NATIONAL OPEN UNIVERSITY OF NIGERIA

SCHOOL OF SCIENCE AND TECHNOLOGY

COURSE CODE:HEM 726

COURSE TITLE:CLINICAL, DIAGNOSTIC AND THERAPEUTIC SERVICES OF HIV/AIDS

COURSE GUIDE

HEM 726
CLINICAL, DIAGNOSTIC AND THERAPEUTIC SERVICES OF HIV/AIDS

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Introduction

HEM 726: Clinical, Diagnostic and Therapeutic Services of HIV/AIDS is a 2-credit course for PGD HIV/AIDs Education and Management and related disciplines

The course is broken into four modules and 12 study units. It introduces the students to basics of HIV/AIDS, types and structure of HIV, HIV modes of transmission as well as replications in HIV. It will further highlight clinical manifestations of HIV as well as several assessment techniques. Furthermore, students will be equipped with classical methods of diagnostic of HIV and finally, it will equip students with various management techniques for HIV/AIDS.

At the end of this course, it is expected that students should be able to understand, explain and be adequately equipped on issues of clinical, diagnostic and therapeutic services of HIV/AIDS.

The course guide, therefore, tells you briefly what the course: HEM 726 is all about, the types of course materials to be used, what you are expected to know in each unit, and how to work through the course material. It suggests the general guidelines and also emphasises the need for self assessment and tutor-marked assignment. There are also tutorial classes that are linked to this course and students are advised to attend.

What You Will Learn in this Course

The overall aim of this course, HEM 726, is to introduce students to the variables associated with clinical, diagnostic and therapeutic services of HIV/AIDS. During this course, you will learn about the concepts of HIV/AIDS, its diagnosis, clinical manifestations as well as its management techniques.

Course Aim

This course aims to give students an in-depth understanding of clinical, diagnostic and therapeutic services of HIV/AIDS.

Course Objectives

Note that each unit has specific objectives. Students should read them carefully before going through the unit. You may want to refer to them during your study of the unit to check on your progress. You should always look at the unit objectives after completing a unit. In this way, you can be sure that you have done what is required of you by the unit.

However, below are the overall objectives of this course. On successful completion of this course, you should be able to:

Illustrate the basics of HIV/AIDS
Understand structure and types of HIV
Define HIV modes of transmission as well as its replications
Illustrate HIV and the immune system
Understand clinical manifestations of HIV/AIDS
Describe various HIV testing techniques
Identify various management techniques of HIV/AIDS

Working through this Course

To complete this course, you are required to read the units, the recommended textbooks, and other relevant materials. Each unit contains some self assessment exercises and tutor marked assignments, and at some point in this course, you are required to submit the tutor marked assignments. There is also a final examination at the end of this course. Stated below are the components of this course and what you have to do.

Course Materials

The major components of the course are:

2.0 Course Guide

Study Units

There are 12 study units and four modules in this course. They are:

Module 1 HIV/AIDS: Definition, Transmission and Replication

Unit 1 HIV/AIDS: Basics
Unit 2 HIV/AIDS: Structure and Types
Unit 3 HIV/AIDS: Modes of Transmission
Unit 4 Replication in HIV/AIDS

Module 2 HIV/AIDS: Clinical Manifestations

Unit 1 HIV/AIDS and the Immune System
Unit 2 Clinical Manifestations of HIV/AIDS
Unit 3 Clinical Manifestations/Assessment of HIV/AIDS

Module 3 HIV Testing

Unit 1 HIV Rapid Testing (Principle and National Algorithm)
Unit 2 Classical Methods of Diagnostic of HIV Infection
Unit 3 Classical Methods of Diagnostic of HIV Infection (II)

Module 4 Management Techniques of HIV/AIDS

Unit 1 Pharmacological management of HIV/AIDS
Unit 2 Eclectic Management Technique for HIV/AIDS

Textbooks and References

These texts will be of immense benefit to students:

Baron S. (1996). *Medical Microbiology*, 4th Edition. The University of Texas Medical Branch at Galveston.

Burton R.W. Engelkirk P.G., (2000). *Microbiology for the Health Sciences,* 6th edition. Lippincott Williams & Wilkins.

Irwin, A., Millen J. and Fallows, D. (2003). *Global AIDS: Myths and Facts.* Cambridge, MA: South End Press.

Lucas, K. and Lloyd, B. (2005). *Health Promotion.* SAGE.

Melia, K. M. (2004). *Health Care Ethic*. SAGE.

Parker, R. (2006). *Global Public Health.* Routledge.

UNAIDS (2002), *Report on the Global HIV/AIDS Epidemic*. Geneva: UNAIDS.

Assignment File

The assignment file will be given to you in due course. In this file, you will find all the details of the work you must submit to your tutor for marking. The marks you obtain for these assignments will count towards the final mark for the course. Altogether, there are 12 tutor-marked assignments for this course.

Presentation Schedule

The presentation schedule included in this course guide provides you with important dates for completion of each tutor marked assignment. You should therefore try to meet the deadlines.

Assessment

There are two aspects to the assessment of this course. First, there are tutor marked assignments; and second, the written examination.

You are thus expected to apply the knowledge, comprehension, information and problem solving gathered during the course. The tutor marked assignments must be submitted to your tutor for formal assessment, in accordance with the deadline given. The work submitted will count for 40% of your total course mark.

At the end of the course, you will sit for a final written examination. This examination will account for 60% of your total score.

Tutor-Marked Assignment

There are 12 TMAs in this course. You need to submit all the TMAs. The best four will therefore be counted. When you have completed each assignment, send them to your tutor as soon as possible and make sure that it gets to your tutor on or before the stated deadline. If for any reason you cannot complete your assignment on time, contact your tutor before the assignment is due to discuss the possibility of extension. Extension will not be granted after the deadline, unless on exceptional cases.

Final Examination and Grading

The final examination of HEM 726 will be of three hour's duration and have a value of 60% of the total course grade. The examination will consist of questions which reflect the self assessment exercise and tutor marked assignments that you have previously encountered. Furthermore, all areas of the course will be examined. It is also better to use the time between finishing the last unit and sitting for the examination, to revise the entire course. You might find it useful to review your TMAs and comment on them before the examination. The final examination covers information from all parts of the course.

Course Marking Scheme

The following table includes the course marking scheme:

Table 1 Course Marking Scheme

Assessment	Marks
Assignment 1-12	12 assignments, 40% for the best 4 Total = 10% X 4 = 40%
Final Examination	60% of overall course marks
Total	100% of Course Marks

Course Overview

This table indicates the units, the number of weeks required to complete them and the assignments.

Table 2: Course Organisation

Unit	Title of Work	Weeks Activity	Assessment (End of Unit)
	Course Guide	Week 1	
Module 1 HIV/AIDS: Definition, Transmission and Replication			
1	HIV/AIDS: Basics	Week 1	Assignment 1
2	HIV/AIDS: Structure and Types	Week 2	Assignment 2
3	HIV/AIDS: Modes of Transmission	Week 3	Assignment 3
4	Replication in HIV/AIDS	Week 3	Assignment 4
Module 2 HIV/AIDS: Clinical Manifestations			
1	HIV/AIDS and the Immune System	Week 4	Assignment 5
2	Clinical Manifestations of HIV/AIDS	Week 5	Assignment 6
3	Clinical Manifestations/Assessment of HIV/AIDS	Week 5	Assignment 7
Module 3 HIV Testing			
1	HIV Rapid Testing (Principle and National Algorithm)	Week 6	Assignment 8
2	Classical Methods Of Diagnostic HIV Infection	Week 6	Assignment 9
3	Classical Methods of Diagnostic HIV Infection Cont.	Week 7	Assignment 10
Module 4 Management Techniques of HIV Infection			
1	Pharmacological Management of HIV/AIDS	Week 8	Assignment 11
2	Eclectic Management Technique for HIV/AIDS	Week 9	Assignment 12

How to Get the Most Out of This Course

In distance learning, the study units replace the university lecturer. This is one of the huge advantages of distance learning mode; you can read and work through specially designed study materials at your own pace and at a time and place that suit you best. Think of it as reading from the teacher, the study guide tells you what to read, when to read and the relevant texts to consult. You are provided exercises at appropriate points, just as a lecturer might give you an in-class exercise.

Each of the study units follows a common format. The first item is an introduction to the subject matter of the unit and how a particular unit is integrated with the other units and the course as a whole. Next to this is a set of learning objectives. These learning objectives are meant to guide your studies. The moment a unit is finished, you must go back and check whether you have achieved the objectives. If this is made a habit, then you will significantly improve your chances of passing the course. The main body of the units also guides you through the required readings from other sources. This will usually be either from a set book or from other sources.

Self assessment exercises are provided throughout the unit, to aid personal studies and answers are provided at the end of the unit. Working through these self tests will help you to achieve the objectives of the unit and also prepare you for tutor marked assignments and examinations. You should attempt each self test as you encounter them in the units.

The following are practical strategies for working through this course

1. Read the Course Guide thoroughly.

2. Organize a study schedule. Refer to the course overview for more details. Note the time you are expected to spend on each unit and how the assignment relates to the units. Important details, e.g. details of your tutorials and the date of the first day of the semester are available. You need to gather together all these information in one place such as a diary, a wall chart calendar or an organizer. Whatever method you choose, you should decide on and write in your own dates for working on each unit.

3. Once you have created your own study schedule, do everything you can to stick to it. The major reason that students fail is that they get behind with their course works. If you get into

difficulties with your schedule, please let your tutor know before it is too late for help.

4. Turn to Unit 1 and read the introduction and the objectives for the unit.

5. Assemble the study materials. Information about what you need for a unit is given in the table of contents at the beginning of each unit. You will almost always need both the study unit you are working on and one of the materials recommended for further readings, on your desk at the same time.

6. Work through the unit, the content of the unit itself has been arranged to provide a sequence for you to follow. As you work through the unit, you will be encouraged to read from your set books.

7. Keep in mind that you will learn a lot by doing all your assignments carefully. They have been designed to help you meet the objectives of the course and will help you pass the examination.

8. Review the objectives of each study unit to confirm that you have achieved them. If you are not certain about any of the objectives, review the study material and consult your tutor.

9. When you are confident that you have achieved a unit's objectives, you can start on the next unit. Proceed unit by unit through the course and try to pace your study so that you can keep yourself on schedule.

10. When you have submitted an assignment to your tutor for marking, do not wait for its return before starting on the next unit. Keep to your schedule. When the assignment is returned, pay particular attention to your tutor's comments, both on the tutor-marked assignment form and also that written on the assignment. Consult you tutor as soon as possible if you have any questions or problems.

11. After completing the last unit, review the course and prepare yourself for the final examination. Check that you have achieved the unit objectives (listed at the beginning of each unit) and the course objectives (listed in this course guide).

Facilitators/Tutors and Tutorials

There are eight hours of tutorials provided in support of this course. You will be notified of the dates, time and location together with the name and phone number of your tutor as soon as you are allocated a tutorial group.

Your tutor will mark and comment on your assignments, keep a close watch on your progress and on any difficulties you might encounter and provide assistance to you during the course. You must mail your tutor-marked assignment to your tutor well before the due date. At least two working days are required for this purpose. They will be marked by your tutor and returned to you as soon as possible.

Do not hesitate to contact your tutor by telephone, e-mail or discussion board if you need help. The following might be circumstances in which you would find help necessary: contact your tutor if:

> You do not understand any part of the study units or the assigned readings.
> You have difficulty with the self test or exercise.
> You have questions or problems with an assignment, with your tutor's comments on an assignment or with the grading of an assignment.

You should try your best to attend the tutorials. This is the only chance to have face to face contact with your tutor and ask questions which are answered instantly. You can raise any problem encountered in the course of your study. To gain the maximum benefit from the course tutorials, prepare a question list before attending them. You will learn a lot from participating in discussion actively.

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MODULE 1 HIV/AIDS: DEFINITION, TRANSMISSION AND REPLICATION

UNIT 1 HIV/AIDS: BASICS

CONTENTS

1.0 INTRODUCTION

HIV is Human Immuno-deficiency Virus while AIDS is the Acquired Immune Deficiency Syndrome. As a syndrome, AIDS is a group of signs and symptoms resulting from the attack of the HIV on the body's immune system.

It is the worst epidemic so far and it affects every part of the globe. Its effect is estimated to that of four World Wars put together and it still defies any cure. Available drugs do not cure but prevent multiplication of the virus.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

define HIV
define AIDS
identify what it means to be HIV positive
identify how HIV is transmitted
identify the difference between risk and vulnerability of HIV/ADS
define prevalence and identify how it differs from incidence.

3.0 MAIN CONTENT

3.1 What is HIV?

Human immuno-deficiency virus (HIV) is the virus that causes AIDS. Once introduced into the bloodstream, HIV attacks certain cells of the immune system called the 'helper T-cells' or CD4 cells, which are responsible for helping the body fight off infections. HIV invades the CD4 cells, reproducing within the infected cells, and then bursting out into the bloodstream. The immune system responds by producing antibodies to fight the virus and making more CD4 cells to replenish those killed. But this immune response is ultimately ineffective. In the late stages of infection, HIV destroys increasing numbers of CD4 cells until the body's capacity to fight other viruses and bacteria gradually begins to decline. Eventually, the immune system stops functioning, leaving the body defenseless against other infectious agents (Irwin, Millen and Fallows, 2003).

3.2 What is AIDS?

Acquired Immuno-deficiency Syndrome (AIDS) is the medical designation for a set of symptoms, opportunistic infections, and laboratory markers indicating that a person is in an advanced stage of HIV infection, with an impaired immune system. Although some people may develop AIDS much sooner, it takes an average of 10 years from the time of infection for the virus to develop clinically. As immune functions begin to decline, the body becomes prone to certain opportunistic infections, so called because they are able to cause illness as a result of weakened immune system. The characteristic spectrum of opportunistic infections that a person is likely to get will vary in different regions of the world, depending upon the locally predominant infectious agents. For example, TB is not frequently encountered in North America or Europe, but it is a common opportunistic infection in many developing countries (Irwin, Millen and Fallows, 2003).

3.3 What does it mean to be HIV Positive?

An HIV serologist test looks for the presence of antibodies against HIV in the blood. A person who is HIV-positive (or seropositive) has been infected but does not necessarily have AIDS. Because of the long delay between the time of infection and onset of the disease, the number of HIV-positive people in a population is always much greater than the number of people with AIDS. In the absence of treatment, however, nearly everyone who is HIV-positive today will develop AIDS within the next decade (Irwin, Millen and Fallows, 2003).

3.4 How is HIV Transmitted?

HIV is spread through having unprotected sex with an infected partner, sharing needles or other drug injection equipment previously used by an infected person or receiving a transfusion of blood or blood products contaminated with HIV. HIV can also be passed from a mother to her infant before or during childbirth or though breast-feeding. Thus, the fact that HIV-positive people can remain free of symptoms (asymptomatic) for years increases the chances that they may unwittingly pass the virus to others through sexual contact, needle sharing or breast-feeding.

