

UNIVERSITY OF PORT HARCOURT

**“THE WOMAN, HER REPRODUCTIVE
TRACT AND MICROBES: THE NORMAL
AND THE ABNORMAL”**

INAUGURAL LECTURE

By

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DEDICATION

With humility I dedicate this lecture to;

1. My parents Late Ambassador Daye Obunge and Lady Emma Obunge
2. My mentor, teacher and academic father Late Professor Mario Coluzzi
3. My lovely wife Mrs Jessey Obunge and my children Tari, Soye and Oprite.

The Almighty God and My Saviour Jesus Christ who made all this possible.

ACKNOWLEDGEMENT

In the course of my academic journey I have been privileged to have been mentored by great men of diverse minds; Emeritus Professor Kelsey Harrison and Emeritus Professor Nimi Briggs both past Vice Chancellors of the University of Port Harcourt, Professor Victor Wakwe, Professor Oseikhuemen Ejele, Professor Simeon Nwosu, Professor SNC Wemambu (Deceased), Professor Ralphael Oruamabo, Professor Kanu Nkangineme and Professor Osaretin Ordia.

I acknowledge Dr. Uriah Etawo and Professor Aaron Ojule, past Chief Medical Directors of University of Port Harcourt Teaching Hospital who gave me the enabling environment to carry out the research activities outlined in this book.

I recognize the great minds outside the shores of this country who contributed in moulding my career path, Professor Mario Coluzzi (Deceased) of University of Rome and Professor Anthony Hart (Deceased) of the University of Liverpool.

I recognize all those who collaborated with our Nigeria Research Teams and made research a rewarding experience; in particular, Dr Loretta Brabin of the University of Manchester, Dr Vera Halpern of Family Health International, 360, Research Triangle, North Carolina USA, Dr Julia Kemp, Department for International Development, UK.

I recognize my co-collaborators in Nigeria: Dr Nneka Onyejebu, Nigeria Institute of Medical Research, Professor Sade Ogunsola, University of Lagos, Mr John Umo-otong who inspired me to achieve success and fulfilment in research. I recognize my graduate students especially Linus Ossai-Chidi, a PhD student who is currently part of my research team.

I recognize my colleagues and friends who shared my academic journey; Professor John Ikimalo, Professor Christie Mato, Professor Iyeopu Siminiliayi, Professor Chijioke Nwauche, Professor Nicholas Etebu, Professors Daye Seleye-Fubara, Hakeem Fawehinmi,

Alash'le Abimiku , Dr Tobin-West, Dr 'Seye Babatunde, Associate Professor Patrick Dakum and Mr Charles Mensah amongst others.

I recognize all the members of the following research groups: Women Health Program, Diacore Project, Environmental Health Project, Family Health International (FHI) Research Family.

I recognize the contributions of the consultants (Dr Kennedy Wariso, Dr Tayo Awopeju, Dr Ibinabo Oboro, Dr Mary Alex-Wele, and Dr John Egbagba), Residents and Laboratory Scientists of the Department of Medical Microbiology and Parasitology who have always been part of my story.

I recognize all my siblings; Tonye, Abiye, Boma, Ibifubara, Ibinabo, Belemina, Asemeye and Onimim for their support through these years. I am unreservedly grateful to my parents: late Sir Ambassador and Lady Daye Obunge who gave me a sound foundation based on integrity, honesty and transparency. They introduced me to a rewarding career, sound Christian learning and living.

My heart is filled with gratitude to my wife Jessey and my children: Tari and Dein, Soye and Ralph and Oprite and Jennifer. Thank you for being so patient with me. I acknowledge their immense encouragement, support and love. They have truly been a great pillar.

I am immensely grateful to the University of Port Harcourt, it is my appointment as a lecturer in this institution that put me on this track.

I acknowledge the General Overseer of the Redeemed Christian Church of God, Pastor Enoch A. Adeboye fondly known as Daddy GO and all the Pastors and Ministers of the mission for the privilege and opportunities for spiritual growth, development and service to God.

I am most grateful to my heavenly father, the most High God, who predestined and conformed me to His perfect will; His grace, endowments and providence have made it all possible. I give him praise and adoration.

Preface

This lecture may seem to be technical for some, some may even encounter words that they do not openly use in a public setting. However, because this lecture, looks at the woman, her reproductive tract, the hidden aspects and not so hidden aspects, as viewed through the lens of a Clinical Microbiologist the use of certain terms are inevitable.

I will do my best to use simplified language to pass on information that I consider important to the health of the woman.

ORDER OF PROCEEDINGS

2.45P.M. GUESTS ARE SEATED

3.00P.M. ACADEMIC PROCESSION BEGINS

The procession shall enter the Ebitimi Banigo Auditorium, University Park, and the Congregation shall stand as the procession enters the hall in the following order:

ACADEMIC OFFICER
PROFESSORS
DEANS OF FACULTIES/SCHOOLS
DEAN, SCHOOL OF GRADUATE STUDIES
PROVOST, COLLEGE OF HEALTH SCIENCES
LECTURER
REGISTRAR
DEPUTY VICE-CHANCELLOR [ACADEMIC]
DEPUTY VICE-CHANCELLOR [ADMINISTRATION]
VICE CHANCELLOR

After the Vice-Chancellor has ascended the dais, the congregation shall remain standing for the University of Port Harcourt Anthem. The congregation shall thereafter resume their seats.

THE VICE-CHANCELLOR'S OPENING REMARKS.

The Registrar shall rise, cap and invite the Vice-Chancellor to make the opening Remarks.

THE VICE-CHANCELLOR SHALL THEN RISE, CAP AND MAKE HIS OPENING REMARKS AND RESUME HIS SEAT.

THE INAUGURAL LECTURE

The Registrar shall rise, cap, invite the Vice-Chancellor to make his opening remarks and introduce the Lecturer.

The Lecturer shall remain standing during the Introduction. The Lecturer shall step on the rostrum, cap and deliver his Inaugural Lecture. After the lectures, he shall step towards the Vice-Chancellor, cap and deliver a copy of the Inaugural Lecture to the Vice-Chancellor and resume her seat. The Vice-Chancellor shall present the document to the Registrar.

CLOSING

The Registrar shall rise, cap and invite the Vice-Chancellor to make his Closing Remarks.

THE VICE-CHANCELLOR'S CLOSING REMARKS.

The Vice-Chancellor shall then rise, cap and make his Closing Remarks. The Congregation shall rise for the University of Port Harcourt Anthem and remain standing as the Academic [Honour] Procession retreats in the following order:

VICE CHANCELLOR
DEPUTY VICE-CHANCELLOR [ADMINISTRATION]
DEPUTY VICE-CHANCELLOR [ACADEMIC]
REGISTRAR
LECTURER
PROVOST, COLLEGE OF HEALTH SCIENCES
DEAN, SCHOOL OF GRADUATE STUDIES
DEANS OF FACULTIES/SCHOOLS
PROFESSORS
ACADEMIC OFFICER

PROTOCOL

- The Vice-Chancellor
- Previous Vice-Chancellors
- Deputy Vice-Chancellors (Admin and Academic)
- Previous Deputy Vice-Chancellors
- Members of the Governing Council
- Principal Officers of the University
- Provost, College of Health Sciences
- Dean, Graduate School
- Dean, Faculty of Management Sciences
- Deans of other Faculties
- Heads of Departments
- Distinguished Professors
- Directors of Institutes and Units
- Visiting Academics and Colleagues
- Esteemed Administrative Staff
- Captains of Industries
- Cherished Friends and Guests
- Unique Students of Unique UNIPORT
- Members of the Press
- Distinguished Ladies and Gentlemen.

