NIGER DELTA UNIVERSITY

WILBERFOCE ISLAND, BAYELSA STATE.

36th INAUGURAL LECTURE

Titled:

VIRUSES: IGNORED, NEGLECTED, POORLY UNDERSTOOD WITH RESULTING DEVASTATING CONSEQUENCES

By:

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PUBLISHERS
Niger Delta University Publishers Ltd.

ISSN. 240848673

Inaugural Lecture Series No 35
Delivered 20th March, 2019

Printed by:
Mascot Dynamic Ventures
08035088684

36th INAUGURAL LECTURER

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NIGER DELTA UNIVERSITY

Motto:

Creativity Excellence Service

Vision

To be a centre of excellence defined by well articulated programmes that will produce creative and innovative minds.

Mission

To strive to maintain an international reputation for high quality scholarship, research and academic excellence for the promotion of the socio-cultural and economic well being of mankind.

NIGER DELTA UNIVERSITY ANTHEM

Like the brightest star we are, to lead the way
To the good education that is all our due,
The dream of our fathers like the seed has grown;
Niger Delta University if here to stay.

Let us build on this noble foundation
And with love, let our dedication increase,
To rise and uphold this noble vision
Ev'ry passing moment let our zeal never decrease.

In all that we do, let us bring to mind
Our duty as staff and students of NDU
Ev'rywhere to promote peace towards mankind,
Creativity, Excellence, Service.

Rejoice, great people old and new, rejoice
For the good fruit through us is sown;
Be glad in our worthy contribution
To the growth of humanity.

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The Deputy Vice Chancellor (Administration).
The Deputy Vice Chancellor (Academic).
Registrar
University Librarian
Members of the University Governing Council here present
Deans of other Faculties/ Directors of Institutes and Centres
Distinguished Professors and Scholars
Heads of Departments
Staff and students of the NDU
Staff of the NDUTH
Members of the Nigerian Medical Association
Ladies and Gentlemen

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DEDICATION

This inaugural lecture is dedicated foremost to the Most High, Almighty GOD for his countless mercies. Also dedicated to:

1. My late parents: Mr. Meliyouwei Miepere Pondei and Ms. Gladys Ere.
2. My late Uncle and Aunts: Chief Abele Alfred Pondei, Mrs. Elmina Ouserigha and Mrs. Dise-ere Nicholas Ere.
3. His Excellency, Late Chief D. S. P. Alamieyeseigha, First Civilian Governor of Bayelsa State.
4. My wife and children: Dr. Juliana Pondei, Oyintokoni, Oyintonye and Oyintariebi Pondei.

1.0. PREAMBLE

First, I want to express eternal gratitude to GOD Almighty for the opportunity and privilege to stand before this august assembly to present an inaugural lecture. I thank the Vice Chancellor, Principal Officers and the entire University for this awesome opportunity.

An inaugural lecture is usually when gown meets town. It is an avenue to inform the general public and University community about a topic, discuss contemporary problems and proffer solutions, while also disclosing research done and contributions to fill gaps in knowledge. The theme of this lecture "Viruses: Ignored, Neglected, Poorly Understood with Resulting Devastating Consequences" was chosen not to frighten anyone, but to state the current knowledge of viruses as at today in Bayelsa State and Nigeria. Very many people have contributed in one way or the other in my journey through life and I wish to from the bottom of my heart thank everyone. Time and space may not afford me the chance to name everyone, but you are all appreciated and GOD who sees in secret will reward you openly.

2.0. INTRODUCTION

2.1. VOYAGE INTO VIROLOGY

My journey into academics began in 2001 with the advice of Dr.Abrakasa Fiepere (then Chief Medical Director, Bayelsa State Hospitals Management Board) to apply to the newly established Niger Delta University, Amassoma, Wilberforce Island, Bayelsa State. With the encouragement and support of Professor Nelson Brambaifa (First Provost of the College of Health Sciences), the Management of the Niger Delta University and the Bayelsa State Government, I was able to undergo postgraduate training in the United Kingdom. I ventured into virology owing to advice from my wife who suggested that I worked on the Human Immunodeficiency Virus (HIV). So I found myself in the Laboratory of Professor Jonathan Ball, Virus research Group, School of Molecular Medical Sciences, University of Nottingham, situated at the Queen's Medical Centre, Nottingham (the Teaching Hospital of the University of Nottingham). I was therefore exposed to molecular and clinical virology.

2.2. HISTORY OF VIROLOGY

Virology is the study of viruses. The word virus is derived from Latin and means “slimy fluid”. It all began in 1884 in Paris when a filter, the Chamberland-Pasteur filter was invented by Charles Chamberland working with Louis Pasteur (Knipe and Howley 2001; Rybicki and Kightley 2015). This filter could be used to completely remove all bacteria and other cells from a liquid suspension. Adolf Mayer in Germany in 1886 showed that despite filtration, a liquid extract from an infected plant could lead to infection

of the leaves of a healthy plant when rubbed on them. Dmitri Ivanovski in Russia in 1892 also used infectious extract of tobacco plants and showed that they remained infectious after filtration, and the agent responsible appeared to be soluble. Martinus Beijerinck conducting similar experiments in Netherlands in 1898, termed the agent as "**contagium vivum fluidum**" or contagious living fluid. The term "filterable agent" was used before the term virus was finally adopted (Knipe and Howley 2001; Rybicki and Kightley 2015).

In 1898, Frederich Loeffler and Paul Frosch concluded that the infectious agent was a tiny particle and not a liquid agent. The first important virus was the Yellow Fever Virus, identified by Walter Reed and colleagues, which killed 13 times more people than the Spanish-American War in Cuba in the 1890s. In 1908, Karl Landsteiner and Erwin Popper in Germany showed that Poliomyelitis was caused by a virus and also in 1908, Oluf Bang and Vilhelm Ellerman associated a virus with leukaemia (cancer of the white blood cells) (Knipe and Howley 2001; Rybicki and Kightley 2015).

Virology is a grossly neglected and under-taught aspect of Medical Microbiology in Nigeria. Most doctors, Nurses, Pharmacists and Medical Laboratory Scientists have just surface knowledge of viruses. This is because virology can only be understood in the context of molecular processes occurring inside the cell (Wagner and Hewlett 2004). Poor public knowledge of viruses has resulted in viruses being misunderstood, underestimated causing occasional panic and pandemonium with attendant consequences.

In the secular world, everyone is aware of the term "virus". It is a code capable of corrupting computer systems and destroying data. Therefore, most people install antivirus software in their laptops, computers and smart phones in order to prevent malfunctioning and system shutdown. When a news item, video or picture is distributed rapidly and widely, it is said to have gone viral. These terminologies were derived from the actions or behaviour of the biological viruses.

2.3. WHAT IS A VIRUS?

A virus in the simplest of terms is a piece of genetic material (DNA or RNA) surrounded by a protein coat. The genetic material (genome) contains the blueprint for virus replication. A virus is not a cell, as it does not have the characteristics or attributes of cells. It is therefore classified among the non-cellular micro-organisms. They cannot be seen with the ordinary light microscope. There was controversy whether viruses were living or non-living things. Viruses are **obligate intra-cellular parasites**, meaning that a virus must be inside a cell to be functional. The virus outside a cell is inert and is therefore referred to as a viral particle. For a virus to enter a cell and cause infection, it has to first bind to receptors on the cell surface to achieve entry. The Human Immunodeficiency Virus (HIV) for instance binds to CD4 receptor and CCR5 and CXCR4 receptors to achieve entry into cells it infects. Red Blood Cells do not have CD4, CCR5 or CXCR4 receptors and so cannot be infected by HIV. So, these receptors act as visas for viruses to enter cells.