SELF ASSESSMENT EXERCISE

1. What is HIV?
2. What is AIDS?
3. What does it mean to be HIV positive?

3.5 What is the difference between risk and vulnerability?

Risk of HIV infection is defined as the probability that a person could become infected. Epidemiologists often look for 'risk factors' or characteristics that correlate with an increased risk of an infection. Behaviours associated with the transmission of HIV, such as unprotected sex, intravenous drug use, etc, are some of the risk factors of HIV infection.

But looking at individual risk factors alone provides only a limited understanding of how to control the spread of HIV. Underlying socio-economic factors – poverty, discrimination and gender inequality – continue to drive the pandemic. It is these socio-economic factors determinants that often lead people to adopt 'risky behaviour' and render them vulnerable to HIV infection.

3.6 What is Prevalence and how does it differ from Incidence?

Prevalence is the percentage of people living in a population with a specific disease or condition at a given moment in time. When we talk about the prevalence of HIV infection in a given community, we mean the percentage of a total population that is HIV-positive. Prevalence is useful for describing the overall burden of disease, but a low prevalence of HIV/AIDS can be falsely reassuring for two reasons:

First, because prevalence is an average value, a low prevalence of HIV/ AIDS in a population with widely varying risks of HIV infection can mask small high-risk groups with high prevalence of HIV/AIDS.

Second, countries with a low prevalence of HIV/AIDS but a very large population can have more total cases of HIV/AIDS than countries with high prevalence but much smaller population. Moreover, prevalence does not provide information about the trends of an epidemic over time. Thus if we would like to know about the dynamics of an HIV/AIDS epidemic – if it is declining, stable or growing – we would need to look at the rates at which new infections are occurring. This number, called the incidence, is usually expressed as the number of new HIV infections per year. By comparing the annual rates of new HIV infections, we can learn how an epidemic is proceeding (UNAIDS, 2002)

4.0 CONCLUSION

In conclusion, we defined Human immuno-deficiency virus (HIV) as the virus that causes AIDS. We also observed that when introduced into the bloodstream, HIV attacks certain cells of the immune system called the 'helper T-cells' or CD4 cells, which are responsible for helping the body fight off infections.

5.0 SUMMARY

In this unit, we provided a simple definition of HIV and AIDS. We identified what it means to be HIV positive and also a brief presentation of HIV transmission routes. We also differentiated risk and vulnerability to HIV and lastly provided information on differences between prevalence and incidence of HIV/AIDS. We hope you found this introductory unit interesting and unambiguous. Now let us attempt the questions below.

ANSWER TO SELF ASSESSMENT EXERCISE

Human immunodeficiency virus (HIV) is the virus that causes AIDS. Once introduced into the bloodstream, HIV attacks certain cells of the immune system called the 'helper T-cells' or CD4 cells, which are responsible for helping the body fight off infections.

Acquired Immunodeficiency Syndrome (AIDS) is the medical designation for a set of symptoms, opportunistic infections, and laboratory markers indicating that a person is in an advanced stage of HIV infection, with an impaired immune system.

An HIV serologist test looks for the presence of antibodies against HIV in the blood. A person who is HIV-positive (or seropositive) has been infected but does not necessarily have AIDS.

6.0 TUTOR-MARKED ASSIGNMENT

What is prevalence of HIV/AIDS and how does it differ from incidence? Describe using HIV statistics from an identified population

7.0 REFERENCES/FURTHER READINGS

Irwin, A., Millen J. and Fallows, D. (2003). *Global AIDS: Myths and Facts.* Cambridge, MA: South End Press.

UNAIDS (2002). *Report on the Global HIV/AIDS Epidemic*. Geneva: UNAIDS.

UNIT 2 HIV/AIDS-STRUCTURE AND TYPES

CONTENTS

1.0 INTRODUCTION

The human immuno-deficiency virus (HIV) is a retro virus so called because this single stranded RNA (ssRNA) virus contains a *pol* gene that codes for a reverse transcriptase. In this unit, we will take a further look at the structure and types of HIV viruses.

7.0 OBJECTIVES

At the end of this unit, you should be able to:

explain brief the history of HIV/AIDS
list and describe the symptoms of HIV/AIDS
list and explain the different types of HIV and their characteristics
differentiate the different types of HIV on the basis of cytopathy and virulence.
describe the structure of HIV
explain the different genes and their functions in the HIV genome.

3.0 MAIN CONTENT

3.1 HIV/AIDS-A Brief History

HIV is the causative agent of the Acquired Immune Deficiency Syndrome (AIDS), which is a pandemic that have spread around the whole world. In 1981, the Communicable Diseases Centre, Atlanta USA noted an increase in requests to use pentamidine for *Pneumocystis carinii* infection in previously healthy individuals who also suffered severe infections by other normally harmless micro-organisms. Those included were Candida albicans oesophagittis, mucocutaneous herpes simplex, toxoplasma CNS infection or pneumonia and cryptosporidial enteritis; and Kaposi's sarcoma was often present. Such patients had evidence of impaired immune function as shown by skin test anergies and depletion of CD4 positive T – helper lymphocytes. This immuno-deficiency syndrome appearing in an individual without a known cause,

such as treatment with immunosuppressive drugs was referred to as "Acquired Immune Deficiency Syndrome" (AIDS).

Signs and symptoms of acute HIV infection usually occur within days to weeks after initial exposure and last from a few days to more than 10 weeks (usually less than 14 days). Unfortunately, the syndrome is often undiagnosed or misdiagnosed because HIV antibodies are not usually detected during this early phase of infection.

AIDS is a severe, life threatening syndrome which represents the late clinical state of infection with HIV. Invasion and destruction of helper T – cells lead to suppression of the patients' immune system. The immune system of the HIV infected person is unable to produce antibodies in response to T – cell dependent antigens. Secondary infections caused by viruses, protozoa, bacteria and or fungi become systemic and caused death of the patients. AIDS patients die as a result of overwhelming infections caused by a variety of opportunistic pathogens. Previously considered to be a universally fatal disease, certain combinations of drugs referred to as cocktail are used in extending life of AIDS patients.

3.2 Different Types of Human Retroviruses

HIV is classified as a *retrovirus* because it contains reverse transcriptase. It is a D.type virus in the Lentivirus family. Retroviruses are ribonucleic acid (RNA) viruses and in order to replicate they must make a deoxyribonucleic acid (DNA) copy of their RNA. It is the DNA genes that allow the virus to replicate.

Like all viruses, HIV can replicate only inside cells, commandeering the cell machinery to replicate (reproduce). However, only HIV and other retroviruses, once inside the cell, uses the enzyme called reverse transcriptase to convert their RNA into DNA which can be incorporated into the host cells' gene.

Infections of cultured T – cells with HIV usually result in cell death. The major antigenic types (HIV – 1 and HIV – 2) have been identified and are readily distinguished by differences in antibody reactivity to the envelope glycoproteins. The two HIV types share approximately 40% genetic identity. There is some disagreement about whether or not they are pathogens. Both apparently cause AIDS, but some researchers think that HIV – 2 is less virulent in causing diseases.

Different isolates of HIV – 1 and HIV – 2 exhibit considerable genomic variation and antigenic heterogeneity. The most variable regions are in the *env gene*. This type of variation is observed in HIV isolates obtained from individuals over the course of their infection. HIV strains often

display differences in replicative capacity and cytopathic effect /cytopathicity.

In 1983, the causative virus of AIDS, HIV was isolated from blood lymphocytes and recognized as belonging to the Lentivirus (slow viruses) group of retroviruses related to similar agents in monkey and to similar virus is sheep and goats.

Table 1 Human Retroviruses

Virus	Characteristics
HTLVI	endemic in W. Indies and SW Japan transmission via blood human milk, can cause adult t – cell leukemia and HTLV 1 associated myelopathy and tropical spastic apararesis,
HTLV2	Uncommon, sporadic, occurrence, transmission via blood can cause hairy T. Cell leukemia
HIV 1, HIV2	Transmission via blood, sexual intercourses responsible for ARC, AIDS, AIDS dementia etc. HIV 2 is West Africans in origin. closely related but anti-genetically distinct
Human foamy virus	Causes foamy vacuolation in infected cells, little is known of its occurrence or pathogenic potential.
Human placental virus(es)	Detected in placental tissues by electron microscopy and by the presence of reverse transcriptase
Human genome viruses	Nucleic acid sequence representing endogenous retroviruses are common in the vertebrate genome, often in well defined genetic loci, acquired during evolutionary history, not expressed as infections virus; function unknown, perhaps should be regarded as mere parasitic DNA.

The human placental and genome viruses are not known to be infectious agents.

An increasing number of different straits of both HIV – 1 and HIV – 2 are being identified by molecular virology and by phenotyping in cell culture. Highly cytopathic and infectious strains of HIV – 1 have been identified in parts of Central Africa. Increases in virulence appear to be due to minor differences in the molecular structure of the virus. Some strains of HIV – 2 appear to cause few symptoms in those known to have been infected for many years.

The molecular biological evidence through nucleic acid sequencing indicates that both HIV – 1 and the closely related HIV – 2, seen in

West African probably arose from closely related primate viruses. HIV – 1 may have been present in humans in Central African for many years but in the late 1970s it began to spread rapidly possibly with change of properties, as a result of increased transmission following major socio – economic upheavals and migration of people from Central to East Africa such as female prostitutes and mobile male soldiers.

SELF ASSESSMENT EXERCISE

Identify the characteristics of the following Human Retroviruses

HTLVI
HTLV2
HIV 1, HIV2
Human foamy virus
Human placental virus(es)
Human Genome Viruses

3.3 The Structure of HIV

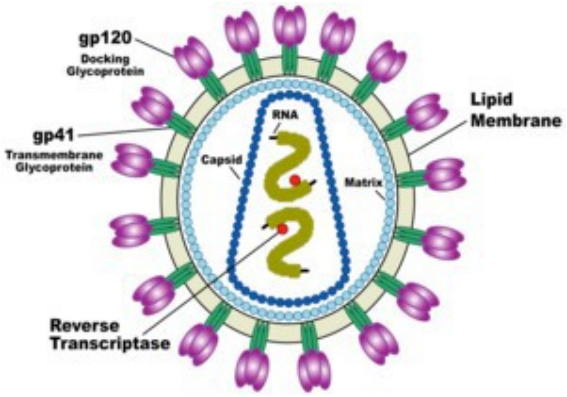

Diagram of HIV

The general structure of HIV is similar to that of Human T – cell Leukemia viruses (HTLV). The virus consists of an external lipid bilayer glycoprotein envelope (including envelopes proteins gp 120 and gp 41), an internal protein core (proteins p15, p17 and p24), a viral RNA complexed with reverse transcriptase. The HIV genome is approximately 10 kilobases which is larger than the HTLV. In addition to the structural *gag*, *pol* and *env* genes and regulatory *lat* (analogous to HTLV rex) genes (*nef, rif, vpu* and *vpr*). HIV -2 does not have sequences for vpu but does encode a novel gene, vpx, that is also found in the simian Immuno-deficiency virus.

A complete HIV particle consists of an envelope, a coat or capsid shell and core. The envelope is the membrane that surrounds the virus. It is a

lipid (fat bilayer), which is derived from the host proteins. Embedded in the envelope is the viral encoded glycoprotein (gp), gp41, bound to this is the outer glycoprotein knob gp120 molecules bind to specific molecules on the surface of the host cell called cluster designation 4 (CD4) receptors. The capsid is the protein coat that surrounds the core (viral genome) of the virus. It is made up of protein (P) p17 and p18 which the icosahedral symmetry. The viral core is the elongated inner mass of the virus which contains two identical single strands of viral RNA, structural protein, the enzyme reverse transcriptase and other enzymes. The main core protein is P25. Serological diagnosis of HIV is based on P24, P26 specific detection of antibiotic to HIV and envelope proteins.

4.0 CONCLUSION

We have seen that HIV/AIDS which is pandemic are retroviruses of the Lentivirus family. HIV/AIDS is associated with opportunistic infections such as *Pneumocystic carinii* infections, *Candida albicans* oesophagitis, toxoplasma CNS infection etc. HIV infected patients had evidence of impaired immunity as shown by skin test anergies and depletion of CD4 positive T-helper lymphocytes. There are two types of HIV i.e. HIV 1 and HIV 2 on the basis of antibody reactivity to the envelope glycol-proteins both share 70% genetic identify. The general structure of HIV is similar to that of HTLV.

5.0 SUMMARY

In this unit, we provided simple illustrations of HIV/AIDS, identified different types of HIV as well as the structure of HIV. Hope you enjoyed your studies.

6.0 TUTOR-MARKED ASSIGNMENT

1. What do you understand by HIV and AIDS?
2. List six infectious agents associated with AIDS
3. What effect has HIV on the T – cell?

7.0 REFERENCES/FURTHER READINGS

Baron S. (1996). *Medical Microbiology* 4th Edition. University of Texas Medical Branch at Galveston pp. 761 – 776.

Burton R.W. Engelkirk P.G., (2000). *Microbiology for the Health Sciences,* 6th edition. Lippincott Williams & Wilkins pp. 309 – 412.

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UNIT 3 HIV/AIDS: MODES OF TRANSMISSION

CONTENTS

1.0 INTRODUCTION

HIV infection is transmitted through several means which are specific, distinct and well understood. The mode of HIV transmission has raised several unanswered questions and thus has aroused the curiosity of man than his knowledge about HIV infection itself. HIV infection originated from homosexuals and later through heterosexual means in the United States and now the world over. Some of the means of transmission include sexual contacts, sharing of sharp objects, trans-placental or perinatal means from mother to child, blood and blood products, organ transplantation among others. A clear understanding of all mode of transmission is therefore an antidote to curtailing the uncontrollable spread of HIV/AIDS.

2.0 OBJECTIVES

In this unit, you will learn about the various modes of HIV transmission within a population, a community and the entire world as well as the high risk population based on age, sex, occupation and general behaviour. You will also learn that arthropod transmission is very unlikely as well as by close contact aerosols, kissing is yet virtually unknown. After going through this unit you should be able to:

explain the mode of transmission of HIV
list and describe each and all means of HIV transmission
list and explain the commonest means of HIV transmission
list and explain factors associated with increased risk
explain how HIV infection can be transmitted from mother to child vertically
list the unlikely methods of HIV transmission
explain why women are more vulnerable to HIV infection in Nigeria .

