**REPORT ON STUDENT INDUSTRIAL WORK EXPERIENCE SCHEME (SIWES)**

**UNDERTAKEN AT ZANKLI MEDICAL CENTRE PHARAMACY**

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CERTIFICATION

This is to certify that this research work was done by **Ereh Deborah Ekojonwa** student of

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CHAPTER ONE: INTRODUCTION

I was posted to the pharmacy department at Zankli Medical Centre Abuja, for my industrial training.

**ABOUT ZANKLI MEDICAL CENTRE PHARMACY**

The Pharmacy at Zankli Medical Centre, like that other departments in the hospital committed to providing first-rate services to our Patients.

The Pharmacy is well stocked with only NAFDAC approved drugs. The drugs dispensed are of highest quality with the aim of giving our patients the best possible care at reliable prices.
With the team of competent Pharmacists and Pharmacy Technicians who are available round the clock, patients are sure that they will receive adequate counselling on how to take their medications. Drug related questions will be answered also.

In the department I had the opportunity of working hand in hand with the chief pharmacist, where I learnt how to:

1. Read and understand doctor’s prescription such as;

b/ds – two times daily

t/ds – three times daily

1. Attended some presentation that talked about new drugs in the market and their effects, and understanding why it is more efficacious than the previous ones.
2. Learn about different drugs in the pharmacy such as anti-malaria drugs, antihypertensive drugs, antidiabetics, anticonvulsant, antibiotics, antiretroviral therapy etc.
3. Had various presentation on some of the drugs such as antiretroviral therapy, antihypertensive, and discuss the next line of drugs and prevention

**DURATION OF WORK**

During my posting to the pharmacy at Zankli Medical Centre, I was instructed to resume work by 9 o’clock in the morning and close by 4 pm in the evening from Monday-Friday. I started my posting on May 3rd and ended August 3rd. ( 3 months).

**SUPERVISOR**

I was supervised by Pharmacist Salamatu Orekwelu, who is the chief pharmacist in the hospital that assigned pharmacist Nishik Ibrahim, to instruct me on what to do during my 3 months training in the pharmacy.

I learnt about various classes of drugs but I will be focusing on Antiretroviral drug in the next chapter.

**HUMAN IMMUNODEFIECY VIRUS (HIV)**

**Epidemiology**: The first two AIDS cases in Nigeria was diagnosed in 1985 and reported in 1986 in Lagos one of which was a young female sex worker aged 13 years from one of the West African countries. The news of this first AIDS case sent panic, doubt and disbelief to the whole nation as AIDS was perceived as the disease of American homosexuals.

Notwithstanding the above misconception by the Nigerian public, since the beginning of the epidemic in the mid-1980s, a total of 220,0000 new HIV infections have been reported in 2014.

Most cases were adults over the age of 15 years. A substantial number of new HIV-infected children (<15 years) was also noted in 2014 (n = 58,000). Notably, previous data had linked the infections of a substantial number of HIV-infected children to their mothers’ infections.

Albeit due to its population size, Nigeria is now the second largest HIV disease burden in the world with 3.2 million after South Africa which has 6.8 million burden of the disease.

**Mode of transmission:**

[HIV](https://en.wikipedia.org/wiki/HIV) is commonly transmitted via [unprotected sexual activity](https://en.wikipedia.org/wiki/Safe_sex), [blood transfusions](https://en.wikipedia.org/wiki/Blood_transfusion), [hypodermic needles](https://en.wikipedia.org/wiki/Hypodermic_needle), and [from mother to child](https://en.wikipedia.org/wiki/Vertical_transmission).

**Can Disease Progression Be Delayed?**

Disease progression may be delayed by:

 • Prevention and early treatment of opportunistic infections (OIs)

• Antiretroviral therapy

• Positive living

**Types of HIV virus**

There are two types of HIV virus:

• **HIV 1** is most common in sub-Saharan Africa and throughout the world. HIV 1 can be divided into groups M, N, and O. The pandemic is dominated by Group M, which is composed of subtypes A – J.

• **HIV 2** is most often found in West Central Africa, parts of Europe and India.

