The various roles of human microbiome in human health and disease have been discussed in the previous sections. Man is now exploring this knowledge of the benefits of the healthy human microbiome to develop novel therapeutics such as prebiotics, probiotics, synbiotics and faecal microbiota transplantation (FMT) (Figure 13-14), to sustain healthy living and to prevent and treat various infectious and non-infectious diseases. <sup>515253</sup> FMT re-establishes a balanced intestinal microbiome and it has been shown to be an effective cure for recurrent Clostridium difficile infection (RCDI).<sup>54</sup> It is now being explored for the treatment of various other gastrointestinal and non-GI autoimmune and inflammatory diseases.<sup>53</sup> A growing body of evidence, including clinical trials, have reported the therapeutic benefits of prebiotics (substances that induce the activity of beneficial microorganisms), growth or probiotics (live microorganisms which beneficial properties) and synbiotics (products that contain both probiotics and prebiotics) in the treatment of various diseases. <sup>5152</sup> However, in view of poor quality of evidence and variable efficacy rates among studies, these agents are only routinely licensed in most countries including the USA as food supplements.



Figure 13: Faecal Microbiota Capsules

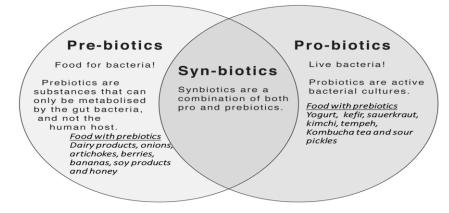


Figure 14: Pre-biotics, Probiotics and Synbiotics

# **Microbes and Genetic Engineering**

Genetic engineering is the direct manipulation of an organism's genome using biotechnology. In genetic engineering, the genetic makeup of a cell or organism is changed by transferring genes across or within species (Figure 15). The resulting organism is called a genetically modified organism (GMO).<sup>55</sup> Microorganisms are indispensable in the process of genetic engineering. Restriction enzymes which are used to slice DNA fragments before the process of gene transfer are produced by bacteria and archaea; these organisms use these enzymes to protect against viruses. Micro-organisms, including bacteria, fungi and viruses have also been widely used as genetically modified microorganisms (GMM) in medicine, agriculture and industrial biotechnology.<sup>55</sup> Using genetic engineering, GMM is being used to synthesise large quantities of pure human products such as human insulin, interferons, interleukins, human growth hormone, and human albumin, as well as monoclonal antibodies, antihemophilic factors and many other human products. <sup>55</sup> GMM and live microorganisms (Oncolytic viruses) are also being explored for the treatment of various cancers such as bladder, ovarian, head and neck cancers, melanoma, among others.<sup>56</sup>

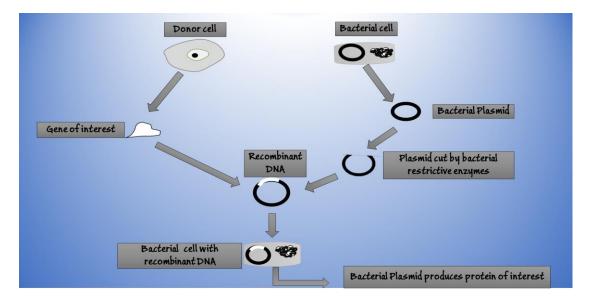


Figure 15: Microbe and Recombinant DNA technology- microorganisms are required for all essential steps in genetic engineering

# Microbes in vaccine production

Since 400BC, scientists and physicians had observed that a prior exposure to microorganisms could protect against subsequent infection with the same microorganisms.<sup>7</sup> Edward Jenner established and popularised the process of vaccination using microorganisms when in 1796 he inoculated a 13-year-old-boy with vaccinia virus (cowpox) and later demonstrated immunity to smallpox.<sup>7</sup> Today, microorganisms in whole or part, live or killed, or their components/products (e.g. toxoids), have been used to produce various vaccines against various infectious diseases (Box 2).<sup>57</sup> Using recombinant DNA technology, GMM are being used to produce vaccines against hepatitis B, human papilloma virus and influenza, among others.<sup>55,57</sup> GMM and microbial derived particles are also being explored to develop vaccines against various non-communicable diseases and their risk factors including hypertension, smoking, obesity and high cholesterol.<sup>57–59</sup>

Box 2: Vaccines derived from microbes			
Live, attenuated vaccine list:			
Vaccinia (smallpox)			
Measles, mumps, rubella (MMR combined vaccine)			
Varicella (chickenpox)			
Influenza (nasal spray)			
Rotavirus			
Zoster (shingles)			
Yellow fever			
Inactivated/killed vaccine list:			
Polio (IPV)			
Hepatitis A			
Rabies			
Toxoid (inactivated toxin) vaccine list:			
Diphtheria, tetanus (part of DTaP combined			
immunization)			
Subunit/conjugate vaccine list:			
Hepatitis B			
Influenza (injection)			
Haemophilus influenza type b (Hib)			
Pertussis (part of DTaP combined immunization) Pneumococcal			
Meningococcal			
Human papillomavirus (HPV)			

# Microbes in antibiotic production

To date microorganisms remain the most important source of antibiotics used in the treatment of infectious diseases (Table 5). The list of antibiotics derived from micro-organisms is still expanding as newer antibiotics are either being identified as products of micro-organisms or being synthesized using microorganisms.<sup>60,61</sup>

Antibiotic	Producer organism
Actinomycetin	Micromonospora spp
Aureomycin	Streptomyces aurofaciens
Amphotericin B	Streptomyces nodosus
Bacitracin	Bacillus subtilis
Cephalosporin	Cephalosporium acremonium
Chloromycetin	Streptomyces Venezuela
Erythromycin	Streptomyces erythreus
Gentamicin	Micromonospora purpurea
Griseofulvin	Penicillium griseofulvum
Neomycin	Streptomyces fradiae
Penicillin	Pencillium notatum
Polymyxin B	Bacillus polymyxa
Rifamycin	Streptomyces mediterranei
Streptomycin	Streptomyces griseus
Terramycin	Streptomyces ramosus
Tetracycline	Streptomyces rimosus
Vancomycin	Streptomyces orientalis

# Table 5: List of some antibiotics produce by microorganisms

#### **MY CONTRIBUTIONS TO RESEARCH AND SCHOLARSHIP**

My VC Sir, let me at this juncture share my contributions to research and scholarship. In the following section, I outline some of my published research as well as conference papers that offer practical examples of the diverse roles of microorganisms in human health and disease. I conclude by highlighting my future interests in research and scholarship.

#### 1. Infections and NCD

i. **Review Article:** The role of infections in the emergence of noncommunicable diseases (NCDs): Compelling needs for novel strategies in the developing world <sup>26</sup>

In this review article, we explored the possible mechanisms by which infections induce NCDs citing examples of studies in Africa and elsewhere where NCDs and infections are proposed or confirmed to be causally linked. We also discussed the implications and challenges of our observations for science and medicine. It was suggested that in view of the emerging associations between infections and NCD, NCD prevention and control strategies must necessarily include preventing of infections.