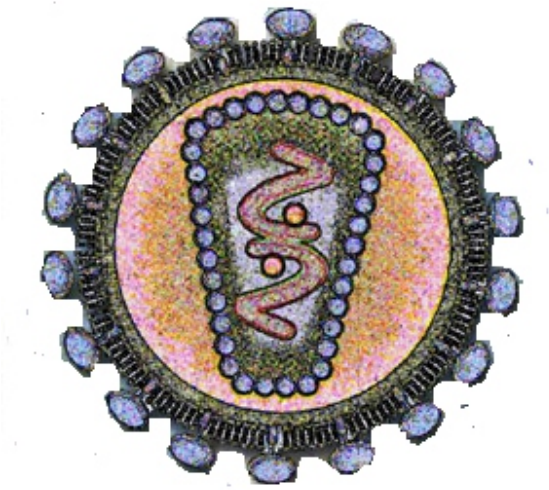


Fig. 1. Schematic drawing of cross-section of HIV-1.
Fromhttp://www.lanl.gov/orgs/pa/newsbulletin/2003/07/14/text02.shtm

The major goal or objective of a virus as it enters a cell is to use the resources available in the cell to mass produce its offspring or progeny. Some viruses can produce millions of progeny in a day. Viruses also aim to produce offspring that are fitter and able to survive hostilities of the host immune system. It is important to note that a virus can infect every type of life form as long as it is cellular – plants, animals, protozoa, fungi and even bacteria.

2.3.1. PECULIAR REPLICATION

Viruses replicate in a peculiar way asexually. The different parts of the virus, the protein coat and the genome, are reproduced separately millions of times and then assembled after which, the newly formed viruses are released to infect

other cells and continue the cycle. On getting into a suitable cell, the protein coat is first removed, exposing the genome to the enzymes involved in reproducing the virus. The enzymes using the information /blueprint contained in the genome produce millions of parts of the protein coat. There is simultaneously also direct reproduction of millions of copies of the genome. The assembly consists of packaging the genome into the protein coat to form new viruses (Fig. 2). More than one virus can infect a cell and this has led to the phenomenon of recombination during viral replication in which parts from different viruses combine to form new offspring.

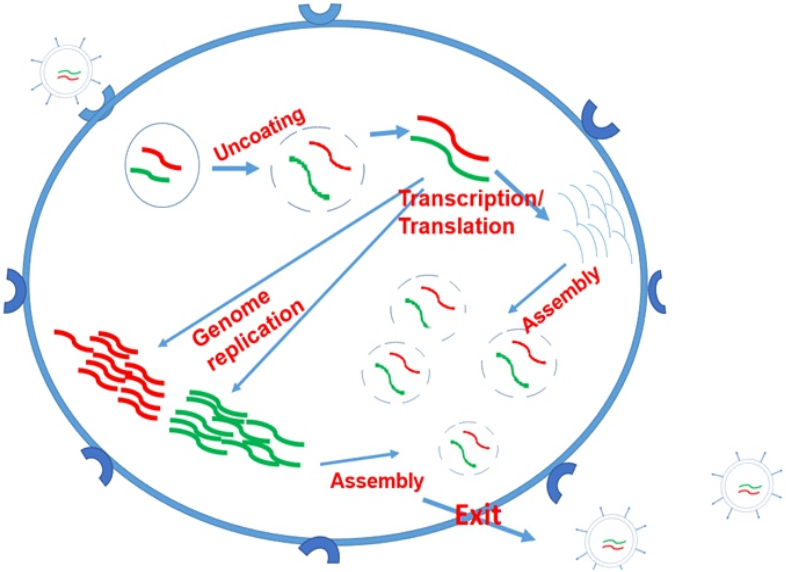


Fig. 2. The viral replication cycle.

2.4. IMPACT OF VIRUSES ON PUBLIC HEALTH

Viruses have been responsible for major public health hazards for centuries. The Spanish flu (infection with the influenza virus) after the First World War was responsible for the death of 10% of the World's population at that time. With advances in science and improved diagnostics, new viruses have been implicated in causing morbidity and mortality every decade. Spread is also easier because the world is now a global village.

Viruses also because of easy transmissibility are responsible for epidemics and pandemics. Of recent there have been outbreaks of Monkey Pox virus, Zika virus, Lassa Fever virus, Ebola virus, Swine flu, Bird flu, HIV. Other important viruses include Rabies virus, Rubella virus, Epstein-Barr virus, Human Papilloma Virus, Hepatitis B virus, Polio virus, Measles virus, Mumps virus.

INFLUENZA VIRUS

There are four types of the Influenza virus – A, B, C and D. Influenza Virus type D is not known to infect or cause disease in humans. Influenza Virus type A has been responsible for the influenza pandemic.

They are spread by aerosols (airborne secretions) – sneezing, coughing. There were three pandemics in the 20th century: the Spanish Influenza 1918 caused by the H1N1 strain affected 500 million people worldwide resulting in the deaths of between 50 -100 million people (10% of the world's population); the Asian Influenza 1957 caused by the H2N2 strain with 2 million deaths; the Hong Kong Influenza 1968 caused by the H3N2 strain with 1 million deaths.

Humans can be infected with avian, swine and other zoonotic influenza viruses. There were thus other epidemics: the Bird flu in 2004 caused by the H5N1 strain involving 701 cases and 407 deaths; Swine flu in 2009 resulting in 14,286 deaths.
Diagnosis is difficult because the symptoms are similar to malaria: fever, chills, cough. The Influenza vaccine has been available for decades. Due to the high mutation rate of the virus, particular vaccines can confer protection for only a few years. Vaccines are therefore reformulated regularly.
SMALL POX: deadly with 30% risk of death. Caused massive scarring of the skin and also caused blindness when the eyes are affected. Eradicated in 1977.

EBOLA VIRUS
A cause of haemorrhagic fever in which 25-90% (average 50%) of infected people die. First outbreak was in 1976 and 24 outbreaks between 1976 and 2013. There have been 28,616 cases with 11,310 deaths between December 2013 and January 2016. First documented case in Nigeria was in 2014 (Shuaib, Gunnala et al. 2014). Death occurs between day 6 and 16 from the first symptoms. Spread mostly by contact with bodily fluids. Dead bodies can remain infectious. A lot is still not known about the Ebola virus and the disease. There is no known effective drug. A vaccine (rVSV-ZEBOV) has been shown to be highly protective against the Ebola virus. Diagnosis can be difficult because the symptoms are not distinguishable from malaria, Dengue fever, typhoid fever and other haemorrhagic viral fevers like Yellow fever, Lassa fever.

Diagnosis is by detection of the virus or antibodies against the virus. Cell culture, ELISA, PCR can confirm infection with the Ebola virus. Biosafety Level 4- equivalent containment is needed for laboratories where testing can be done. The Light Mix ® Ebola Zaire rRT-PCR test can detect Ebola infection.

The Ebola incidence in Nigeria, arose from a single importation into the country. On the 20th of July 2014, a traveller from Liberia, who had been hospitalized and travelled against medical advice, collapsed at the Lagos airport. Doctors in Nigeria were on a National strike, so he was taken to a private hospital in Lagos. Dr. Stella Adadevoh, a Consultant Physician was able to suspect Ebola and confined the patient to the hospital while informing the health authorities. Her singular heroic action saved Nigeria from a calamity. The patient died on the 25th of July 2014 and Dr. Adadevoh on 19th August 2014. Out of the 20 confirmed cases in Nigeria , 8 died, a case fatality rate of 40% (Fasina, Shittu et al. 2014; Shuaib, Gunnala et al. 2014; Patel, Pharr et al. 2016).

A lot of misinformation occurred during the Nigerian Ebola scare in 2014, with people bathing with salt, drinking salt, using ewedu leaves etc (Fasina, Shittu et al. 2014; Patel, Pharr et al. 2016). However, the virus can be inactivated by boiling or heating, the use of bleach (sodium hypochlorite) or bleaching powder (calcium hypochlorite). Standard precaution, hand-washing are effective in preventing spread.