1.0 Introduction

*Mr. Vice-Chancellor,
Deputy Vice-Chancellors,
Provost, College of Health Sciences,
Chief Medical Director, University of Port Harcourt Teaching
Hospital,
Registrar and other Principal Officers of the University,
Professors Emeriti
Deans of Faculties and Professors,
Distinguished guests of the University,
Colleagues,
My wife and children
Unique Students,
Ladies and Gentlemen*

One of the most daunting tasks about professorial inaugural lectures is that on one hand, one is expected to stimulate almost all of the esteemed audience and on the other, to convince colleagues that one's academic journey has been worthwhile. It is however also an opportunity for one to thank loved ones, friends and colleagues, both senior and junior, whose supports have led one to this moment.

So today is a key milestone of my journey. I will attempt to keep your interest alive as I take you through my journey; my academic journey.

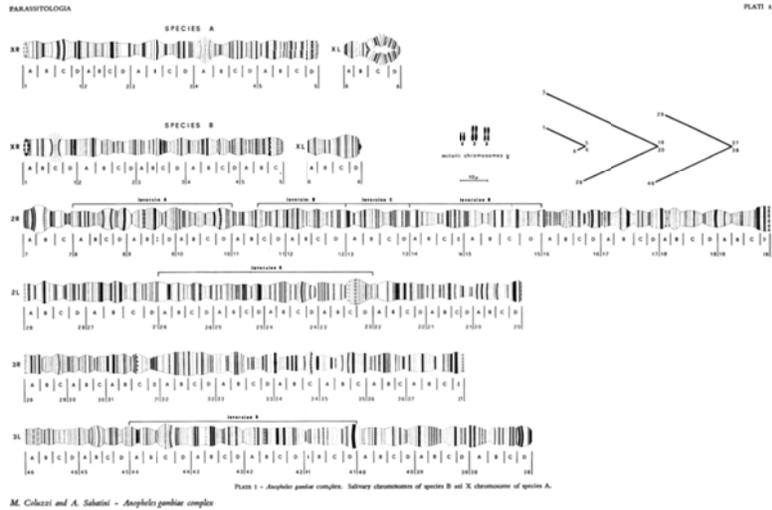
In my early secondary class it was made very clear to me and my teachers that I was going to study medicine. Despite my A grades in General Classics, Latin and Modern Languages, despite the attempt by my teachers to get me a scholarship into Cambridge University, my path was pre-determined. In spite of my attempt at rebellion and my acts of escapade leading to an honours degree in Biochemistry at the Ahmadu Bello University, that was not to be my final path. I eventually found myself at the University of Rome "La Sapienza" applying my knowledge of Latin to learn Italian to study Medicine.

My interest in research really started in 1985, at the end of my third year in medical school after my parasitology examination when a

certain Professor Mario Coluzzi, now late, who was then the Director of the World Health Organization Centre of Malariology in Rome, took an interest in me and began the task of mentoring me. He placed me in a cubicle, gave me a dissecting microscope and convinced me that to be a neurosurgeon, which I had wished to be, I must first learn to dissect a mosquito. That cubicle became my reading place and laboratory throughout my stay at the medical school. By the end of my years in the school, my interest shifted from neurosurgery to pathology and parasitology.



Professor Coluzzi was one of the world's foremost experts on malaria vectors. His research area of focus was medical entomology. He developed a simple and reliable technique to examine polytene chromosomes in the ovarian nurse cells in half gravid female anopheles mosquitoes, and trained scientists from all parts of the world, particularly Africa, to master the technique.



With over 35 years of research in Africa, he unravelled the existence of at least nine cryptic taxa of the complex and demonstrated the existence of high levels of chromosomal polymorphisms which enabled these vectors to colonize different environments.



Emeritus Professor Kelsey Harrison, former Vice Chancellor of the University of Port Harcourt believed in me and introduced me to the Women Health Program of the Liverpool School of Tropical Medicine and Hygiene as a lead Medical Microbiologist, even as a Registrar and Lecturer II, thus diverting my research interest to

Women's Health; I am grateful to this great mentor who taught me by his actions, the act of mentorship.



Emeritus Professor Nimi D. Briggs, former Vice Chancellor of the University of Port Harcourt with an open door policy led the Nigerian research team of the Women Health Programme to incredible heights. He taught me to recognize that the least qualified person in the team may be the one to come up with an idea that may be the next major thrust of the research group. I appreciate all the members of the research team.



The late Professor Anthony Hart, former Head of Medical Microbiology and Genitourinary Medicine of the University of Liverpool believed in my ability to set up a functional quality assurance system even when my initial results from the laboratory

differed significantly from existing data. He taught me to be a Consultant Medical Microbiologist while also being a researcher.



Dr Vera Halpern of FHI research triangle partnered with me as co-principal Investigator in a pioneer four-year, phase three clinical trial on the use of microbicide as a preventive tool against heterosexual transmission of Human Immunodeficiency Virus (HIV). The secondary outcome of the study was to determine the burden of sexually transmitted infections (STIs) in high risk women. The result of that trial has given insight to other research activities that followed in that field globally. I recognize the 70 men and women in Port Harcourt who worked with me on that project. They were all outstanding.



Professor Odia as the head of the Ethical Committee often travelled with the research team to help unravel complex ethical questions that arose in the course of our research efforts. We look forward to his advice as we press forward in our attempt to seek answers to more complex questions.

It is a rewarding experience to work with all my mentees who themselves have become mentors; the members of staff of the department of Medical Microbiology and parasitology and members of the various research teams I have worked with some holding key positions in other research institutions in the country.

**2.0 The topic of this professorial inaugural lecture is
“The Woman, her Reproductive Tract and Microbes; the
Normal and the Abnormal”**

Why Women?

Infections of the reproductive tract, also known as reproductive tract infections (RTI) affect both men and women, but in many cases the complications and consequences they cause can be more severe for women. When the infection is transmitted following sexual intercourse it is known as sexually transmitted infection (STI). A man with a sexually transmitted infection (STI) such as penile discharge is symptomatic in about 98% of the cases and therefore knows he has an infection and with proper health seeking behaviour will get appropriate treatment. However about 50-70% of women with such infections may not know until complications such as

pelvic inflammatory disease and subsequently chronic pelvic pain, ectopic pregnancy and secondary infertility sets in.

The biblical book of Revelation, in chapter 12 describes a battle between the woman, her child, the earth and the serpent. The serpent represents all that can do harm to the woman and her child. There have been many interpretations of this account. I believe one can take it quite literally especially Revelation chapter 12:16:

“And the earth helped the woman”

The earth represents nature as created by God and the immediate environment of the woman including her symbiotic relationship with microbes and their ability to protect and preserve the external part of her reproductive tract thus allowing for the cushioned passage of the baby through the birth canal.