3.0 MAIN CONTENT

3.1 Mode of Transmission of HIV

In developed countries, homosexual men have so far been the group most vulnerable to HIV infection and AIDS, especially the passive partners in anal intercourse. Haemophiliacs who received contaminated blood products have also been infected, though less commonly, as well as intravenous drug abusers. HIV infection is transmitted primarily from male to male and from male to female, although not very efficiently compared with other sexually transmitted diseases. Transmission from female to male, however, is a common and well established feature of HIV infection in Africa. In randomly selected rural communities in parts of central and East Africa, seropositivity rates of up to 40% are encountered mostly in young adults. The demographic predictions are for a disastrous mortality, with major economic and political implications in these countries.

The main modes of HIV transmission in both developed and developing countries are through:

1) Sexual Contact.

a. In the United State of America the type of sexual contact carrying the greatest risk is male to male (homosexuals) followed by male to female and female to male (heterosexuals). Heterosexual transmission is considerably more common in third-world countries but it is also on the rise in the United States of America.

b. Factors associated with increased risk of venereal transmission include receptive anal intercourse within intravenous drug abusers, presence of genital ulcers and multiple sexual partners.

2) Sharing of needles, blades and syringes among intravenous drug users.
3) Transplacental or perinatal transmission from mother to child.
4) Blood and blood products transmission is unlikely because donated blood is tested for HIV and blood from potential donors who engage in high risk activities or who are HIV positive is declined. Some hospitals may use unscreened blood, or even collect blood from high risk individuals thereby may contribute to the high prevalence of HIV in developing countries.
5) Organ transplantation transmission is unlikely because organ donors must be HIV negative.
6) In developed countries. HIV infected women are advised to avoid breast-feeding. In regions of the world where infectious diseases

and malnutrition are important causes of infant mortality, breast-feeding is still recommended.

So far, heterosexual transmission has not been notable in developed countries. One possible explanation for the greater heterosexual spread in Africa is that ulcers and other lesions due to other sexually transmitted agents are very common on the cervix of African females and could be a source of infected lympocytes and monocytes. But there are signs that transmission by heterosexual intercourse is beginning to be more important in developed countries. It is not clear whether HIV can infect males by the urethra or whether pre-existing genital skin breaks are necessary. There is however, evidence that those possessing a foreskin are more likely to be infected.

HIV can also be transmitted vertically from infected mother to offspring. Little is known about this but it occurs in about 20% of cases especially in utero but also peri- and postnatally. At least half of the infected offspring developed AIDS within the first year of life but at this age there are fewer latent infections available for reactivation. Over a million infants have been infected mainly in sub-Saharan Africa and it is predicted that, AIDS will be a major cause of death, with over 10 million infants affected by the year 2010.

The fact that infection in Africa does not generally occur until after the onset of sexual maturity indicates that arthropod transmission probably does not occur, transmission by close contact, aerosols, kissing and so forth is virtually unknown.

SELF ASSESSMENT EXERCISE

Identify the main modes of HIV transmission in both developed and developing countries.

3.2 HIV Exposure Groups

1. Individuals with AIDS in the United States are grouped according to risk factors or probable mode of transmission. The ranking of exposure groups in most industrialized countries is similar:

a. Homosexual or bisexual men (43%)
b. Heterosexual intravenous drug users (26%)
c. Homosexual or bisexual intravenous drug use (5%)
d. Heterosexual individuals (10%)
e. Children (1%)
f. Recipients of blood, blood components or organ transplants (2%)

g. Haemophiliacs (1%)
h. Other or risk not reported or identified (6%)

2. In the United States, the fastest increasing rates of new HIV infection are among adolescents (especially gay males) and women through needlestick, scalpel or broken glass injury

3. Most children infected with HIV (90%) have a mother with or at risk of HIV infection usually through transplacental transfer (the risk of contracting HIV from an infected mother is approximately 30%). The remaining children acquire HIV through blood transfusion (10%) or through administration of coagulation factors or through breast feeding by HIV infected mothers.

3.3 HIV Transmission in Nigeria

About 60 of the HIV transmission in Nigeria is through heterosexual sex. This is because other forms of sex like anal, oral, homosexualism and lesbianism are less common here. This points to the fact that majority of Nigerian are heterosexuals.

Several factors contribute to the high incidence/prevalence of HIV in Nigeria. Some of these factors include:

1. Lack of information about sexual health on HIV
2. Low level of prevented sexual intercourse especially the use of condoms
3. High level of sexually transmitted infections which often remain a symptomatic especially in women.

About 10% of infections is though blood transmission. This is because there is a high demand for blood due to many cause of anemia. However, there is no coordinated blood supply stem. Note that about 10% of HIV infections is through other routes particularly mother-to-child-transmission (MYCT), intravenous drug use (IDU), and use of unsterilized instruments. Nigeria is a male dominated country and women are often seen as inferior to men; so men often decide to do whatever they like without considering the woman's opinion and plight. It is believed women's traditional role is to have children and take care of every responsibility in the home.

Women therefore do not have the same status as men, and do not have the same access to education which increases their vulnerability to HIV infection. Other factors predisposing women to HIV/AIDS include:

1. Female Circumcision

a. Female circumcision is still practised in many parts of the country
b. Such practices with the use of crude methods, unsterilized equipment as well as infected personnel put the women and girls at risk of contracting HIV.

2. Commercial Sex Work

a. Although prostitution is illegal in Nigeria, the practice is still relatively rampant, especially among young girls, particularly those in higher institutions and cities
b. HIV infection rates among commercial workers have been estimated to be as high as 30% in some areas especially in town and cities.
c. Low level of condom use by CSWs due to ignorance about the routes of transmission and poor acceptance by clients

3. Marriage Practices

a. Harmful marriage practices violate human rights and contribute to increasing HIV infection in women and girls.
b. Such young women and girls are at risk of being infected as a man can have many sexual partners even outside marriage
c. Majority of such young women are uneducated and thus can not negotiate safe sex with their husbands or men as the case may be.

3.4 Socio-economic Factors Facilitating HIV Transmission in Nigeria

Several factors contribute to the high prevalence of HIV in Nigeria like other countries in Africa.

Some of These Factors Include

1. Lack of sexual health information and education

a. Sex is a very private subject in Nigeria
b. Frank and detailed discussions about sex with teenagers is seen and even regarded as being indecent
c. Just recently has sexual health education for young people which had been a major barrier to reducing sexually transmitted infection STIs and HIV introduced.
d. Myths and misconceptions about sex and HIV abuse.

2. Poor health care awareness and services

a. There is extreme deterioration of health services due to political instability, corruption and mismanagement of the country's economy.
b. There is lack of basic health care provision in many parts of the country. It is difficult to establish HIV testing and prevention services e.g. Prevention of MTCT
c. Sexual health clinics providing contraception, testing and treatment for other STIs are also few.

3. Stigma and discrimination

a. These are very common in Nigeria
b. The major religions see immoral behaviours as being the cause of the HIV/AIDS epidemic. This is perhaps because of the low level of awareness of the likely means of transmission
c. These affect attitudes towards people with HIV.
d. PLWHA often loses their jobs or are denied health care services as a result of ignorance and fear.

4.0 CONCLUSION

The several means of HIV transmission discussed in this unit show that the most vulnerable group of people to HIV infection and AIDS are mainly passive partners, those involved in unprotected heterosexual intercourse etc. The mode of transmission varies from population to population as well as in urban settings. HIV infection can as well be transmitted to people through non-sexual means like sharp objects, blood transfusion and even vertically from mother to child.

5.0 SUMMARY

HIV/AIDS has been accepted as a pandemic currently devoid of any known cure, but could only be managed especially by the use of anti-retroviral drugs. In addition to heterosexual mode of transmission, there are several ways by which this infection/disease is transmitted. The erroneous impression that those infected are as a result of sexual promiscuity is unfounded. Certain occupations even expose people to infection. A few of the means by which HIV infection is transmitted include: blood transfusion, intravenous drug use, organ transplantation, artificial insemination and maternal milk. HIV is unlikely to be transmitted through close contact, hugging among others.

ANSWER TO SELF ASSESSEMENT EXERCISE

The main modes of transmission of HIV in both developed and developing countries are through:

Sexual contact.
Sharing of needles, blades and syringes among intravenous drug users.
Transplacental or perinatal transmission from mother to child.

6.0 TUTOR-MARKED ASSIGNMENT

1. Discuss briefly the mode of transmission of HIV in developed and developing countries.
2. Several factors contribute to the high incidence/prevalence of HIV in Nigeria. Identify the factors.

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UNIT 4 REPLICATION IN HIV

CONTENTS

1.0 INTRODUCTION

In this unit, we shall identify and explain various stages of replications in HIV.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

Explain all the processes involved in replication in HIV.

3.0 MAIN CONTENT

3.1 Replication in HIV

Viral replication is regulated by the products of the genes. The replication cycle is often halted after integration of the provirus, so that the infection remains latent in the cell. The *lat* and *ref* genes, for instance, function as transactivating factors and can increase production of viral RNAs and proteins when latently infected cells are stimulated to differentiate (e.g. T-helper cell by antigen) or stimulated by infection with certain other viruses (e.g. HSV, cytomegalovirus)

The life cycle of HIV involves eight steps namely:

1. Attachment / Entry
2. Reverse transcription and DNA synthesis
3. Transport to the nucleus
4. Integration
5. Viral transcription
6. Viral protein synthesis
7. Assembly of virus
8. Release of virus

1) Entry of HIV into Cells

Infection typically begins when an HIV particle, which contains two copies of the HIV RNA, encounters a cell with a surface molecule called

cluster designation 4(CD4). Cells carrying this molecule are known as CD4 positive cells.

One or more of the virus pg120 molecules bind tightly to CD4 molecules (s) on the cells surface. The binding of gp 120 to CD4 results in conformational change in the gp 120 molecule allowing it to bind to a second molecule on the cell surface known as coreceptor. The envelope of the virus and the cell membrane then fuse, leading to the entry of the virus into the cell. The gp41 of the envelope is critical to the fusion process. Drugs that block either the binding or the fusion process are being developed and tested in clinical trials.

Studies have identified multiple coreceptors for different types of HIV strains; these coreceptors are promising targets for new anti – HIV drugs, some of which are now being tested in pre-clinical and clinical studies. In the early stage of HIV diseases, most people harbour viruses that use, in addition to CD4, a receptor called CCR5 to enter their target cells. With disease progression, the spectrum of coreceptor usage expands in approximately 50 percent of patients to include other recetors, notably a molecule called CXCR4. Virus that utilizes CCR5 is called R5 HIV and virus that utilizes CXCR4 is called X4 HIV.

Although CD4+ T – cells appear to be the main target of HIV, other immune system cells with and without CD4 molecules on their surfaces are infected as well. Among these are long – lived cells called monocytes and macrophages, which apparently can harbour large quantities of the virus without being killed, thus acting as reservoirs of HIV. CD 4 T – cells also serve as important reservoir of HIV: a small proportion of theses cells harbours HIV in a stable, inactive form. Normal immune processes may activate these cells resulting in the production of new HIV virions. Cell to cell spread of HIV also can occur through the CD 4 – mediated fusion of an infected cell with an uninfected cell.

2) Reverse Transcription

In the cytoplasm of the cell HIV reverse transcriptase converts viral RNA into DNA, the nucleic acid form in which the cell carries the genes. Nine of the 15 antiviral drugs approved in the United States of America for treatment of people with HIV infection, AZT, ddC, ddI, d4T, 3TC nevirapine, delavirdine abacavir, and efavireng- work by interfering with this stage of the viral cycle.

3) Integration

The newly made HIV DNA moves to the cells nucleus, where it is sliced into the list of DNA with the help of HIV intergase. HIV DNA that

enters the DNA of the cell is called a "provirus". Intergase is an important stage for the development of new drugs.

4) Viral Transcription

For a provirus to produce new viruses, RNA copies must be made that can be read by the host cell's protein making machinery. These copies are called messenger RNA (mRNA) and production of mRNA is called transcription, a process that involves the host cell's own enzymes. Viral genes in concert with the cellular machinery control this process, the *lat* gene for example encodes a protein that accelerates transcription. Genomic RNA is also transcribed for later incorporation in the budding virion. Cytokines proteins involved in the normal regulation of the immune response may also regulate transcription. Molecules such as tumour necrosis factor (TNF) – alpha and interleuckin6 (IL – 6), secreted in elevated levels by the cells of HIV – infected people may help to activate HIV proviruses. Other infections, by organisms such as Mycobacterium tuberculosis, may also enhance transcription by inducing the secretion of cytokines.

5) Translation

After HIV mRNA is processed in the cell's nucleus, it is transported to the cytoplasm. HIV proteins are critical to this process. For example, a protein encoded by the *rev* gene allows mRNA encoding HIV, structural proteins to be transferred from the nucleus to the cytoplasm. Without the *rev* protein, structural proteins are not made. In the cytoplasm, the virus co-opts the cell's protein making machinery including structures called ribosome – to make long chains of viral proteins and enzymes using HIV mRNA as a template. This process is called translation.

6) Assembly and Budding

Newly made HIV core-proteins, enzymes and genomic RNA gather just inside the cell's membrane while the viral envelope proteins aggregate within the membrane. An immature viral particle forms and buds off from the cells, acquiring an envelope that includes both cellular and HIV proteins from the cells membrane. During this part of the viral life cycle, the core of the virus is immature and the virus is not yet infectious. The long chains of the proteins and enzymes that make up the immature viral core are now cleaved into smaller pieces by a viral enzyme called protease. This step results in infectious viral particles. Drugs called inhibitors interfere with this step of the viral life cycle. Six of such drugs are saquinavir, ritonavir, indinavir, amprenavir, nelfinavir and lopinavir –have been approved for marketing in the United States of America.

SELF ASSESSMENT EXERCISE

The life cycle of HIV involves eight steps. Mention and describe each of them

4.0 CONCLUSION

The viral replication is regulated by the production of genes. Eight steps are involved in HIV replications which include attachment / entry, reverse transportation and synthesis, transportation to the nucleus, integration, viral transcription, protein synthesis assembly and release of viruses. Careful and in-depth examination of patients is required so as not to miss out something vital in clinically diagnosing HIV.

5.0 SUMMARY

Hope you enjoyed your studies. In this unit, we presented a brief summary of replications in HIV and identifying the replication steps.

ANSWER TO SELF ASSESSMENT EXERCISE

The life cycle of HIV involves 8 steps namely:

Attachment / Entry of HIV into the cells
Reverse transcription and DNA synthesis
Transport to the nucleus
Integration
Viral transcription
Viral protein synthesis
Assembly of virus
Release of virus

6.0 TUTOR-MARKED ASSIGNMENT

Brief describe the following:

1) Entry of HIV into the cells
2) Reverse transcription of HIV
3) Viral transcription
4) Assembly and budding of HIV

7.0 REFERENCES/FURTHER READINGS

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MODULE 2 HIV/AIDS: CLINICAL MANIFESTATION

Unit 1 HIV/AIDS and the Immune System
Unit 2 Clinical Manifestations of HIV/AIDS

Unit 3 Clinical Manifestations/Assessment of HIV/AIDS

UNIT 1 HIV/AIDS AND THE IMMUNE SYSTEM

CONTENTS

1.0 INTRODUCTION

The human immuno-deficiency virus (HIV) is a deadly virus that attacks the immune system of the patient/host and rendering the patient's immuno-deficiency weak, leading to the disease called AIDS. The virus invades the tissues and cells of its host and manipulates the mechanism of the infected cells to replicate itself. This lead to reduction in the number of T-cells and other lymphocytes, paving way for opportunistic infection, which may lead to the death of the patient.