HEPATITIS B VIRUS (HBV)

Hepatitis B virus causes acute and chronic infections of the liver. It can be transmitted by blood and body fluids, sexually and vertically (mother to child). There were 257 million people living with Hepatitis B virus and 887000 deaths in 2015 mostly from complications. Infection with Hepatitis B virus is an occupational hazard for health workers. Data from Nigeria is very poor. HBV can cause chronic liver infection which will lead to liver cirrhosis and /or liver cancer. It has been shown that 80-90% of infants infected in the first year of life and 30-50% of children infected before the age of 6years will develop chronic infections. 20-30% of adults with chronic infections will develop liver cirrhosis and/or liver cancer. Diagnosis is by detection of the Hepatitis B surface antigen (HBsAg). There is no specific treatment for acute infections. Tenofovir which is expensive, is used for chronic infections.

The aim of treating chronic infections is to slow down progression to liver cirrhosis and reduce the incidence of cancer. A vaccine has been available for decades. All healthcare workers who may be exposed to blood and blood products are required to be vaccinated against Hepatitis B virus. However, we observed in a study the low rates of Hepatitis B vaccination coverage of Healthcare workers (Ogoina, Pondei et al. 2014).

HEPATITIS C VIRUS (HCV)

Also causes acute and chronic infection of the liver. 71 million people living with chronic Hepatitis C infection,

with 400,00 deaths yearly. There are 6 genotypes of the Hepatitis C virus, and the response to drug treatment varies with each genotype. Diagnosis is by detection of antibodies against Hepatitis C virus (screening) and confirmation by nucleic acid test for HCV RNA. Direct-acting antivirals (DAAs) are used for the treatment of HCV infections and are capable of curing 95% of people infected. There is paucity of data about HCV infection in Nigeria. There is no vaccine against HCV.

HERPES SIMPLEX VIRUS

There are two types of the Herpes Simplex Virus – HSV-1 and HSV-2. HSV-1 is spread orally and HSV-2 sexually. Infection with HSV is life-long. There are 3.7 billion people under the age of 50 years infected by HSV-1 (67% of the global population), while 417 million people (11%) of the population are infected with HSV-2. Majority of these infections are asymptomatic. HSV-2 increases the risk of acquiring HIV, and more women than men are infected with HSV-2.

Complications associated with HSV infection include encephalitis, keratitis, neonatal herpes.

HUMAN PAPILLOMA VIRUS (HPV)

Infection with the Human papilloma virus (HPV) is very common worldwide. There are more than 100 types of HPV, with 13 types known to cause cancer in humans. They are transmitted sexually and known to cause most all cases of cervical cancer (HPV Types 16 and 18). They are also associated with cancer of the penis, anus, vulva and vagina as well as oro-pharyngeal cancer. Cervical cancer is the

second most common cancer in women in developing countries. In 2012 there were 270,000 deaths from cervical cancer. The greatest incidence of acquiring HPV infection in both sexes has been shown to occur shortly after becoming sexually active. HPV Types 6 and 11 are known to cause genital warts. Diagnosis is by pap smear.
A vaccine is available against HPV types 16 and 18 which cause 70% of cervical cancers. Vaccines cannot treat HPV infection and are effective if administered prior to exposure to HPV.

LASSA FEVER VIRUS
A cause of acute haemorrhagic fever. Spread through contact with the urine or faeces of infected multimammate rat (*Mastomys natalensis*). The first case was among missionary healthcare workers in Lassa, Borno State in 1969. All bodily fluids from an infected person are potential sources of infection. About 80% of people infected are asymptomatic. In 2018, there were 1081 suspected cases, out of which 317 were confirmed with 72 deaths.

Clinical diagnosis is difficult because the clinical course of the disease vary widely and cannot be easily distinguished from malaria and other haemorrhagic viral illnesses. Some patients present with symptoms of acute abdomen and indeed undergo surgery (Dongo, Kesieme et al. 2013). Diagnosis is by virus isolation from cell culture, ELISA or RT-PCR. Early treatment with ribavirin is effective. Loss of hearing occurs in 25% of infected patients who survive. Healthcare workers are at risk of infection. Prevention includes control of rodents from gaining access to food

supplies and human residences. Maintaining standard precautions including the efficient use of persona protective equipment (PPE) help to reduce the risk of infection in healthcare workers. However, we also observed in another of our studies poor adherence to infection control practices among health care workers(Ogoina, Pondei et al. 2015).

MEASLES VIRUS

A highly contagious virus that is spread by aerosols (suspended droplets) and saliva from infected people. Death rate used to be 30%. Despite the availability of vaccination against the virus for decades, more than 20 million people are affected yearly. In 2011 there were 158,000 deaths, in 2014 there were 73,000 deaths from this vaccine-preventable disease, rising to 110,000 deaths in 2017 due to decreased immunization. Complications include corneal ulceration (loss of vision), pneumonia, panencephalitis (SSPE which is fatal). Measles was eliminated in the Americas in 2016, only for new cases to arise the next year (Fiebelkorn, Redd et al. 2017).

POLIO VIRUS

Causes poliomyelitis, an illness characterized by paralysis of the limbs. One in 200 infections result in irreversible paralysis. There were 350,000 cases reported in 1988 and 22 in 2017. Poliomyelitis was almost eliminated/eradicated in the world until the debacle in 2013 in Kano State when vaccination was stopped due to misinformation and ignorance. Endemic transmission is continuing in Afghanistan, Nigeria and Pakistan. There is now in Nigeria what is known as circulating Vaccine-derived Polio (cVDP).

The oral polio vaccine contains a weakened form of the polio virus, which when administered replicates in the intestine of the child for a period heping to build immunity by producing antibodies against the polio virus. However, during this period the virus is shed in the faeces of the child. Due to poor sanitary habits and conditions, this vaccine-derived virus shed in the faeces can spread in the community and infect others. The vaccine-derived virus can undergo genetic changes into a form that can cause paralysis in infected people. There is no treatment and no cure for poliomyelitis, only prevention.

RABIES VIRUS

A vaccine-preventable viral disease. Dogs are associated with most human rabies infections and deaths. There are presently no diagnostic tools to detect rabies infection. There are also no drugs. There is pre-exposure immunization and post-exposure prophylaxis for those exposed.

YELLOW FEVER VIRUS

The Yellow fever virus is spread by the bite of infected female mosquitoes (*Aedes aegypti*). The Yellow fever virus was the first virus isolated from humans (1927). The name was coined because of the jaundice seen in most patients. It is vaccine-preventable, with a vaccine available since 1937. There were 170,000 infections in 2013 with 60,000 deaths. It is endemic in 47 countries: 34 in Africa, 13 in Central and South America. Clinical diagnosis especially in the early stages is also difficult, and malaria and other haemorrhagic fevers have to be ruled out. There is no effective treatment or

cure. A single dose of the vaccine can confer life-long immunity. Latest outbreaks: Nigeria in 2017 and 2018; Brazil in 2018.

MONKEYPOX VIRUS
Similar to but milder than human smallpox, but can be fatal. It was first identified in humans in 1970 in the Democratic Republic of Congo (Zaire). Outbreak in Bayelsa State and Nigeria in 2017.

In making a diagnosis, other similar illnesses have to be ruled out: smallpox, chickenpox, measles, scabies, syphilis and medication-associated allergies. There is no specific treatment and no vaccine is available.

ZIKA VIRUS
A virus also spread by the Aedes mosquito. Infection during pregnancy can cause infants with microcephaly and other congenital malformations. The symptoms are similar to malaria. There is presently no effective treat or vaccine.

HUMAN IMMUNODEFICIENCY VIRUS (HIV)
The causative agent of the Acquired Immune Deficiency Syndrome (AIDS). Story began in 1981 with the discovery of peculiar symptoms in five otherwise healthy men who have sex with men in the USA. Similar condition was later associated with people receiving blood transfusions, people from Haiti and then infants. The virus was isolated in 1983 (HIV-1) and a second variant in 1986 (HIV-2) originally and still mainly limited to West Africa. As at 2016, there were 36.7 million people living with HIV, one million yearly deaths and 1.8 million new cases.

