"BE FRUITFUL AND MULTIPLY"

THE TURBULENT JOURNEY OF UNCERTAINTY

BY INFERTILE COUPLES

THE 134TH INAUGURAL LECTURE OF UNIVERSITY OF NIGERIA

DELIVERED ON THURSDAY MAY 10, 2018

BY

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OUTLINE

1. **PROTOCOL**
2. **BIBLICAL PERSPECTIVE OF CHILDBEARING**
3. **ATTACHMENT PLACED ON CHILDREN AND CHILDBEARING (NIGERIAN PERSPECTIVE)**
4. **WHAT CHILDLESS WOMEN GO THROUGH**
5. **WHAT DOES IT TAKE TO GET PREGNANT**
6. **BEST TIME TO GET PREGNANT**
7. **FECUNDITY**
8. **INFERTILITY**

    A) **Definition**

    B) **Causes of infertility**

    C) **Investigations**

    D) **Treatment options**

        a) **Traditional**

        b) **Modern**

        c) **Future**

PROTOCOLS

The Vice Chancellor, Professor Benjamin Chukwuma Ozumba

- Deputy Vice chancellors
- Other Principal Officers of the University
- Members of the University of Nigeria Governing Council
- Provost college of Medicine
- Deans of Faculties, Postgraduate School and student Affairs
- Directors of institutes and centres
- Professors and other members of the University Senate
- Past Inaugural Lecturers
- Heads of Departments and other Academic Colleagues
- Members of Administrative and Technical Staff
- Members of my Family, Nuclear and Extended
- My Lords Spiritual and Temporal
- Distinguished Guests
- Gentlemen of Print and Electronic Media
- Great Unmsites
- Lions and Lionesses

- Ladies and Gentlemen

I am very grateful to Almighty God for guiding every step climaxing with this inaugural Lecture: the 134th Inaugural lecture of University of Nigeria and the fourth from the Department of Obstetrics and Gynaecolgy. The first lecture from the department delivered by our indefatigable VC, Professor B.C. Ozumba focused on "Improving maternal Health in developing countries" while Professor U.I. Nwagha in the second lecture explored "Motherhood from conception to reproductive Annihilation". Professor H.U. Ezegwui in the third lecture looked at "The human drama of contraception". The three lectures were very captivating and contain far reaching ideas.

While I stand here before you as the 4th Obstetrician and Gynaecologist to deliver an inaugural lecture in our great University, I have come thus far by standing on the shoulders of giants. To this end, I must acknowledge my teachers in the department namely Professor W. Chukudebelu, Late Dr. G. Uche, Professor V.E. Egwuatu, Late Professor Uchenna Megafu, Late Dr. P.C. Nweke, Dr. P.C. Gini, Late Professor G.C. Iloabachie, Late Dr. J.M. Okaro, Professor A.C. Ikeme, Professor B.C. Ozumba and many others for stimulating my interest in the field of Obstetrics and Gynaecology quite early in my medical student days.

After my NYSC, I was opportune to work as a medical Officer with an orthopaedic Surgeon in Aba and my interest in orthopaedics heightened while dampening my earlier interest in Obstetrics and Gynaecology. I was already discussing with my boss in the hospital on how to write Primaries in surgery. This euphoria however, was short lived following an incident involving a 12 year old girl referred to us as an emergency. According to her parents, she had corrective surgery for genu varum (bow leg) at the referral hospital and after the surgery POP

was applied to the leg and the surgeon travelled for the week end. In the wee small hours the blood supply to the leg was compromised because the POP was very tight and the leg became gangrenous. The young girl eventually had above the knee amputation of the leg in our hospital. The emotional impact of that singular event was a turning point in my career resulting in my switching back to Obstetrics and Gynaecology without consulting with my boss and he felt disappointed when I left to do residency in Obstetrics and Gynaecology.

My six year residency period was greatly influenced by 2 academic giants in the department of Obstetrics and Gynaecology namely Late Professor G.C. Iloabachie who taught me the basic principles of surgery and most of the surgical skill I acquired. His surgical skills was second to none and with him the surgical field was always very clear and all structures within can easily be identified. The second person is Professor B.C. Ozumba who taught me the rudiments of paper writing and stimulated my interest in research and academic life. His singular impact in my academic life is the reason why I am standing before you today delivering this lecture.

Mr. Vice Chancellor Sir, it is with great humility and honour that I stand before you and members of the university community to deliver this 134th edition of the inaugural lecture of this great University titled:

"Be fruitful and multiply" The Turbulent Journey of Uncertainty by Infertile Couples. It is indeed a moment to reflect on problems of infertility in our environment

Introduction

At creation God said; "Let us make man in our image, after our likeness: and let them have dominion over all the earth". So God created man in his [own] image. And God blessed them and said unto them: "**Be fruitful and multiply, and replenish the earth, and subdue it**: [1]. Ever since God issued this command, man has known no rest until this biblical injunction is fulfilled.

The word "**fruitful"** signifies fertility while "**multiply"** refers to the reproduction of the human species. It is when this ability to reproduce ones kind fails that the adventure of infertile couples in the domain of the Gynaecologist begins.

ATTACHMENT PLACED ON CHILDREN AND CHILD BEARING IN NIGERIA

There is no doubt that children are indeed a blessing and one of the God's purposes for creation.

Among the Igbo population in Nigeria, children are pivotal in marriages as is evident from some common Igbo names given to the child like:

Nwakego, a child is more valuable than money

Chinenyenwa- child is a gift from God

Nwabu-uwa - a child is the entire world to me

Nwabugwu _ child is a thing of prestige and honour

Childless marriage is always a source of conflict in the family and more often than not the woman takes the bulk of the blame as is often said that her womb is unable to produce fruit. This is because it is generally believed that every womb must bear "fruit".

It is not uncommon to find engaged couples putting their marriage on hold until the female prove her fertility by becoming pregnant. Until this happens the position of a wife in her husband's family remains unstable, unpredictable and she is often an object of conversation and ridicule. This is further compounded by the fact that the extended family and the society in general absolve the man who often tells his wife to go and see a doctor to sort out her fertility problem. Most often these husbands will even refuse to carry out basic investigations requested by the Gynaecologist.