The soldiers / army of a country are meant to defend the territorial integrity of that country. When during a war and the army of a country is defeated, so goes down the country. In other words, the infrastructure, social and economic factors of the country is destroyed. The lymphocytes, leukocytes and macrophages are the armies of the body. When these are overcome by any invading organisation, a disease situation will set in.

In this unit, you will learn about the human immuno-deficiency virus (HIV) and how it affects the immune system of the host.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

explain the meaning of acquired immunity
differentiate between humoral immunity and cell mediated immunity
differentiate between T lymphocytes and B – lymphocytes and interferon
understand how the HIV infects and destroys the T – cells.
explain the immunological changes associated with HIV infection.

3.0 MAIN CONTENT

3.1 Immune System

The meaning of the term "immunity" as it is used today derives from its earlier usage referring to exemption from military service or paying taxes. It has long been known from time immemorial that persons who suffered from diseases such as smallpox, plague or measles, resisted it on subsequent exposures and rarely contracted it a second time. This is referred to as acquired immunity and is generally effective only against the same type of infection as that previously suffered.

These immune individuals were often used in an epidemic to nurse those suffering from active diseases.

The acquired immunity takes two forms:

Humoral Immunity: This is the appearance of antibodies or immunoglobulin produced by plasma cells in the blood. These antibodies combine with the antigen, which stimulates their production leading to the clumping of the antigen molecules, neutralization of the toxins, or the uptake and subsequent digestion of the antigen by phagocytes.
Cell–Mediated Immunity: This is the response in which antibodies play a subordinate role. It depends mainly on the development of T-cells that are specifically responsive to the inducing agent and is generally active against intracellular organisms.

Lymphocytes originate from stem cells in bone marrow and migrate into the blood stream. Those that finally matured in the thymus gland are called T-cells (T-lymphoid tissue matured into B – cells (B – lymphocytes)

3.2 Function of T-Cells

Although T – cells do not produce antibodies, they do produce antigen – binding protein called receptor always remain firmly bound to the cytoplasmic membrane of the cell that produces it. Each T – cell receptor is a dimmer composed of two non-identical polypeptides and

possess a variable domain and a constant domain in addition to a region of hydrophobic amino acid at the COOH – terminal end of the polypeptides that anchors the receptors of the membrane.

The T-cell controls the response of B – cells to antigens and also mediates other immune functions such as attraction of the leukocytes at site of inflammation. The T – cells produced lymphokines in response to specific antigens. The lymphokines in turn attract macrophages and other leukocytes to a site of inflammation. The T – cells also inhibit the migration of macrophages away from a site of inflammation. The macrophages release a protein known as interleukin – 1 which binds the antigen on their surfaces, so that T-cells with receptor for the antigen binds to it. The B-cells produce antibodies when they are stimulated to differentiate into plasma cells by lymphocytes released from T-cells.

SELF ASSESSMENT EXERCISE

What do you understand by acquired immunity?

3.3 Interferons

These are naturally occurring antiviral compounds produced by mammalian cells in response to viral infection, and can protect other cells from being attacked by the same or other quite different species of virus. They are non-specific.

Interferons bind to the cell surface receptor and interfer with the synthesis of new virus by tissue cells of the host, thereby inhibiting viral replication and activate host defence mechanism.

3.4 HIV/AIDS

Viruses have developed different mechanism for exploiting weakness in the host immune system, and avoiding (and sometimes actually subverting) immune mechanism. Some cleverly avoid the host defense that they persist in the host indefinitely, sometimes in a latent form without producing diseases.
One of the strategies developed by viruses is to infect cells of the immune system itself, thereby rendering the normal functioning of the cell type that has been infected ineffective e.g. the human immuno-deficiency virus (HIV).

The HIV causes permanent depression of immunity in the host to unrelated antigens and occasionally to antigens of the infecting virus. Hence the patient/host becomes susceptible to otherwise harmless protozoan, bacteria, viruses and fungi.

The virus upon entering the cytoplasm of a host cell synthesizes its DNA which becomes integrated into the host chromosome and takes over the mechanism of the host cells to replicate itself.

4.0 CONCLUSION

In this unit, you have learnt that immune response is a physiological reaction to the introduction of foreign material into the body irrespective of whether it is harmful or not. Also a disease condition may or may not arise depending on the result of the reactions between the foreign body and the host immune system.

5.0 SUMMARY

In this unit, you have learnt the basic acquired immune system; the humoral and cell – mediated immunity. You have also learnt how the T – cells and interferons function in eliminating foreign bodies (antigens) from the body system, and how the human immuno-deficiency virus (HIV) invade and attack the cells of the immune system, destroying the T – cells and progressively leading to the establishment of a disease condition known as AIDS.

ANSWER TO SELF ASSESSMENT EXERCISE

Acquired immunity is the process whereby persons who suffered from diseases such as small pox, plague or measles resisted them on subsequent exposures and rarely contracted it a second time. It is thus immunity or resistance acquired at some point in an individual's lifetime

6.0 TUTOR-MARKED ASSIGNMENT

1) Differentiated between humoral immoral immunity and cell-mediated immunity.
2) Briefly describe the function of the T – cell.

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UNIT 2 CLINICAL MANIFESTATION OF HIV/AIDS

CONTENTS

1.0 INTRODUCTION

Adult T – cell lymphoma was first recognized in Japan. The diseases is an acute T – cell proliferative malignancy. Clinically, the features are leukaemia, generalized lymphadenopathy and diseases associated with bone marrow and skin involvement. It is now clear that less dramatic form exists. Another disease, a non – Hodgkin T – cell lymphoma, and few cases of encephalitis have also been recognized. The average incubation period to AIDS onset is about 10 years. Overall, almost half of those who have been diagnosed as AIDS cases are dead.

The enormous variety of infections – including protozoan fungal, bacterial and viral infections and tumors indicate clearly the extent of the immunosuppressant that develops and the magnitude of the diagnostic and therapeutic problems presented by patients.

2.0 OBJECTIVES

At the end of this unit, you should be able to explain:

the different diseases which may progress to AIDS
the opportunistic infections that are involved in HIV infections and the organisms involved
the different symptoms produced by these opportunistic organism / infections.

3.0 MAIN CONTENT

3.1 Clinical Manifestation of HIV/AIDS

The initial stage of HIV infection is the process of being exposed to HIV and becoming antibody – positive (serconversion). Some patients experience this as a mononucleosis-like illness consisting of fever, lymphadenopathy, rash and at times aseptic meningitis, others remain asymptomatic throughout this phase. The initial infection is usually asymptomatic, the length of this phase varies, ranging from five to ten years.

HIV diseases begin to develop as progression occurs in increasing evidence of immuno-deficiency with common recurrent infections or resulting from the virus effect on the T – helper cell. This may lead to increasing constitutional symptoms and finally opportunistic infections and the occurrence of unusual turnovers. These lead to early death.

3.2 Acute Infections

This usually occurs between 1 – 6 weeks after infection and may be asymptomatic. A mononucleosis-like illness may occur with fever, diarrhoea, myalgia, arthralgia, headache, nausea, sore throat, rash, transient lymphadenopathy and rarely meningo-encephalitis. A period of asymptomatic infection then follows and this may last for a few months to many years.

3.3 Persistent Generalized Lymphadenophathy

This is present in 25 – 30% of patients who are otherwise asymptomatic. The enlarged lymph nodes which are not more than 1 cm in diameter are painless and symmetrical in distribution for more than 3 months. There is usually no evidence of any other symptoms or signs of disease at this time.

3.4 Opportunistic Infections (OIs)

This is a term used in describing an infection that probably would not be occurring if the individual were not infected with HIV or suffering from some other conditions that might cause lowered resistance to diseases. Sometimes, many diseases – causing agents are common in our environment but generally does not cause diseases because the healthy immune system disposes it off before it causes any problem. Hence an opportunistic infection takes advantage of the facts that the body's normal defenses are down, giving it an opportunity to cause diseases. Examples that are often seen in AIDS patients include:

Pneumocyitis Carinii Puenmonia (PCP)

This is a life-threatening lung diseases caused by an organism called *Pneumocyptis jiroveci*. It is the number one killer of patients with AIDS. This organism can also infect and cause diseases in other organs, including the skin.

The clinical manifestation includes:

Fever
Fatigue
Weight loss
Cough and dyspnea
Clear lung sound

Tuberculosis

This is a chronic infection caused by mycobacterium tuberculosis. The primary infection is usually the lungs involving the lung parenchyma and the regional lymph nodes (usually mediastinal). If the initial site of infection is the tonsil or the ileum, the affected nodes will be the cervical or mesenteric respectively. Rarely haematogenous spread may occur to produce military tuberculosis with widespread involvement of lungs, bone marrow, kidneys, liver, brain, bones joints, and heart.

The clinical manifestation, if systemic includes:

Lassitude
Weight loss
Might sweats
Malaise
Fever and
Anorexia

And local in lung include: cough, sputum, haemoptysis, breathlessness. Pleura: include pain, breathlessness, effusion.

Percardium / Heart: include pain arrhythymias, constructive pericarditis, intestine include: diarrhoea, malabsorption, obstruction. Genito urinary tract include: venal failure, heamaturia, epididymitis, salpingitis, infertility.

Skin include: lupus vulgaris, erythema nodosum. Eye include choroiditis, iritis, phlyctenular kerato conjunctivitis, Lymphatics include

cold, abscesses, lymphadenopathy, sinuses. Brain include: meningitis, tuberculoma. Adrenal glands include Addison's diseases.

Toxoplasmosis

This is a disease caused by the organism *Toxoplasma gondii*. The common source of this organism includes cats, birds and undercooked meat such as pork, lamb or venison. The organism causes a disease called Toxoplasma encephalitis when it affects the brain. It can also infect and cause diseases in other organs, including the eyes and lungs.

Clinical manifestations include:

Headaches
Seizures
Hemiparesis
Lethargy
Personality changes and change in cognitive ability.

Cryplococcosis

This is caused by the organism *Cryptococcus neoformaris*. Cryptococcal meningitis is the most serious manifestation of infection with this organism. Patients often complain of headache, nausea, and fever. Other manifestations include. Subtitle mental changes i.e. changes in personality and alternations in level of consciousness, seizure and coma.

Cryptococus neoformans have the ability to spread to the central nervous system. Infection of skin, bone, lymphnodes, heart have also been described as well.

Candidiasis

This is a mucocutaneous infection caused by the fungus *Candida albicans* and other species. It commonly occurs in patients with HIV diseases. The fungus causes infection of the mouth, oesophagus, skin and vagina.

Thrus: this is the most common fungal diseases in HIV – infection. Patients are diagnosed early in the epidemic and are independently predictive of progression of AIDS. The likelihood of thrus, which generally develops in patients with CD_4 count less than $500/mm^3$, increases as the CD_4 count declines. The most frequent manifestation of candidiasis is white patches or "Pendomembrances" on the tongue or oral mucosa. Removal of this material leaves an erythematious base that may ooze or bleed. Clinical variants include: an atrophic form (smooth

red patches on affected mucosa), candida leukoplakia (firm, adherent white patches that are difficult to remove), and angular chitis (erythemations tissues at the corner of the mouth.)

Candidal oesophagitis is a frequent AIDS – defining diagnosis, occurring most often when the CD4 counts below 100/mm^3. Patients may complain of dysphasia, retrosternal pain and odynophagia.

In women, recurrent or chronic vulvovaginal cadidcasis is a common early manifestation of HIV – infection, although it may also occur in immunocompetent host as well.

Cytomegalovirus Infections

This is a herpes virus which is present in more than 75% of all HIV infected patients. Cytomegablvius (CMV) can cause diseases in one or several parts of the body. These include:

i. CMV Rectinitis: CMV can cause damage in the back of the eye or the retine, which may lead to blurred vision, blind spots or moving spots and blindness.

ii. CMV Encephalitis: CMV can also cause damage to the brain. If CMV reaches the brain and the immune system is unable to control it, death may occur within weeks or months.

iii. CMV Radiculopathy: This is the disease of the nerves. It can cause pain or tingling in the limbs, particularly the legs and feet. It can also lead to loss of urinary or bowel movement control.

iv. CMV Colitis: This is a disease of the colon and is often associated with symptoms of abdominal pain, weight loss, diarrhoea, and cramping. Most forms of CMV almost always occur in patients, with less than 50 T- cells /mm^3. CMV colitis has been reported in patients with higher T – Cells counts, and even in those who are receiving anti – HIV therapy.

v. CMV Gastristis; CMV of the upper gut, including the stomach can lead to symptoms like those seen in patients with CMV colitis.

vi. CMV Esophagitis: This is a disease of the throat. It can lead to pains while swallowing, chest pain and hiccups.

Oral Hairy Leuckoplakia (OHL)

This is a unique feature of HIV – infected patients. The margins of the tongue show white ridges of folds on the epithelium. OHL looks like thrus, but the difference is that thrus usually comes off when it is slightly scraped with a toothbrush, whereas OHL does not. OHL caused by the Epsteim – Bar virus (EBV) is considered to be a benign disease, meaning that it rarely causes serious physical problems and does not progress to more serious complications.

3.4.8 Wasting Syndrome and Weight Loss

Weight loss and wasting syndrome are two AIDS related complications, that if not adequately treated, can be life threatening. Weight loss refers to loss of body weight while wasting syndrome refers to a loss of body mass or size, most notably muscle mass (sometimes refered to as “lean body mass”). Very often, both occur at the same time. However, this is not always the case. It is possible that someone who is losing weight might not lose muscle mass. It is also possible that someone losing muscle mass might not lose a lot of weight. For example, some HIV – POSITIVE people lose a lot of muscles, yet they may experience an increase in fat, this can cause weight to stay, even though muscle wasting is going on.

Clinical manifestation include: cachexia, persistent fever and diarrhoea. Dementia develops in 25% of patients with AIDS and is marked by a gradual loss of cognitive functions. Progressing to overt dementia in some patients is the main feature of the disease. Brain scan shows a loss of tissue, with widening of the sulci and ventricles.

Lymphomas

Non Hodgkin’s Lymphoma and Hodgkin’s Diseases: Lymphoma is a cancer of the lymphatic system, a network of lymph nodes organs, including the spleen, thymus, and tonsils) and vessels that help make up the immune system. Lymphoma is sub divided into two groups: Non-Hodgkin’s Lymphoma (NHL) and Hodgkin’s diseases (HD). The major difference between the two is the type of cells involved.