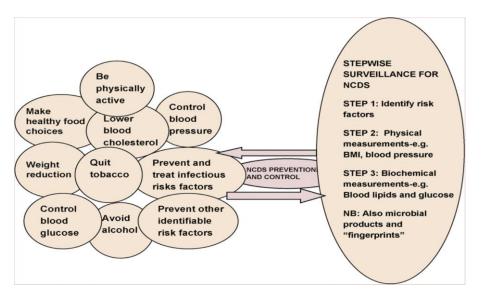


Figure 16: Novel integrated approach to NCDs prevention and control in developing countries: this approach must include identifying and targeting associated infectious risk factors. NB: microbial fingerprints may include microbial DNA, RNA or protein detected by molecular biology techniques.

ii. **Review Article:** *Malaria is a risk factor for chronic noncommunicable diseases; a narrative review of scientific evidence* <sup>62</sup>

We reviewed scientific articles published between 1947 and 2014 to provide evidence of a causal relationship between malaria and NCDs. There were plausible causal association between malaria and chronic diseases such as Burkitt's lymphoma, red cell genetic polymorphism, chronic anaemia, neurocognitive impairment, malnutrition and growth stunting, as well as nephropathy and tropical splenomegaly syndrome. Malaria was hypothetically linked to pre-eclampsia, splenic lymphoma, and endemic Kaposi's sarcoma, as well as cardiomyopathy, new born high blood pressure and fetal programming for adult atherosclerosis and cardiovascular diseases. The aetiopathogenetic pathways were multifactorial, including immune-complex formation, polyclonal B cell activation and placental inflammation, as well as blood vessel inflammation, red cell destruction and sequestration. Malaria-induced natural selection accounted for perpetuation of genetic polymorphisms.

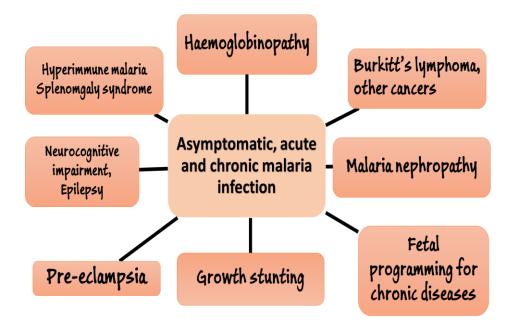


Figure 17: The aetiological associations between malaria and chronic non-communicable diseases.

#### 2. HIV/AIDS

i. **Original Article:** Factors Associated with Timing of Initiation of Antiretroviral Therapy among HIV-1 Infected Adults in the Niger Delta Region of Nigeria<sup>63</sup>

To provide evidence on benefits of starting ART early in Nigeria, we reviewed the hospital records of ART ineligible HIV-infected adults who enrolled into HIV care between January 2008 and December 2012 at two major tertiary hospitals in Bayelsa State. We found that ART-ineligible HIV-infected adults on follow up in South-South Nigeria are more likely to require earlier initiation of ART if they have stage 2 HIV disease or CD4+  $\leq$ 500 cells/ul at presentation. Our findings suggest faster progression of HIV-disease in these groups of individuals and corroborate the growing evidence in support for earlier initiation of ART.

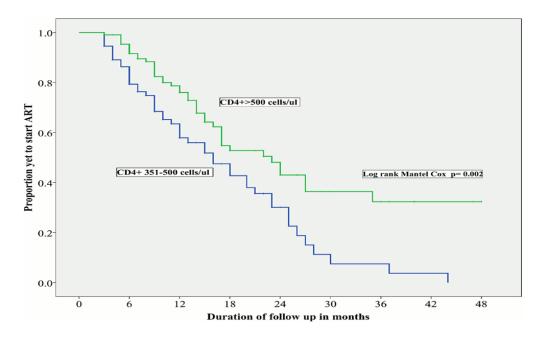


Figure 18: Kaplan-Meier curves of time to initiation of ART in relation to CD4 cell count group. The median time to ART initiation was significantly shorter in participants with CD4 cell count of 351-500cells/ul than those (16months) with CD4 count >500cells/ul (23months).

 Original Article: Morbidity and Mortality Patterns of Hospitalised Adult HIV/AIDS Patients in the Era of Highly Active Antiretroviral Therapy: A 4-year Retrospective Review from Zaria, Northern Nigeria <sup>64</sup>

To describe common morbidity and mortality patterns among adult HIV/AIDS patient, we reviewed admission records and causes of deaths of hospitalised medical HIV-infected patients admitted at ABUTH, Zaria between January 2006 and December 2009. Of the 207 HIV/AIDS patients reviewed, majority were newly diagnosed (73.4%). Disseminated tuberculosis and sepsis were the most common cause of morbidity and mortality. Immune-inflammatoryreconstitution-syndrome, **ART-toxicity** and ART-failure, contributed to morbidity and mortality in patients receiving ART. Sixty-six (31.9%) patients died; hospital stay  $\leq 3$  days and severe anaemia (PCV < 24%) were independent predictors of mortality. Our study suggested that late presentation and tuberculosis significantly contributed to HIV/AIDS morbidity and mortality.

s/n	Diagnosis on presentation	n/%	M/F
1	Tuberculosis	69(33.3)	0.87/1
2	Sepsis	21(10.1)	1.1/1
3	Chronic diarrhoea	14 (6.8)	1.8/1
4	Typhoid fever	8(3.9)	1.7/1
5	Non-TB Pneumonia	11 (5.3)	0.4/1
6	Disseminated Kaposi's sarcoma	8(3.9)	2/1
7	Cerebral toxoplasmosis	7(3.4)	2.3/1
8	Viral meningoencephalitis	6(2.9)	0.7/1
9	Demyelinating polyneuropathy	5(2.4)	0.7/1
10	Cryptococcal meningitis	5(2.4)	4/1
11	AIDS encephalopathy	3(1.4)	2/1
12	Non-Hodgkin's lymphoma	3(1.4)	0.5/1
13	Acute gastroenteritis (Food poisoning)	4(1.9)	0.7/1
14	Steven Johnson's syndrome	4(1.9)	1/1
15	Herpes zoster	3(1.4)	0.5/1
16	Acute bacterial meningitis	2(0.9)	2/0
17	Wasting syndrome	2(0.9)	1/1
18	Acute viral hepatitis (HBsAg positive)	2(0.9)	1/1
19	HIV nephropathy	2(0.9)	1/1
20	Candidiasis (esophageal; disseminated)	2(0.9)	1/1
21	Vacuolar myelopathy	1(0.5)	0/1
22	Disseminated herpes simplex	1(0.5)	0/1

Table 6: Clinical presentation of hospitalised HIV/AIDS patients in ABUTH, Zaria (2006-2009)

23	Severe malaria	1(0.5)	0/1
24	Dilated cardiomyopathy	1(0.5)	0/1
25	Primary CNS lymphoma	1(0.5)	1/0
26	Glioblastoma multiforme	1(0.5)	1/0
27	Stroke-like state? cause	6(2.9)	3/1
28	Primary liver cell carcinoma	1(0.5)	1/0
29	Zidovudine-related severe anaemia	4(1.9)	2/1
30	Nevirapine-induced hepatoxicity	2(0.9)	2/0
31	Nevirapine-induced Steven's Johnson syndrome	2(0.9)	2/0
32	Hypertensive heart failure	2(0.9)	1/1
33	Hypertensive renal failure	3(1.4)	0.5/1
34	Hypertensive haemorrhagic stroke	1(0.5)	0/1
35	Peripartum cardiac failure	1(0.5)	0/1

iii. **Original Article:** Human Herpesvirus 8 Infections and AIDS-Associated Kaposi Sarcoma in Zaria, Northern Nigeria.<sup>65</sup>

In 2007, 20 histologically confirmed adults with AIDS-KS were evaluated clinically and serologically for presence of HHV8 antibodies. Kaposi sarcoma skin lesions were diverse, and majority (18 cases) had poor risk AIDS-KS. Females had a more severe disease. Seventeen patients (85%) were HHV8-seropositive.