WHAT CHILDLESS WOMEN GO THROUGH IN MARRIAGE

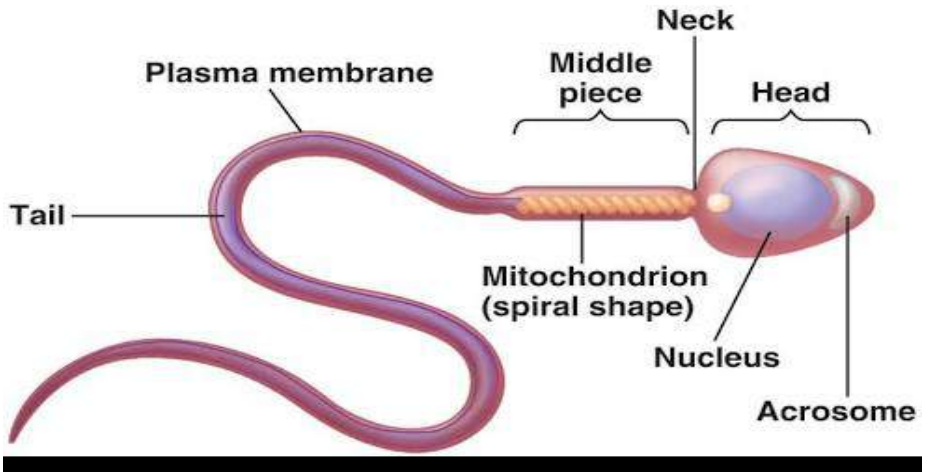
In many cultural settings, childless women suffer humiliation, stigmatization and often are considered as persons of less value than ones with children [2]. They are also exposed to domestic violence especially sexually related violence as reported in our study that evaluated factors associated with domestic violence in south east Nigeria[3] . For these childless women their problem is not absence of people to help but that the society does not respect them except when they become mother of children [4]. There is therefore the need for more attention to be paid on the ways in which the experience of infertility is shaped by social context [5]. The story below will illustrate what women pass through during the period of their childlessness.

Mrs. ABK has been married for 7 years without a child and her husband's relatives have made life unbearable for her because of her childless status. She became an object of ridicule as she kept jumping from one prayer house to the other praying for a child commonly referred to as the "**fruit of the womb"**. Her husband further compounded her problem by not only been on the side of his relations but he also refused to visit the clinic with her. All the medical investigations she did in the hospital were normal. Post coital evaluation of the husband semen (done without his consent) showed no sperm cells. All effort to get her husband to visit the clinic was unsuccessful as the husband responds is always "**There is nothing wrong with me**". She was under pressure to engage in extra-marital sex which our previous study [6] documented a high rate among infertile women and the commonest reason given by women in the study was procreation and continuity of the family name. For the men however, such extramarital sex was a way to satisfy their unmet sexual need [7]. Mrs. ABK rather than embark on such dangerous adventure however, chose to remain childless until she was eventually thrown out of the husband's house by her husband's family member and a new wife brought into the house. She remarried two years later and till date she is a proud mother of 3 children but her former husband unfortunately still remained childless.

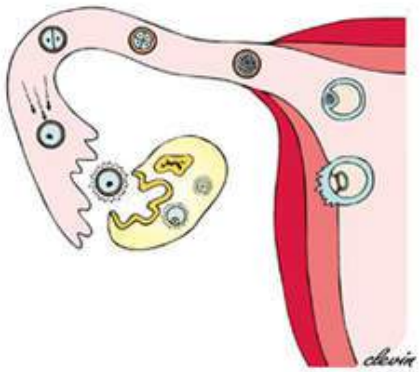
WHAT DOES IT TAKE FOR A WOMAN TO GET PREGNANT

Although conceiving a child may seem to be simple and natural, the physiological process is quite complicated and depends on the proper function of many components as follows:

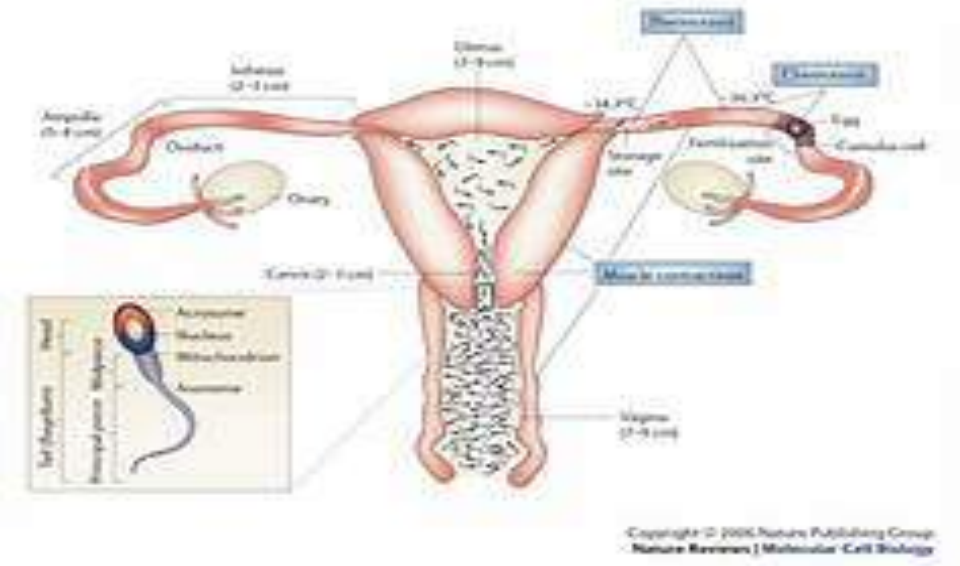
- **Production of healthy sperm by the testes of the man.**



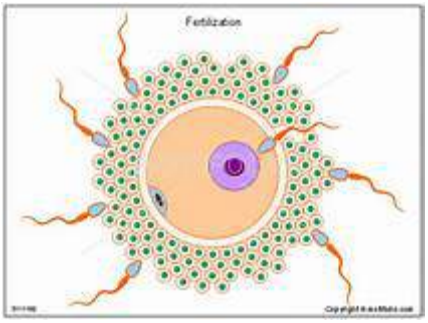
- **Production and release of healthy eggs from either ovaries of the woman**