Lymphoma is more likely to occur in HIV – positive people with fewer than 200 T – cells, while lymphoma of the brain (primary CNS lymphoma) is more likely to occur in people with fewer than 100 T – cells.

Spread of the disease occurs both via lymphatic channels and the blood stream, thus the diseases may be widely disseminated at the time of

diagnosis. While the causes of lymphoma are still unknown, it is believed that radiation chemicals such as pesticides can cause this form of cancer. The Epstein Bar virus (EBV) has also been found to play a major role in the development of the diseases particularly in HIV – infected patients.

Clinical manifestations include, painless lymphadomopathy (enlarge lymph nodes) lassitude, weight loss, fever, night sweats, and anorexia.

Kaposi's sarcoma (KS)

This is the most common neoplasm affecting AIDS patients and was one of the earliest features used in defining AIDS. It is often aggressive and arises in many sites including the skin, mouth, gut and eye. The tumors arise from endothelial cells of blood vessels causing bluish purpose and raised irregular lesions. It was seen almost entirely in homosexual men. There is also an increase in incidence of B cell lymphoniata and other tumours.

3.5 AIDS

This results from severe immunodeficiency due to HIV infection. There is evidence of life threatening opportunistic infections and / or unusual tumours (Pneumocystis pneumonia, cerbral toxoplasmosis, CMV, cryptosporidiosis, cerebral lymphomas, non Hodgkins lymphoma, mycobacterial infection, Kaposis sarcoma). Neurological problems (encephalopathy, myelopathy, neurophpathy, encephalitisu, demyelination and retinitis) are all common and may be present in up to 50% of cases.

SELF ASSESSMENT EXERCISE

Identify the signs and symptoms of acute infection associated with HIV

4.0 CONCLUSION

It is found that the Human immunodeficiency virus (HIV) infection is asymptomatic, at the initial stage, but progressively develops into immuno deficiency with recurrent common infections, increasing common symptoms and finally, opportunistic infections and the occurrence of unusual turnovers. These lead to an early death.

5.0 SUMMARY

Infections with HIV usually occur within 1 – 6 weeks and may be asymptomatic. This period ranges between 5 – 10 years. As the number

of T – cells infected increases, so also is the constitutional symptoms and other infections by opportunistic organism. The combination of all these finally lead to AIDS and eventually death. We also learnt that the clinical features present which will eventually lead to AIDS include candidiasis of the lungs, oesophagus and throat, cryptococcosis, mycbacteriosis, toxoplasmosis of the brain, CMV rectinitis, HIV dementia, wasting syndrome and kaposi sarcoma.

ANSWER TO SELF ASSESSMENT EXERCISE

Acute infection of HIV usually occurs between 1 – 6 weeks after infection and may be asymptomatic. A mononucleosis – like illness may occur with fever, diarrhoea, myalgia, arthralgia, headache, nausea, sore throat, rash, transient lymphadenopathy and rarely meningo-encephalitis. A period of asymptomatic infection then follows and this may last for a few months to many years.

6.0 TUTOR-MARKED ASSIGNMENT

Identify and briefly explain five opportunistic infections associated with HIV

7.0 REFERENCES/FURTHER READINGS

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UNIT 3 CLINICAL MANIFESTATION/ASSESSMENT OF HIV

CONTENTS

1.0 INTRODUCTION

Once it enters the body, HIV infects a large number of CD^{4+} cells and replicates rapidly. During this acute or primary phase infection, the blood contains many viral particles that spread throughout the body organs, particularly the lymphoid organs. Lymphoid organs include the lymph nodes, spleens, tonsils and adenoids. Two to four weeks after exposure to the virus, up to 70% of HIV – infected persons suffer flu-like symptoms related to the acute infection. The patient's immune system fights back with killer T-cells ($CD8^+$ T cells) and B-cells produced antibodies, which dramatically reduce HIV levels. A patient's $CD4^+$ T cell count may rebound somewhat and even approach its original level. A person may then remain free of HIV – related symptoms for years despite continous replication of HIV in the lymphoid organs that had been seeded during the acute phase of infection. HIV escapes the body's aggressive immune responses, which sufficiently clear most viral infections due to the high rate of mutations that occur during the process of HIV replication. The subsets of killer T cells that recognize HIV may either be depleted or become dysfunctional. The virus may hide within the chromosomes of an infected cell and be shielded from surveillance by the immune system. Such cells serve as latent reservoir of the virus, thus contributing to the median time from infection with HIV to the development of AIDS – related symptoms to be approximately 10 to 12 years in the absence of antiretroviral therapy.

2.0 OBJECTIVES

At the end of this unit, you should be able to understand:

the various stages involved in transition from HIV to AIDS
why it takes many years for HIV to manifest as full-blown AIDS
the clinical features associated with HIV/AIDS
the distinctive characteristics of HIV/AIDS infected patients.

3.0 MAIN CONTENT

3.1 Clinical Features (Symptoms and Manifestation) of HIV

The initial infection may be accompanied by a mild mononucleosis – type illness characterized by fever, malaise, weight loss, diarrhoea etc. Antibodies often take many months to become detectable and cytotoxic T – cells are formed. There is probably some curtailment of viral replication and the individual remains well. Infected cells, however, are still present and at a later stage the infected individual may show weight loss, fever, persistent lymphadenopathy, oral cadidiasis and diarrhoea. This is the AIDS Related Complex (ARC). Further viral replication takes place until finally some years after initial infection, there is development of full blown AIDS.

What determines progression through the cycle of seropositivity to ARC and AIDS still remains unclear. The virus exercises complex control over its own replication. Replication is also influenced by the response to other infections, which act as antigenic stimuli and some of them directly as transactivating agents.

Sub-acute encephalitis, sometimes with dementia may occur, and also a variety of reactivating infections of the CNS. In fact, the CNS picture may include arrested CNS development with microencephalophathy. Some patients, especially in Africa, develop a wasting disease (‘slim’ disease) possibly due to unknown intestinal infections or infestations and perhaps also due to the direct effects of the virus infecting cells of the intestinal wall. The disease, AIDS, consists of the microbial diseases acquired or reactivated as a result of the underlying immunosuppression due to HIV. In other words, the entire disease picture is an indirect result of infection with HIV, which by itself causes only a minor clinical illness. The neurological disease is an independent and direct result of neural invasion by HIV although, complicated by reactivation or infection with other infectious agents.

3.2 Physical Examination

The physical examinations of patients, which may progress rapidly to AIDS, include

i. Lymphademopathy
ii. Skin rashes
iii. Fevers
iv. Fatigue
v. Drenching night sweats
vi. Persistent diarrheas
vii. Weight loss and wasting syndrome
viii. Oral thrush
ix. Vaginal yeast infection
x. Pains related to peripheral neuropathies, nyalgies or malignancies.

3.3 History Taking

Find out the following

Activities of Daily Living

Nature of job
What do you do for a living?
How often do you go out?
Where do you go often?

Major Illness

What is your major illness
How often does it occur?

Substance Use

What means of treatment do you often employ
Local drugs? Traditional medicine?
Orthodox drugs?
How often do you use these treatment(s)?
Sexual practices
Married / single?
If married, how many wives?
Have you multiple sex partners?
Do you use any form of production/contraceptive?

Medication

What type of medication do you use?
Do you complete the drugs?
If not, why?
How effective is this medication?

Occupation

What is your occupation?
Does your occupation expose you to women/men.
What effect has your occupation on you?

Social

How do you socialize?
How often do you have sexual intercourse?
Do you have sexual partners outside marriage?

Travel

How often do you travel?
Does your journey expose you to women/men?
How often do you have sexual intercourse during travels?

3.4 Physical Examination

Body System

General appearance
Cardiovascular system
Respiratory system
Head and neck
Ear, nose and throat
Eyes
Skin and hair
Abdomen
Also find out history of

Bowel movements: any constipation or diarrhea?
Fluid intake and output: any dysuria or haematuria?

Chest pain
Genitals
Loss of sensation any where in the body

SELF ASSESSMENT EXERCISE

1. List four examples of lymphoid organs.
2. List four areas the clinician considers when examining an HIV patient.

4.0 CONCLUSION

HIV infection progresses slowly because antibodies often take many months to become detectable. This perhaps is due to high rate of mutation of HIV which occurs during the process of HIV replication. This among other factors prolong the time for the development of AIDS – related symptoms to between 10 to 12 years, especially in patients that have not been receiving antiretroviral therapy. The disease, AIDS, consists of the microbial diseases acquired or reactivated as a result of the underlying immunosuppression due to HIV.

5.0 SUMMARY

HIV is often initially accompanied by a mild mononucleosis – type illness characterized by fever, weight loss, malaise, diarrhoea etc. The HIV infected individual remains free of HIV – related symptoms for years despite continuous replication of the HIV. A sub acute encephalitis, sometimes with dementia, may occur as well as a variety of re-activating diseases or slim diseases which maybe possibly due to unknown intestinal infections or infestations and direct effect of the various infecting cells of the intestinal wall. The medical diagnosis which is based on careful history of the symptoms especially opportunistic infection associated with AIDS is necessary.

ANSWER TO SELF ASSESSMENT EXERCISE

12. Lymph nodes, spleens, tonsils and adenoids.
13. Daily activities, sexual practices, major illness, medication used occupation, social activities, body systems etc.

6.0 TUTOR-MARKED ASSIGNMENT

Identify and briefly explain the steps in HIV assessment.

7.0 REFERENCES/FURTHER READINGS

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MODULE 3 HIV TESTING

UNIT 1 HIV RAPID TESTING (PRINCIPLE AND NATIONAL ALGORITHM)

CONTENTS

1.0 INTRODUCTION

In addition to the classical HIV diagnostic tests, rapid testing, are also used. As the name implies, these tests appear simpler to perform, observe and interpret within a relatively shorter period of time to conventional HIV tests. Most of the widely available HIV tests are either by detection of HIV antibodies in serum plasma whole blood or oral fluids preferably with rapid HIV tests. Rapid HIV tests are comparatively simpler to use, require fewer equipment, cheaper, faster and extremely reliable. These among others are the advantages of the rapid HIV test. Like all diagnostic HIV tests, they have one disadvantage which is testing during the window period.

2.0 OBJECTIVES

At the end of the unit, you should be able to:

explain the benefits of rapid HIV tests
accurately interpret individual test results as positive, negative or invalid
describe the approve testing process
interpret the HIV status using the testing process.

3.0 MAIN CONTENT

3.1 Benefits and Challenges of HIV Rapid Testing

Rapid HIV testing is very easy to use:

The diagnosis and counseling of HIV can be carried out on the same day
This method reduces the time between testing and treatment of those that are positive
It enhances prompt access to treatment thus lowers treatment cost.

3.2 Body Fluids and Formats of Rapid Testing

The body fluids used for rapid testing of HIV include the serum, plasma, whole blood and oral fluids. Three major formats are commonly used for the HIV rapid testing. They include:

(1) Immunnoconcenration (flow through device).
(2) Immunichronatograph (lateral flow device) e.g. Determine, stat–pak.
(3) Particle agglutination e.g. caliphs.

There are a number of different tests which can be used to diagnose HIV, and the most commonly used test to diagnose and confirm HIV in Nigeria is based on the presence HIV –specific antibodies. All diagnostic tests have both advantages and disadvantages.

3.3 HIV Diagnostic Testing

The laboratory diagnosis of HIV series on the presence of HIV specific antibodies, antigens or genetic materials in the patent's blood or contain body fluids.
An antibody is a protein made by the body's immune system to attack, and destroy foreign substances. A person infected with HIV will produce antibodies specific to the virus

An antigen is a foreign substance recognized by the body's immune system.
The genetic material of HIV is responsible for making HIV particles (i.e encodes viral antigens.
Rapid HIV antibody test is the most available test by detection of HIV antibodies in serum, plasma, whole blood or oral fluid.
Rapid HIV tests are relatively simple to use requires minimum equipment, cheap, fast and extremely reliable in testing during the "window period".

3.4 The Window Period

It takes time for the body's immune system to produce antibodies to HIV after infection, thus giving false negative result.
The "window period" is that period it take to produce some level of antibody that can be detected by a rapid HIV test
It takes 2-3 weeks from initial infection for most individuals to become positive using a HIV rapid test
It is therefore crucial, especially, for high risk individuals, to get retest three months after receiving a negative test result
Length of the window period often depends upon the test used.

3.5 Use of Rapid Tests on Adults and Children and the Need for More Than One Test

It is possible for HIV to be passed from mother to child
It is also possible for HIV antibodies to be passed from mother to child
Children up to 18 months old may have antibodies to HIV that have been passed from the mother. These antibodies may give rise to a false positive HIV antibody test
It is the therefore necessary to use antigen or RNA – based HIV tests in this age group.
At least two different rapid tests must be used to diagnose HIV clinically
Rapid tests are very efficient but it is always better to use more than one test because individuals respond differently to the virus
The federal Ministry of Health should endeavour to evaluate test kits to make since they work properly. A list of kits can then be used together in what is called a "testing algorithm"

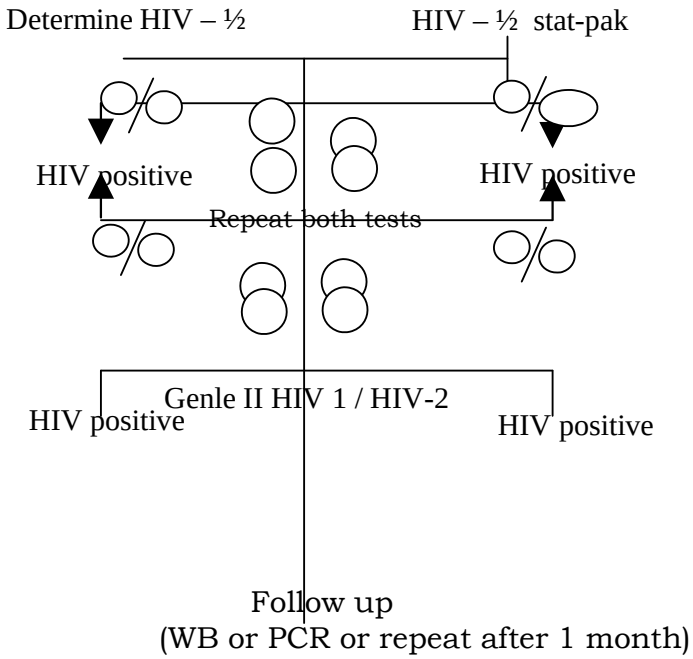
3.6 Four Possible Test Results of HIV Rapid Testing

A test result can either be:

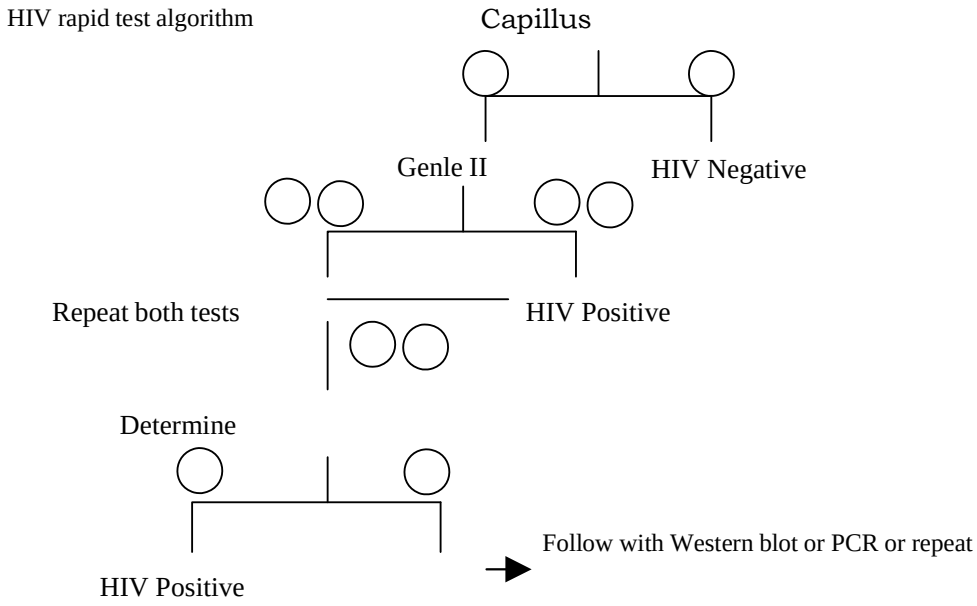
Reactive
Non-reactive
Discordant
Invalid.