Figure 19: Two cases of AIDS-associated Kaposi's sarcoma with multinodular (left) and ecchymotic lesions (right).

iv. **Original Article:** Seroprevalence and determinants of human herpes virus 8 infection in adult Nigerians with and without HIV-1 infection<sup>66</sup>

To describe the epidemiology of human herpes virus 8 (HHV8) among HIV-positive and negative individuals, we conducted a cross sectional study in 2007 in ABUTH Zaria. The seroprevalence of HHV8 infection was 62% in HIV-1 positive patients and 25.9% in HIV negative adults (p<0.001). A past history of STD [OR=

2.88, 95% CI= 1.0 - 8.2] and advanced HIV/AIDS (WHO stage 3 and 4) [OR=3.5, 95% CI= 1.21-10.1] were the only variables independently associated with HHV8 seropositivity in HIV-infected patients. In HIV-negative adults, none of the variables was significantly associated with HHV8 seropositivity. The study findings suggested an adverse interaction between HHV8 and HIV-1. The higher prevalence of HHV8 infection in HIV-infected patients and its association with STD supported a predominant sexual route of HHV8 transmission among adult Nigerians.

v. **Original Article**: Clinical presentation and outcome of toxoplasma encephalitis in HIV-infected patients from Zaria, Northern Nigeria: a case series of 9 patients.<sup>67</sup>

Here, we described clinical, serological and brain imaging findings, as well as outcome of cerebral toxoplasmosis among HIV-infected patients. There were 9 cases of cerebral toxoplasmosis seen at ABUTH between January 2006 and December 2010. All 9 patients had CD4 count of less than 50 cells/mm (3); 7 were antiretroviral therapy (ART)-naive, while 2 were cases of ART-induced TEreconstitution inflammatory After immune syndrome. administering dexamethasone for intravenous cerebral decompression and specific antitoxoplasma therapy, symptoms and signs resolved in 8 patients within 4 to 14 days, but 1 patient died.



Figure 20: Brain computer tomography scan of one of the cases of cerebral toxoplasmosis showing single right parietal lobe ring–enhancing lesion with mass effect

vi. Original Article: Seroprevalence of IgM and IgG antibodies to Toxoplasma infection in healthy and HIV-positive adults from Northern Nigeria<sup>68</sup>

In 2008, sera of 219 adults, including 111 consecutive HIVinfected adults and 108 healthy HIV-negative adult volunteers from Zaria, Northern Nigeria, were examined for IgG and IgM antibodies to toxoplasma by ELISA. The seroprevalence of toxoplasma infection (IgG positive and or IgM positive) was 32.4% in HIV-negative healthy adults and 38.7% in HIV-infected adults (P > 0.05). The rate of IgM seropositivity was 4.6% in healthy adults and 1.8% in HIV-infected patients, while the rate of IgG seropositivity (without IgM seropositivity) was 28.7% in healthy adults and 37.8% in HIV-infected patients (p > 0.05). Toxoplasmosis was equally prevalent in HIV-infected patients and healthy adults from similar environments in Northern Nigeria.

vii. **Case Reports:** Disseminated infections due to Immune Reconstitution Inflammatory Syndrome after Highly Active Antiretroviral Therapy - Report of 3 cases from Nigeria.<sup>69</sup>

Immune Reconstitution Inflammatory Syndromes (IRIS) are exaggerated pathological inflammatory reactions occurring after initiation of highly active antiretroviral therapy (HAART) due to exuberant immune responses to occult or apparent opportunistic infections or cancers. We reported 3 cases of IRIS presenting as disseminated infections in HIV-1 infected patients initiating HAART. The cases were disseminated tuberculosis, disseminated herpes zoster infection and disseminated Kaposi's sarcoma. We highlighted the need for clinicians to be alert to the possibility of IRIS in HIV-infected patients initiated or re-initiated on HAART



Figure 21: Two cases of immune reconstitution inflammatory syndrome (IRIS) in HIV presenting as disseminated Kaposi's sarcoma (left) and disseminated herpes zoster infection (right).

viii. **Case Report**: Dermatomyositis associated with HIV-1 infection in a Nigerian adult female: a case report.<sup>70</sup>

Human immunodeficiency virus (HIV) infection has been implicated as a trigger for various autoimmune diseases, one of which is dermatomyositis. Dermatomyositis is a very rare autoimmune disease characterised by myopathy, typical cutaneous signs and variable systemic manifestations. To our knowledge, the association of this rare disease with HIV infection has not been previously reported in Nigeria. We therefore decided to report the case of a 40-year-old HIV-1 infected Nigerian female who presented to us with muscle, skin, and systemic manifestations of dermatomyositis. Our aim is to show the effect of HIV infection, as well as HAART-induced immune reconstitution on the clinical course of dermatomyositis.



Figure 22: A case of Dermatomyositis associated with HIV-1 infection. Images show macular hyper-pigmented lesions on knees, hands and face all typical of the disease.

ix. **Case Series:** *Peculiarities of genital ulcer diseases in HIV-infected patients: Report of four cases from Zaria, Nigeria.*<sup>71</sup> We reported four peculiar cases of genital ulcers in HIV-infected patients who presented with lesions that were atypical, chronic, aggressive and unresponsive to therapy. They include 2 cases of genital herpes, one case each of Chancroid and Inguinal bubo.



Figure 23: Peculiar cases of genital ulcer disease associated with HIV/AIDS

x. **Case Report:** *HIV Wasting Syndrome in a Nigerian Failing Antiretroviral Therapy: A Case Report and Review of the Literature.*<sup>72</sup>

The HIV wasting syndrome represented the face of HIV/AIDS before the advent of highly active antiretroviral therapy (HAART). Although the incidence of wasting has declined since the introduction of HAART, weight loss remains common in patients receiving HAART, especially in the setting of a failing HAART regimen. As we were not aware of any previous reports from Nigeria, we reported a case of the classical wasting syndrome in a Nigerian female who had both virological and immunological HAART failure due to poor adherence. The influence of a failing HAART regimen, socioeconomic status, and other clinical variables in the wasting syndrome were discussed.



Figure 24: A case of HIV wasting syndrome showing severe muscle wasting and prominent bones

xi. **Case Report:** Acute Marjolin's ulcers following Genital Ulcer Disease in an HIV-infected Adult Nigeria. <sup>73</sup>

At the time of this publication, Acute Marjolin's ulcer had not been previously reported in HIV/AIDS patients with genital ulcer disease (GUD). A 28-year-old HIV-1-infected Nigerian female presented with a three-month history of chronic genital ulcers associated with fistula and sinuses, as well as bilateral inguinal lymphadenopathies and right leg lymphedema. After about two months of follow up, the genital ulcers evolved into a fungating proliferative ulcer. A biopsy of the ulcer revealed a well differentiated invasive squamous cell carcinoma-a typical feature of Marjolin''s ulcer. This case is reported to alert clinicians on the need for prompt recognition and treatment of all cases of GUDs in HIV/AIDS patient, in order to mitigate the potential of malignant transformation of HIV-related chronic genital ulcers to Marjolin's ulcers.



Figure 25: A case of acute Marjolin's ulcer complicating chronic genital ulcer diseases in an HIV-infeced patient. Irregular vulvovagina ulcers (left) with transformation to fungating ulcer-proliferative mass (Marjolin's ulcer)

#### **Other HIV/AIDS Research**

- xii. Prevalence Pattern and Determinants of Disclosure of HIV Status in an Anti-Retroviral Therapy Clinic in The Niger Delta Region of Nigeria.<sup>74</sup>
- *xiii.* The frequency and outcome of neuropathies among HIV/AIDS adults treated at a tertiary hospital in Kaduna State, Nigeria. <sup>75</sup>
- *xiv.* Types and predictors of partner reactions to HIV status disclosure among HIV-infected adult Nigerians in a tertiary hospital in the Niger Delta. <sup>76</sup>
- xv. Human papilloma virus (HPV) infection is associated with HIV-1 infection and AIDS in HIV-infected adult patients from Zaria, Northern Nigeria.<sup>77</sup>
- *xvi.* Antiretroviral Drug Resistance- implications for HIV/AIDS reduction in Sub-Saharan Africa and other developing countries. <sup>78</sup>
- xvii. Prevalence and predictors of HIV serodiscordance and concordance among HIV-infected patients in the Niger Delta Region of Nigeria (In press)
- xviii. An assessment of nutritional status of HIV/AIDS adult patients attending an antiretroviral clinic in the Niger Delta (In press)
- *xix.* Serum leptin levels in HIV-1 infected Nigerians receiving highly active antiretroviral therapy.<sup>79</sup>
- *xx.* Serum leptin levels in antiretroviral therapy naïve HIV-1 infected patients in Zaria, Nigeria. <sup>80</sup>
- xxi. Determinants of risky sexual behaviour among HIV-infected patients in the Niger Delta. (In Press)
- 3. Infection control and Healthcare associated infections

### i. Guest Lecture

*Healthcare-associated infections: when hospitals fail to protect.* Guest lecture at the 5th Prof TI Francis Memorial Lecture. Held at University of Port Harcourt, Rivers State-August 30th 2016. In this lecture, I discussed healthcare-associated infections (HCAI) as a consequence of failure of hospitals and other healthcare facilities to protect patients, healthcare workers and other service users from harm. I gave an overview of the burden, types and risks factors for HCAI and also outlined evidence-based guidelines that should be implemented by all healthcare facilities to protect against HCAI.