Both produce the same patterns of illness. HIV 2 causes a slower progression of disease than HIV 1. It is important for tests to detect the HIV subtypes that are present in the region. Otherwise, testing may lead to false negative results.

**Pathophysiology:**

* HIV gradually destroys the [immune system](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/347/immune-system/) by attacking and destroying a type of white blood cell called a [CD4 cell](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/113/cd4-t-lymphocyte). CD4 cells play a major role in protecting the body from infection.
* HIV uses the machinery of the CD4 cells to multiply and spread throughout the body. This process, which is carried out in seven steps or stages, is called the HIV life cycle. HIV medicines protect the immune system by blocking HIV at different stages of the HIV life cycle.

Upon acquisition of the virus, the virus replicates inside and kills [T helper cells](https://en.wikipedia.org/wiki/T_helper_cells), which are required for almost all [adaptive immune responses](https://en.wikipedia.org/wiki/Adaptive_immune_system). There is an initial period of [influenza-like illness](https://en.wikipedia.org/wiki/Influenza-like_illness), and then a latent, asymptomatic phase. When the [CD4](https://en.wikipedia.org/wiki/CD4) lymphocyte count falls below 200 cells/ml of blood, the HIV host has progressed to AIDS, a condition characterized by deficiency in [cell-mediated immunity](https://en.wikipedia.org/wiki/Cell-mediated_immunity).

**Symptoms**:

Within a few weeks of HIV infection, flu-like symptoms such as fever, sore throat and fatigue can occur. Then the disease is usually asymptomatic until it progresses to AIDS. AIDS symptoms include weight loss, fever or night sweats, fatigue and recurrent infections.

 CHAPTER TWO: HIV: A GLOBAL PANDEMIC

Since the beginning of the epidemic, 75 million people have been infected with the HIV virus and about 32 million people have died of HIV. Globally, 37.9 million [32.7–44.0 million] people were living with HIV at the end of 2018. An estimated 0.8% [0.6-0.9%] of adults aged 15–49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. The WHO African region remains most severely affected, with nearly 1 in every 25 adults (3.9%) living with HIV and accounting for more than two-thirds of the people living with HIV worldwide.

**HIV epidemic in sub-Saharan Africa**

Sub-Saharan Africa bears the highest burden of HIV infection globally. Notwithstanding success in a growing number of countries with stabilized epidemics and or reductions in new HIV infections, the continued high burden of new HIV infections in South Africa, Swaziland, Lesotho, Zimbabwe, Botswana, Mozambique, Namibia and Zambia contribute to new infections globally.

Globally, 15% of women living with HIV are aged 15-24 years, of whom 80% live in sub-Saharan Africa. In this region where just over 70% of all new HIV infections occur, young women bear a disproportionate burden of HIV infection. Not only do young women aged 15-24 years have HIV rates higher than their male peers, they acquire HIV infection 5-7 years earlier than their male peers. Although there are some declining trends in the 15-24 year age group, HIV prevalence is consistently higher among young women compared to young men throughout eastern and southern Africa.

A geospatial prioritization with targeted HIV prevention services within and between countries could reduce the burden of HIV in sub-Saharan Africa and impact on the global burden of HIV. A better understanding of structural, biological and behavioral factors, including the chains of transmission by applying molecular methods and phylogenetic analysis of HIV-1 sequences could improve the efficient targeting of HIV prevention efforts.

**Testing for viral infection and immune response**

HIV infection can be measured in terms of:

- The amount of virus circulating in the body –called the viral load

- The amount of antigen – p24 antigen – circulating in the body

- Proteins or cells that protect the body against infection – IgG and IgM antibodies, and CD4 cells

**Window period**

Window period is the phase when you have been infected with HIV, but antibody levels are not detectable. One may test false negative for HIV antibodies, and can still pass the virus to others during this period. What occurs during the window period is called Seroconversion:

* “Seroconversion” is a term used to describe the change from non-detectable to detectable antibody levels. Specimen may test initially non-reactive, but change to testing reactive after a certain time period.
* Seroconversion occurs generally 3-8 weeks after the initial infection.