3.0 The Normal Vaginal Flora

The common wisdom of the vaginal flora of the healthy woman of reproductive age is that the lactobacillus dominates the microbiota and the growth of non-indigenous organisms including pathogens is restricted. Although the mechanism is not very clear, glycogen in the lumen of the lower genital tract is an important determinant of Lactobacillus colonization and a high vaginal acidic level.

Unlike the normal flora of the gut, the vaginal flora has a life of its own from birth to menopause;

At birth the passive passage of oestrogen from the mother allows for transient accumulation of glycogen in the vaginal epithelium leading to a predominance of lactobacillus spp. By pre-pubertal age the oestrogen is eventually metabolized leading to a loss of lactobacillus and a shift towards strict anaerobes dominance.

At puberty, increased secretion of oestrogen leads to higher concentration of glycogen, progressive vaginal community shift and at reproductive age, once again there is a dominance of lactobacillus spp.

This association between colonization with *Lactobacillus* and deposition of intraepithelial glycogen has led to the hypothesis that glycogen serves as an important energy source for lactobacilli and their ability to colonize and produce lactic acid in the female lower genital tract. At menopause there is decreased oestrogen, less glycogen, less lactobacillus and less lactic acid.

God has established the normal flora to protect the woman from microbes that can cause harm. When there is a deviation from what God has established, we run into trouble!

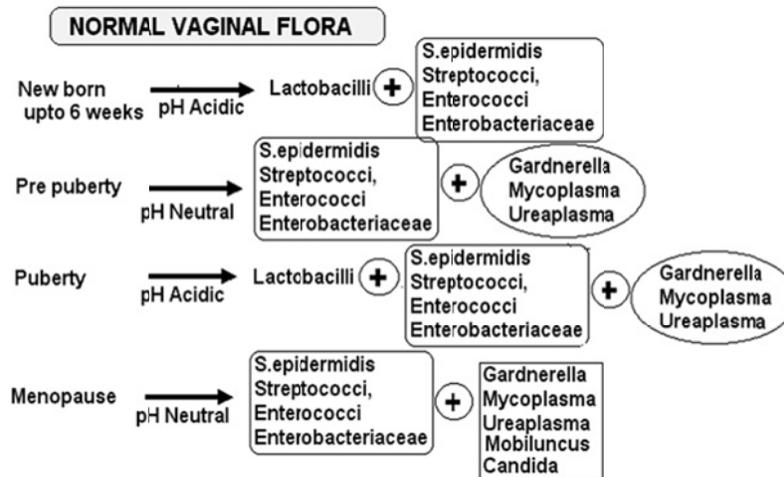


Figure 1: Changing flora of the vagina with age

4.0 The Female Genital Microbiome

4.0 The Female Genital Microbiome

Antonie van Leewenhoek using handcrafted microscopes was the first to notice the diversity of the human microbiota in the year 1680. He noted the striking differences in microbial flora in oral and faecal samples and also between samples from individuals in states of health and disease. Therefore studies of the different types of microbes at different body sites, and between health and disease, are as old as microbiology itself.

We now know that the human microbiota consists of trillions of symbiotic microbial deoxy nucleic acid (DNA) found in each person, primarily in the form of bacteria in the gut; Microbiome projects worldwide have been launched with the goal of understanding the roles that these symbionts play and their impacts on human health.

“What is the human microbiome?”

This remains a question that is yet to be fully answered. The interchangeable use of the word “microbiota” (the microbial taxa associated with humans) and “microbiome” (a collection of microbes and their genes) adds to the confusion of terminology.

The Nugent method is an acceptable approach to appreciate and classify vaginal flora according to morphotypes seen under the microscopes. The Nugent score is calculated by looking for the presence of large Gram-positive rods (*Lactobacillus* morphotypes; decrease in *Lactobacillus* scored as 0 to 4), small Gram-variable rods (*Gardnerella vaginalis* morphotypes; scored as 0 to 4), and curved Gram-variable rods (*Mobiluncus* spp. morphotypes; scored as 0 to 2). The net score can range from 0 to 10. A score of 7 to 10 is traditionally consistent with bacterial vaginosis, a state conventionally considered as “a diseased vagina”.

Table 1: Nugent Classification of Vaginal Communities

<i>Lactobacillus</i> Morphotype (Gram Positive Rods)	Score	<i>Gardnerella</i> Morphotype (Gram variable coccobacilli)	Score	Curved Bacteria Morphotype (Curved Gram negative rods)		Net Score
>30	0	0	0	0	0	0
5 – 30	1	<1	1	<1	1	3
1 – 4	2	1 – 4	2	1-4	1	5
<1	3	5 – 30	3	5-30	2	8
0	4	≥30	4	≥30	2	10

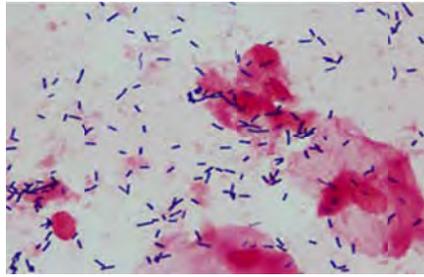
In this manner, we divide the human vaginal communities into three types based on the total net scores:

Type 1 or normal flora: 0-3

Type 2 or intermediate flora: 4-6

Type 3 or Bacterial vaginosis: 7-10

Figure 2: Types of Vaginal Communities according to Nugent Classification.



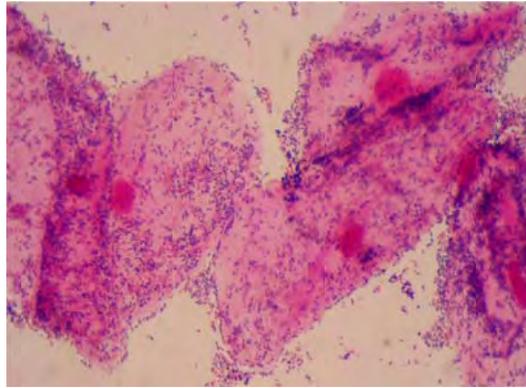
Type 1: Gram stain of vaginal show normal flora



Type 2: Progressive loss of lactobacilli and evidence of mixed flora



Type 3: Absence of lactobacilli and predominance of Gram variable and Gram negative organisms



Type 4 Gram variable microbes surrounding epithelial cells (clue cells)

Type 1 is therefore considered as a normal vaginal community and type 4 as an abnormal vaginal community.

Several types of vaginal communities exist in normal and otherwise healthy women, each with markedly different bacterial species composition.

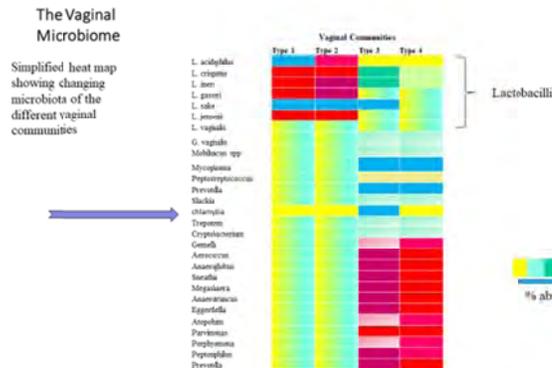
These communities are usually either dominated by one of four common *Lactobacillus* sp. (*L. crispatus*, *L. iners*, *L. gasseri* and *L. jensenii*) or lack significant numbers of lactobacilli, but have a diverse array of strict and facultative anaerobes.