*Healthcare-associated infections: Yesterday, Today and the Future*. Guest lecture at the 5<sup>th</sup> Annual General Meeting and Scientific Conference of the Nigerian Infectious Disease Society. Held at Abuja November 25-26<sup>th</sup> 2016.

In this lecture, I discussed the past history, current knowledge and future prospects of healthcare-associated infections epidemiology, prevention and control. I emphasized the roles of antimicrobial resistance and inappropriate antibiotic use in emergence of healthcare-associated infections, as well as the critical role of implementing standard infection prevention and control programs in all hospitals to guarantee quality healthcare.

ii. **Original Article:** *Status of the infection control program in a Nigerian tertiary hospital before and after implementation of an improvement plan.*<sup>81</sup>

In this study, conducted at NDUTH Bayelsa, we reviewed our infection control program before and after implementation of an improvement plan. Our results suggested that significant improvements in infection control programs and activities among hospitals in resource-limited settings is achievable (table 7). However, sustainable implementation of the improvement plan was challenged by poor cooperation, inadequate staff, lack of required infrastructure and irregular supply of IPAC resources, mainly due to funding gaps.

Table 7: Baseline and final infection prevention and control assessment scoresfollowing implementation of an improvement plan at NDUTH, Bayelsa

s/n	Modules assessed	Baseline score	Final score	Baseline	Final
		(%)	(%)	rating	rating

1	Health facility information	54.5	72.7	В	В
2	Pharmacy	60	78	В	А
3	Microbiology	55.3	76.6	В	А
4	Infection control programs	21.3	69.1	С	В
5	Isolation and standard precautions	15.6	68.9	С	В
6	Tuberculosis precautions	25	63.2	С	В
7	Waste Management	33.3	66.7	С	В
8	Hand Hygiene	54.6	70	В	В
9	Injections	70	77.5	В	А
10	Surgical antibiotic use and surgical equipment procedures	38.5	57.7	С	В
11	Surgical area practices	56.3	68.8	В	В
12	Labour and delivery	65.5	69.1	В	В
	Total	48.6	70.9	В	В

iii. **Original Article:** Prevalence and determinants of occupational exposures to blood and body fluids among health workers in two tertiary hospitals in Nigeria.<sup>82</sup>

This study was undertaken in two tertiary hospitals in North-central and South-south Nigeria in 2011 among 290 health workers of various professional groups. Our results suggest high rates of occupational exposures to blood/body fluid among health workers in Nigeria, especially among newly qualified medical doctors and nurses (Figure 24).

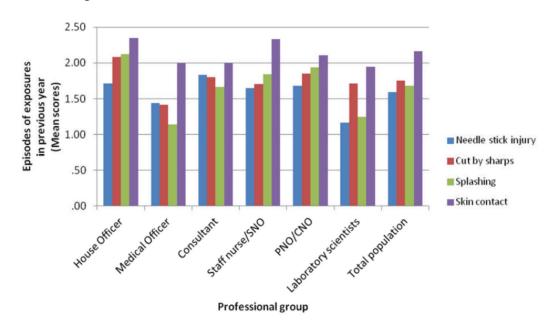


Figure 26: Bar Chart Showing Average Episodes of the Various Types Occupational Exposures across Professional Groups in the Previous 1year.

**Original Article:** *Prevalence of hepatitis B vaccination among health care workers in Nigeria in 2011-12.*<sup>83</sup>

This cross-sectional study was undertaken in 2011 and 2012 in two teaching hospitals (BHUTH) in Jos, North-Central Nigeria, and (NDUTH) Yenagoa, South-South Nigeria. The study findings are as summarised in box below.

#### TAKE-HOME MESSAGE

- We found low rates of hepatitis B vaccine coverage among health care workers in two teaching hospitals in Nigeria
- Among 290 health care workers studied, 64.5% received at least one dose of hepatitis B vaccine; only 36.2% had full coverage of three doses of the vaccine
- Receiving hepatitis B vaccine was independently associated with professional group and prior training in infection control. House officers and laboratory scientists had significantly lower vaccine uptake rates compared to resident doctors, consultant doctors and nurses.
- iv. **Original Article:** *Knowledge, attitude and practice of standard precautions of infection control by hospital workers in two tertiary hospitals in Nigeria.*<sup>84</sup>

A cross-sectional study was undertaken in 2011/2012 among HCW in two tertiary hospitals (BHUTH, Jos, NDUTH Yenagoa) in Nigeria. A total of 290 HCW participated in the study. The majority of the HCW had poor knowledge of injection safety and complained of inadequate resources to practise standard precautions.

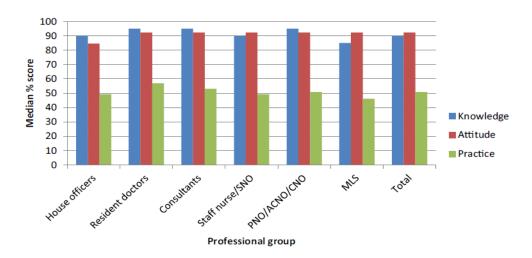


Figure 27. Distribution of median knowledge, attitude and practice (KAP) scores across professional groups of health workers. NB: House officers, staff nurses/senior staff nurses and medical laboratory scientists (MLS), generally had lower KAP scores than other cadres of health workers.

v. **Original Article:** Peri-operative Antibiotic Use and Compliance with Surgical Antibiotic Prophylaxis Guidelines in a Tertiary Hospital in Nigeria.<sup>85</sup>

We retrospectively reviewed the hospital records of adult surgical patients who had surgical operations between April 2012 and April 2013. The prevalence of pre- and post-operative antibiotic use was 50.8% and 100%, respectively. The choices of antibiotic were variable but ceftriaxone and metronidazole were most commonly used. Overall, antibiotic use among surgical patients in study site was variable and inconsistent with established standards. We recommended institution and implementation of local and national surgical antibiotic guidelines in study centre.

*vi.* **Original Article:** *Antimicrobial consumption in a tertiary hospital in the Niger Delta Region of Nigeria (Preliminary findings)* 

We measured antimicrobial consumption based on prescriptions received at the pharmacy department of NDUTH, Bayelsa in 2015. There were 7380 antimicrobial prescriptions in 2015 with total defined daily dose (DDD) of 29046. The average DDD/patient/year was 3.9. Metronidazole, Ceftriazone, Ciprofloxaxin and Cefuroxime were the most frequently prescribed antimicrobial drugs. Metronidazole, Ciprofloxacin and Cefuroxime had the highest DDD.