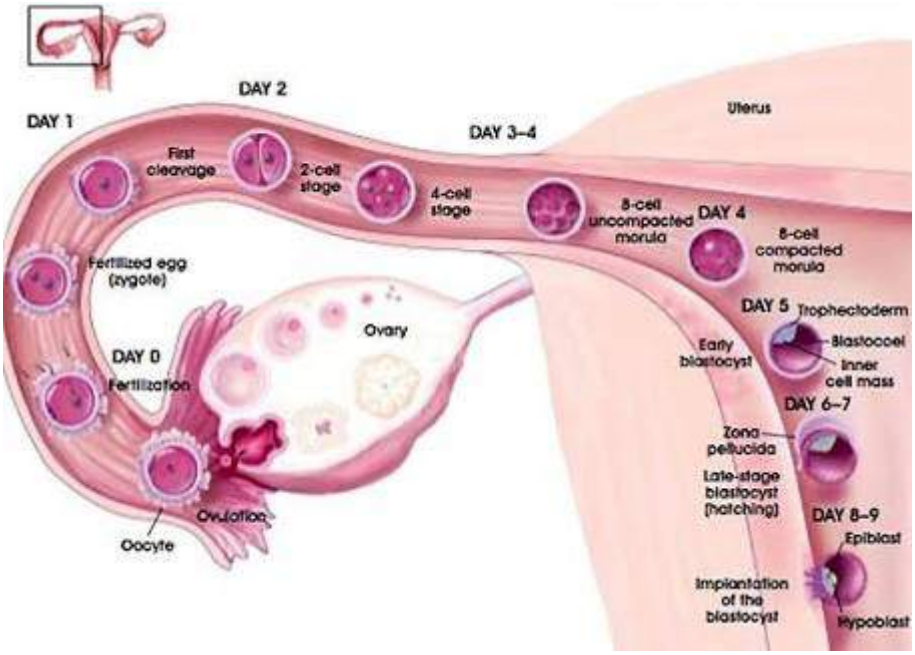
- **Ability of the sperm deposited into the vagina during intercourse to travel through the womb and make contact (fertilization) with the mature female egg in the fallopian tube.**



- Following contact with the egg, the sperm breaks through two barriers surrounding the egg and once it reaches the inside of the egg it sheds its tail and the two nuclei fuse.



- **The fertilized egg (zygote) must go back through a fallopian tube towards the uterus (womb) and get attached to the inside of the uterus (implantation).**



- This zygote begins a process of development that eventually results in the birth of a baby after a period of gestation which is approximately 280 days (40 weeks).

WHEN IS THE IDEAL TIME IN A WOMAN'S CYCLE TO ACHIEVE PREGNANCY

For normal couple, the woman's **menstrual cycle** (interval between the beginnings of one menstruation to the next) is the key determinant of the time for conception to take place. This is because ovulation (release of egg) is dependent on it. For a woman with menstrual cycle length of 28 days, ovulation is most likely to occur mid cycle which is 14^{th} day.

Research has shown that among healthy women trying to conceive nearly all pregnancies occurred following intercourse during a six-day period ending on the day of ovulation[8]. From basic physiology we know that the duration of Sperm survival inside the female genital tract is up to 5 days and an egg can be fertilized for up to 1 day after ovulation [9].

How Long Will It Really Take Newly Married Couple to Get Pregnant

Fecundity is the probability of a woman becoming pregnant within a given period of time.

For couples ready for child bearing, the odds of getting pregnant are shown in a study we carried out among Igbo women [10].

In this study, we interviewed 331 women with planned pregnancies on the time it took them to achieve pregnancy. Of the 331 women in the study, 294 (89%) achieved pregnancy in the first year. The breakdown showed that:

26 percent were pregnant after 1 month.
53 percent were pregnant after 3 months.
70 percent were pregnant after 6 months.
77 percent were pregnant after 9 months.
89 percent were pregnant after 12 months.

"Our conclusion was that the time to conception among Nigerian Igbo women demonstrated a high fertility and this was in agreement with an earlier study [11]. And after a year of trying without conceiving, there is need for the 11% who did not conceive to see a fertility specialist.

INFERTILITY

Infertility is defined as the inability of couple to achieve pregnancy (conceive) after 12 months of frequent, regular (at least 3 times weekly), **unprotected sex (intercourse).** The single most important factor affecting the chances of achieving pregnancy is the timing and frequency of intercourse. This is important because it is not uncommon to find couples coming to the infertility clinic after one year of marriage complaining of infertility when in actual fact the couple reside in different cities and only have coitus when the husband visits which is mostly on weekends.

For women who are 35 years of age or older, we will start evaluation after six months of unsuccessful attempts at pregnancy. This is because from 35 years approximately 9.1% of the remaining follicles (egg) in the ovaries disappear annually [1 2, 13].

Other reasons include:

- Her ovaries find it increasingly difficult to release eggs.
- Most of the eggs left behind are unhealthy.
- She is more likely to have health conditions that can affect fertility.
- Her chances of pregnancy loss or **miscarriage** increases [13]. Our study on pregnancy loss among Nigerian women showed that 30 percent of them were above 30 years and most of them suffer some level of depression especially when there is no living child[15].

It is therefore not surprising that the peak age incidence of women who presented for infertility in our study were within the age group of 30-39 years[16].

Infertility is primary if the couples have never achieved pregnancy, while secondary infertility is the inability to get pregnant after an earlier pregnancy.

Infertility is a universal issue existing in virtually all countries. In Britain the reported prevalence of infertility was 12.5 percent among women and 10.2 percent among men[17]. Levels vary widely within and between countries. The incidence was 26.8% in Lagos (south west) [18] , 15.7% in Sokoto (North west) [19], while in the study we carried out in this institution (south east) the prevalence of infertility was 12.1% with primary infertility constituting about a third (28.4%) [16]. Primary infertility is the most common type world-wide, but in Sub-Saharan Africa (Nigeria inclusive) more infertile couples suffers from secondary infertility. According to WHO[20], more than half of the infertility cases in Africa are due to genital tract infection involving both male and female. From our studies the risk factor for secondary infertility include STI from risky sexual behavior [21, 22], chorioamnionitis from prolonged membrane rupture [23] and unbooked obstetric emergencies[24]. Provision of proper information on reproductive health according to our studies will invariably result in reduction of in risky sexual behavior and STI prevalence[25, 26].