Lactobacillus spp. are gram-positive, highly pleomorphic bacilli, which may appear as Gram positive rod-shaped organisms. There are more than 100 species of *Lactobacillus*.

Lactobacilli produce lactic acid from glycogen which lowers the vaginal pH and suppresses the overgrowth of organisms such as *Mobiluncus*, *Prevotella*, and *Gardnerella vaginalis*.

The level III type dominance of the vaginal community is also known as bacterial vaginosis and may result if the delicate balance between lactobacilli and other bacteria representing the normal vaginal biota is disrupted.

In this context, different types of vaginal microbiota represent different vaginal communities which could be considered ‘healthy’ in the absence of symptoms, with or without lactobacilli, while having differing degrees of predisposition to infection by sexually transmitted pathogens. A young Gynaecologist was asked by his house officer whether to send a vaginal swab to the laboratory or not and his response was “they will always grow something” so why bother. From what has been outlined thus far he is correct. But there is a difference between a laboratory result and a laboratory report.



One of the key roles of the Clinical Microbiologist is to make sense of all the microbes that grow from the sample obtained from the woman, thus separating the “heroes” from the harmful bacteria based on an understanding of not just the laboratory result, not just the scientific knowledge of the role of the microbes but also the clinical presentation of the woman in question. The outcome of this exercise is what is called a laboratory report.

Bacterial vaginosis, currently considered as a vaginal disease, is not therefore a specific microbiological process but rather a spectrum of changes within the bacterial community that makes up the vaginal microbiome.

The microscopic criteria for the diagnosis of bacterial vaginosis should always be supplemented with those proposed by Amsel. The criteria include at least three of the following four characteristics: vaginal discharge with a pH of less than or equal to 4.5, presence of a homogeneous discharge, a fishy amine odour when the discharge is mixed with a potassium hydroxide solution on a slide, and microscopic visualization of squamous epithelial cells surrounded with bacteria (known as clue cells).

5.0 Sexually Transmitted Infections in Nigeria

There are a myriad of sexually transmitted infections that may affect women, as shown below

Table 2: Sexually Transmitted Infections, Associated Symptoms and Treatment.

Disease	How you get it	Symptoms	Treatment
Chlamydia Infection of mucous membranes lining the genitals can lead to inflammatory disease (PID) in women and infertility in men and women.	By having vaginal or anal sex without a condom with someone who has the infection; from mother-to-baby (eye)	Women often have no symptoms or may have pain with sexual intercourse, lower abdominal pain, changes in bleeding pattern. Men may have no symptoms or but usually have watery or thick discharge from penis, pain or urinating.	Antibiotics.
Gonorrhoea Bacterial infection of genitals, throat or anus, can lead to infertility particularly in women.	By having vaginal or anal sex without a condom with someone who has the infection;	Women usually have no symptoms, but may have pain with sex, vaginal discharge, lower abdominal pain. Men may have no	Antibiotics.

Disease	How you get it	Symptoms	Treatment
	from mother-to-baby (eye infections).	symptoms or but usually have discharge from penis, discharge from anus, pain in testicles, pain on urinating.	
Syphilis Bacterial infection entering the body through breaks in skin or linings of the genital area; over time, goes on to damage internal organs (heart, brain, spinal cord)	By having vaginal, anal or oral sex without a condom with someone who has the infection; from mother-to-baby across placenta during pregnancy (congenital syphilis).	Painless ulcer (chancre) usually on genitals; later swollen glands, rash, hair loss.	Antibiotics with follow-up blood tests.
Genital warts <i>Human papillomavirus</i> (HPV) causes fleshy or flat lumps – may be present even if not visible	HPV transmitted by direct skin-to-skin contact, from mother-to-baby. Sometimes no identifiable source of transmission.	Fleshy or flat lumps on or around genitals, anus, groin or thigh.	Visible warts can be treated, but the infection cannot be cured. Patient should be followed up as patient could be at risk for cervical cancer. Discuss vaccination with your health professional.

Disease	How you get it	Symptoms	Treatment
Genital herpes <i>Herpes simplexvirus</i> causes skin infection usually on mouth and lips (cold sores) or on genitals.	Close skin contact with someone with the virus; usually during sex and from mother-to-baby.	Painful, red blisters, little sores or ulcers, flu-like symptoms, and sometimes a vaginal discharge.	Anti-herpes drugs and pain relief can be given to treat symptoms, but the infection cannot be cured. Some may need medication to prevent further outbreaks.
Non-specific urethritis (NSU) Infections that cause inflammation of the urethra.	Can be caused by chlamydia, gonorrhoea or by other bacteria, viruses or other organisms.	Women usually have no symptoms. Men have discharge from the penis, pain on urinating, but sometimes there are no symptoms.	Antibiotics.
Trichomoniasis <i>Trichomonas vaginalis</i> , a small parasitic organism, causes irritation in the vagina in women and can cause an irritation inside the penis in men.	During sexual intercourse with an infected person.	Women may have no symptoms, but there may be a yellowy-green frothy vaginal discharge. Men usually have no symptoms.	Cured by the use of antibiotic tablets and/or vaginal pessaries.
Hepatitis A Viral infection which affects the liver.	Mainly through contaminated food or water or not hand-washing after toilet, before food etc. Can	Often no symptoms, or may have mild flu-like illness, or vomiting, abdominal pain, dark urine and yellowing of the	Immunisation for prevention. Good hygiene and hand-washing. Avoid alcohol and drugs. Eat a well-

Disease	How you get it	Symptoms	Treatment
	be through anal sex and oral-to-anal contact (rimming).	skin and whites of the eyes.	balanced low-fat diet.
Hepatitis B Viral infection which affects the liver.	By having vaginal, anal or oral sex without a condom with someone who has the infection; from mother-to-baby. By sharing needles, syringes, toothbrushes, razors and unsterilized instruments that pierce the skin. Blood transfusion in countries that do not pre-test blood for transfusion.	May have no symptoms or mild flu-like illness or vomiting, abdominal pain, dark urine and yellowing of the skin and whites of the eyes.	Rest, exercise and avoid alcohol, drugs and smoking may control progression and limit complications. Eat a well-balanced low-fat diet.
Hepatitis C Viral infection which affects the liver.	After contact with infected blood or by sharing needles or syringes or possibly through sexual contact. Blood transfusion in	Often no symptoms or may have mild, flu-like illness or vomiting, abdominal pain, dark urine and yellowing of the skin and whites of the eyes.	Rest, exercise and avoid alcohol, drugs and smoking and a well-balanced low-fat diet will control progression.