Figure 28: Word cloud showing relative frequency of antibiotic consumption at NDUTH. Metronidazole was the most frequently consumed antibiotic; size of the words reflects frequency of consumption.

vii. *Original Article:* Prevalence of healthcare associated infections in a tertiary hospital in the Bayelsa State.<sup>86</sup>

Between July 2013 and June 2014, the prevalence of healthcare associated infections among 2611 patients admitted at NDUTH Bayelsa was 2.6%. Among 264 patients who had microbial evaluation for HCAI, 69 (26.1%) were culture positive. Surgical sites were more infected than other sites. *Pseudomonas Auregenosa, Staph Aureus and Klebsiella spp* were the most common pathogens isolated.

viii. **Original Article:** An Assessment of Hand Hygiene Resources and Practices in a Tertiary Hospital in The Niger Delta Region of Nigeria.<sup>87</sup>

Ten wards and 102 HCWs (41 doctors, 36 nurses, 25 other health staff) were observed for compliance with recommended hand hygiene (HH) practices, facilities and supplies. Compliance with HH facilities/supplies ranged from 28.6-100% (average 74.9%,). Of 150 opportunities for HH, overall compliance rates before and after patient contact ranged from 37-100% (average 72%). HCWs were significantly more likely to perform HH after than before patient contact (83% vs 60.7%, p<0.00001). In almost all components of HH practices observed, doctors generally had lower compliance rates than other HCWs.

ix. **Original Article**: Bacterial contamination of the hospital environment- the experience of an infection control team in a tertiary hospital in Niger Delta Region of Nigeria. <sup>88</sup>

We surveyed the bacterial flora of the hospital environment in a tertiary hospital in Nigeria to identify possible environment sources of healthcare-associated infections (HCAI) and to guide development of infection control policies. Twelve (27.3%) out of the 44 samples were culture positive, including samples from hospital water, nine baby cots and one stethoscope. Of the 15

isolates, 9 (60%) were *Pseudomonas aeruginosa*, 4 (26.7%) were *Klebsiella pneumonia* and 2 (13.3%) were *Staphylococcus aureus*. Majority of the isolated organisms were multi-resistant. After this survey, the infection control committee of the hospital developed policies and implemented remedial measures according to established guidelines for environmental infection control in hospitals. Our study had shown that the hospital environment is a potential source for acquisition of HCAI. Hospitals ought to strictly adhere to infection control guidelines, including environmental infection control measures

### **Other studies on Infection Prevention and Control**

- x. Prospective Audit of Compliance with Utilization of World Health Organization Surgical Safety Checklist as Part of Quality Improvement Program in a Tertiary Hospital in Bayelsa State, Nigeria.<sup>89</sup>
- xi. Prospective Randomised Comparison of Ceftriaxone Versus Ampicillin/Cloxacillin and Metronidazole for Prevention of Post-Caesarean Section Infection (Ibrahim I, Ogoina D et al Ongoing)
- xii. One-year retrospective review of Peri-operative antibiotic use and surgical site infection among Obstetrics and Gynaecology patients in a tertiary hospital in Bayelsa State, Nigeria. (Ogoina D, Abasi J. In preparation)

### 4. Emerging infections and public health

i. **Case Series**: Acute meningococcemia complicating epidemic meningitis in Zaria.<sup>90</sup>

We reported 3 cases of meningococcemia during the 2009 epidemic meningitis outbreak in Nigeria. The patients presented with features of meningitis associated with systemic inflammatory response syndrome, haemorrhagic tendencies and haemorrhagic skin lesions.



Figure 29: Various degrees of haemorrhagic skin lesions including purpura and ulcers on Left foot of a patient with meningococcemia

ii. **Review Article:** Lassa Fever: A Clinical and Epidemiological Review. <sup>43</sup>

Literature published between 1969 and August 2012 was reviewed. The study summarised the history, aetiology, clinical presentation, management and prevention of Lassa fever, with emphasis on the epidemiological findings from Nigeria.

Year	States/cities affected	Cases	Deaths	Case Fatality Rate (%)
1969	Borno (Lassa Town), and Plateau (Jos)	3	2	66.7
1970	Plateau (Jos and Vom)	28	10	58
1974	Anambra (Onitsha)	3	1	33.3
1975	Kaduna (Zonkwa), and Plateau (Vom)	4	1	25
1980	Kaduna (Zaria)	1	1	100
1989	Imo	34	22	64.7
1993	Plateau	13	8	61,5
1994	Edo	20	11	55
	Enugu	54	0	0
	Lagos	2	2	100
	Yobe	1	0	0
1995	Akwa Ibom	8	0	0
	Anambra	7	0	0
	Enugu	1	0	0
	Imo	2	0	0
	Taraba	51	0	0
1998	Anambra	1	0	0
	Rivers	2	0	0
1999	Zamfara	46	0	0
2000	Edo	60	26	43.3

Table 8: REPORTED OUTBREAKS OF LASSA FEVER IN NIGERIA 1969-2006.

	Nasarawa	26	0	0
2002	Edo	55	15	27.3
	Lagos	1	0	0
2003	Edo	31	18	58.1
2004	Edo	50	21	50
2005	Edo	25	10	40
	Ebonyi	6	4	66.7
	Ogun	5	2	40
2006	Edo	19	1	5.3

### iii. **Original Article**: A Multi-Site Knowledge Attitude and Practice Survey of Ebola Virus Disease in Nigeria.<sup>91</sup>

Between July 30th and September 30th 2014, we undertook a cross sectional study on knowledge, attitude and practice (KAP) of Ebola Virus Disease (EVD) among adults of the general population and healthcare workers (HCW) in three states of Nigeria, namely Bayelsa, Cross River and Kano states. Our results reveal suboptimal EVD-related knowledge, attitude and practice among adults in Nigeria. We recommended that to effectively control future outbreaks of EVD in Nigeria, there is a need to implement public sensitization programmes that improve understanding of EVD and address EVD-related myths and misconceptions, especially among the general population.

## iv. **Review Article**: Behavioural and emotional responses to the 2014 Ebola outbreak in Nigeria: a narrative review.<sup>92</sup>

This paper reviews the behavioural and emotional responses to the 2014 Ebola virus disease (EVD) outbreak in Nigeria as documented in scientific publications and portrayed in the media between 21 July 2014 and 30 March 2015. The study reported the fears, myths and misconceptions associated with EVD outbreaks.

Box 3. Fears associated with outbreaks of Ebola virus disease Fear of infection with Ebola virus Fear of suspected Ebola patients Fear of places with Ebola patients Fear of Ebola treatment centres Fear of healthcare workers who treat Ebola patients Fear of stigma and discrimination if infected Fear of dying from Ebola Fear of Ebola dying process Fear of corpse or remains of Ebola cases

v. **Original Article**: Preparation and Response to the 2014 Ebola Virus Disease Epidemic in Nigeria—The Experience of a Tertiary Hospital in Nigeria.<sup>93</sup>

Between 4th August and 31st October 2014, we conducted a mixed cross sectional and qualitative study to ascertain the Ebola (EVD)-related fear, myths and misconceptions among healthcare workers (HCWs) in NDUTH Bayelsa, and also evaluated the plans, activities and challenges faced by the hospital during the outbreak. More than 40% of respondents rated their fear of EVD greater or equal to 7 out of 10. The hospital reported three cases of false alarms erroneously labelled as suspected cases of EVD by admitting clinicians. During the outbreak, the hospital designed an isolation ward, built a field incinerator, and produced hand sanitizers.



Figure 30: Field incinerator (left) and hand sanitizers designed and produced during the Ebola outbreak

vi. **Original Article**: Diagnostic utility of non-contact infra-red thermometers in body temperature measurements – a hospital based study.<sup>94</sup>

The demand and utilization of non-contact infrared thermometers among healthcare workers increased during the 2014 Ebola outbreak. To determine the accuracy and agreement of non-contact infra-red thermometers (NCIT) with axillary thermometry we studied 67 neonates, 117 children and 223 adults, including healthy non-febrile and febrile participants who were all Nigerians living in Bayelsa state. Our results revealed that body temperature measured by mercury-in-glass thermometers agreed with digital axillary thermometers. There was however poor agreement between noncontact infra-red thermometers and mercury-in-glass thermometers (Accuracy (74-90%), sensitivity (58.5-82.4%), specificity (76-97%)). Our study data suggested that in view of the underestimation of body temperature, NCIT might not be a suitable alternative to mercury in-glass thermometers for routine body temperature measurements.