2.5. IMPORTANCE OF VIRUSES

2.5.1. Diversity

Viruses are very diverse with about 5450 species of viruses. Classification was a nightmare for virologists and presently the Baltimore Classification System is used.

There is further diversity even within species. For instance, there are two types of HIV (HIV-1 and HIV-2). HIV-1 has four major groups (M, N, O and recently P). Group M responsible for most of the global infections has 9 subtypes (A, B, C, D, F, G, H, J and K). Subtype A has 5 sub-subtypes (A1, A2, A3, A4 and A5), while Subtype F has sub-subtypes F1 and F2 (Fig. 3.)

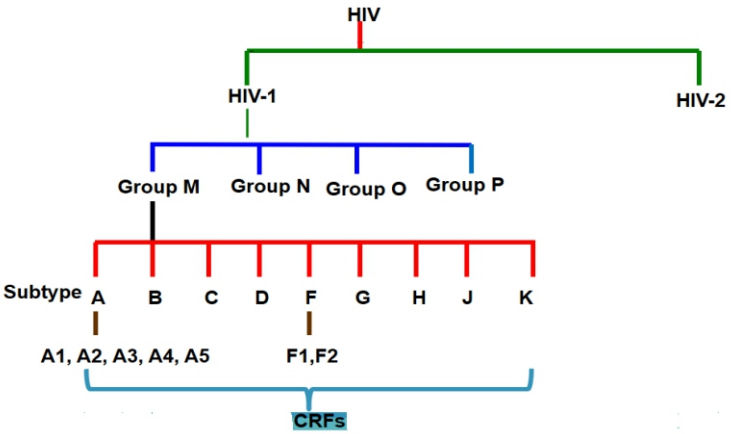
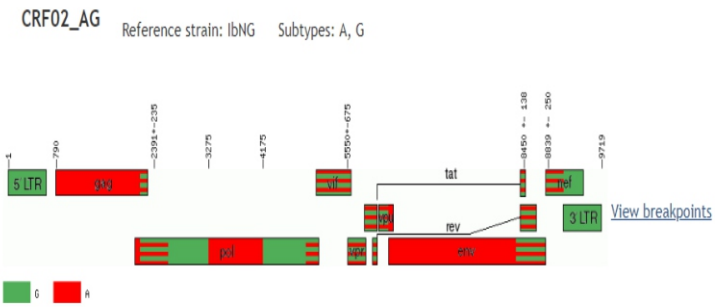


Fig. 3. Diversity of the Human Immunodeficiency Virus

There are also Circulating Recombinant Forms (CRFs) which are viruses made up of parts from different HIV-1 subtypes. There are currently 98 CRFs (Fig. 4).



CRF02_AG (Howard and Rasheed 1996) is a subtype A/G recombinant form that is circulating widely in West and Central Africa (Carr et al. 1998), but has also been reported in Taiwan (Lee et al. 1998).

Fig. 4. An example of a CRF, first isolated from a patient in Ibadan, Nigeria

Unique Recombinant Forms (URFs) are made up from different subtypes but are not yet common in the population. Diversity has implication for disease progression, vaccine design, transmission, drug resistance and diagnosis.

2.5.2. Persistence/Latency of the virus:

Certain viruses are difficult to eliminate from the body as they integrate their genome into the host chromosome e.g. (HIV) or deposit the genetic material in the nervous system e.g.(Herpesviruses). They remain dormant and can be reactivated, especially when the immune system is weakened.

2.5.3. Evading the Host Defence Mechanisms

Viruses while trying to perform their sole obligation of replicating themselves, also have to evade the host immune responses/defences. Different viruses have developed

different mechanisms to overcome immune pressure from the host. The Influenza viruses have used re-assortment of segments of their genome to not only increase their virulence but also confuse and evade the host immune responses. That is why the strains of influenza virus are identified by the sequential arrangement of segments of their genome (Neuraminidase (N) and Haemagglutinin (H)). The strains responsible for the pandemics have been H1N1, H2N2, H3N2, H5N1 etc.

HIV on its part, forms on its surface what is known as a "glycan shield" composed partly of carbohydrates derived from the host (Doores 2015). This shield hides epitopes or areas of vulnerability to host antibodies, and is also recognized by the immune system as "self" and is therefore not marked for destruction. HIV also uses recombination as a tool to produce fitter offspring.

2.5.4. Diagnostic Challenges

Diagnosis of viral infections is usually difficult clinically, because the symptoms are not distinguishable in the early stages of illness from endemic illnesses like malaria. Unlike bacteria that can easily be grown in culture media and with available biochemical tests to aid easy affordable diagnosis, viruses can only be grown in cell culture and the facilities for cell culture are greatly lacking in Nigeria.

Laboratory diagnosis usually consists of a screening test to detect specific antibodies against the particular virus. Confirmatory tests are done to detect viral antigens or isolate the virus from a clinical specimen (PCR, ELISA, cell

culture). Rapid diagnostic kits have been developed to detect a number of viral infections, but there are still many that cannot be easily diagnosed. Also, facilities to conduct most of the confirmatory tests are presently lacking. So, most viral illnesses remain unconfirmed since diagnoses are simply presumptive.
Rapid diagnosis is important because the disease course from infection to death can be rapid in many of these viral infections e.g. Ebola and Lassa Fever.

2.5.5. Treatment Challenges

Also, unlike bacteria that can be treated with a wide range of antibiotics, anti-viral drugs are relatively virus-specific, because the drugs are designed to interfere with either the structure or replication cycle of the virus. Most of the drugs are expensive and not readily available. Ribavirin, used for the treatment of Lassa Fever was initially stored by the FMOH and only released on requisition. There are also no effective drugs against some viral infections e.g. Ebola virus.

2.5.6. Association with Cancer

A number of viruses have been associated with the development of cancer e.g. the Human Papilloma virus, Hepatitis B virus, Hepatitis C virus, Epstein-Barr virus, Human Herpes virus - 8. There is an upsurge in the number of people diagnosed with cancer in Nigeria. The increase can mainly be attributed to improved and relatively early diagnosis of cancer, with the availability of more non-invasive diagnostic procedures – CT scan, MRI. We will

never be able to estimate how many cancers were preventable, how many were due to environmental hazards and importantly to us in virology, how many were due to viral illnesses.

It is obvious that improved early diagnosis of viral illnesses with attendant early treatment can significantly reduce the incidence of viral-associated cancers.

3.0 CONTEMPORARY VIROLOGY IN NIGERIA

3.1. IGNORANCE

Ignorance about viruses and the public health burden they constitute has led to misinformation, denial, miseducation, misapplication of knowledge and wrong decisions which have led to unnecessary increased morbidity and mortality.

In 2003, the Government of Kano State acting on the stand of the Supreme Council for Sharia in Nigeria, stopped vaccinations especially against polio because of suspicion that intentionally-contaminated vaccines were used to make people infertile and introduce HIV to the muslim population (Fleck 2004; Larson, Cooper et al. 2011; Ghinai, Willott et al. 2013; Verma, Iliyasu et al. 2018). This was at a time when polio had been largely reduced globally and was about to be eradicated. Fifteen years later, polio is still very much around and the Boko Haram insurgency in the North Easter Nigeria has hampered immunization. There is re-emergence of wild type strains of the polio virus.

This ignorance is not limited to only Nigeria or Africa. There was a call for boycott of polio vaccinations by the Catholic Bishops of Kenya, due to the fact that tetanus vaccine was alleged to be contaminated with contraceptives (Njeru, Ajack et al. 2016). Also, there was refusal of certain people to have the Measles Mumps Rubella (MMR) vaccine to be given to their children in the United Kingdom, believing that the vaccine was associated with the development of autism in children (Godlee, Smith et al. 2011; Larson, Cooper et al. 2011; Fiebelkorn, Redd et al. 2017). There has since been a resurgence of measles in the United Kingdom.