CHAPTER THREE: ANTIRETROVIRAL THERAPY

**7 stages of HIV life cycle:**

The seven stages of the HIV life cycle are:

1. [Binding](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/4597/binding/): The first of seven steps in the HIV life cycle. When HIV attacks a CD4 cell, the virus binds (attaches itself) to molecules on the surface of the CD4 cell.
2. F[usion](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/3320/fusion/): The second of seven steps in the HIV life cycle. After HIV attaches itself to a host CD4 cell, the HIV viral envelope fuses with the CD4 cell membrane. Fusion allows HIV to enter the CD4 cell. Once inside the CD4 cell, the virus releases HIV RNA and HIV enzymes, such as reverse transcriptase and integrase.
3. [Reverse transcription](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/3321/reverse-transcription/): The third of seven steps in the HIV life cycle. Once inside a CD4 cell, HIV releases and uses reverse transcriptase (an HIV enzyme) to convert its genetic material—HIV RNA—into HIV DNA. The conversion of HIV RNA to HIV DNA allows HIV to enter the CD4 cell nucleus and combine with the cell’s genetic material.
4. [Integration](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/381/integration/): Once inside the host CD4 cell nucleus, HIV releases integrase, an HIV enzyme. HIV uses integrase to insert (integrate) its viral DNA into the DNA of the host cell.
5. [Replication](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/1648/replication/): Once HIV is integrated into the host CD4 cell DNA, the virus begins to use the machinery of the CD4 cell to create long chains of HIV proteins. The protein chains are the building blocks for more HIV.
6. [assembly](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/4593/assembly/): During assembly, new HIV RNA and HIV proteins made by the host CD4 cell move to the surface of the cell and assemble into immature (non-infectious) HIV.
7. [Budding](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/814/budding/): The final step of seven steps in the HIV life cycle. During budding, immature (non-infectious) HIV pushes itself out of the host CD4 cell. (Non-infectious HIV can't infect another CD4 cell.) Once outside the CD4 cell, the new HIV releases protease, an HIV enzyme. Protease breaks up the long protein chains in the immature virus, creating the mature (infectious) virus.

Treatment

HIV can be suppressed by combination ART consisting of 3 or more ARV drugs. ART does not cure HIV infection but suppresses viral replication within a person's body and allows an individual's immune system to strengthen and regain the capacity to fight off infections.

In 2016, WHO recommended that all people living with HIV be provided with lifelong ART, including children, adolescents and adults, and pregnant and breastfeeding women, regardless of clinical status or CD4 cell count. By mid-2019, 182 countries had already adopted this recommendation, covering 99% of all people living with HIV globally.

**Antiretroviral therapy**

 There are 5 classes of ART known as:

1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
2. Non-nucleoside reverse transcriptase inhibitors (NNRTI)
3. Protease inhibitors (PI)
4. Entry Inhibitors
5. Integrase inhibitors

**Mechanism of action: Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**

The NRTI class of antiretroviral drugs are chemical compounds that are nucleotide base analogues. They function as chain-terminators during the extension of the DNA chain during the reverse transcription process which is carried out by HIV reverse transcriptase. The NRTI compounds permit correct base-pairing and incorporation into the DNA chain, however, an important hydroxyl group required for addition of the next nucleotide has been replaced by a non-reactive chemical group.

With the exception of Tenofovir, the NRTI compounds that are taken up by the cell do not contain phosphate groups and require three phosphate groups to generate the triphosphate form of the base analogue before it can be used as a substrate by reverse transcriptase. Tenofovir contains a single phosphonate group to which only two phosphate groups need to be added to generate the active compound. The additional phosphorylation is carried out by host cellular enzymes (kinases).

**Mechanism of action : Non-nucleoside reverse transcriptase inhibitors (NNRTI)**

The NNRTI class of antiretroviral drugs are small hydrophobic chemical compounds that have high affinity for a hydrophobic binding pocket located near the active site of HIV reverse transcriptase. Binding of the drug to the enzyme results in a change in structural conformation of important residues required for optimal ability of the enzyme to catalyse DNA polymerisation.

