

All About Antiretrovirals

A Nurse Training Programme

Trainer's Manual

Written & Developed by
Marcus McGilvray & Nicola Willis

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We would like to thank all the people who have contributed towards the development of this manual:

All the nurses who assisted us with our assessment and pilot of this manual, for not only giving up their time but also their invaluable thoughts and ideas on nurses' training needs, enabling us to develop a nurse-focused training manual.

Dr Janet Giddy for her motivation and allowing us to use some of her training slides.

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NAM for making this training manual freely available to people involved in ARV training.

The Peer Review Committee, a team of six nurses from Chelsea & Westminster Hospital, UK, who each have considerable experience of ARV training in resource limited settings, and Dr David Ferris, Research Fellow, Columbia University.

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The potential benefits of Antiretrovirals for people living with HIV/AIDS are great. With ARVs becoming increasingly more accessible in resource-limited settings it is hoped that people with HIV/AIDS will now face a manageable chronic disease as opposed to a progressive, debilitating disease resulting in death. As a result, people will live longer and enjoy a better quality of life.

However, there are significant challenges associated with Antiretroviral therapy. Rapid emergence of resistant viral strains have, for a long time, been recognised in the US and Europe. Multi-drug resistant HIV infection rapidly develops through the sub-optimal use of ARVs, curtailing future treatment options for the patient.

Due to the paucity of doctors in resource-limited settings, ARV administration will, to a large part, rely on nurses and health care workers.

Enhancing Care Initiative KZN Plus kindly allowed us to visit their six hospital/clinic sites in KwaZulu Natal, South Africa, to carry out a number of informal assessments with nurses working in the field of HIV/AIDS. These assessments were carried out in order to recognise nurses' perceived training needs for successful ARV administration.

As a result, this training manual has been developed by nurses for nurses to equip them with the knowledge and skills required to rise up and meet the greatest health challenge in the world today. We do not profess to have designed a manual that covers every single aspect associated with ARVs and their delivery. However, we do hope that this training manual will be seen as a comprehensive nurse teaching pack, which offers a clear introduction into ARVs and the role of the nurse.

On completion of this training it is hoped that the nurse will feel empowered by having a basic understanding of ARVs and the challenges they commonly present. Furthermore, nurses will gain an increased sense of importance and confidence in the role that they have to play in the professional, holistic care of people living with HIV/AIDS and the overall success of ARV treatment.

Dr Janet Giddy from McCord Hospital, Durban very kindly allowed us to use some of her training slides in this manual. Her quip, "With so much work to be done we need to freely share materials rather than keep reinventing the wheel", rings very true. Whilst we appreciate that training materials must vary if they are to meet the needs of each particular audience, we also believe that a lot of time, money and effort can be saved by encouraging people to simply adapt existing materials rather than starting from scratch!

We hope that you will find the Training Manual to be of benefit and wish you good luck in your training.

Marcus McGilvray
HIV Nurse Specialist

Nicola Willis
Paediatric HIV Nurse Specialist

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The training manual has been designed to provide trainers with a flexible tool, which may be utilised and adapted according to their specific needs. The course can be delivered as a whole or used in part, according to the needs of the nurse and health care worker, work setting and the time available.

Based on our own experiences, we suggest that each teaching session take one hour to complete. Ideally, a further half an hour is required for the group exercises. In total, allow 1 hour 30 minutes for each module.

Training Course Modules

Module 1: Let's Talk About HIV

Module 2: Let's Talk About ARVs

Module 3: Side Effects

Module 4: Resistance

Module 5: Adherence

Module 6: ARVs in Children

Module 7: The Role of the Nurse

Each module contains:

Learning objectives: to inform trainer and trainees of module content and expected learning outcomes.

PowerPoint slides with accompanying lecture notes: to assist trainers in the delivery of training sessions. The lecture notes have been written as a guide, to be enhanced by the local, personal experience of the trainer.

Learning Exercises: to reinforce module content and help facilitate the application of theory in to practice

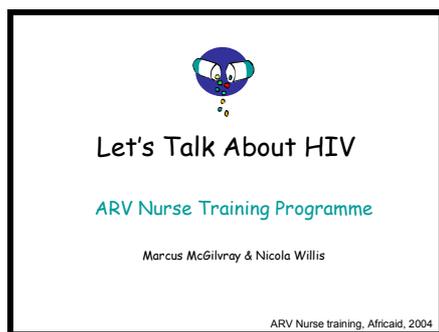
Suggested Handouts: to provide nurses with a continual source of reference on ARV drugs.