Despite all the knowledge of what these viruses can do, there is the tendency to overlook viral illnesses. Only when outbreaks occur do health professionals and the Government attempt to contain the particular epidemic and after that, everyone goes to sleep. Lack of sustained efforts to prevent and control viral infections is worrying.

3.2. FACILITIES

As earlier stated, most viruses are highly contagious and laboratories where testing of samples or research can be done must have some level of containment to prevent the viruses from being inadvertently spread and to protect the workers/researchers. There are thus four levels of biosafety containment.

Table 1. Biosafety Levels

Biosafety Level	Description of agent of risk	Examples
Biosafety Level 1 (BSL-1)	Agents not associated with disease in healthy adult humans	*Escherichia coli*, *Bacillus subtilis*
Biosafety Level 2 (BSL-2)	Agents associated with human disease which is rarely serious and for which preventive and therapeutic interventions are **often** available	*Staphylococcus aureus*, Herpes simplex virus, Salmonella species
Biosafety Level 3 (BSL-3)	Agents associated with serious or lethal human disease for which preventive and therapeutic interventions **may be** available	*Mycobacterium tuberculosis*, HIV, *Bacillus anthracis*
Biosafety Level 4 (BSL-4)	Agents likely to cause serious or lethal human disease for which preventive and therapeutic interventions are **not usually** available	Ebola virus, Lassa virus, Marburg virus

Work on viruses like the Ebola virus and the Lassa fever virus need to be carried out in a Biosafety Level-4 containment facility. However, there are only two of such in Africa: one in Gabon and the other in Gauteng, South Africa.

The International Centre for Medical Researches of Franceville **(**CIRMF**)** was founded in 1974 by His Excellency El Hadj Omar Bongo Ondimba, President of the Gabonese Republic, and Mr. Pierre Guillaumat, the Chairman of the petroleum company, Total Gabon. The

Centre was inaugurated on December 5th, 1979. The first BSL3+ (including negative pressure and glove box) laboratory was built in 1997, mostly financed by the Foreign Ministry of France. A second, high security laboratory for Risk Group 3/4 Agents, mostly funded by the Total Gabon oil company and the Gabonese Government, was built between 2003 and 2008 on CIRMF campus (Leroy and Gonzalez 2012) Figs 5, 6, 7 and 8.

Figure 5. The International Centre for Medical Research of Franceville (CIRMF), Gabon. Campus aerial view: the P4 laboratory: **A** = P4 laboratory facilities; **B** = Main Building; **C** = P3 Laboratory; **D** = Primatology Center.

Fig. 6. Initial Laboratory with BSL-3 facility.

Fig.7. The Present CIRMF High Security P4 Laboratory with "Glove Box".

Fig.8. Field Biosafety and Trapping Potential Ebola Virus Reservoir Bats in Gabon.

Even though Lassa Fever virus infection is endemic in certain parts of Nigeria and spreading gradually, there is only one centre for the diagnosis of Lassa Fever infection; the Irrua Specialist Teaching Hospital (ISTH), Irrua, Edo State (Asogun, Adomeh et al. 2012).

The cost of unsubsidized treatment at ISTH, Irrua has been shown to be high, average of N205,558.99. Some medications and investigations are highly subsidized (Asogun, Tobin et al. 2016). The lack of facilities has been attributed to lack of vision as stated in a 2009 paper: "There is a **lack of an overall vision of the critical role of the laboratory** in health care delivery by the governments of such countries. Hence, investments in laboratories are absent or inadequate at best, resulting in rundown services and unreliable laboratory results" (Abimiku 2009).

Fig.9. BSL-2 Cabinet used at Irrua Specialist

Teaching Hospital

Infectious Diseases Hospitals and standard isolation wards are generally lacking. The Ebola outbreak was an indication for Government to establish isolation wards with well trained staff in every State in the country.

3.1. Consequences

1. Nigeria continues to appear in the WHO AFRO Outbreaks and other emergencies bulletins. This has consequences for tourism as different embassies

warn their nationals not to visit because of these outbreaks. The following statement is from the bulletin: "**Nigeria has never stopped circulation of indigenous wild poliovirus and is currently affected by circulating vaccine-derived polio virus".** As at the 21st of December 2018, there were 32 cases of poliomyelitis in Nigeria.

2. Nigeria has the highest number of unvaccinated children against measles worldwide.

3. There are avoidable deaths of Medical doctors and other healthcare workers from complications arising from hospital-acquired Lassa fever infections.

4. Preventable morbidity and deaths from cervical cancer due to no active sustainable programmes to vaccinate young girls.

5. Preventable deaths from undiagnosed infections with viruses associated with cancer.

Table 2. WHO AFRO Outbreak update for viral illnesses in Nigeria. December 2018

EVENT	Reporting period	Total cases	Confirmed cases	Deaths	CFR	Comments
Lassa fever	1st Jan 2018 - 9th Dec 2018	3,276	588	166	5.10%	Five states in active outbreak phase: Edo, Ondo, Plateau, Gombe and Kano
Measles	1st Jan 2018 - 11th Nov 2018	15,723	1,110	123	0.8%	4,604 fewer cases than in 2017
Monkeypox	24th Sept 2017 - 13th Nov 2018	300	126	8	2.7%	Rivers State and Bayelsa State remain the most affected
Yellow fever	7th Sept 2017 - 16th Dec 2018	3,902	78	73	1.9%	Confirmed cases have been recorded from 14 states
Poliomyelitis (cVDPV2)	1st Jan 2018 - 19th Dec 2018	31	31	0	0.0%	The country continues to be affected by two separate cVDPV2 outbreaks

4.0 CONTRIBUTION TO KNOWLEDGE

I have been privileged to conduct research in molecular virology and contribute a little to gaps in knowledge.

4.1 VIROLOGY

My PhD thesis was "**Genetic Variation and Intrahost evolution ofthe Human Immunodeficiency Virus Type-1 envelope gene in different body compartments".** This work examined the variation of HIV-1 between different parts of the body of an individual and the evolution of the virus within each host. It showed the existence of distinct variants in the brain, male genital tract, secondary lymphoid tissue and the blood in most of the patients studied. The virus was shown to be more diverse in the blood and lymphoid tissue compared with those in the brain and semen(Pondei 2009).

Expanded further work on the same subjects and others from Cameroun and including phenotypic analysis confirmed that the virus exists as different entities in different parts of the human body, and viruses from these compartments combine to form more efficient and infective viruses which now determine the receptors they use to achieve infection and their response to a class of antiviral drugs – the co-receptor antagonist Maraviroc (Brown, Peters et al. 2011).

We had also compared the effect of using unquantified DNA in PCR versus using approximately a single molecule of DNA obtained by limiting dilution (Single-genome amplification). This work showed that single genome

amplification was more reliable compared with bulk sampling corroborating the hypothesis of Pete Simmonds (Simmonds, Balfe et al. 1990; Simmonds, Balfe et al. 1990). Single-genome amplification therefore reduces PCR-induced recombination and artefacts. Efficient detection of viruses using PCR for a recombinogenic virus like HIV can only be possible using single genome amplification (Pondei and Wankasi 2013).

Analyzing HIV-1 sequences obtained from different body compartments, we observed that the virus uses different co-receptors to achieve infection even in the same person. This has implications and calls for caution in the use of new anti-HIV drugs like Maraviroc (Pondei, Wankasi et al. 2013).

HIV and tuberculosis have a clinical relationship and investigating testing for HIV and TB revealed disjointed services in the detection and treatment of HIV and Tuberculosis, and we recommend a co-ordinated collaborative service (Pondei and Lawani 2013).

Knowing that the HIV-1 subtype has a bearing on disease progression and drug treatment, we investigated the subtype distribution across Africa, and observed that due to the lack of infrastructure and knowledgeable personnel, what is represented as the distribution of HIV-1 subtypes is inaccurate. Nigeria has only 21 documented full-length HIV-1 sequences (Pondei, Abdu et al. 2014).

Infection with the Hepatitis B and C viruses remain underestimated public health problems in our environment.