Female/male ratio of infertility

In United States infertility affects men as well as women in the following proportion [27]:

- One-third of infertility is due to male factors
- One-third is due to female factors.

- Another one-third is combined male/female factors or the problem cannot be identified

However, our study[16] showed that infertility was due to female factors in 32.1% of couples, male factors in 26.1% of couples, and a combination of male and female factors in 29.4% of couples. The cause of infertility could not be determined in 12.4% of couples. The level of unexplained infertility varies from place to place and is dependent on the level of technology available in each place.

Since both the husband and the wife have a stake in issues of infertility, it becomes very necessary for both of them to seek medical help.

Psychological stress and infertility

There is no doubt the heightened importance of parenthood affects infertile couples' adjustment to infertility. It has been shown that 18% of men and 16% of women have significant psychological distress including high level of depression and somatization [28]. For these women the coping strategies were perceptive personal control, optimism that they would eventually have a child and intensity of motivation to have a child [29]. The infertility related distress is more on women with high income because this failure is a crisis for someone who is used to having control over her environment and equally meeting goals set for her [30]. For the men they display impaired self-esteem and inadequacy in relation to their societal role as well as feeling guilty for denying their wives a child [31]. This later aspect of the men feeling are often not shown physically because of our culture and environment. The psychological stress in men is further worsen by

sexual performance anxiety and the pressure to time intercourse to the woman' ovulation. Ultimately erectile dysfunction, frustration and marital disharmony set in.

CAUSES OF INFERTILITY

Male factors: This will include**:**

(A) Sperm abnormalities:

Types of Abnormal Sperm

- **Normozoospermia**: Describes normal sperm parameters.
- **Oligozoospermia**: when sperm **count is lower** than normal.

  It can further be described as mild, moderate or severe oligozoospermia.
- **Asthenozoospermia**: Describes abnormal sperm **motility**. Normal sperm should move in a progressive direction. This is in a straight line or very larger circles.
- **Teratozoospermia**: Describes **abnormally shaped** sperm. Normal sperm have an oval head with a long tail. Abnormally shaped sperm affect the ability of the sperm to reach and penetrate an egg.
- **Oligoasthenoteratozoospermia**: Is when all sperm parameters (**count, movement, shape**) are abnormal.
- **Azoospermia**: when there are **zero s**perm in the ejaculate.
- **Necrozoospermia**: when all the sperm are either **dead or non-moving.**
- **Leukocytospermia**: when there is **high WBC** count in the semen. It indicates possible infection.

- **Hypospermia**: when the **total ejaculate is low**, or less than 1.5 milliliters of fluid.

Sperm Morphology and motility

The shape (morphology) of a sperm is an important determinant of its ability to fertilize the female egg (**fertilizability).** In addition the sperm must be vigorously motile

The protein that covers the female egg (zona pellucid) determines the sperm that will fertilize the the egg on the basis of the above two factors.

Therefore, nature has evolved a way to keep abnormally shaped sperm from getting inside the egg and thereby maximizing the genetic development potential of the embryo.

(B) Ejaculation problems due to:

- Premature ejaculation (semen is discharged before or immediately after penetration)
- Retrograde ejaculation, which occurs when the semen is forced back into the bladder
- Erectile dysfunctions (very weak or no penile erection). This has a prevalence of one in six infertile men [32].
- Failure of ejaculation (anejaculation)

Risk factors for infertility in men

These affect fertility in men by reducing sperm count and/or motility

- **Anti-inflammatory drug** eg Sulfasalazine used in treatment of rheumatoid arthritis.
- **Anabolic steroids** used commonly by bodybuilders and athletes.

- **Chemotherapy (anti-cancer drugs)**.
- **Illegal drugs (marijuana)**.
- **Age**: Male fertility starts to fall after 40 years.
- Exposure to **chemicals** (Pesticides)
- **Excess alcohol** consumption. Moderate alcohol consumption has not been shown to lower fertility in most men, but it may affect those who already have a low sperm count.
- **Obesity:** Obesity causes alteration in hormone profile **(↑estrogen**), increase scrotal temperature which impair semen parameters (sperm count, motility etc) [33].

- **Stress:** Stress will activate the release of glucocorticoid that affect the metabolism of carbohydrate, protein and fat which could **reduce testosterone** level and sperm production. It also triggers oxidative stress-physiological stress on the body caused by damage from **unneutralized free radicals**-which has been associated with semen quality and fertility [34].

Causes of infertility in women

The following increases a woman's risk of infertility:

- **Age** as explained earlier.
- **Smoking**. This is associated with prolonged and dose-dependent adverse effect on ovarian function [35].

- **Excessive alcohol** use. (The excessive sugar in alcohol decreases fertility by contributing to hormonal imbalance, insulin resistance etc). It is associated with altered levels of estrogen and progesterone and irregularities in menstrual cycle and ovulation [36].
- **Extreme weight gain**. Weight reduction in this group of women leads to high spontaneous conception rate [37].
- Risky sexual behaviour. [21, 22]
- Exposure to some chemical (pesticides, herbicides, metals, such as lead, and solvents)
- Stress: This may affect female ovulation and can lead to reduced sexual activity.