Disease	How you get it	Symptoms	Treatment
	countries that do no pre-test blood for transfusion.		
HIV <i>Human Immunodeficiency Virus</i> attacks the white blood cells and causes damage to the immune system so that it can be difficult to fight off infections.	HIV is transmitted through blood, semen and vaginal fluids, sharing needles and from mother-to-baby. Blood transfusion in countries that do not pre-test blood for transfusion.	Usually no obvious symptoms for many years. The number of years varies according to individuals. It may range from 2 – 10 years.	No immunisation or cure available although some secondary infections can be treated or prevented. The use of highly active antiretroviral therapy (HAART) has been known to prolong lives.
Pelvic inflammatory disease (PID) An infection of the womb and fallopian tubes that can cause infertility.	Can be caused by chlamydia, gonorrhoea	Pain during sex, sore abdomen or back, heavy, irregular or painful periods, spotting, high temperature, feeling sick; sometimes no symptoms.	Antibiotics and rest.
Pubic lice – crabs Small lice that live in the pubic hair and cause irritation.	By close body contact, usually during sex with an infected person. Can be spread via infected bedding and clothing.	Intense itching in the pubic area, small nits (eggs) on pubic hair.	Special shampoo, cream or spray applied to pubic area. Wash all clothing and bed linen.

Disease	How you get it	Symptoms	Treatment
<p>Scabies Small mites that burrow into the skin cause irritation.</p>	<p>By close body contact, sometimes during sex. Can be spread by sharing clothes or bedding.</p>	<p>Itching, worse at night, and a rash on the body.</p>	<p>Special lotion, cream or ointment. Wash all clothing and bed linen.</p>
<p>Thrush or candidiasis Irritation of mucous membranes from a yeast organism. It can occur in or around the vagina, and on the tip of the penis.</p>	<p>Yeast overgrowth may occur when antibiotics are used, during pregnancy, with diabetes, or when immunity is lowered. It can occur after sex, but also without sex.</p>	<p>Women have vaginal or vulval itching and a thick, whitish vaginal discharge. Men have itching and may have a red rash on the head of the penis or a discharge under the foreskin.</p>	<p>Creams and pessaries for local treatment. Anti-fungal tablets may be given in severe cases. Salt water baths for men are usually effective.</p>
<p>Bacterial vaginosis If the control of the normal bacteria in a healthy vagina fails, an overgrowth of certain bacteria can occur. The acid/alkaline balance is upset and irritation results.</p>	<p>It may be brought on by anything that changes the balance in the vagina, e.g, new sexual partners, increased sexual activity.</p>	<p>Greyish white, smelly vaginal discharge.</p>	<p>Oral tablets and/or vaginal pessaries.</p>

Source: <https://www.healthed.govt.nz/resource-table/table-sexual-health-sti-chart>

Each year, an estimated 500 million people become ill in Africa with one of 4 STIs: Chlamydia, Gonorrhoea, Syphilis and Trichomoniasis.

The classic sexually transmitted diseases enable us to outline the infections responsible for two major types of inflammation that affect the reproductive tract: Vaginitis (inflammation of the wall of the vagina) and Cervicitis (inflammation of the uterine cervix).

The female reproductive organs can be subdivided into the internal and external genitalia. The internal genitalia are those organs that are within the true pelvis. These include the vagina, uterus, cervix, uterine tubes (oviducts or fallopian tubes), and ovaries. The external genital organs include the mons pubis, labia majora, labia minora, Bartholin glands, and clitoris. The area containing these organs is called the vulva.

The vaginal canal and ectocervix are made of stratified squamous non-keratinized epithelium rich in glycogen while the endocervix and cervical canal are made of pseudo-stratified columnar ciliated epithelium which is rich in mucus secretion.

Major pathogens causing STI have selective tropism for either the squamous (vaginitis) or the columnar epithelium (cervicitis).

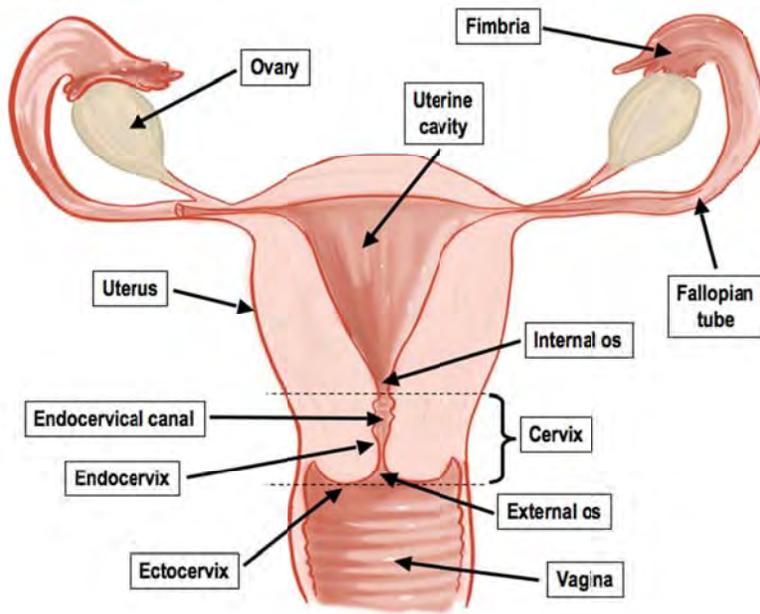


Figure 3: The Female Reproductive tract

Gonorrhoea

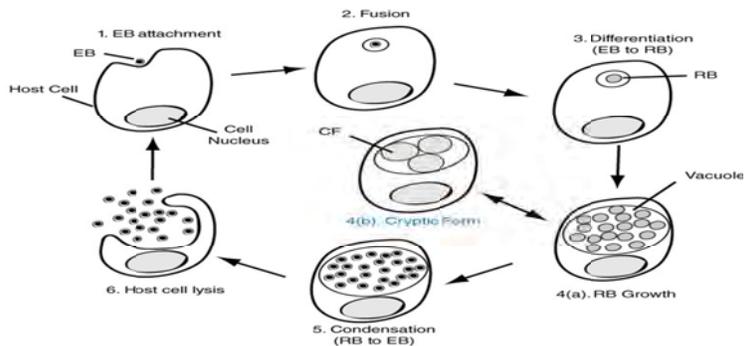
This is caused by *Neisseria gonorrhoeae*, microscopically gram negative diplococci that sometimes appear to be intracellular i.e. located inside the white blood cells. The organism has affinity for the inner lining of the urethra, cervix, throat and the conjunctiva of the eye. It may spread through the bloodstream to other parts of the body, especially the skin and joints.

In women, untreated gonorrhoea may through ascending infection progress from cervical infection which may or may not be symptomatic (abnormal vaginal discharge) to an intermediary outcome of pelvic inflammatory disease to the longer term complications of chronic pelvic pain, ectopic pregnancy and infertility.

The laboratory procedure commonly used for its detection involves an appropriately taken sample depending on the method of identification to be employed, followed by either phenotypic diagnosis which is based on a biological amplification (search for the organism or its products) or molecular methods based on amplification and detection of a target nucleic acid sequence.

Chlamydia

Genital chlamydia is caused by *Chlamydia trachomatis*, an obligate intracellular organism. It is likened to viruses in its intracellular characteristics so cannot be grown in artificial media and like bacteria in certain aspects including its ability to respond to antimicrobial therapy.



The organism has affinity for the columnar epithelium of the cervix. Most women infected with Chlamydia have no symptoms. If untreated a chlamydial infection often like gonorrhoea can ascend to the fallopian tubes, where inflammation may cause pain and scarring which may cause infertility and ectopic pregnancy. Chlamydia may also cause conjunctivitis and lead to neonatal eye discharge.