**Mechanism of action: Protease Inhibitors (PI)**

The protease inhibitors are small chemical compounds that mimic the natural peptide substrate of the enzyme, but do not allow for a cut to be made due to chemical modifications. Binding of the inhibitor to the active site of the enzyme prevents the enzyme from targeting its natural substrate since the inhibitor can only be released from the enzyme after the substrate has been cleaved.

**Mechanism of action: Integrase Inhibitors (**Raltegravir)

Integrase enzyme brings about the insertion of HIV DNA into human DNA, thereby helping to hide HIV’s DNA inside the host cell’s DNA (see figure 1). Once this provirus is formed the cell begins producing genetic material for new viruses. Raltegravir inhibits integrase from performing this essential function limiting the ability of the virus to replicate and infect new cells, thus preventing HIV DNA from meshing with healthy cell DNA (see figure 2). There are drugs in use that inhibit two other enzymes critical to the HIV replication process – protease and reverse transcriptase – but Raltegravir is the only drug approved that inhibits the integrase enzyme. For this reason Raltegravir is a significant milestone in the history of HIV/AIDS therapy.

**Mechanism of action: Entry Inhibitors**

Entry Inhibitors interfere with the receptor-mediated entry of the virus into a cell. Two subclasses known as “fusion inhibitors” and “CCR5 antagonists”, are new classes of antiretroviral drugs used in combination therapy for the treatment of HIV infection.

This class of drugs interferes with the binding, fusion and entry process of HIV into a human cell.

Entry inhibitors**(a) Subclass: fusion inhibitor (eg. Enfuvirtide)**

**MOA**

The FDA approved fusion inhibitor Enfuvirtide is a peptide chain that mimics the structure of the HR2 region of gp41 that binds to the HR1 region and facilitates fusion of the viral envelope with the cell membrane. Binding of the inhibitor to the HR1 region prevents the HR2 region from access to HR1 and inhibits the fusion process.

Entry inhibitors**(b) Subclass: CCR5 antagonist (eg. Maraviroc)**

**MOA**

The recently FDA approved CCR5 antagonist Maraviroc is a small chemical compound that binds to the external part of the CCR5 transmembrane receptor that serves as the co-receptor for virus entry. Binding of this inhibitor to CCR5 prevents HIV gp120 from access to the co-receptor and prevents the fusion process involving gp41 from proceeding.

 **Some short-term side effects from Antiretroviral Therapy**

People starting an HIV medicine for the first time may have side effects that last a couple of weeks. These short-term side effects can include:

* Feeling tired
* Nausea (upset stomach)
* Vomiting
* Diarrhoea
* Headache
* Fever
* Muscle pain
* Occasional dizziness
* Insomnia

**Some long-term side effects from Antiretroviral Therapy**

Some side effects from HIV medicines can appear months or even years after starting a medicine and can continue for a long time. Examples of long-term side effects include:

* Kidney problems, including kidney failure
* Liver damage ([hepatotoxicity](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/776/hepatotoxicity/))
* Heart disease
* [Diabetes](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/202/diabetes/) or [insulin resistance](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/791/insulin-resistance/)
* An increase in fat levels in the blood ([hyperlipidaemia](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/785/hyperlipidemia/))
* Changes in how the body uses and stores fat ([lipodystrophy](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/417/lipodystrophy-syndrome/))
* Weakening of the bones ([osteoporosis](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/815/osteoporosis/))
* Nerve damage ([peripheral neuropathy](https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/563/peripheral-neuropathy))

**CONCLUSION**

My experience at Zankli Medical Centre was a memorable one. All my fellow I.T colleagues were easy to work with; my supervisors were very strict but in a good way that benefited me at the end. Assignment and presentations were given to me every 3 weeks to improve my understanding on broad classes of drugs like antiretroviral therapy. Every Mondays we usually go on rounds with the chief pharmacist, and the doctors usually throw random questions at us to test our knowledge. I found this very helpful because it kept me on my toe throughout my stay at the pharmacy.

**REFRECENCE**

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