Our studies observed asymptomatic Hepatitis B and C virus infections among pregnant women (Pondei and Ibrahim 2013); and in women attending gynaecology clinic for other reasons (Ibrahim and Pondei 2014), thus our recommendation for routine screening of all women attending antenatal and gynaecology clinics.
We had also shown poor rates of vaccination coverage against Hepatitis B virus among healthcare workers in Bayelsa and Plateau States (Ogoina, Pondei et al. 2014).

4.2. ANTIMICROBIAL RESISTANCE/INFECTION CONTROL

Microorganisms are increasingly developing resistance against not only commonly prescribed antibiotics, but also against new and not commonly prescribe antibiotics. We sampled nasal passages of apparently healthy people and isolated bacteria already resistant to Linezolid, a relatively new antibiotic used for treatment of infections caused by bacteria resistant to other antibiotics (Abdu, Pondei et al. 2016). Earlier, our investigation of microorganisms infecting wounds at the NDUTH had shown high rates of resistance to antibiotics (Pondei, Fente et al. 2013) and informed the decision of the Department of Surgery to stop empirical treatment with cloxacillin.

Considering the need for new antibiotics in the face of increasing resistance to antibiotics, we investigated the antibiotic properties of a commonly used herbal plant, the Goat weed (*Ageratum conyzoides*). Extracts from the plant were able to inhibit growth of bacteria isolated from clinical specimens and already resistant to commonly prescribed

antibiotics (Ere, Pondei et al. 2014). More work is required to explore the commercial potential of this plant.
Infection prevention and control is very important in keeping the patient attending hospital and healthcare workers safe. However, our study of the knowledge and practice of standard precautions showed poor compliance with infection control procedures among health care workers in Nigeria (Kunle-Olowu, Pondei et al. 2013; Ogoina, Pondei et al. 2015; Oyeyemi, Ogoina et al. 2018).

We also observed that there were high rates of occupational exposures to blood and body fluids among health workers, especially among newly qualified medical doctors and nurses. There is a need for increased infection prevention and control measures (Ogoina, Pondei et al. 2014).

Studies by the Infection and Prevention Control Committee of the NDUTH identified bacterial contamination of the hospital environment with most of the isolated bacteria being highly resistant to commonly prescribed antibiotics (Oladapo, Pondei et al. 2017).

4.3. URINARY TRACT INFECTION (UTI)

Asymptomatic urinary tract infection is common and we detected this in pregnant women attending antenatal clinic and found that the causative organisms exhibited a high degree of resistance to amoxicillin-clavualanic acid (Pondei, Ibrahim et al. 2012). Other studies we conducted among patients with symptoms revealed varying degrees of resistant microorganisms in the NDUTH (Pondei, Oladapo et al. 2012), in a private hospital setting (Pondei, Orutugu et

al. 2012) and in Maiduguri (Kachallah, Abdu et al. 2018). The studies showed differences in the commonest causative organism in the different study sites.

4.4. PAEDIATRICS

Children are vulnerable to infection by microorganisms even from birth. We characterized sepsis in neonates and found about 44% of them infected with bacteria within the first 28 days of life. Majority had early-onset sepsis, and there is thus a need to investigate the risk factors associated with early-onset sepsis in our environment (Peterside, Pondei et al. 2015). Further analysis of older children observed that childhood sepsis is a common cause of morbidity and found that rates of infection decreased with increasing age of the children, and most of the isolated bacteria were susceptible to the quinolones (Peterside, Pondei et al. 2017).

We had also shown that almost half of children presenting with fever (48.4%) actually had confirmed malaria. There is thus rampant over-treatment of malaria and a need for consideration of other causes of fever (Pondei, Kunle-Olowu et al. 2012). We also showed the causes of non-malarial febrile illnesses in children (Pondei, Kunle-Olowu et al. 2013; Pondei, Peterside et al. 2017), including infection of the middle ear (Pondei, Peterside et al. 2017).

4.5. GENERAL

We examined blood already screened for transfusion and found the presence of malaria parasite in 12.6%. We therefore recommended routine screening of blood for

malaria parasite before transfusion (Pondei, Lawani et al. 2012).

We also showed that anaemia was common in pregnant women (Isa, Pondei et al. 2012) and that blood donor /transfusion services were poorly organized (Pondei, Lawani et al. 2013).

We also sampled eating utensils (spoons, forks, knives) and the bowls of water they were kept in prior to usage by customers in some restaurants in Amassoma. Microorganisms resistant to commonly prescribed antibiotics were isolated (Abdu, Orutugu et al. 2017).

We also investigated women presenting with vaginal symptoms and observed that symptomatic vulvo-vaginal candidiasis and *Trichomonas vaginalis* infections were common, and that clinical guidelines were generally needed in their management (Pondei, Jeremiah et al. 2017).

These contributions to knowledge through peer-reviewed publications have increased the visibility of the Niger Delta University because authors and researchers from institutions across the world have cited and are still citing these works, which are thus productive works.

5.0. THE WAY FORWARD

1. Review of the undergraduate curriculum for training of doctors, dentists, nurses, pharmacists and medical laboratory scientist to include the basics of virology and contemporary knowledge of viral infections.

2. Establish a Virology Institute that will co-ordinate viral research, especially the role of viruses in cancer in Bayelsa State. The establishment of standard viral diagnostic centres and the appropriate training of the staff.

3. The establishment of Infectious Diseases Hospitals with standard isolation wards and well-trained requisite staff, ready for any emergency.

4. Continuous public education on infection prevention and control measures, especially hand hygiene and waste disposal/management.

5. Widespread screening of the populace for viral illnesses and early treatment for cases.

ACKNOWLEDGEMENT

I wish to acknowledge the Vice Chancellor, Prof. Samuel Gowon Edoumiekumo, the Deputy Vice Chancellor (Academic), Prof. DonbebeWankasi; Past Vice Chancellors, Prof. John Cecil Buseri, Prof. Humphrey Ogoni; The Registrar, Mrs. EffuaBerepubo and other Principal Officers, Mr. Seth Tueridei and Dr. Joyce Oyadongha. The pioneer Provost of the College of Health Sciences, Prof. Nelson Brambaifa; former Provost, Prof. K. K. Imananagha and the current Provost, Prof. BeleudanyoFente for guidance. My former Deans, Prof. OwunariGeorgewill and Prof. Stephen Elesha. The pioneer Chief Medical Director NDUTH, Prof. OnyayeKunle-Olowu and the current CMD, Prof. DimieOgoina.

I appreciate members of the **Governing Council**: Mr. Mathew Seiyefa, Prof. Steve Azaiki, Chief (Dr.) Allen Ameri, Chief AzibaodusiAduba, Elder (Chief) MarksonMieyebo, Hon. Donald Daunemigha, Mr. Anthony Howells Ikobho, Barr. Albert Karikarisei, Dr. InetiminebiOgidi, Dr. Mercy Orukari, Dr. Stanley Ogoun, Mr. IneinkiyeOgidi, Ms. Ifiemi Theresa Otobo.

I acknowledge my King, the Ebenanaowei of Ogboin Clan, His Royal Majesty Dele Oweipa Jones Ere; the Amananaowei of Amassoma, His Royal Highness, Major (Rtd). Graham Naingba, Oboro VI and the Council of Chiefs; the entire Pondei Family and Ibenikiri-ama; the Ere Family of Ogbopina-ama, the Okosi family of Agbedi-ama and the Efeke family of Efeke-ama. Special acknowledgement of the MM Pondei Family, especially my

brothers Mr. Preye Pondei and Engr. Sidney Pondei. Also special acknowledgement of my in-laws: The family of Late Damian Ashikeni.