Laboratory techniques we use for the diagnosis of this infection include enzyme immunoassay (EIA), immune fluorescence (IMF) and molecular methods.

Trichomoniasis

The causative agent is a protozoan, *Trichomonas vaginalis*. It is highly motile and easily diagnosed using wet mount microscopy. It is the most common curable STI affecting women. It may be symptomless but when symptomatic it presents as an itchy purulent vaginal discharge. The infection usually facilitates infectiousness to other STIs including the human immune deficiency virus (HIV).

Candidiasis

A vaginal yeast infection is an infection caused by yeasts (*Candida* species). Vaginal yeast infection is sometimes referred to as *Candida vulvovaginitis*.

Over 90% of vaginal yeast infections are caused by the species known as *Candida albicans*. Other *Candida* species make up the remainder of yeast infections. *Candida* species can be present in healthy women in the vagina without causing any symptoms. In fact, it is estimated that 20% to 50% of women have *Candida* already present in the vagina. For an infection to occur, the normal balance of yeast and bacteria is disturbed, allowing for overgrowth of the yeast. While yeast can be spread by sexual contact, vaginal yeast infection is not considered to be a sexually-transmitted disease because it can also occur in women who are not sexually active. The infection affects up to 75% of women at some point in life.

6.0 At this point, I would like to share some of my contributions from key studies over the last 25 years:

Study 1

- Funding was obtained from Overseas Development Agency (ODA) now Department For International Development (DFID), UK
- Community based prospective study
- Six hundred and eighty four (684) consenting sexually active women enrolled
- Ethical approval obtained

- Laboratory Method: conventional methods with immuno-enzyme assay and immuno-fluorescent microscopy for chlamydia assay

Findings

- 1 in every 10 female aged 17-19 years had genital Chlamydia infection while 1 in every 20 female aged 20-29 years had genital Chlamydia infection
- 1 in every 4 female aged 17-19 years had itchy vaginal discharge due to yeast infection but did not access medical care
- 1 in every 50 female aged 17 -19 years had gonorrhoea infection

Study 2

- Five hundred and fifteen (515) consenting senior secondary school girls from five different schools in Port Harcourt City who self-reported as being sexually active
- Community based prospective study
- Ethical approval obtained
- Laboratory Method: Conventional method with Immuno-enzyme assay and immuno-fluorescent microscopy for Chlamydia assay

Findings

- Mean age 17 years
- 1 in 50 girls had genital Chlamydia infection
- 1 in 50 girls had gonorrhoea
- Only half of the girls with gonorrhoea complained of abnormal vaginal discharge

- Only 10% of the girls with genital Chlamydia complained of abnormal vaginal discharge

Study 3

- Case control Study
- Forty (40) women with pelvic inflammatory disease (PID) and 27 women with no apparent symptom (control)
- Ethical approval obtained
- Laboratory Method: conventional with Immuno-enzyme assay and immuno-fluorescent microscopy for Chlamydia assay

Findings

	PID (LAP, AVD)	Control
Average age	26	26
Chlamydia	12%	4%
Gonorrhoea	0	0
Yeast cells	55%	48%
Bacterial Vaginosis (Type 3 Vaginal Community)	17%	4%

PID - Pelvic Inflammatory Disease;
LAP - Lower Abdominal Pain
AVD - Abnormal Vaginal Discharge

Study 4

- Funded by United States Agency for International Development
- 820 women enrolled
- Self-reported high risk sexual behaviour
- Written consent from all women
- Ethical approval obtained
- Molecular methods for identification of gonococci and chlamydia

Findings

- Mean age of 23 years
- 95% not married
- Average 17 sexual partners in the last three months
- Gonorrhoea- 7%
- Chlamydia- 5%
- Bacterial vaginosis (Type 4 Vaginal Community)- 57%

Table 3: Prevalence Values of STI from various studies (1999-2008)

	Gonorrhoeae	Chlamydia	Trichomoniasis	Candidiasis	BV	Comment
L Brabin, J Kemp, N Dollimore, <u>OK Obunge</u> , J Ikimalo et al. The Lancet, 1995	2.9	4.9	6.2	25.6		Adolescent girls (17-19yrs): Chlamydia 10.5%
J Ikimalo, <u>OK Obunge</u> , <u>S Babatunde</u> et al. Sexually Transmitted Infection, 1999.	2.1	2.1	9.1	-	-	Average Age: 16.8yrs Chlamydia 2.1%
<u>OK Obunge</u> , CT John - African Journal of Clinical and Experimental Microbiology. 2007	0	12.5	10.0	55.0	17.5	Chlamydia prevalence is doubled in PID. BV associated with PID
V Halpern, F Ogunsola, <u>O Obunge</u> , CH Wang et. al. PloS one. 2008	5	2.0	5	25.0	56	High risk group. BV measure of High risk sexual behaviour?

The salient issues arising from these studies were as follows:

1. Chlamydia is an important infection in adolescent girls and young women.

Genital chlamydia is known as the silent epidemic and can linger for months or years and usually recognized through its complications. The question does arise: Should we then screen for Chlamydia in women?

Active case finding for genital chlamydia infection through screening of "at risk" populations can reduce the prevalence of infection if coverage is sufficiently high. The approach for screening for chlamydia in developing countries remains unresolved as the techniques involved requires expensive reagents or kits. The syndromic management of STI is likely to have little impact on chlamydial infections.

Most adolescent infections are asymptomatic and consistent risk markers for repeat infections have not been identified to date. Although not universally supported, the epidemiological treatment of those at high risk could be one such approach. Epidemiologic treatment refers to antibiotics administered when a diagnosis is considered likely on clinical, laboratory, or epidemiologic grounds, but before the results of confirmatory laboratory tests are known. This treatment is justified on the grounds that the potential benefits of treating the patient outweigh the potential harm of not treating. Fear of overtreatment in this case is a major reality. The question remains largely unresolved.

We need to start looking at the Know-Do gap. Knowing the science is one thing to address the factors that hinder us from putting it into practice is another. Implementation research is an important tool to help us move forward.

2. The second issue arising from the data is that Type 3 vaginal community is significantly associated with PIDs and is common in women with self-reported high risk sexual behaviour.

In our studies we observed that woman can present with all possible types of vaginal communities and still be asymptomatic therefore it may well be that the different types may represent states of being at risk for infection. To attempt to answer this question we looked at the immunologic responses elicited in the various types of vaginal communities.

Local Immunological response and the vaginal microbiota

The research team designed studies to understand the role of innate immunity such as cytokine production in the reproductive tract of the woman

We know that in the early stage of local immunological response to the reproductive tract infection, activated macrophages produce a large quantity of cytokines. Rather than systemic immunity, local immunity is critical for protection against infection. Many clinical studies have reported elevated production of pro-inflammatory interleukins such as TNF- α , IL-6 and IL-8 in women with reproductive tract infections. The local production of cytokines is important for the regulation of immunity in the genital tract.

Age, ethnicity, reproductive hormones, nutrition, socioeconomic and psychosomatic stress, physical fitness and exercise, and diurnal variations have all been suspected to be factors in the regulation of cytokine networks but the influence of this network on the female genital tract is rarely studied.

My research team therefore carried out studies to examine the role of the cytokines in the various vaginal microbial communities.