(A) Ovulatory disorders

Ovulatory disorders can be due to:

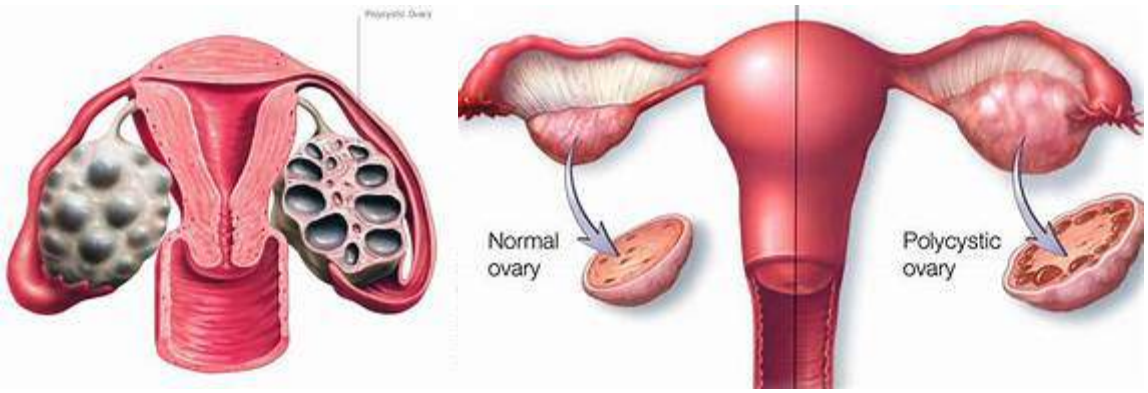
➢ Hyperprolactinemia (Excess prolactin in the bloodstream)

This hormone allows for breastfeeding after giving birth. An elevated level outside the period of breastfeeding suppresses the menstruation and prevents ovulation. Our recent study showed that hyperprolactinemia is the commonest cause of anovulatory infertility [16].

➢ Pituitary hormone dysfunction

Ovulation relies on a balance between two hormones (FSH and LH) secreted by the pituitary gland which are important for follicular growth and ovulation. If the pituitary gland doesn't release enough of either one of these hormones, or if the balance is disturbed, the egg follicles may fail to develop and ovulation will not occur.

➢ Polycystic Ovary Syndrome (PCOS)



In this condition, a number of tiny cysts usually begin to form on the surface of the ovaries. The hormone imbalances (elevated androgens and reversal of the FSH/LH ratio) that occur as a result affect the rate at which the ovarian follicles develop and therefore prevent ovulation. PCOS is fairly common occurring in approximately one in six (17%) infertile Nigerian women in Enugu [38] and in the southwest Nigeria it was present in 12.2% of women during pelvic ultrasound [39]

- **Luteinized unruptured follicle syndrome (LUFS)**

Although the follicle matures and makes its transition into corpus luteum (the progesterone-releasing structure), ovulation (release of the ovum or egg cell) did not occur. It's thought that this often occurs in conjunction with endometriosis [40].

- **Premature ovarian failure/ Premature Menopause**

All the egg follicles in each individual are present at birth and it will continue to be depleted with each ovulation and will start to run out as menopause approaches. The average age of menopause in our environment according to our study is 49.4 [41, 42] but in some women it begins before 35 years (Premature menopause). The early depletion of

these follicles resulting in anovulation (absence of ovulation), amenorrhoea may be due to genetic disposition, effect of radiation therapy, chemotherapy etc. with premature ovarian failure the women occasionally menstruate but they cannot get pregnant naturally.

- **Obesity/ Being underweight**

Fatty tissue plays an important role in managing hormone levels. Consequently, a high level of body fat can **trigger hormone imbalances leading to ovulation problems** and this has been shown to be detrimental for fertility [43]. For the obese women who ovulate and eventually become pregnant the complications that follow such pregnancy will further impair future fertility [44]

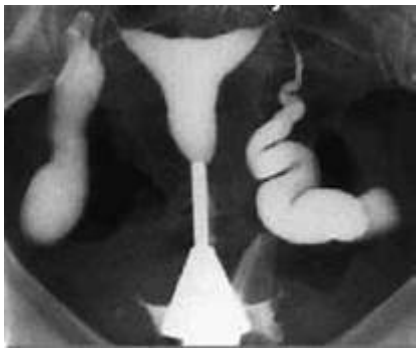
Being on the slim side is one thing, but extreme weight loss from crash dieting, severe stress, and eating disorders like anorexia nervosa is dangerous for the entire body, and can disrupt the menstrual cycle. Left untreated, this can result in failure to ovulate or even no menstruation at all.

- **Other potential causes** of irregular or absent ovulation:

- Extreme exercise
- Thyroid dysfunction (hyperthyroidism)
- **Ovarian cysts**. The role of cysts in infertility is controversial. It appears that the effects of surgical treatment are often more harmful than the cyst itself to the ovarian reserve [45].

- **Scarred Ovaries** from physical damage to the ovaries from multiple surgeries may result in failed ovulation.

(B) Tubal/Peritoneal factor (picture of blocked tubes)



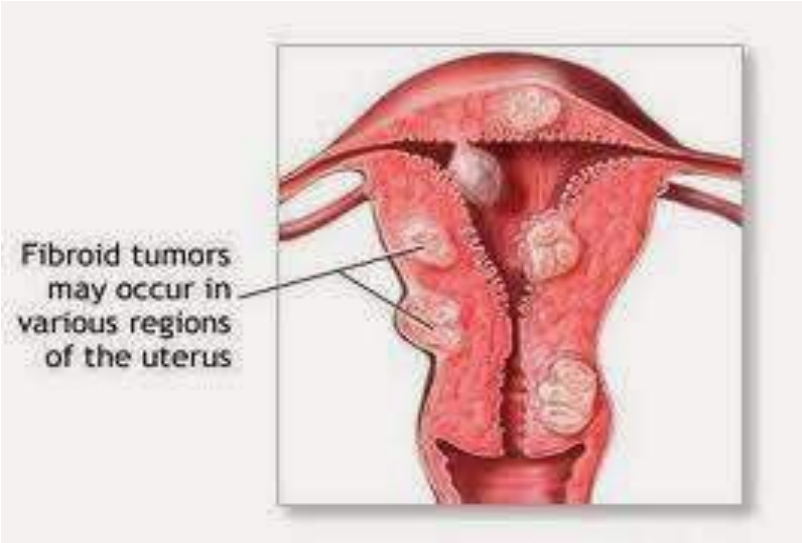
This is the commonest cause of female infertility in our environment [46].