I wouldn't be here without the work done on me by my teachers. Primary school: Mr. Eze, Mr. Nwala, Mr. Mannah of Christ the King Primary School, Oromineke, Diobu; Mrs. Sarah T. Jack, Mr. Dokubo, Mrs. Soberekon, Ms. Akpughunum of State School I, Churchill, Road, Port Harcourt. My teachers in FGC PH: Mrs. Mather, Mrs. Abegunde, Mr. Hussain, Mr. Jafri, Mr. Achaya, Mr. Ohayi, Mrs. Adeniran, Mr. Offor, Mr. Nawaz, Dr. Singh, Mr. and Mrs. NnachiEnwo, Mrs. Ofoluwa, Mr. Okoye, Mrs. Leton, Miss. Eseonu etc.

My teachers in medical school: Prof. Elesha, Prof. Ashiru, Dr. Noronha, Prof. Sofola, Prof. Odunjo, Prof. Abudu, Prof. Rotimi, Prof. Odugbemi, Dr. Abosede, Prof. Foulkes-Crabbe, Prof. Mabadeje, Prof. Ojikutu, Dr. Abosede.

The Virus Research Group, University of Nottingham: Prof. Jonathan Ball, Prof. Will Irving, Dr. Richard Brown, Dr. Patrick McClure, Dr. Tim Hickling, Dr. Alex Tarr, Dr.ChiambahAnkghuambom, Dr. Victoria Arandhra, Dr. Victoria Juttla, Dr. Nader Tagiuri, Dr.Deboeetta Chatterjee, Dr. Rajiv Tawar, Dr. Kristelle Brown, Dr. Mohammed Hamed, Dr. Jessie Bwanali, Dr.Amanj Saeed, Dr.DhanyaSrikanth, Dr.Shafiq Rahman.

My bosses: Dr. AbrakasaFiepere, Dr. AyibapreyeBaralatei, Dr. MarksonAmaegbe, Dame (Dr). EbimieOkara, Dr. Peter

Singabele, Dr. Solomon Sagbe, Dr. LishmanKosipre, Dr. Miebodei, Dr. Benjamin Tabowei, Prof. EbitimitulaEtebu, Dr. AmatareDinyain, Dr. Isaac Oworodo, Dr. ZuboemiAgadah.
Dr. Diepreye Ere, Surv. IgoGoin, Dr. NimibofaAyawei, Mr. Mike GbolodiWenibowei, Mr. Imiebo Ere, Mr. Egbon Ere, Mr. Johnbull Pondei, Dr. Godwin Ogobiri, Dr. Collins Ouserigha, Hon. And Mrs. Ambrose Oyovwe, Mr. Glasgow Akaranbiriowei, Pharm (Dr.) OtakhoOrunwense, Hon. Joe Akedesuo, Hon. KuroakeghaDorgu, Hon. Vivian Ere, Chief Ebifemowei Abel, Barr. Carter Cleopas,Mr. and Mrs. Couple Ingibina, Dr. WakienteOmubo, Dr. Jones Stow, Dr. KolapoOyeniyi, Julius Chinedu, Dr. Malcolm Brisibe, Chief OkoyeEzeali (P. Noble), Mr. SuotonAmade, Mr. Jude Patrick, Arch. Ere Efeke.

My Nigerian Medical Association (NMA) Ogas: Dr. James Omietimi, Prof. Israel Jeremiah, Dr. NgowariTorunana, Dr. NonsoOkoye, Dr. Williams Appah, Dr. Tony Godfrey, Dr. Vivacious Otiti, Dr. EbiOkpomu, Dr. Newton Igwele.

All staff of the College of Health Sciences: Mrs. EbiIzonfuo, Mr. Benjamin Yebufura, Ms. BolouyeOmemu, Prof. SeiyefaBrisibe, Dr. Izibeloko Jack, Mr. Benedict Ateboh, Mr. Kojo Paul, Mr. BoukaziEbrakumo, Ms. Funge-Ere Kenkayoro, Engr. Millionaire Woyengikuro, Mr. Oti Thompson.

Staff of the **Faculty of Basic Medical Sciences**: Ms. Cynthia Bindei, Ms. Stella Konboye, Mr. W. Kayopa, Ms.

Gladys Dudafa; the Heads of departments: Dr. EzenwaUdoye, Mr. Charles Oyinbo, Dr. Marcel Arhoghro, Dr. Benedicta Kasia, Dr. CrosdalePughikumo, Dr. Peter Erigbali, Dr. Ferdinand Ezeiruaku, Prof. ChingPoh, Prof. FiekumoBuseri, Dr. SuleJimoh, Dr. Faith Robert, Dr. BonsomeBokolo, Dr. Koikoibo, Dr. MieebiWankasi, Dr. Gborienemi George, Dr. Michael Egbejimi.

Staff of the Department of Medical Microbiology and Parasitology: Dr. AbdulRasheed Abdu, Dr. JubrilAshiru, Dr. Ben Owhe-Ureghe, Mr. Langley Orutugu, Ms. Ndutimi, Bikpobigha, Ms. Glory Birikidi, Mr. DedeZiteide, Mr. Clement John, Mrs. Amos.

NDUTH Staff: Mr. Allen Isaac, Pharm (Dr.) Austin Onabor, Mr. Mologe, Mr. Oduru, Mr. Ebigoni Edgar. All past and present members of the Quality Improvement Committee, Infection Prevention and Control Committee and Research and Ethics Committee of the NDUTH.

My research collaborators: Prof. OliemenPeterside, Prof. Felix Akinbami, Dr. Chika Duru, Dr. DejiAdeyemi, Prof. Isa Ibrahim, Dr. AbisoyeOyeyemi, Mrs. EbidorLawani, Mrs. Oladapo, Mr. Wisdom Olomo, Pharm. Nanakede.

The NDU Staff Club (Wednesday Table): Prof. Agbonlahor, Prof. Egumu, Prof. Tatfeng, Prof. Ogaga, Dr. Tiemo, Dr. Kashimawo, Dr. Eni, Dr. Akpotohwo, Dr. Ayunku, Ms. Ese Okpako, Dr. Joy Hamilton-Ekeke, Dr. MacIver, Mrs. Wellington, Mr. TimiBinafeigha, Mrs. Dagana.

Esteemed NDU Staff: Prof Osa Tawari, Prof. Adeleke A. Adeyinka, Prof. OluOsinowo, Prof. Hope Obianwu, Prof. Ismail Sulaiman, Prof. Eniojukan, Dr. DiepreyeOkodoko. Prof. (Mrs.) Abiodun O. Adeyemo**,** Prof. Munakurogha E. Adigio, Prof. Solomon T. Ebobrah, Prof. Ibaba S. Ibaba, Prof. Allen AzibodumomsiAgih, Dr. Christine O. Odi, Prof. EbimieoweiEtebu, Prof. Prohp The Prophet, Prof. Helen Madukosiri, Prof. Tuemi T. Asuka, Prof. Martin Allison, Prof. Domingo A. Okorie**,** Prof. Kolawole K. Ajibesin, Prof. Zaccheaus A. Jeremiah**,** Prof. Chabovie M. Sorgwe**,** Prof. Bismarck B. Kombo**,** Dr. OdoguBinabindor, Dr. Paul C. Onyeabo, Prof. Woyengi- EbinipreBurubai, Dr. Salome T. Farrow, Dr. ChukwudiNjoku, Dr. Godwin Jackson, Dr. Gideon Alade, Dr. (Mrs.) Oluwayemisi A. Olorode**,** Prof. Jasper F. Nestor Abowei, Dr. Timi Jack F. Tarawou, Prof. AmbilyEtekpe, Dr. Perekibina A. Bariweni, Dr. TebekemeOkoko, Prof. Dau S. Zibokere**,** Prof. Ezekiel Dikio, Prof. Tubonye C. Harry, Dr. Tonbarapagha Kingdom, Dr. (Mrs.) NnennaBenwari, Dr. TuboOkumoko, Dr. Michael Amaegberi, Dr. PreyeAngaye, Ms. Margaret Ekeins, Mr. Korikiye Isaiah, Ms. Flora Apreala.