The sample size was 100. The stages recognized using the Nugent classifications were the normal stage 0-1, the intermediate stage 2-3, the BV (Type 3) stage 4-6 and the BV (Type 4) stage 7-10. The cytokines TNF α , IL-10 and IL-2 were assayed using the ELISA method.

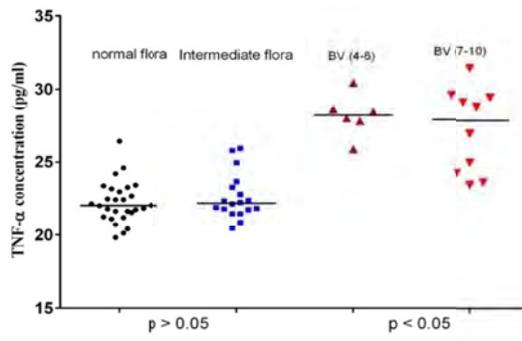


Fig 4: Graphical Representation of TNF- α activity

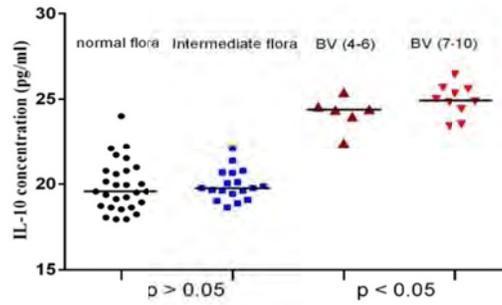


Fig 5: Graphical Representation of IL-10 activity

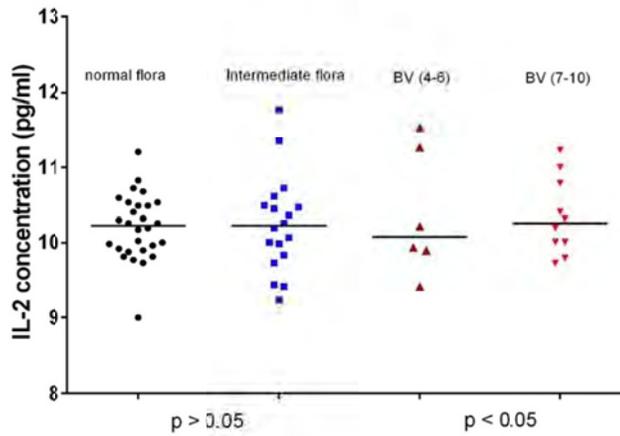


Fig 6: Graphical Representation of IL-2

It is possible that the more a woman's vagina becomes more bacterially diverse, the more its immune response, including the secretion of inflammatory chemicals, leading to local accumulation of immune cells. On the other hand we believe that the increase of TNF alpha, a pro-inflammatory cytokine with concomitant increase of IL10 an anti-inflammatory cytokine seen in asymptomatic women defines a state of risk of the vaginal milieu to inflammation rather than a state of disease.

We also looked at the level of these cytokine when the vaginal canal was colonized by yeast. We believe that the concomitant elevated levels of TNF- α and IL-10 in yeast colonization observed in our studies is an important factor in preventing a systemic spread of the infection.

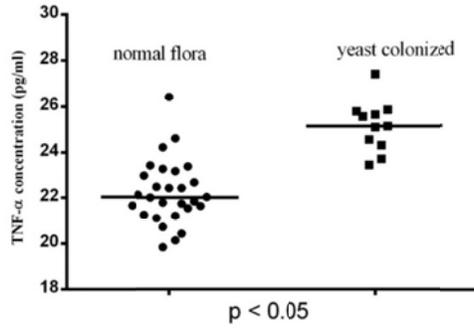


Fig 7: Graphical Representation of TNF- α activity in Candidiasis

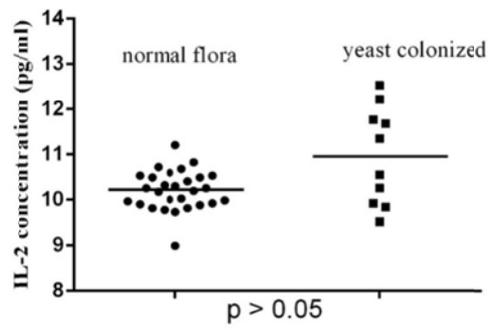
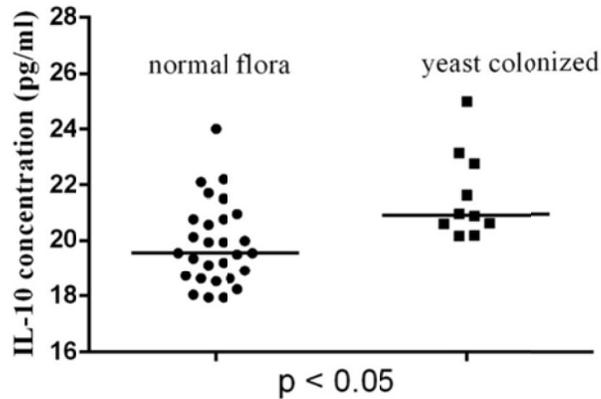


Fig. 8: Graphical Representation of IL-2 activity in Candidiasis



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7.0 Other than Scientific Successes

Mr Chairman, one of our major achievements from these grants and projects is what I call “other than scientific successes”. Beyond the primary scientific outcome of a research project we have been able to

- Through the earlier studies, the team revitalized the health services of K-Dere in Ogoni land. The community responded by conferring a chieftaincy title on the then team lead (then Professor Nimi Briggs).
- Established a rural research post in K-dere which was subsequently used by the university in training its medical students in their community health postings.
- Through the grant facilitated three persons, non-Nigerians to register with their universities in the UK and obtained PhDs.

As a Principal Investigator I was able to

- Develop a new level of collaboration between the academic communities, non-governmental organizations, Community based organizations and policy makers leading to a better understanding of research, its ethics and implementation.

- Upgrade our departmental facilities of medical microbiology to partake in molecular biology-based research thus attracting more collaborative research.
- Facilitate the sponsored training of both technical and academic staff of this university outside and within the country leading to increased skills for independent research.
- Develop community mobilization models and strategies and the lessons learned have contributed to the global pool of resources in the area of STI/HIV/AIDS prevention strategies, research ethics and laboratory management.

Conclusion and Recommendation

The next decade of systems biology and epidemiologic research on the vaginal microbiota is expected to lead to antibiotic-sparing strategies designed to manage, modulate, and restore a robust vaginal microenvironment and ultimately improve the health of the woman and her child.

Vice Chancellor Sir, I believe our work and the global recognition of our work places us, the researchers, this University and Nigeria in a position to be at the cutting edge of research in this area of interest. We must however be prepared to play that role.

I therefore make these recommendations:

- The university should consider establishing a reproductive health institute with multi-sectorial, multi-professional involvement that span from medical anthropology to medical sociology to ethics, from molecular research to implementation research to medical science. Implementation research should be a key agenda.
- Transfer of higher level molecular tools such as gene level sequencing should also be an important focus for the linkage program of this University.