Risk factors for blocked fallopian tubes (tubal occlusion) can include a

- History of pelvic infection which distort the pelvic anatomy because of adhesions. Increasing incidence of sexually transmitted infections, use of IUCD are all predisposing factors [47].
- Ruptured appendicitis,
- Endometriosis, presence of endometrial tissue (uterine lining) outside the uterus. It causes adhesion formation and commonly manifest with chronic pelvic pain of varying degree. It has a prevalence of 4.3% at Enugu [48] and 4.9% at Nnewi [49] and 48.1% at Ibadan [50] among women scheduled for their first diagnostic laparoscopy for gynaecological indications. The incidence of infertility amongst women suffering from endometriosis ranges from 30%-40% [51].
- Previous abdominal surgery with subsequent adhesion formation [52, 53].

(C) Uterine factor

- **Fibroids**



This is an abnormal growth in the womb of women. This womb is supposed to be carrying a baby and if there is delay in carrying a baby, something else would grow there. That is why it is usually said that **"bad girls have babies while the good girls have fibroid"**. If a womb is not carrying a baby, then something else (fibroid) grow there. These fibroid are located in different parts of the womb and they are the most common benign tumours of the genital organs in women of childbearing age [54]. There is a general agreement that submucosal fibroid and intramural fibroid above 4cm in size negatively affect fertility via alteration of local anatomy, functional changes of myometrium and endometrium and finally endocrine and paracrine molecular mechanism [55]. Fibroid is associated with significant morbidity [56, 57] and surgical removal enhances fertility and successful pregnancy outcome [58, 59].

- **Asherman's syndrome** (intrauterine adhesion). It manifest with menstrual irregularities ranging from hypomenorrhoea to amenorrhoea. Here the cavity of the uterus is obliterated making it impossible for the fetus to implant in the endometrial cavity. It is commonly due to a combination of trauma to the endometrium from overzealous endometrial curettage and infection.
- **Others**: anatomic abnormalities (uterine malformation), endometrial polyps, cervical mucus.

Unexplained infertility

In these cases abnormalities are likely to be present but not detected by available methods. In other words, this diagnosis is dependent on the level of equipments available for investigation. So what is unexplained in one institution or country may become explained in another.

Possible causes of unexplained infertility:

- The egg is not released at the optimum time for fertilization
- The egg may not enter the fallopian tube but end in the peritoneal cavity
- Sperm may be unable to reach the egg for fertilization
- Transport of the zygote (fertilized egg) may be disturbed
- Implantation fails.
- Poor egg quality in women of advanced maternal age have reduced capacity for normal and successful fertilization.

INVESTIGATIONS

Semen Analysis.

Preparation for semen collection

- 2-5 days of abstinence
- Semen collected by masturbation into special container
- Collected semen sample needs to be examined in the laboratory within an hour

A typical semen analysis will report on the following parameters with lower Reference limit (WHO 2010) [60]:

- **Liquefaction:** After ejaculation, the sperm sample coagulate and will totally liquefy in 60 minutes
- **PH:** Should be greater than 7.1(7.2-7.8)
- **Semen volume** (1.5 milliliters)
- **Sperm count (**15 million per milliliter)
- **Sperm morphology (**4% with normal shape)
- **Motility** (32% progressively motile).
- **Leucocytes** (less than 1 million)
- **Vitality** (60% live spermatozoa)

It is important to note that one poor result doesn't necessarily mean the man is infertile because semen can be affected by recent illness, anxiety and other factors.

There is therefore the need to order one or two follow-up tests to confirm the results, to see if the abnormality persisted.

Further Male Fertility Testing

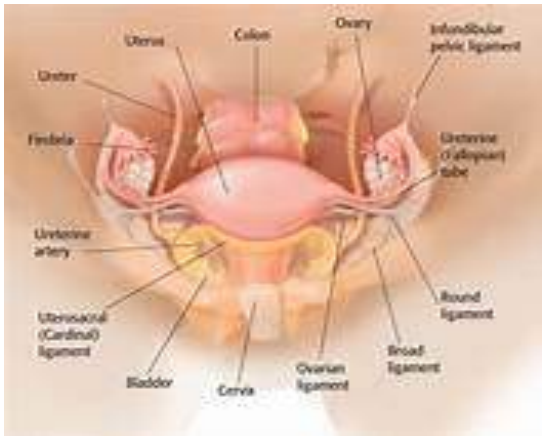
Beyond the basic semen analysis, the doctor may also order the following male fertility test:

- **Hormonal assay levels** including follicle stimulating hormone (FSH), testosterone, luteinizing hormone (LH), estradiol, and prolactin.
- **More advanced semen analysis testing,** which may include Computer Assisted Semen Analysis (CASE), **anti-sperm antibodies testing, sperm DNA testing**, hypo-osmotic swelling testing, and others.
- **Post-coital test** (PCT), to evaluate the sperm interaction with the woman's cervical mucus after intercourse.
- **Genetic testing**, for chromosomal disorders that can cause male infertility
- **Genetic karyotyping,** especially if recurrent miscarriage is occurring
- **Ultrasonography** (Trans rectal, scrotal, or renal). This may reveal issues such as ejaculatory duct obstruction or retrograde ejaculation.

- **Magnetic Resonance Imaging** (MRI) of Pelvic or cranial.
- **Post-ejaculatory urinalysis** (urine testing), to check for retrograde ejaculation
- **Testicular biopsy**
- **Vasography-** an X-ray of the vas deferens to see if there is blockage

FOR THE FEMALE

- **Hormonal assay (FSH, LH, Prolactin, thyroid hormones, Progesterone etc):** This will assess hormone levels in the blood and establish whether a woman is ovulating.
- **Hysterosalpingography (HSG)**: This is a radiological procedure where dye is injected via the cervix (neck of the womb) to visualize the shape of uterine cavity as well as tubal patency. It is very vital in detecting birth canal pathologies [61].
- **Laparoscopy**: A thin, flexible tube with a camera at the end is inserted into the abdomen and pelvis, allowing the gynaecologist to look at the pelvic organs (fallopian tubes, uterus, and ovaries). This when combined with dye test will provide information as to the possible cause/causes of the infertility like endometriosis, pelvic adhesions, tubal blockages, and some irregularities of the uterus, ovaries and fallopian tubes. Laparoscopy has the advantage of detecting peritubal adhesions and other pelvic pathologies that may compromise the functionality of the tubes [62].