A result is said to be reactive when it gives a result teamed "Reactive result" and it is termed non-reactive when the result shows a non-reactive result. Such patients are then referred for further tests in the laboratory. When the result of one or both tests cannot be determined, the test is regarded as invalid. Such patents should be referred for further tests at the laboratory.

3.6.1 HIV Rapid Testing Algorithm



3.6.2 HIV Testing Algorithm



3.7 How to Know if the Test Kit Is Working: Quality Control

Use "known" positive and negative samples. Both DETERMINE & STAT –PAK include an "internal control". The internal control confirms that you have added your sample correctly. The only way to be certain your kit is working is to test known positive and negative control everyday. If the controls do not work, do not use the kit. Repeat controls with new kit. The equipment used is transfer pipette and mechanical pipette

SELF ASSESSMENT EXERCISE

Identify and briefly explain four possible test results of rapid testing

3.8 How to Perform HIV Rapid Tests

Collect test items and other necessary laboratory supplies.
Use 1 strip per test. Preserve the lot number on the best of the strip
Always check that the test is within date
Label the test strip with client identification number
Put off the protective foil cover
Collect specimen using a precision pipette or l drop using a plastic transfer pipette.
Apply the specimen to the absorbent pad on the strip
For whole blood, add 1 drop of chase buffer to the specimen pad.

Read and record results and other pertinent information on the worksheet.

3.9 Principles of STAT–PAK

This employs a combination of specific antibody binding protein, which is conjugated on colloidal gold dye particles and antigens to HIV1/2, which are bound to the membrane solid phase. The ringing buffer facilitates the lateral flow of the released products from the sample as well as promoting binding of antigen and antibodies.

In each case the sample continues to migrate along the membrane and produces a pink/purple line in the CONTROL area answering the validity of the assay.

In a positive sample, the dye conjugated – immune complex migrates on the nitrocellulose membrane and is captured by the antigens immobilized at the TEST (I) areas, producing a pink/purple line. In the absence of HIV- 1/2 antibodies, there is no pink/ purple line in the TEST (I) area.

4.0 CONCLUSION

HIV infections, till date has no known cure. This is a pandemic the globe has to contend with. Millions of adults and even infants are lost to this infection because there is still no known cure. Attempts have therefore been made to employ rapid testing procedures and their interpretation so as to employ prompt antiretroviral therapy. This would definitely make life meaningful for those already infected with HIV/AIDS

5.0 SUMMARY

In this unit you have learnt the various rapid testing techniques, the testing algorithm, the body fluids used for rapid testing and the attendant benefits of HIV/rapid testing. In addition to the formats of rapid HIV tests, the application of the rapid HIV test as well as how the rapid test can be quality controlled was also discussed.

ANSWER TO SELF ASSESSMENT EXERCISE

Four Possible Test Results of HIV Rapid Testing are

A test result can either be:

1) Reactive
2) Non-reactive
3) Discordant
4) Invalid.

6.0 TUTOR-MARKED ASSIGNMENT

1) Identify the benefit of HIV rapid testing.
2) Identify the characteristics of the window period.
3) Illustrate how to know that one's HIV testing kit is working properly.

7.0 REFERENCES/FURTHER READINGS

Baron, S (1996). *Medical Microbiology*. University of Texas Medical Branch: Galceton Galveston Texa.s

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UNIT 2 CLASSICAL METHODS OF DIAGNOSING HIV INFECTION

CONTENTS

1.0 INTRODUCTION

Laboratory tests for HIV infection depends on the demonstration of specific antibodies. AIDS itself is a clinical definition and in the presence of antibodies to HIV any or some of the opportunistic infections regardless of the presence of other causes of immunodeficiency indicate AIDS. Initially, an ELISA test is carried out. A positive result is confirmed on a further blood sample by either Western blotting, radioimmunoassay, or immunofluorescent testing. This is done because ELISA test very occasionally gives a false positive report and (b) to eliminate possible clerical errors in the clinic or laboratory. Tests to distinguish between antibodies to HIV – 1 and HIV – 2 are however available in specialized laboratories. Diagnosis of HIV infection in newborn infants is a problem. If 1gG antibodies are present they are presumably of maternal origin and test for virus specific IgG antibodies, which would signify in utero infection, are not yet available. The various classical HIV diagnostic tests procedures, observation and interpretation are discussed in this Unit.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

understand the various classical methods of diagnosing HIV
identify the advantages and disadvantages of the various methods of HIV diagnosis
explain the various test procedure
record and interpret the outcome/ result of each test.

3.0 MAIN CONTENT

3.1 Classical Methods of Diagnosing HIV Infection

Among the methods used in the diagnosis of HIV- infection includes: Antibody test (ELISA& Western – Blot), T4/T8 ratio, HIV cultures and HIV p24 antigens. Other tests includes: HIV polymerase chain reaction (PCR). Two types namely PCR DNA and PCR RNA exist.

3.2 Types of HIV Antibody Testing

HIV – Antibody Testing: this can be broadly divided or subdivided into two namely (i) screening assays (ii) confirmatory assays.

Using the old ELISA Kit, antibodies could be detected between six and twelve weeks because they can only detect IgG. Newer generation assays can detect antibody at between 3 to 4 weeks, after initial infection. This ability is due to a higher sensitivity to antibodies. They are able to detect both 1st immunoglobulins IgM as well as IgG.

The methodology of conducting Enzyme-linked-immunosorbent assay (ELISA) is:

> Collection of specimen 5 to 7 ml of whole clotted blood (specimen should be refrigerated). HIV– antigens purified from viral lysate or prepared from recombinant DNA technology are coated into microwells of plate or into beads that are placed in the wells depending on preference, to form solid phase or assay. The patient's serum is placed in the wells and allowed to react for about 30 mins at a temperature of between 37- 40^{0}C.
>
> The serum is then washed away. An indicator reagent consisting of an anti-human antibody bound to the enzyme is added to the well. The HIV specific antibodies in the patient's serum if present will remain attached to solid- phase antigen, the enzyme conjugated antihuman antibody will attach to these antibodies and thus to the solid phase. Another washing step follows. If the patient's serum contains antihuman antibody, it will attach to these antibodies and thus to the solid phase. Another washing step follows. If the patient's serum contains antibody to HIV, the enzyme remains attached to the solid phase and is available to catalyze a colour-producing reaction, when an appropriate substrate is added to the well. The colour change is reassured with a spectrophotometer.

This colour change is proportional to specific HIV antibody concentration in the sample. Optical density values (OD) are produced, the coloured solution absorbs transmitted light, and provides an indication of the amount of colour, which is proportional to the amount of antibody bound (i.e. antibody concentration). A calculation based on the OD of negative controls multiplied by a factor produces a cut off value (CO) on which the OD of the sample is compared to determine the antibody status. Sample with OD/CO rations greater that 1.0 are considered an antibody reactive i.e. Positive

3.3 Simple Tests

This type of HIV test requires no instrumentation. They include agglutination assays in which antigen coated particles (red blood cells (RBC), latex particles or gelatin particles) are allowed to react with serum antibodies to coagulate (agglutination).

When RBCs are used the method is known as passive haemagglutination (PHA).

When latex particles are used, the method is known as latex agglutnation (LA) and when HIV gelatin particles are used, it is known as HIV particle agglutination test (PAT).

The test takes about two hours and it is conducted under temperature controlled conditions. It is sensitive, costs less and it is easy to perform.

The methods described above fall under screening assays in HIV – Antibody Testing. The methods involved in confirmatory assays include. Western Blot Test, Immunifluorescence Assay (IFA), Line Immune assay (LIA) and Radioimmunoprecitation (RIPA).

Western Blot

This detects immune response to specific viral proteins. This method involves the layering of a purified HIV- antigen mixture onto an SDS polyacrylamide gel slab, followed by electrophoresis. The viral proteins (HIV antigens) migrate through the molecular pores of the gel rates, determined by electrical change and molecular weight. The higher molecular weight proteins migrate less and forms bands closer to the starting point.

The proteins on the gel are blotted to a nitrocellulose paper by an electrophoretic procedure. The paper is cut into thin strips, each with the

full distribution of viral protein antigen bands. A single test strip is incubated with a 1:50 or 1:100 dilution of a test sample or a control and then washed and incubated with a labelled antihuman ‘globulin. The label is usually an enzyme (horse radish peroxidase or alkaline phosphatase) that will react with a specific colourless substrate to produce an insoluble coloured band on the strip where there is an antigen- antibody complex. Reaction with a positive serum sample produces a pattern of bands on the strip that is characteristic of HIV. These bands represent viral genes product. A test is said to be positive if it contains two out of three of the specific bands p24, gp 41, and gp 120 or gp 160 The molecular weight of the antigens of HIV – 1 are for genes p 55, p 17, p24, p9, p6. For pol genes they are p10, p50, p15, p31, and for glycoproteins in env genes they are gp160 or gp120 and gp41.

The molecular weight of the antigens of HIV – 2 for gag genes is p56, p26 and p16. For the pol genes in HIV –2 the molecular weights of the proteins are p68 and p34; while the molecular weights of the envelope gloycoproteins are gp36 or (gp 41), gp 140 and gp 105.

Immubifloresecence Assay (IFA) is less expensive than Western blot and it is a very sensitive assay. It is performed by preparing a suspension of a lymphocyte cell culture infected with HIV. The suspension is placed on a microscope slide, air-dried and fixed in acetone or methanol. Uninfected controls are put on separate spots on the slide to provide means of detecting non- specific reactions. Diluted sera is added to the cells spots, the slide is washed, incubated with fluoresces – conjugated antihuman globulin, using an ultraviolet microscope. Localized fluorescence of infected cells is observed in a positive sera while little or no fluorescence is observed in a negative sera. The control uninfected cells serves as to eliminate unspecific reactions. Unspecific reactions (e.g. Antinuclear antibody) as fluorescence is observed in the control cells too.

The disadvantages of this method are the fact that a highly trained personnel who cultivates cells and also interprets results correctly is needed. It also requires an expansive microscope.

3.4 Radio Immunoprecepitation Assay

This is primarily used for research purposes and it is highly technical. The methodology involves culturing HIV in cells radio, labelled with cysteine or gloucosamine, or the viral proteins are labelled by direct reaction with 1:125. The disrupted virus is exposed to the test specimen and specific antigen–antibody complexes are concentrated and isolated by immuno-precipitation. After extensive washing, electrophoresis

disrupts and distributes the precipitate through a polyacrylamide gel. Authoradiography detects antigen antibody bands. This technique is very sensitive to the higher molecular weight envelope, glocoproteins gp160 and gp120, which some, Western blot techniques miss. This method can be used to resolve conflicting results from HIV antibody assays e.g. When Western blot methods report probably false positive results (such as p24 alone) are often negative to RIPA.

Line Immunoassay: In this assay recombinant or synthetic peptide antigens are applied on a nitrocellulose strip. The use of artificial antigens strip reduces the risk of contaminants derived from cell culture. This method is as accurate as the Western blot. It is in use in Europe but has not been licensed for use in the United States.

3.5 HIV–Antigen Test

HIV – p24 Antigen serological test measures the presence of HIV core antigen in serum. This represents either recent infection or an antigen excess state from unchecked viral replication.

It is used to detect HIV positive infants during the neonatal period. HIV p24 antigen test in cerebrospinal fluid is also used to monitor central nervous system involvement by HIV.

HIV – antigen detection was formerly immuno fluorescent staining of peripheral blood mononuclear cells, using antibody directed to HIV antigens (p24). This method is very inefficient since less than 0.01% of mononuclear cells are infected with HIV. Through research, improvements have been made and commercial HIV – antigen assays are now available, which are solid phase antigen and captures enzyme immunoassays.

Principle of Test: A specific monoclonal antibody to HIV p24 antigen is attached to the solid phase (microtitre plate – well or polystyrene bead). When sample is added to such microtitre plate-well or polystyrene bead, the viral antigen is captured.

Methodology: - The sample is diluted in Triton x100 detergent to disrupt the virions, antigen thus becomes attached to the monoclonal antibody in the solid phase if present in the serum. Addition of antibody detector, followed by incubation, is preceeded by a wash step. The reagent used as the detector usually has high-titres antibody to 24 antigens coupled with biotin. Following incubation with a conjugate (Streptavidin- peroxidase), the complex is labelled by attaching it to biotin. An avidin-biotin system acts as an amplifier to generate

additional signals to detect the minute quantities of antigen in the sample.

A substrate is added which mediates a colour production as the enzyme cleaves the substrate. The reaction is stopped after a defined period of time by adding a weak acid (e.g. 2M sulfuric acid). The optical density (O.D.) is measured with a spectrophotometer of 450nm; and the optical density is proportional to the quantity of HIV –1 P24 antigen in the specimen. This assay is capable of detecting p24 antigen in the pg/ml to ng/ml range.