Mr. Emma Amaegbe, Mr. BolouYalah, Mr. Benjamin Joffa, Engr. Emmanuel Frank-Opigo, Engr. Emmanuel Egbekun, Dr. KomonisoOnu, Dr. ThankGodApere, Mr. Kingsley Amabie, Mr. Frank Ogbotobo, Barr. Keme Sogo,Mr. Duncan Ubarugu, Mr. Domo J. Alagoa, Ms. UkieUgulafa, Mrs. SeiyefaTaylor-Harry, Ms. Tare Apre, Ms. AyibatariInanabor, Mrs. Ebiye Colman, Mr. Thomas, Mrs. Achimota F. Amazama, Mr. Kokobaiye O. Angaye, Mrs. TarikiyeAngaye, Mr. WoneOkumoko, Ms. Anita Allagoa,

Mrs. Tare-ela D. Abite, Mr. Simon Ineidou, Mr. TonbraKime, Mr. IyekorogheIwerikumo, Mr. Julius Ofonibengha, Mr. Keme Zaukumo, Mr. Fidelis Allagoa.

My FGC PH mateleens: Sir Isaac Gomba Chu, Sir Clifford Dikibugerere, Dr. Amejima Chu, Prof. Edward Fubara, Dr. ProtaseOpara, Dr. Sunday Amadi, Hon. Charles Zuofa, Chief AlwellHanachor, Dr. Abiye Hector-Goma, Arch. Nathan Job Otokwala, Mr. PreborOruambo, Mr. OkechukwuOlisa, Ms. Rita Wai-Ogosu, Ms. IkwoUloh, Ms. Henrietta Isokpan, Dr. Musa Umar, Prof. Masaudu Ado, Mr. DayoAwosika, Mrs. Glory Ogugua, Mrs. Hajo Ali Daggash, Arch. Charles Egbudom, Pharm. NimiAbili, Engr. Kalada Tobin, Arch. IliyaZangoTabakwot, Mr. Ibrahim Shehu, Mrs. Elizabeth Ogundayo, Mr. John Ode Ogboji, Mr. Paschal Essien, Mr. NsikakArchibong.

My College of Medicine, University of Lagos (Medilag) family: Dr. Ime Isa, Dr. AnietieAkpan, Dr. Jude Ughovwa, Dr. Remi Olaosun, Dr. Ugo Osuji, Dr. Irikefe Edu, Dr. Ajibayo and Dr. FunkeAdeyeye, Dr. Olumide Amos-Oluwole, Dr. Sola and Dr. BukiAdeyemo, Dr. AjikeOladoyin, Dr. Greg Onwueme, Dr. JibrilAlhassan, Dr. AbayomiAjigini, Dr. AsongalemiFortaboh,Dr. BiodunBadewa, Dr. EbeleChira, Dr. Remi Banjoko, Dr. NnekaNdiomu, Dr. Vincent Ahonsi, Dr. LawalSolarin, Dr. GbengaOdubela, Dr. Sola Adeyemo, Dr. BolajiPopoola (Oyebanjo), Dr. BayoFapohunda, Dr. Tony Nwabudike, Dr. SegunDosunmu, Dr. IretiFajolu, Dr. Dupe PopoolaAdemola, Dr. Ezi Abigail Akaji, Dr. AbduljalilAdebesin, Dr. Victor Odunlami, Dr.

OlumideAnifowoshe, Dr. NafisahWali, Dr. Olusegun Sholanke, Dr. Deji& Dr. WunmiSorinmade, Dr. JideAjetunmobi, Dr. Bisi Alder Ogunbase, Dr. Adebayo Okesola, Dr. AgwuUgochukwuUmahi, Dr. DapoOshinowo, Dr. Beatrice Egbeogu, Dr. TemisanEtikerentse, Dr. YinkaAdeyinka, Dr. DuroAkindutire, Dr. Yusuf Habeebu, Dr. Enitan Ibrahim, Dr. Susan Dim, Dr. Loretta Ugwueke, Dr. AbisoyeOyenaike, Dr. BodunOluwadare, Dr. KejiKuteyi Akin, Dr. Aide & Dr. KumbiOnime, Dr. Adebayo Adeyemi, Dr. NgoziIfezue, Dr. ChinyereEkechukwu, Dr. BabatundeAriyibi, Dr. OmotayoBolu, Dr. Raqibat Idris, Dr. Cyril Adegbulu, Dr. IjeomaIbeleme, Dr. GbengaDaini, Dr. Michael Afolayan, Dr. Chidozie David Ibeh, Dr. LanreSomorin, Dr. Ayo Ajim, Dr. Aderibigbe, Dr. DamilolaOyebajo, Dr. SegunOkeowo, Dr. BunmiOgunsanwo, Dr. UjuIbekie, Dr. IdowuAjiboye, Dr. TokunboShangobiyi, Dr. Oladapo Gabriel Awodein, Dr. ToluOlufunlayo, Dr. ToluFagorala, Dr. David BabalolaOlalekan, Dr. Maxwell Adeyemi, Dr. Emmanuel OnomeItobi, Dr. KayodeOgunnaike, Dr. TinuOyekan, Dr. Bode Obayelu, Dr. Demola Hakeem-Davies, Dr. Taiwo Oni, Dr. Olaseni Oyedele, Dr. Wale Oyerinde, Dr. Femi Olufowobi, Dr. Yusuf, Dr. DejiAfilaka, Dr. Adewusi, Dr. Damola Orimolade, Dr. NosaAkpata, Dr. Lanre Esan. Dr. Lola Mabadeje, Dr. YinkaOgunye.

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Above all, to **HIM** who has been faithful throughout all generations!

PROFILE

Professor Kemebradikumo Daniel Pondei

Professor of Medical Microbiology (Virology)

Professor Kemebradikumo Daniel Pondei was born in Lagos to the family of Late Meliyouwei Miepere Pondei and Late Gladys Ere, both of Amassoma, Southern Ijaw Local Government Area of Bayelsa State.

He had his primary education at both the Christ the King Primary School, Oromineke, Diobu, Port Harcourt and State School I, Churchill Road, Port Harcourt. Secondary education was at Federal Government College, Port Harcourt. He was briefly at the University of Benin, Benin to study Dentistry and was later admitted to study Medicine and Surgery at the University of Lagos, Lagos, graduating with the MBBS in 1991.

After housemanship at the Military Hospital, Yaba, Lagos, his National Youth Service was in Lagos, with his place of primary assignment being the Maryland Specialist Hospital, Maryland, Lagos. He was retained after service and spent three years there. He worked at the Cosmoderm Medical Centre, Awolowo Road, Ikoyi, Lagos (1997-1998); Plateau Specialist Hospital, Jos and the General Hospital Langtang, both in Plateau State (1998-2000); General Hospital, Okolobiri, Bayelsa State (2000-2002).

He joined the Niger Delta University as a Lecturer II in February 2002. He obtained a PhD in Microbiology from the University of Nottingham in 2009. Rising through the ranks from Lecturer I, Senior Lecturer, Reader, he was appointed Professor with effect from 1st October 2017.

He was Acting Head, Department of Medical Microbiology and Parasitology (2013-2016); Sub-Dean, Faculty of Basic Medical Sciences (2013-2016); Acting Dean, Faculty of Basic Medical

Sciences (2016 to 2019) and currently the Provost of the College of Health Sciences. He is a Senate Representative in the Governing Council of the Niger Delta University (2017 to date); Chairman, Housing Committee College of Health Sciences (2014 to date).

He was appointed Honorary Consultant Virologist, Niger Delta University Teaching Hospital, Okolobiri in 2010. He has been twice Chairman of the NDUTH Quality Improvement Committee. He is a member of the Board of the Bayelsa Health Insurance Scheme, representing public interest.

He was Editor (2014-2016) and then Chairman (2016-2018) of the Nigerian Medical Association (NMA), Bayelsa State. He is the Chairman of the NMA National Committee on Research Grants (2018-2020).

He is married to Dr. Juliana Okwena Pondei PhD, and they are blessed with three children.

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