- **Hysteroscopy** allows for direct visualization of the endometrial cavity and pathologies like uterine polyps, uterine synerchia, uterine abnormalities etc can be detected and treated appropriately. This procedure can detect significant number of incidental findings missed by HSG [63].

- **Ultrasound**: It is an important tool in evaluation of infertile couple and visualizes the uterus, tubes, and check for ovarian reserve, PCO, tract the egg through growth, to ovulation and after ovulation. Its use reliably, efficiently and cost-effectively assesses female infertility [64].
- **Genetic testing**, to see if a genetic abnormality is interfering with fertility
- **Culture swab** for organisms that affect fertility

TREATMENT

The following will be taken into consideration in deciding the treatment options for the couple:

- Age of the couple especially the female
- Duration of infertility
- Individual preferences after counseling on risks and benefits of each treatment option.
- General state of health of the couple

General advice

- Counseling of the couple which will involve the Gynaecologist, Urologist, Clinical psychologist and a priest.

- The psychological aspect of the infertility need to be discussed with the couple and appropriate advice and treatment given.
- The couples are advised to time intercourse around the period of ovulation bearing in mind the duration of Sperm survival inside the female tract (up to 5 days) and the fact that an egg can be fertilized for up to 1 day after ovulation.
- They should refrain from taking recreational drugs.
- Men to avoid taking long hot showers, using hot tubs and should wear loose underwear such as boxer.

Treatment option for men

Treatment will depend on the underlying cause of the infertility. Often times the treatment of the male partner is handled by the urologist and will only be highlighted here.

- **Erectile dysfunction**: Ejaculation is achieved with electric or vibratory stimulation. Medication, behavioral approaches.
- **Varicocele**: Surgical removal of varicose vein in the scrotum.
- **Blockage of the ejaculatory duct**: Direct surgical sperm aspiration from the testicles and subsequent injection into an egg in the laboratory.
- **Epididymal blockage**: This is repaired surgically to ensure proper transport of sperm.
- **Retrograde ejaculation:** Recovery of the sperm directly from the bladder and its injection into an egg in the laboratory.
- **Medications** to help increase sperm production
- **Infections** are treated with antibiotics

- **Low sperm count/ Azospermia (no sperm cells)** is treated by artificial insemination (AIH or AID). The sperm is collected, treated and manually placed in the female's uterus or fallopian tubes.

  The culture surrounding sperm donation is changing dramatically. Today there is much more openness and sharing of information between the parties involved as opposed to secrecy associated with it in the past. In our study among 180 medical students on use of donated sperm for infertility, it was discovered that their knowledge on the subject matter was very high but it was rather surprising that only about 15% of the male students were willing to donate their sperm [65]

  When we reviewed 200 infertile couples on their acceptability of artificial donor insemination, the acceptability rate was 43% and it was significantly higher among female respondents, women with primary infertility, and those whose infertility had lasted for 5 years and beyond [66].

Intrauterine insemination (IUI):

This procedure involves placing sperm inside the womb of the woman to facilitate fertilization. It is carried out at the time of ovulation and the aim is to increase the number of sperm that reach the tube thereby increasing the chances of fertilization. A fine catheter is inserted through the cervix into the uterus to place a sperm sample directly into the uterus. The sperm undergoes washing and the best specimens are selected subsequently introduce through a fine catheter inserted through the cervix into the uterus.

It is a less evasive procedure with a success rate of 15.6% per treatment cycle [67]. Although it is a cheaper fertility treatment option compared to ART, it must be remembered that couple may need multiple IUI cycles to achieve success.

The woman may be given a low dose of ovary stimulating hormones to ensure that ovulation occurs.

Indications for IUI include the following:

- When the man has a low sperm count,
- When there is decreased sperm motility, or
- When infertility does not have an identifiable cause.
- In cases of severe erectile dysfunction.

Treatment of infertility in women

OVULATION INDUCTION:

In our evaluation and follow up of infertile couple in this institution, it was observed that 24% of the female benefitted from ovulation induction [16]

The following drugs are used:

- **Clomiphene citrate** induces ovulation by acting on the pituitary gland. Has successful induction rate of 81.1% [68].

- **Bromocriptine** is used for women who do not ovulate because of high levels of prolactin. Prolactin is a hormone that causes milk production. Treatment with this drug results in pregnancy rate of 66.7% to 90.7% [69].
- **Human menopausal gonadotropin** or hMG acts directly on the ovaries to stimulate ovulation.
- **Follicle-stimulating hormone** (FSH): It also acts on the ovaries and induces ovulation.
- **Gonadotropin-releasing hormone (Gn-RH) analog**
- **Metformin** is used for women with insulin resistance and/or PCOS. It helps lower the high levels of male hormones in women with these conditions.

The success rate of the ovulation inducing agents varies depending on the cause of the anovulation and the agents used in treatment.

Surgical procedures for women

- **Laparoscopic burning in cases of Endometriotic tissue**. A small incision is made in the abdomen, and a thin, flexible microscope with a light at the end, called a laparoscope, is inserted through it. The endometrial lesions are excised or burned away using high energy heat like laser. Spontaneous pregnancy was achieved in 33.1% of infertile women treated by this method [70].

- **Laparoscopic drilling of ovary** for PCOS. This procedure has 53.5% pregnancy rate among infertile women treated for anovulatory infertility [71].

- **Laparoscopic adhesiolysis** for peritubal adhesions and bilateral hydrosalpinges. The pregnancy rate after adhesiolysis and cuff salpingostomy is up to 35% [72].
- **Hysteroscopic adhesiolysis, polypectomy, tubal cannulation** (for Asherman's syndrome, endometrial polyp or corneal block respectively). When used in treating Asherman syndrome, it has a pregnancy rate of 32% [73].

Assisted reproductive technology (ART)

Assisted Reproductive Technology (ART) is a novel technology which encompasses all fertility treatments in which both eggs and sperm are handled outside of the body. In this procedure eggs surgically removed from a woman's ovaries are combined with the sperm in the laboratory and subsequently returned to the woman's body or donating them to another woman.