Figure 31: Infra-red non-contact thermometers being used for body temperature measurement

### 4a. Geographical information system and health

i. **Original Article**: Geospatial and epidemiological determinants of sexual behaviour among adult HIV-1 infected patients receiving antiretroviral therapy in a tertiary hospital in Bayelsa state, Nigeria.<sup>95</sup>

This study aims to evaluate the determinants of sexual behaviour among patients receiving anti-retroviral drugs and to ascertain if there is geographical clustering of risky sexual behaviour. Sixty (24.9%) patients engaged in risky sex, 86 (35.7%) used condom consistently and 95 (39.4%) abstained. Female sex, age>35years and being currently married were the only independent predictors of risky sex. There were significant hot spots of patients with risky sex in Ahoada-West LGA in Rivers state, and 5 LGAs in Bayelsa state (Yenagoa, Ogbia, Kolga, Brass and Sagbama)-Figure 28.

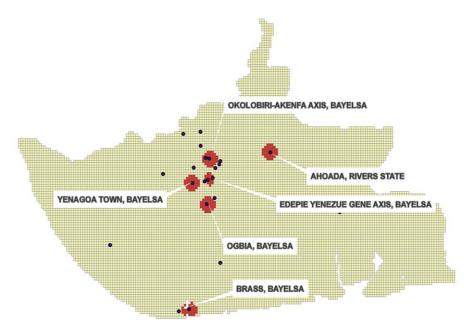


Figure 32: Map of Bayelsa showing location or hot spots (red dots) of HIV/AIDS patients seen at NDUTH with high risk sexual behaviour

# ii. Original Article: A Geospatial assessment of HIV vulnerability in Nigeria. <sup>96</sup>

We used geospatial analysis to map the state-wide differences in HIV- vulnerability in Nigeria. This is an ecological study based on the data provided by the National HIV/AIDS and Reproductive

Health Survey 2012 and the Nigerian Demographic and Health Survey 2013. Using ArcGIS software (13.1), these data were represented geographically, rastarized and then used to develop geospatial models that calculated state-wide HIV exposure index, HIV sensitivity index and HIV adaptability index. These indices were then used to construct state-wide HIV vulnerability maps, with vulnerability patterns reclassified and ranked as very low, low, moderate and high. The results indicate that Bayelsa, Rivers, Akwa-Ibom, Imo, Benue and Taraba States had the highest ranked HIV exposure; Akwa-Ibom, Benue, Ondo and Taraba had the highest ranked HIV sensitivity; while Anambra, Kogi, Enugu and all south-west states had the highest ranked HIV adaptability. Vulnerability maps revealed that Akwa-Ibom, Benue and Taraba were the States most vulnerable to HIV in Nigeria. The lowest HIV vulnerabilities were observed mainly in the south-west, northeast and north-west parts of the country.

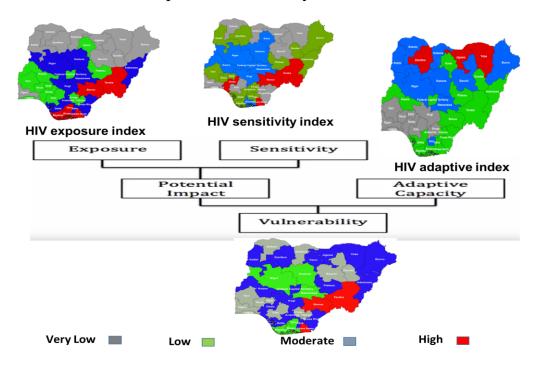


Figure 33: Geospatial maps showing state-wide differences in HIV-related exposure, HIV sensitivity, HIV adaptive capacity and composite HIV vulnerability in Nigeria. Akwa-Ibom, Benue and Taraba were the States most vulnerable to HIV in Nigeria.

*iii.* Applications of GIS in health- a case study of NDUTH-15<sup>th</sup> Dean's Lecture of Faculty of Clinical Sciences. (Ogoina D, Sept 2015)

I explored the various applications of GIS in health and also used, ArcGIS-a GIS-based software, to evaluate its potential applications in the overall delivery of healthcare in the Niger Delta University Teaching Hospital (NDUTH), Bayelsa state, Nigeria. Working in collaboration with some staff at Bayelsa state geographical information system, we evaluated geographical clustering of HIV/AIDS patients and geographical relationship between HIV/AIDS and Brothels in Yenagoa. Of 966 HIV/AIDS patients who presented to NDUTH, 151 (15.6%) lived within 1km of a Brothel. There were more clustering around Brothels situated along Imiringi road.

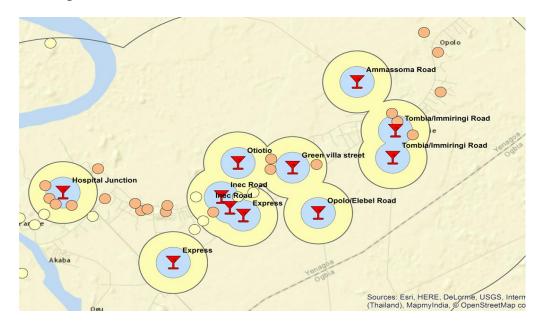


Figure 34. Geographical distribution of HIV/AIDS patient seen at NDUTH in relation to location of Brothels in Yenagoa, Bayelsa State. Red dots indicate clustering of patients, red symbol indicate location of brothels, blue and yellow circles indicate buffers around Brothels at 500m and Ikm respectively

# *iv.* **Original Article:** *Geospatial trends of infectious disease epidemics in Nigeria: a 5year review. (Ogoina D -in press)*

We conducted an ecological study to describe the geographical trends of infectious disease outbreaks in Nigeria. The study data were based on Weekly Epidemiological Reports (January 2011 to December 2015) provided by the Federal Ministry of Health of Nigeria. The number of cases, number of deaths, case fatalities and population incidence (incidence/100,000 population) were

ascertained for Cholera, cerebrospinal meningitis, measles and Lassa fever epidemics over the 5year period. The yearly and 5year trends in incidences and case fatalities of these epidemics were represented geospatially using a mapping software. Over the 5year period there were 236272 cases of ID outbreaks with 3762 deaths (CFR 1.6%). The average annual incidence (attack rate) was 33.8 per 100000 persons. The highest number of cases and attack rates were observed in Yobe, Bauchi, Sokoto, and Kebbi, while the lowest rates were observed in Akwa Ibom, Cross River, Ondo and Kwara states.