A blocking assay is usually performed to confirm the presence of p24 antigen. It includes incubation of the sample containing the antigen with a neutralizing reagent, which is human anti-p24 antibody. During the incubation, if antigen is present, it is complexed with the neutralizing antibody and this prevents p24 antigen from being bound to the solid-phase captured reagent in the p24 antigen assay. The antigen assay is repeated on the pre-incubated sample along with an aliquot sample that has not been pre-incubated with neutralizing reagent. The optical density readings is compared and the optical density for reading the sample that has been pre-incubated with the neutralizing reagent should be at least 50% less than the reading of the neutralized aliquot.

The quantity of p24 antigen in the blood is determined by diluting HIV-1 antigen standard to prepare series of six standards of varying concentrations. Concentration varies between 0.0 and 125 pg/ml. The concentration of HIV – p24 antigen standard (p/ml) on x axis is plotted against the optical densities for each standard on y axis; to obtain a linear graph from which a standard curve is derived. If the value of the unknown sample happens to be higher than the value of the highest standard, the sample is diluted with normal human serum and the neutralization procedure is repeated.

Disadvantages of this test includes

It is expensive
It requires large volumes of sample (about 1 ml of serum)
HIV – 1 p24 antigen rapidly degrades in improperly stored sample, thus fresh samples are often required

4.0 CONCLUSION

We have indeed seen that laboratory tests for HIV infection depends on the demonstration of specific antibodies. Initially, testing for HIV is carried via an ELISA. A positive result is confirmed on a further blood sample by either Western blotting, radioimmunoassay, or

immunofluorescent testing. This is done because ELISA test very occasionally gives a false positive report and also to eliminate possible clerical errors in the clinic or laboratory.

5.0 SUMMARY

In this unit, we have been able to understand various classical methods of diagnosing HIV, explain the various test procedures as well as identify the advantages and disadvantages of the various methods of HIV diagnosis

6.0 TUTOR-MARKED ASSIGNMENT

1) Define HIV Antigen Test.
2) Identify the advantages and disadvantages of HIV Antigen Test.

7.0 REFERENCES/FURTHER READINGS

Baron, S (1996). *Medical Microbiology*, University of Texas. Medical Branch: Galceton Galveston Texas.

Jametz E. Melunick J.L. and Adelberg E.A (1998). *Medical Microbiology.* Prentice Hall Int: New Hersop, pp202-212.

UNIT 3 CLASSICAL METHODS OF DIAGNOSTIC HIV INFECTION (II)

CONTENTS

1.0 INTRODUCTION

This unit is a continuation of the previous one. Here, we will look at other classical methods of diagnosing HIV infection.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

describe HIV culture test
illustrate T4/T8 ratio
explain HIV polymerase chain reaction test
identify alternative classical tests.

3.0 MAIN CONTENT

3.1 HIV Culture Test

HIV can be cultured from lymphocytes in peripheral blood. The numbers of circulating infected cells vary with the stage of the disease.

HIV isolation and culture is achieved by culturing the clinical sample (PBMCS or plasma), phytohaemagglutinin (PHA), stimulated peripheral blood, mononuclear cells, PBMCS obtained from buffy coat preparation from HIV- negative donors. Active replication of the virus is observed in the stimulated PBMCS.

There are two types of HIV culture tests, namely the quantitative culture test and qualitative culture test.

The qualitative assay takes eight days (range 3 to 21 days) to detect HIV from a patient PBMCs and 14 days (range 7 to 30) to detect it from plasma. To qualify p24 antigen in culture supernatants, it takes additional seven days. Larger volumes of stock virus are usually generated by method for research purposes.

The quantitative PBMCs and plasma culture are maintained for 14 days, and then it is evaluated for evidence of viral replication by testing for the presence of 24 antigens in the culture supernatants.

Final dilution of cells or plasma that yields a positive HIV – 1 culture method is used to evaluate the number of infected cells or infectious viral particles.

The cell culture supernatant fluids can also be tested for reverse transcriptase. The sensitivity of the test has been confirmed to 50% of infection at birth and over 90% by the age of three months. The test specificity and positive predictive value is close to 100 percent. Positive test results indicate HIV infection, but it must be confirmed with a second test.

Disadvantages of these methods include the following:

(i) It is technically demanding
(ii) It is expensive
(iii) It is time consuming
(iv) Because of varying sensitivity with age and viral burden, negative result from a single test should be reconfirmed to exclude infection.

3.2 T4/ T8 ratio

CD4+ T lymphocytes are the major target of the HIV, it is responsible for production of the virus. Research has shown that CD8+ cells too are vulnerable to HIV infection. CD4+ T cells also known as the T- inducer or T helper cells are disabled during HIV infection. CD8+ T cells (suppressor cytotoxic cells) kills cells infected with HIV or other viruses.

Immunocompetent host usually have twice as many helper cells as suppressor cells; thus the ratio is approximately one to two. On the other hand, in HIV infected individuals the ratio can be as low as 0.01 to 0.50.

A CD4+ *T cell count less than 200/mm*^{3} is an indication of immunodeficiency from HIV.

In infants less than 12 months old, a CD4+T lymphocyte count, less than 750 peruL is an indication of HIV. In children of age range 1-5 years, a CD4+ T cell count of less than 500/uL indication severe immunosuppression. While a CD4 + Tcell count less than 200 per/uL indicates severe immunosuppression in children with age range 6-12 years.

SELF ASSESSMENT EXERCISE 1

There are two types of HIV culture tests. Name them.

3.3 HIV polymerase chain reaction (PCR) test

The PCR assay was invented by Mullis in 1985. Its fundamental form detects a small known sequence of designated DNA in the midst of larger quantities of DNA. This is achieved by selectively making copies of the desired DNA sequence, but not of the remainder of the DNA in the sample.

HIV PCR test can be divided into two: The HIV- DNA PCR and HIV – RNA PCR.

The DNA PCR determines the presence of viral RNA in the plasma.

Methodology: - DNA PCR is prepared either by the manual method or the automated method. The manual method requires between 5 to 7 ml of blood to yield enough DNA. Numerous steps, including treatment with density separation agent (e.g. ficoll), centrifugation, cell washing and lysis are used. DNA is thus extracted and suspended in buffers. This method takes 8 hours in all. It requires a highly skilled personnel and it promotes some errors due to repeated handling and pipetting. The automated method takes less time (less than or equal to 4 hours) and requires a smaller sample (0.5 to 2ml of whole blood). The sample is incubated for 45 minutes with proteinase K to remove proteins, and DNA is quantified, usually a fluoresent dye assay, a known quantity (usually 1/ug) is used in PCR. The advantages of this method includes: shorter time of extraction, less chance of contamination and also does not require a highly skilled personnel.

The extracted DNA is incubated with a thermostable DNA polymerase, deoxynucleotide triphosphates, and oilgonucleotide primers that define the proportion of HIV genome to be amplified. Series of temperature shift cycles typically 30 to 35^{0}C result in an exponential increase in the

copy number of the HIV sequence, usually in multiples of several hundred thousands. Before, amplified DNA sequence of HIV was detected by hybridization with a radioactive- labeled probe, but presently, chemiluminescence or calorimetric methods which are more sensitive and easier to use are in use. The PCR method is so sensitive that it can detect a single molecule of target. DNA from 15,000 PBMCs (100uLin newborns, 500uL in adults). It can provide results in 48 hours. Positive tests indicate HIV infection but it should be confirmed as contamination of uninfected patient's sample. Amplified product from prior assays can result in false positive results. Negative result should also be reconfirmed, as the results of PCR test may be negative in as many as 50% of neonates who are infected with HIV.

HIV PCR RNA: Research is on the use of HIV RNA PCR for diagnosing HIV infection in new born. RNA amplification may be a reliable factor for indicating HIV infection.

RNA PCR is highly sensitive for diagnosing plasma viremia in HIV infected infants but false positive results have been reported in some cases. The use of DNA PCR for integrated cellular provirus is more specific.

3.4 Alternatives to Classical Tests

Urine Test: - Samples of urine contain immunoglobulin G but their exact origin is not known. Advantage of this form of test includes the fact that the collection of urine is simple, non-invasive, inexpensive and can be stored at room temperature. The disadvantage is that there is no approved confirmatory assay resulting in the collection of blood when results are reactive. An ELISA has been approved by Federal Drug Agency (FDA) to screen urine for antibodies of HIV-1.

Saliva Test: - Oral fluids have been used for HIV testing as an alternative to blood samples. The saliva contains crevicular fluid capillaries between the tooth and gum, and are transudes of blood. Therefore they include plasma which is used for testing with serum based test. Very sensitive test used in detecting this minute concentration of antibodies is now available

A newer technology is now being developed known as the "One Step". Its reagents are contained in a tube-like device that has a strip containing antigens. Whole blood, oral fluid or serum is placed at the tip of the device and allowed to diffuse along the strip with impregnated reagents where reaction with antigens occurs.

These are the assays of the future and they have the advantage that they contains an in built quality control advantage (contains in built quality control) reagent and thus requires no addition of reagent. Apart from this, it also has the advantage that the test can be completed within a short period (less than 10 minutes).

SELF ASSESSMENT EXERCISE 2

1. List five of the classical methods used in diagnosing HIV infection.
2. Which of these tests confirms HIV infection?

4.0 CONCLUSION

HIV infection is diagnosed by several methods most of which are based on HIV – specific antibodies, which usually appear at some interval after infection. The emphasis have been on the most commonly used methods in HIV diagnosis such as ELISA, Western Blot, T4/T8 ration, HIV culture, PCR etc. Detection of the p24 core antigen in serum also indicates HIV infection. AIDS is diagnosed mainly on the basis of specific opportunistic infection or cancers coinciding with a T4 cell defect in the absence of other known causes of immunodeficiency.

5.0 SUMMARY

In this unit you have learnt the classical methods of diagnosing HIV/AID infection. The procedures and the advantages and disadvantages and discussed. You have also learnt how to carry out these methods, observe and even interpret the various procedures used classically to diagnose HIV infection. In addition, the alternative tests to classical tests have also been elucidated.

ANSWER TO SELF ASSESSMENT EXERCISE 1

1. Antibody tests which include ELLSA and Western Blot, T4/T8 ration, HIV cultures HIV P24 antigens test, HIV PCR DNA HIV PCR RNA Urine test, Saliva test and one step test

2. Western Blot, Immunofluorescence assay (IFA) Line immuno assay (IJA) and Radio immunoprecipitation (RIPA)

6.0 TUTOR-MARKED ASSIGNMENT

1. Why is laboratory diagnosis of HIV difficult?
2. List two of the confirmatory tests of HIV infections and state their immolation.
3. Which of the method of HIV diagnosis appears to be more reliable?

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MODULE 4 MANAGEMENT TECHNIQUES OF HIV/AIDS

UNIT 1 PHARMACOLOGICAL MANAGEMENT OF HIV/AIDS

CONTENTS

1.0 INTRODUCTION

Several pharmacological products which include anti-retroval drugs (ARVs) and antibiotics are used in the treatment of HIV/AIDS. ARVs are more effective and are better prescribed in triple combination otherwise known as standard combination therapy or triple cocktail party. Most antiviral agents attack viruses at either the point of penetration and uncoating or viral DNA/RNA synthesis. These drugs among others contribute to the lengthening of the asymptomatic stage of HIV disease and prolong lives of infected individuals.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

Identify the two major problems associated with the therapy of vital infections
Explain the two groups of ARV drugs which are: inhibitors of reverse transcriptase and inhibitors of viral protease
Illustrate mechanism of action of some antiviral drugs.

3.0 MAIN CONTENT

3.1 Phamacological Treatment

Although, there is yet no known curative therapy for HIV/AIDS, there are available therapies which can lengthen the asymptomatic stage of the HIV diseases and prolong life. Like most viral infections, there is no specific treatment. Effective antiviral drugs are few in number, in contrast to the great range of successful antibiotics available for bacterial infections. The shortage of antiviral drugs is partly due to the difficulty of interfering with viral activity in the cell without adversely affecting the host. However, the advent of AIDS has stimulated intensive research, and new antiviral drugs have undoubtedly appeared. Antiviral agents are few in number and narrow in their spectrum of activity.

There are two problems with the therapy of viral infections:

The incubation period is often a week or more, and by the time the patient becomes ill most of the spread and replication of virus has already taken place. Infection cannot be diagnosed during the incubation period and even after the patient becomes ill. Laboratory diagnosis often takes several hours.

Viruses that are latent in cells and not actively replicating are generally insusceptible to antiviral agents.

3.2 Groups of Antiviral Medications for HIV/AIDS

The antiviral medication for HIV/AIDS falls into two groups:

Inhibitors of reverse transcriptase and inhibitors of viral protease.

Inhibitors of reverse transcriptase include Zidovudine (AZT) Stavudine (D4T), Didanosine (ddI), Zalcitabine (ddC) and Lamivudine (3TC). All these are nucleoside analogues, but they differ chemically and in terms of site of action on the enzyme.

Protease inhibitors include saquinavir and indinavir. They are unlike the reverse transcrptase inhibitors which prevent the virus from reproducing.

Antiretrovoral (ARV) drugs are far more effective and are usually prescribed in triple combination. The standard combination therapy or “triple cocktail party” is also known as highly active antiretroviral

therapy (HAART). For example, a combination of lamindudency, stavudene and nevirapine known as Triomune is being used by over 60% of ARVs used in Uganda. Similarly, a combination of zidovudine, lamivudine and nevirapine is known as Diuvir – N.

The use of combined therapy is employed to delay the development of HIV resistance to medication, which frequently develops during therapy with single medication. Another major limitation of anti – HIV therapy is the toxic effects of the drug. Zidovudine, for example can cause anaemia, low white blood cell counts, vomiting, fatigue, headache as well as muscle and liver damage. The biggest limitation perhaps in the use of ARVs is their cost. When the cost of ARVs is added to the cost of prevention and treatment of opportunistic infections and other conditions, it is far beyond the reach of millions of impoverished HIV victims, particularly in the developing and underdeveloped countries.