Common methods of ART:

- **In vitro fertilization (IVF),** in which fertilization takes place outside of the body and the zygote is transferred back to the womb. This is the most common form of ART.
- **Zygote intra fallopian transfer (ZIFT**) or tubal embryo transfer. This is similar to IVF. Fertilization occurs in the laboratory and the very young embryo is transferred to the fallopian tube instead of the uterus.

- **Gamete intra fallopian transfer** (**GIFT**) involves transferring eggs and sperm into the woman's fallopian tube. Fertilization occurs in the woman's body. Few practices offer GIFT as an option.

- **Intra cytoplasmic sperm injection** (**ICSI**). In ICSI, a single sperm is injected into a mature egg as opposed to "conventional" fertilization where the egg and sperm are placed in a petri dish together and the sperm fertilizes an egg on its own. It is often used for couples with male factor infertility. Sometimes it is also used for older couples or for those with failed IVF attempts.

In vitro fertilization (IVF): The work of **Robert Geoffrey Edwards** (27 September 1925 – 10 April 2013) and the gynaecologist, **Patrick Christopher Steptoe** (9 June 1913 – 21 March 1988) which began in the 1950s, resulted in the first child, **Louise Brown** born on 25th July 1978 as a result of IVF.

There are basically five steps involved in the standard IVF procedure. These are:

1. Stimulating and monitoring the development of healthy egg(s) in the ovaries.
2. Collection of the eggs through laparoscopy.
3. Sperm is obtained from the husband and prepared for mixing with the eggs.
4. The eggs and sperm are combined in the laboratory for fertilization and early embryo growth.
5. Embryos formed are subsequently transferred into the woman's uterus where implantation and foetal growth continues till delivery.

Success rates of IVF/ART vary and depend on:

- The clinic performing the procedure
- Infertility diagnosis

- Age of the woman undergoing the procedure.
- Quality of the woman's egg
- Quality of the sperm
- The receptivity of the endometrium

According to the 2015 IVF Success Rates from National ART Outcome Report in the United States involving 231,936 IVF cycles [74], the success rate in different age group were:

- 47.5% in women less than 35 years of age.
- 39.6% in women aged 35–37 years.
- 28% in women aged 38–40 years.
- 15.7% in women aged 41–42 years.

ART has brought a ray of hope for the infertile couple but unfortunately in Nigeria it is mainly private sector driven and only a few government health institutions currently offers the service. Hence it is still expensive and unaffordable for majority of the populace that needs the service. Despite this the success rate in Nigeria is improving and is currently at 30% [75].

Donor eggs (eggs from another woman), donor sperm, or previously frozen embryos are sometimes used in ART.

Donor eggs/sperm are indicated for

- Those who cannot produce eggs/sperm,
- When the woman or man has a genetic disease that can be passed on to the baby.

An infertile woman or couple may also use **donor embryos.** These are embryos that were either created by couples in infertility treatment or were created from donor sperm and donor eggs. The donated embryo is transferred to the uterus. The child will not be genetically related to either Parent.

Assisted hatching involves making a small hole in the outer membrane of the embryo (the zona pellucid) improves the ability of the embryo to implant into the uterine lining.

The indications are:

- If IVF has not been effective,
- Where there has been poor embryo growth rate
- In older woman where the membrane becomes harder making it difficult for the embryo to implant.

Surrogacy

A surrogate is a woman who agrees to become pregnant using the man's sperm and her own egg. The child will be genetically related to the surrogate and the male partner. Infertile women with unhealthy eggs might also want to consider surrogacy.

Gestational Carrier

In this case, the woman’s egg is fertilized by her partner's sperm and the embryo is placed inside the carrier's uterus. Women with ovaries but no uterus may be able to use a gestational carrier. This may also be an option for women who shouldn't become pregnant because of a serious health problem.

Adoption

This is a process whereby a person assumes the parenting of another, usually a child, from that person's biological or legal parents and in so doing permanently transfers all rights and responsibilities along with filiations from the biological parents [76].

Despite the advances in fertility management, some infertile couples eventually do not achieve a pregnancy. Child adoption is one option available to such couples. In our study of 279 consecutive infertile couples in Enugu on their attitude toward adoption, one- third (33%) of them were disposed favourably to adoption as a treatment option for their infertility especially when the probability of cure of infertility is small [77]. A similar study from Ibadan and Sokoto showed acceptability rate of child adoption to be 17% [78] and 27.2% [79] respectively. The acceptance of adoption as a treatment option in our environment is important as there are many children for adoption. This is further collaborated in our study on unmarried adolescent expectant mothers which showed that majority of them are willing to consider the option of giving up their babies for adoption [80, 81.] However, among poor women and those with limited education the acceptability rate was significantly lower [82].

CONCLUSION

About 50 million couples across the globe are experiencing one form of infertility or the other and majority of them are from developing countries. In Nigeria the prevalence has continued to rise and the most common cause is infection. Addressing the preventable causes of infertility like reducing risky sexual behaviour, educating the populace on the need to avoid going to the quack for abortion and prompt treatment of STI will help reduce infection which contribute significantly to secondary infertility

The availability of ART gives a ray of hope to the infertile couples in Nigeria that childlessness will be a thing of the past as conception moves from bedroom to laboratory. Unfortunately for most women in developing countries, infertility services especially IVF are not widely available and where available, it is not unaffordable to majority of the populace.

Mr. Vice Chancellor Sir, we optimistically look forward to the future where

(a) Fertility treatments become better (with higher success rate), cheaper and more widespread so that the rural/urban populace can easily access it.

(b) With genetic screening pregnancy rates will show remarkable improvement.

(c) More women will freeze their eggs at younger age to preserve their fertility

(d) Stem cells from infertile couple could produce sperm and egg

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To the wonderful audience especially those on the turbulent journey of trying to fulfill the biblical injunction "**BE FRUITFUL AND MULTIPLE**" rejoice for there is light at the end of the tunnel.

To everlasting, immortal, invisible, the only wise God be honour and glory forever and ever.

Mr Vice Chancellor Sir, distinguished audience, I thank you for your attention.

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