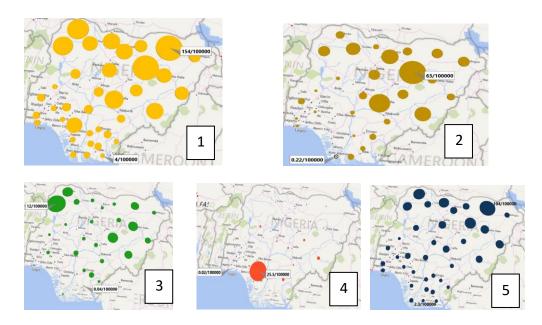


Figure 35: Geographical representation of state-wide differences in incidence of infectious disease epidemics in Nigeria. Circles represent incidence rates- Plate 1-overall incidence for all four epidemics, Plate 2 -Cholera, Plate 3- Cerebrospinal meningitis, Plate 4- Lassa fever, Plate 5- Measles

## 5. <u>MY RESEARCH ON OTHER CLINICAL INFECTIOUS</u> <u>DISEASES</u>

i. **Case Series:** Clinical presentation and outcome of severe malaria in adults in Zaria, Northern Nigeria.<sup>97</sup>

Severe malaria is rare in adults living in malaria endemic countries. Here we reported 12 cases of severe malaria in adults among 3464 adult non-pregnant medical patients admitted between January 2006 and December 2009 at ABUTH, Zaria, Nigeria. These patients had varied clinical and laboratory manifestations with majority presenting with multiple convulsions and features of cerebral malaria. Patients were treated with parenteral quinine and artemether. Mortality was 25%. We identified delayed treatment and advanced HIV as risk factors for severe malaria in adult Nigerians.

ii. **Review Article**: Fever, fever patterns and diseases called 'fever'-a review. <sup>98</sup>

In this widely cited review article, I discussed the pathophysiology of the febrile response and described the fever types and patterns, including their clinical significance. The various medical illnesses called "fever' were also listed and the origins of their appellations discussed.

iii. **Case Report**: Neurobrucellosis--a case report and review of literature.<sup>99</sup>

Neurobrucellosis is a rare form of systemic brucellosis, a disease acquired through ingestion of unpasteurized dairy products, which may manifest as stroke, encephalitis, meningitis, or psychiatric disorders. At the time of this report we were not aware of previous published report of neurobrucellosis in Nigeria. We reported the case a 28year old spinster with history of significant ingestion of unpasteurized cow milk and brucellosis of the brain diagnosed using brain magnetic resonance imagining (MRI) and brucella antigen agglutination test. Because of the indolent nature of brucellosis infection, it should be suspected in individuals with pyrexia of unknown origin so that early detection and treatment could prevent long-term sequelae such as focal neurologic deficits, hydrocephalus and psychiatric illness.

iv. **Original Article**: An Eight-Year Review of Morbidity and Mortality among Adult Patients with Tetanus at a Tertiary Hospital in Zaria, Northern Nigeria.<sup>100</sup>

This review studied morbidity and mortality patterns among adults treated for tetanus at a tertiary hospital in Zaria from January 2006 to December 2013. Forty-seven tetanus patients aged 15-65years, 70.2% males, were admitted during the period. 51.2% of patients were students. The lower limbs were portal of entry in 70.6% of cases, and 52.9% of the wounds were dirty. 82.4% of the patients were unimmunized and overall mortality was 40.4%. Predictors of mortality were short incubation period, short onset time, severe muscle spasms, non-immunization and presence of complications.

# 6. OTHER ACTIVITIES IN SCHOLARSHIP, RESEARCH AND COMMUNITY SERVCE

i. The CRAQ RESEARCH TEAM- Creating a culture of asking questions (CRAQ)

Together with some colleagues working with FHI 360 Bayelsa, we constituted the CRAQ research team in 2016 to develop and implement health research that would ultimately decrease the burden of HIV/AIDS and other infectious diseases in Bayelsa. Currently, several research topics are being explored and some completed proposals have been sent for ethical approval.

ii. Infection prevention and control manual

I initiated and developed the infection prevention and control manual of NDUTH Bayelsa in collaboration with other members of the infection control team of the hospital

iii. Software development-

Designed a data entry software based on Excel and Epi Info now used by Health Information Management and Pharmacy Departments of NDUTH for electronic health database and drug utilization monitoring.

iv. Medical Animations for medical education-

I am currently developing interactive medical lectures using animations.

v. Community service

I am actively involved in various community services as coordinator, member and or resource person for health-related activities organised by NDUTH Bayelsa, NMA Bayelsa, Nigerian Infectious Disease Society, Bayelsa State Lassa fever Committee, West African College of Physicians Lassa Fever Committee and MDCAN NDUTH Branch, as well as some Faith-based organisations. Served as Resource person to World Health Organization (WHO) organized training workshop on viral hemorrhagic fever held 12th-14th May 2016 at Yenagoa, Bayelsa state.

## 7. My Future Research interests

- i. Infection Prevention and Control
- ii. Comprehensive review of Epidemiological, Social, Clinical and Laboratory aspects of HIV/AIDS in Bayelsa
- iii. Clinical trials in infectious diseases
- iv. Outbreak investigation
- v. Clinical aspects of infectious diseases
- vi. Immunology of Infectious diseases
- vii. Genomics of Infectious diseases
- viii. Infectious diseases and public health
  - ix. Healthcare-associated infections, including Antibiotic use and resistance patterns
  - x. Microbial markers in non-communicable diseases
  - xi. Applications of geographical information system in infectious diseases epidemiology and control
- xii. Quality improvement and clinical governance
- xiii. Software and apps development for medical education and health

## THE PREVENTION AND CONTROL OF INFECTIOUS DISEASES-PERSPECTIVES

My VC Sir, it is evident from all forgoing sections that micro-organisms are active and indispensable players in the ecosystem, where they could interact with man as associates, adversaries and adjutants. In view of their divergent roles in human health and disease, the successful prevention and control of diseases due to microorganisms (infectious diseases) must be based on strategies that take advantage of their benefits, avoid their deleterious effects and or eliminate the pathogenic micro-organisms altogether. Such strategies must also restore the imbalance in the host, microbial and environment interactions as well as break the chain of infection that leads to disease.

Since a healthy human microbiome is required for protection against infectious diseases and for normal healthy living, there is need for institution and adoption of strategies that improve and sustain the robustness and resilience of human microbiome from birth to old age<sup>101,102</sup> Figure 33 summarises the various ways the human microbiome can be protected, preserved and enriched.

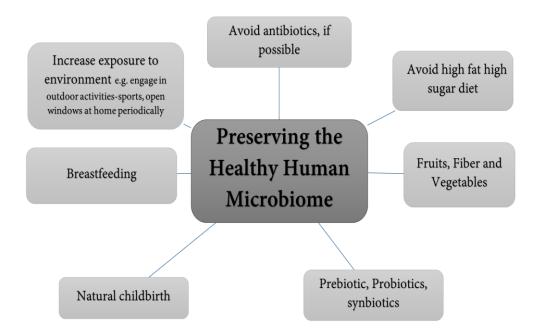


Figure 33: Preserving the healthy human microbiome.

In restoring the balance between the man, microbe and the environment, man ought to also devise strategies to increase resistance to infections, to interrupt transmission of pathogenic of microorganisms and to control or eliminate infections that have evolved to cause disease. Figure 34 illustrates the various ways these could be achieved, while Box 4 highlights the critical role of vaccination in the prevention of infectious diseases.

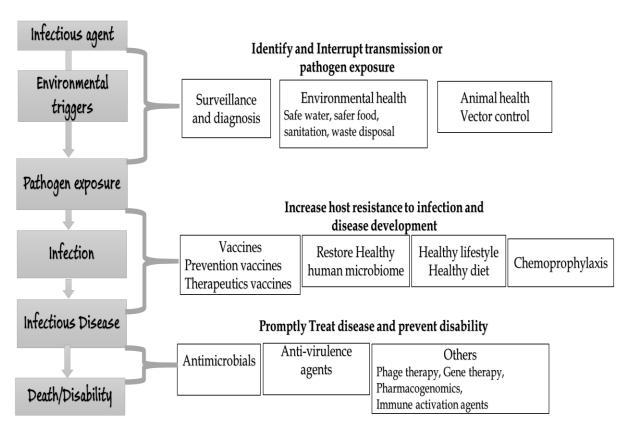


Figure 34: Strategies to interrupt transmission and progression of infectious diseases

#### Box 4

Vaccines stimulate the body's own immune system to protect the person against subsequent infection or disease. Vaccination is a proven tool for controlling and eliminating lifethreatening infectious diseases and is estimated to avert between 2 and 3 million deaths each year. It is one of the most cost-effective health investments. WHO 2016