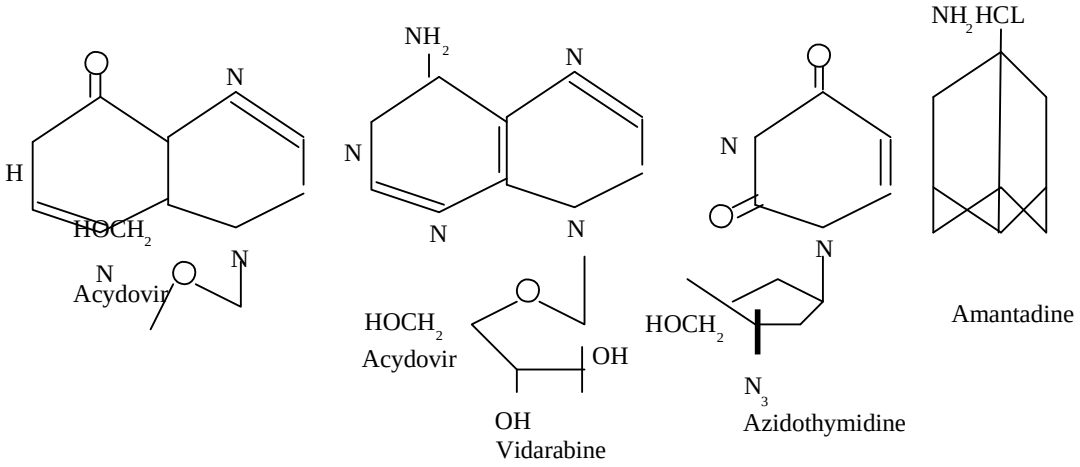

Fig 1: Structure of Antiviral agents

Table 1: Site of action of antiviral agents

	Replication Stage	**Drugs Available**
1.	Absorption	None available
2.	Penetration and uncoating	Amantadine
3.	Viral DNA/RNA synthesis	Idoxuridine, vidarabine, acydovir, zidovudine, ribarin
4.	Viral protein synthesis	Interferons
5.	Assembly	None available
6.	Release	None available

Viruses are resistant to antibacterial antibiotics, although the latter may be needed to control secondary bacterial infection, for example in influenza pneumonia and HIV/AIDS.

3.3 Mode of Action of Antiviral Drugs

Acydovir is phosphorylated by the herpes virus thymidine kinase and the monophosphate is then converted by cellular kinases to the tripphosphate, which acts by inhibiting the herpes virus DNA polymerase. The drug is also incorporated into the viral DNA polymerase, resulting in chain termination. Acyclovir is inactive until phopshorylated and it is only phosphorylated in infected cells. Toxic side – effects (neutropenia, thromobocytopenia) are usually not severe. The drug acts on herpes simplex and varicella – zoster viruses but is almost inactive against bacteria infections.

Acycohir is used topically to treat primary genital herpes, herpes simplex virus dendritic ulcers and less effectively for cold sores and zoster. Systemic acyclovir has revolutionized the treatment of herpes simplex encephalitis, herpes simplex and V – ZV infection in immuno compromised patients.

Another nucleoside analogue is Zidovudine in which the hydroxyl group on the ribose is replaced by an azido group. After conversion to the triphosphate by cellular enzymes, it acts as an inhibitor of and substrate for, the viral transcriptase. Proviral DNA formulation is blocked because the drug is incorporated into the DNA with resulting chain termination. Zidovudine is currently the most useful drug for patients with AIDS – related complex (ARC) and AIDS, and when used in the early asymptomatic stages of HIV infection, will decrease progression to ARC and AIDS.

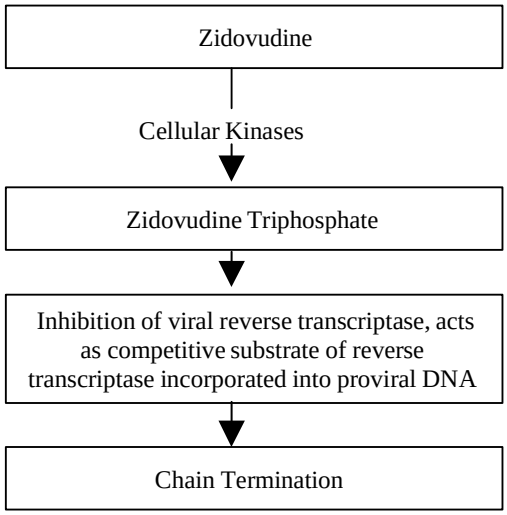

Fig. 2: Antiviral action of Zidovudine

Other antiviral drugs include amantidine, vidarabine, dexoycytidine (ddc) and deoxyinosine (ddi), ribavirin and use of interferons.

Amantidine specifically inhibits the replication of influenza A viruses but influenza B and other respiratory viruses are not affected. Amantidine acts by inhibition to the penetration of the virus into the cell or its uncoating. With the standard dose (200mg/day orally) there are minor neurological side effects (insomnia, dizziness, headache etc), especially in elderly patients which has discouraged its wide use. When given prophylactically during community outbreaks, amantidine is as effective as influenza vaccine in preventing illness. It is also used for treatment and if taken within 48 hours of symptoms, there is a reduction in disease that far outweighs the drugs toxic effects.

Vidarabine is a nucleoside analogue which is converted to the triphopshate by cellular kinases and then inhibits the viral DNA polymerase. It is less effective than acyclovir but can be used topically for herpetic dendritic ulcers.

Another antiviral agent, ribavirin is a guanosine analogue with various actions including inhibition of production of guanosine triphosphate pools needed for viral nucleic acid synthesis. It is used clinically as an aerosol for severe respiratory syncytial virus (RSV) infection in infants, for severe influenza B and for a renavicus infection such as lassa fever.

SELF ASSESSMENT EXERCISE

1. List at least five ARV drugs you know.
2. Combined therapy in which three ARV drugs are used is called ……..?

4.0 CONCLUSION

Like most viral infections, there is no specific treatment for HIV and effective antiviral drugs are few in number. The shortage of antiviral drugs is partly due to the difficulty of interfering with viral activity in the cell without adversely affecting the host. Antiviral agents are few in number and narrow in their spectrum of activity.

5.0 SUMMARY

Certain drugs like the ARVs are specifically used in the treatment of HIV. The antiretroviral drugs are grouped into two: (1) Inhibitors of reverse transcriptase and (2) inhibitors of viral protease. These mechanisms of actions also differ considerably.

We also learnt that ARVs can be administered singly, in dual combination and in triple combination. One of the major limitations of ARVs is the toxic effects of the drugs which negates the principle of selective toxicity. The biggest limitation of ARVs however is their cost which is usually beyond the reach of the average man on the street who is more prone to HIV infection. The mechanism of actions of antiviral drugs such as zidonvudine, acyclovir, amantidene, vidarabine and vibarin are also explained.

ANSWER TO SELF ASSESSMENT EXERCISE

1. Zidovudine, Stavudine, zalcitabine, lamivudine, saquinavir.

2. Standard combination therapy or triple cocktail party or highly active antiretroviral thrapy (HAART)

6.0 TUTOR-MARKED ASSIGNMENT

1. With the aid of annotated diagram describe the mode of action of zidovudine.
2. How affordable are ARV drugs to the common man?

7.0 REFERENCES/FURTHER READINGS

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UNIT 2 ECLECTIC MANAGEMENT TECHNIQUES FOR HIV/AIDS

CONTENTS

1.0 INTRODUCTION

Unlike several other infectious diseases which kill within a short period of time, HIV progresses gradually from the day of infection to about 10-12 years before a fully, blown HIV infection otherwise known as AIDS manifests.

The management of HIV/AIDS does not aim at curing the infection as till date there is no known cure at the moment except vaccines that prolong the life of the infected.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

explain how to manage HIV/AIDS
explain how to apply ARVs in HIV/AIDS
explain the various vaccine trials against HIV/AIDS
understand the prospects of HIV/AIDS vaccines
understood the nutritional requirements of HIV/AIDS
economically empower PLWHA
understand how PLWHA can live normal lives
explain the consequences of stigmatization and discrimination.

3.0 MAIN CONTENT

3.1 Pharmacology

Pharmacology of HIV and AIDS are similar to those for HTLV infection: therapy education, public health and vaccination. Therapeutic categories for HIV include antiviral therapies, immunomodulators and therapies which are usually specific to treat and prevent opportunistic diseases. Several nucleoside analogues, are currently the only anti HIV agents that have been shown to significantly improve area survival in AIDS-patients. Additional nucleoside analogues, as well as other potential antiviral agents, are undergoing clinical trials. Owing to the persistence of HIV infections, lifelong antiviral to the treatment will probably be necessary.

In addition to the antiviral agents, several immunomodulatory agents are undergoing clinical trial. As regards treatment of opportunistic infections, the use of aerosolizer pentamidine has brought about a major advance in preventing P.carinii pneumonia. Since P. carinii pneumonia is the commonest cause of death in AIDS patients, aerosolized pentamidine can greatly improve survival in these patients.

3.2 Vaccine against HIV

One obstacle to the development of vaccine against HIV is that the relation of immunity to HIV infection is not understood. The experience gained in developing a vaccine against an animal retrovirus, feline leukaema virus suggests that immunity to the viral envelope protein is crucial for prevention of infection. Efforts have therefore been made to develop HIV vaccines that use the processor HIV glyprotein (gp 160) with external subunit (gp120), as immunogens which are being evaluated in phases.

Because of the difficulty of ensuring safety against probable vector-induced disease, vaccines based on attenuated or inactivated HIV or on simian isolates are viewed with apprehension. Recombinant viral proteins-especially those of the envelop of glycoproteins-seem to be more likely bandiates whether delivered with adjuvants or with heterologous viral vectors. In effect, sub-unit vaccine must be able to protect antibodies against natural isolates of HIV as well as the laboratory strain used for production.

Novel methods are under investigation e.g. a soluble form of CD4 has been made recombinant DNA techniques, and is being studied as a viral blocking agent. As CD4 is the HIV receptor on cells, it may block

gp120. Immediate events such as fusions may serve as a targeting signal to direct cytotoxical agents (e.g. CD4-nicin) to HIV-infected cells.

Geje theraphy approaches are also being developed. They are designed to achieve "intracellular immunization, i.e. genetically alter target cells to make them resistant to HIV. Two strategies are employed. One strategy aims to express an altered from an HIV replication protein in that it interferes with wild type function, disrupting viral replication and thereby protecting the engineered CD4-T cells. Another concept uses ribozymes- RNA molecules that enxymalically cut targeted RNA into fragments-to block HIV replication in cells.

A major hindrance to vaccine development is the act of an appropriate animal model for HIV. Chimpanzees have been mostly used as an animal susceptible to HIV, it is however scarce in supply and even develop only vicimia and antibodies but do not develop immunodeficiency.

3.3 Nutrition

Consequent upon the devastating nature of HIV/AIDS on the infected individuals they often appear malnourished. They therefore required energy/high energy food and protein to supply the required energy and repair and replace worn-out tissues and even build up the CD4 in HIV/AIDS.

A Patient undergoing a history and physical examination should be asked questions to help intensify those high risk patients and given further evaluation for malnutrition. Meals must be regular and available. Intake of food or body weight, use of special diets or dietary supplements, use of alcohol, drugs or medications, food preference and food allergies and the presence of opportunistic infection, nutritional intakes losses or requirements should be evaluated. Elderly and adolescent patient, pregnant or lactating women, and the poor and socially isolated HIV patients are at particular risk of nutritional problems.

Initial efforts should be directed at correcting fluid and electrolyte abnormalities and opportunistic infections. Of particular concern are depletion of potassium magnesium and calcium and acid base abnormalities. The second phase of treatment is directed at repletion of protein, energy and micronutrient. Treatment is started with modest quantities of protein and calories calculated according to the patients actual body weight. Adults are given 1g of protein and 30kcal/kg.

Concomitant administration of vitamins and minerals is obligated. Either the enteral or parepleral route can be used, although the former is preferable. Patients with low protein-calories under nutrition can be given calories and proteins simultaneously, with the correction of fluid and electrolyte abnormalities and similarly, protein and calories are recommended for initial treatment.

Patients treated for protein-energy malnutrition require close follow up. In adults both calories and protein are advanced as tolerated, (adult to 15g/kg/d of protein and 40/kcal/kg/d of calories).

SELF ASSESSMENT EXERCISE

1. List three groups of drugs used in HIV/AIDS
2. Give at least five forms in which HIV/AIDS is managed

3.4 Social

HIV/AIDS infection has dire social consequences. These arise from the individual understanding, perception as well as beliefs on HIV/AIDS. Victims lose self-esteem because they assume that they are in the society. Some believe that they had better die than live with the infection, as they don't accept the fact that they can live a normal life with HIV. Other believes that by using ARVs and taking necessary precaution they will help in preventing further spread. When a man writes himself off there is nothing somebody else could do to convince such a man, so he loses his self esteem, human dignity and undermines his potential as person who can successfully live for yeas with HIV patient. This perhaps is one of the major causes of high mortality of HIV in the developing counties, especially in the sub-Saharan Africa. This is one major reason while counseling is very important. This is self stigmatization. The truth is that no one ever said "yes" to AIDS and no one has asked for it. Most of us who have it now had never heard of it when we caught it. You cannot attach blame or assign guilt to anyone as it does not matter who was responsible. The most important thing is to think and live positively. Discrimination is composed of actions or treatment based on the stigma and directed towards the stigmatized.

Some sources of stigma include self stigmatization, family, community, workplace, religious institutions, health care and existing laws.

Certain managerial responsibilities with the health facility such as non-discriminatory policies, confidentiality policies, universal precaution policies, including provision of necessary materials for its application and post exposure prophylaxi policies should be fully implemented.

Health facilities must be more friendly and above all, training of healthcare providers on HIV management is very important.

At the family and community levels the males must be enlightened on support of choices, avoidance of abuse and violence particularly if the woman is first diagnosed. The role of men in HIV transmission, in addition to peer support and community support should be publicized by governments, religious institutions and well-meaning individuals. This means that provision of community mobilization and education should reduce the reported high prevalence of HIV/AIDS. Advocacy and sensitization of individuals, communities and opinion leaders are seriously required. Community awareness of voluntary counselling and treatment (VCT) and its benefits should be encouraged, including the establishment of VCT services so that more people can know their HIV status. Involvement of faith based organizations should be encouraged.

3.5 Economic

As HIV/AIDS progresses in an infected individual it does affect his/her productivity, especially when the individual does not know his/her HIV status. This means several man-hour are wasted which has adverse economic consequences on the individuals, institutions and the country at large. It is therefore advocated that when the HIV status of the population in a country is known, interventions policies from government would yield the desired results. Those infected must be placed on ARVs to boost high C4 counts and allow viral loads and hence higher productivity. Provision of free ARVs especially the HAART cocktail would also enhance their productivity. Those orphaned and widowed should also be catered for both in terms of health and economic empowerment. Provision of interest free loans by well-meaning individuals, organization and government is strongly recommended. This will make life meaningful to those infected and thus enable them to live dignified lives. The community and government should therefore provide mandatory economic and educational empowerment to HIV/AIDS positive individuals so that they can live fruitful lives.

4.0 CONCLUSION

We have seen that there are many way to manage HIV, (medical, social, economic, etc) to produce a healthier and happier HIV positive individuals.

5.0 SUMMARY

In order to manage HIV/AIDS, several important factors need to be considered. This unit therefore provided the different management approaches to HIV.

ANSWER TO SELF ASSESSMENT EXERCISE

Antiviral therapies, immunomodulators, pharmacological vaccine production, nutrition pharmacology, economic and social

6.0 TUTOR-MARKED ASSESSMENT

1. What are the problem militating against vaccine production for HIV/AIDS?
2. What do you understand by stigmatization and discrimination?

7.0 REFERENCES/FURTHER READINGS

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