Having done all, Vice Chancellor Sir we too can be part of that prophesy of Revelation 12:10

“And the earth helped the woman”

REFERENCES

- Brabin L, Kemp J, Obunge OK, Ikimalo J, Dollimore N, Odu N, Hart C A, Briggs N D.(1995). Reproductive tract infections and abortion among adolescent girls living in rural Nigeria, *Lancet*. 345:300-304.
- Feldblum PJ., Halpern V, Lie C, **Obunge O** , Ogunsola Ampofo FW, Opoku K.(2011) What predicts non-retention in microbicide trials? (2011) *Contemporary Clinical Trials* 32:512–516
- Halpern V, Lie C1, Feldblum P, Van Damme L, Weaver M, Mauck C, Guédou F, Mirembe F , Govinden R, **Obunge O**, Ogunsola F.(2011)Predictors of Pregnancy in Microbicide. *Contraception*83:436–440
- Halpern V, **Obunge O**, Ogunsola F, Otusanya S, Umo-Otong J, Wang C, Mehta N. (2009). Interim data monitoring to enroll higher-risk participants in HIV prevention trials *BMC Medical Research Methodology*doi: 10.1186/1471-2288-9-44
- Ikimalo J, **Obunge OK**, Babatunde S, Ikoku-Wonodi C, Briggs ND, Kemp J, Dollimore N, Brabin L, Agbaje O, Hart CA (1999). Sexually transmitted infection among Nigerian adolescent schoolgirls. *Sexually Transmitted Infections*.75:121
- Halpern V, Ogunsola F, **Obunge O**, Wang C, Onyejebu N, Oduyebo O, Taylor D, McNeil L, Mehta N, Umo-Otong J, Otusanya S, Crucitti T, Abdellati S. (2008). Effectiveness of Cellulose Sulfate Vaginal Gel for the Prevention of HIV Infection: Results of a Phase III Trial in Nigeria. *PLoS ONE*, 3:e378
- Obunge OK**, Awah I, Onyejebu N.(2006) Prevalence rate of syphilis among pregnant women attending antenatal care in a teaching hospital. *Nigerian journal of Genitourinary Medicine*6:28-30
- Obunge OK**, Brabin L. (1995)The stimulus of research for development of microbiological services - an example from Nigeria. *Africa Health*. May Suppl: viii - ix.
- Obunge OK**, Brabin L, Dollimore N, Kemp J, Ikoku-Wonodi C, White S, Briggs ND, Hart CA. (2001) A flowchart for managing sexually transmitted infections in Nigerian

- adolescent females. *Bull World Health Organ.* 2001; 79(4):301-305
- Obunge OK**, John CT. (2007). The role of genital Chlamydia infection in acute pelvic inflammatory disease in Port Harcourt. *Africa Journal of Clinical and Experimental Microbiology.* 89:23-27
- Obunge OK**, Umo-otong JC, Onyejebu N. (2006). Premarital HIV screening by faith-based organizations in Rivers State Nigeria. *Nigerian Journal of Genitourinary Medicine* 6: 43-45
- Ossai-Chidi LN., **Obunge OK.**, C. Nnadi, Awopeju ATO, Alex-Wele MA (2016) Expression of Cytokines in Vaginal Secretion of Women with Yeast Colonization *BMRJ.* 16(4): 1-5
- Ossai-Chidi L, **Obunge OK**, Oboro LI. (2017) Comparison of Local Cytokine Expression in Vaginal Secretions of Women with Normal and Abnormal Microbiota. *International Journal of Medical Sciences and Technology.* 7(3):18.
- Taylor DJ, Lie C, Weaver MA Tolley E , Van Damme L , Halpern V , Feldblum P , Ogunsoola F, **Obunge O**, Ramjee G , Alary M, Mirembe F.(2011). Notes on the Frequency of Routinely Collected and Self-Reported Behavioral Data in HIV Prevention Trial. *AIDS Behavior*15:389–395



PROFESSOR ORIKOMABA KORIFAMA OBUNGE

[B.Sc (ABU, MD (Rome), Ph.D (Rome), FWACP, FIIA]

Orikomaba Obunge was born to Sir Ambassador Daye and Lady Emma Obunge both of Abonnema, Rivers State, Nigeria.

He completed his secondary education at Brighton College, Brighton, England. His University Education started at the Ahmadu Bello University Zaria where he studied Biochemistry from 1976 to 1979. He proceeded to the University of Rome to study Medicine and Surgery(1982-1989).

In Medical School, Prof Obunge obtained distinctions in various courses earning him a degree in Medicine and Surgery with summa cum laude.

He returned to Nigeria late 1989 and was accepted as Lecturer 11 at the Department of Medical Microbiology and Parasitology of the University of Port Harcourt in 1991. He completed his fellowship in Laboratory Medicine (sub-speciality Medical Microbiology) in 1997

being the first to do so in that field at the University of Port Harcourt Teaching Hospital.

In 1996 on invitation from his mentor and MD supervisor Professor Mario Coluzzi, he initiated a Ph.D. program in Public Health which he completed during his sabbatical leave in 2009.

Professor Obunge early in his career as a resident doctor followed a path in reproductive health and venereology while also actively contributing to the hospital service as clinical microbiologist.

He has been a consultant to many organizations including Crowns Agent UK, Department for International Development UK, United State Agency for International Development (USAID), Pathfinder International, Liverpool Associates in Tropical Health, Family Health International Research triangle USA, Society for Family Health and World Health Organization.

His consultancy activities resulted in significant contribution to the development of sexually transmitted infection and tuberculosis program in Nigeria. Professor Obunge has been a member of many state and national technical committees; chairman of the State STI technical working group, chairman of the State global fund Project Committee and a member of several national technical committees including STI technical working group, HIV technical working group, HIV research policy development committee, National tuberculosis technical working group, and Viral Haemorrhagic Fever steering committee amongst others.

While on Sabbatical in 2009, he was Director of Clinical Laboratory services at the Institute of Human Virology Nigeria where he had oversight function over 98 laboratories all over Nigeria offering free HIV support to those infected with HIV as well as free tuberculosis management to those who are in need of it. On his return to Rivers State he was instrumental in negotiating for free HIV treatment to be available at the University of Port Harcourt Teaching Hospital, a service to the people of Rivers State.

Within the University he was head of the Department of Medical Microbiology and Parasitology for several years where he trained a pool of professionals who now hold senior positions in this University including the immediate past and present heads of department. He has been a member of several university committees. Professor Obunge has supervised many post graduate projects including fellowship projects, MSc and PhDs. He has also assessed several persons for the Professorial cadre from Nigerian Universities and has been external examiners to many universities. He is also a reviewer of several journals. One of the unique aspect of the work of Professor Obunge is that most of his literary works are outcomes of grants from various international bodies.

The outcome of the research works have been widely presented in conferences globally including united kingdom, United States, Canada, Italy, Australia, India, South Africa and Nigeria.

Outside the academic world, Professor Obunge is a Pastor of the Redeemed Christian Church of God.

He is married to Jessey, an educationist and has three children all married and has two grandchildren.

Mr Vice Chancellor Sir, Colleagues, Ladies and Gentlemen, I present to you an honest gentleman, a scholar, a researcher par excellence, a teacher, a Pastor, a husband and a father Professor Orikomaba Korifama Obunge.

Professor N. E. S. Lale
Vice-Chancellor