It is now established that the ecosystem can only guarantee healthy living for man in the presence of a healthy environment – defined as a healthy state for all the physical, chemical, and biological factors external to a person, and all the related behaviours.<sup>50</sup> The recognition of the role of the environment, especially pivotal role of animal reservoirs and vectors, in the emergence and reemergence of infectious diseases, has now led to the adoption of the concept of 'One Health' in the prevention and control of infectious diseases.<sup>50</sup> One Health recognizes that the health of humans is intricately connected to the health of animals and the environment. It encourages collaboration between multiple disciplines including human, animal and environmental disciplines, to address potential or existing risks that originate at the animal-human-ecosystems interface.<sup>50</sup>

Perhaps, the greatest challenge faced in the prevention and control of infectious diseases lies in the ability of microorganisms, especially pathogenic microorganisms, to constantly evolve and adapt to new host, new environments and new control measures.<sup>7,42,103</sup> It is for this reason that the emergence and reemergence of infectious diseases will likely remain a perpetual challenge to man. To successfully prevent and control current and future infectious disease challenges, man must also continually enrich its ingenuity in developing novel countermeasures to prevent, detect, treat and control infectious diseases. Such countermeasures should include development of novel diagnostic techniques, novel vaccines, novel therapeutics, including alternatives to antibiotics and pharmacogenomics, as well as strengthening and advancement of public health interventions using modern technology (Figure 35). To this end, healthcare professionals, policy makers, scientists, academicians and other health stakeholders must be prepared to work collaboratively and to integrate interventions at the bench, bedside and the community for the health and wellbeing of humanity.

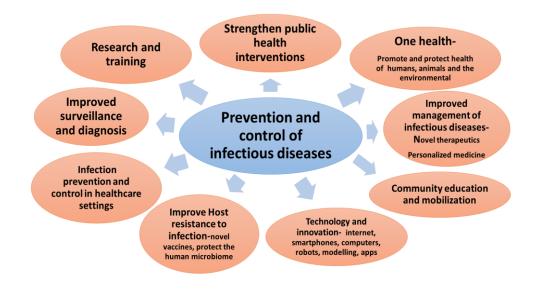


Figure 35: Contemporary measures to prevent and control infectious diseases

### Conclusion

My VC Sir, in our ecosystem, we live and will always live with microorganisms as our associates, adversaries and adjutants. It is hoped that in the future man can fully exploit the beneficial effects of microorganisms to promote human health and at the same time successfully tame their potential to cause human diseases. In this undertaking, man must not never forget their dominant role over all species of the ecosystem as established in the scriptures (Box 5).

#### Box 5

Then God said, "Let us make man in our image, after our likeness. And let them have dominion over the fish of the sea and over the birds of the heavens and over the livestock and over all the earth and over every creeping thing that creeps on the earth." Genesis 1:26

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To all of you distinguished ladies and gentlemen, I thank you for taking time to attend this lecture. We are greatly honoured by your presence.

God bless us all.

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## PROFILE OF PROF DIMIE OGOINA

# (MBBS, FWACP, FMCP-Infectious Diseases, FACP, Certificate Clinical Leadership)

Prof Dimie Ogoina was born in Port Harcourt, Rivers State on 2nd February 1974 to the family of Col SB Ogoina (Rtd) and Mrs Victoria O Ogoina (Nee Izonfuo), both of Odi in Yenagoa LGA, Bayelsa. He is an indigene of Amakirebiama, Odi, Kolokuma-Opukuma Local Government Area of Bayelsa State, Nigeria. He attended Command Children School, Calabar from 1981-1985 and then Command Secondary School, Lagos from 1986 -1991 for his primary and secondary education respectively. He completed his secondary education with distinctions in seven subjects. He was accepted into the Ahmadu Bello University Zaria, Kaduna State in 1991 to Study Medicine and Surgery. His undergraduate training was interrupted by closure of the university and strike action by university staff. In 2000, he successfully completed his undergraduate medical training winning two Prizes, including the Professor's Bandipo's prize as the overall best graduating doctor in Community Medicine and the best continuous assessment in Community Medicine.

After his undergraduate medical training, he undertook his compulsory housemanship in Ahmadu Bello University Teaching Hospital, Zaria between 2000and 2001, and then proceeded for his National Youth Service at FCT, Abuja in 2002. On completion of his NYSC in 2002, Professor Ogoina worked briefly as a medical officer in the Federal Medical Centre, Yenagoa and left FMC Yenagoa in October 2003 to enrol into the Residency Programme in Internal Medicine at the Ahmadu Bello University Teaching Hospital, Zaria, Here he trained in the field of infectious diseases and Kaduna State. immunology in both the West African College of Physicians (WACP) and the National Postgraduate Medical College of Nigeria (NPMCN). During his residency training he was awarded the Ayo Iyun Prize for the overall best Part 1 Candidate in West Africa in the Faculty of Internal Medicine, West Africa College of Physicians. He completed his residency training in 2009 with fellowship in both West Africa (FWACP) and National (PMCP) Postgraduate Colleges in infectious disease and immunology sub-speciality. Prof Ogoina then worked at the Bingham University/Bingham University Teaching Hospital, Jos Plateau State as a Lecturer 1/Consultant Physician from October 2010 to April 2011. He was appointed Senior Lecturer/Consultant in Internal Medicine at the

Niger Delta University/Niger Delta University Teaching Hospital, Bayelsa State in June 2011.

Prof Ogoina has held several leadership and administrative positions. He was the Chief resident of the department of Internal Medicine, ABUTH, Zaria from 2006-2008. He was appointed Head of Department of Internal medicine, Niger Delta University from June 2012 to June 2013, and elected Chairman, MDCAN, NDUTH branch from July 2012 to June 2013. He was appointed Chairman, Medical Advisory Committee, (CMAC) NDUTH Bayelsa in June 2013 and served in the positon until November 2015 when he was appointed as the Ag. Chief Medical Director, NDUTH, Bayelsa. He also served as the Ag. Provost of the College of Health Sciences, Niger Delta University from September 2014 to February 2015.

Professor Ogoina has keen interest in Clinical medicine and research, especially in the field of infectious diseases and immunology. His research interests include clinical infectious diseases, immunology of infectious diseases, public diseases, translational aspects of infectious research. quality health improvement and use of technology in health and medical education, among others. He has published over 45 scientific papers, presented over 30 conference papers and 25 public lectures both nationally and internationally. He has served as a reviewer for various scientific journals including most BMC journals, Journal of Infection Prevention, African Health Sciences, African Journal of Infectious diseases, Nigerian Journal of Clinical Practice, among many others. In 2016, he was appointed as a reviewer for the 2017 National Abstract Competitions for the American College of Physicians as part of the ACP Internal Medicine meeting for 2017. He has also served as an external examiner for Masters in Immunology programme in the Ahmadu Bello University, Zaria. He is a member of various reputable international organisations including Infectious Disease Society of America (IDSA), International Society of Infectious Disease (ISID), Association of Professionals in Infection Control (APIC), European Society of Clinical Microbiology and Infectious Disease (ESCMID), among others. He is a foundation member of the Nigerian Infectious Disease Society (NIDS) and currently the Society's 1st Vice President.

Professor Ogoina obtained a certificate in Management and Leadership in Health from the University of Washington USA in March 2015 and a certificate in Clinical leadership from the National Health Service, United Kingdom in May 2016. He also obtained a certificate in Principles of STD/HIV Research from the University of Washington USA in 2015. He was elected as Fellow of the American College of Physicians in September 2015. He was appointed Professor of Medicine by the Niger Delta University in October 2014, about 5years after qualifying as a Consultant Physician.

Professor Ogoina is happily married to Mrs Hembafan Ogoina. As a hospital administrator he is interested in quality improvement and the use of data to improve service delivery. As a medical educator he is interested in the use of technology to improve the ease of learning. As a clinician and researcher, he is interested in translational research, where research on the bench or the community can be translated to the bedside and vice versa. He enjoys teaching and giving scientific presentations. He is a proficient Chess Player having won Gold Medals in Chess both as a medical student and resident doctor. He values hard work, integrity and creativity.