Reference and Resource List included at the end of the manual to provide trainers with further background information for the preparation and delivery of training sessions.

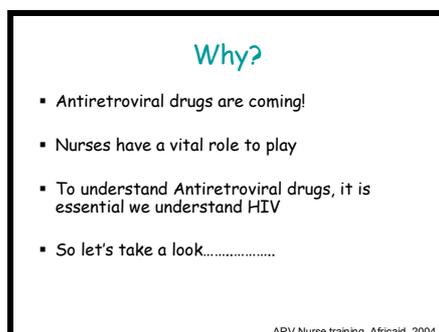
Module Objectives

- To ensure nurses have a basic understanding of HIV infection and its effect on the immune system
 - To provide nurses with an understanding of the usual clinical course of HIV infection
 - To describe the general management of patients throughout the stages of HIV infection
 - To equip nurses with the skills required to explain the basics of HIV infection to their patients
 - To differentiate between HIV and AIDS
-

Slide Presentation: Let's Talk About HIV



1. Welcome trainees and introduce yourself. Give a brief background of your area of practice, role & experience in the provision of care for patients with HIV. If there is time, trainees may be asked to share with one another their own experiences, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage trainees to feel free to interrupt with questions at any time.



2. ARVs are becoming increasingly available to people living with HIV/AIDS. A lack of human resources and the traditional holistic role played by the nurse means they will have a central role to play in ARV administration. To understand the impact of ARVs on HIV disease, first, we must be sure we understand HIV.

What is HIV?

- Human
- Immunodeficiency
- Virus



Like all viruses, HIV must enter other cells in order to replicate

HIV is a **retrovirus**, and its genetic material, RNA, must be converted in to DNA during replication

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3. Viruses are simple in structure and cannot replicate alone. They require the components of other cells for replicating. HIV, like all viruses, must therefore enter other cells if they are to replicate and survive. HIV is from a special family of viruses known as *Retroviruses*. *Its genetic material is* carried in the form of RNA, rather than DNA. This RNA must be converted in to DNA during replication.

HIV & the Immune System

- HIV uses **CD4 cells** for reproduction
- CD4 cells are cells that carry **CD4 receptors** on their surface
- CD4 receptors are found on a variety of cells, but mainly on **T4-lymphocytes (T-helper cells)**
- T4-lymphocytes are a type of white blood cell that **'switch on'** the immune system to fight disease

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4. HIV primarily targets cells known as CD4 cells. These cells are called CD4 cells as they carry CD4 receptors on their surface. These are protein molecules and are found on the surface of a variety of cells of the immune system. HIV 'looks' for these CD4 receptors. When it finds them, HIV binds to the CD4 receptor on the surface of the CD4 cell like a 'lock and key'. Most CD4 cells are T4 lymphocytes which coordinate the immune system response.

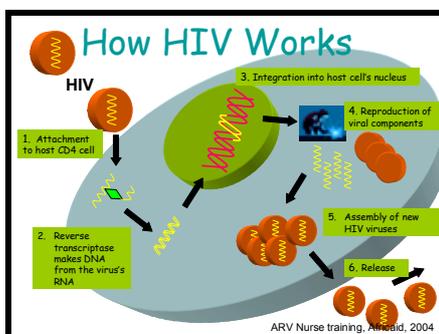
HIV & the Immune System

- The CD4 cells are like soldiers
- Strong CD4 cells are able to fight off infection
- BUT, when HIV enters CD4 cells for reproduction, it damages the CD4 cell, eventually killing it.
- So, HIV damages the very system that usually protects the body from infection



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5. Many people find it helpful to think of CD4 cells as 'soldiers' in the body. Usually any infection entering the body is fought off by the soldiers (CD4 cells). Strong soldiers make a strong immune response and the infection is fought off. However, HIV damages these soldiers, finally killing them. The soldiers are either too weak or too few in number to fight off infection. The immune system is progressively weakened.



6. The 6 stages of the HIV life cycle are essential if we are to understand the effect of ARVs on HIV. 1) HIV attaches to the CD4 cell & releases RNA & enzymes. 2) The enzyme *Reverse Transcriptase* makes a DNA copy of the viral RNA. 3) New viral DNA is then integrated using the enzyme *integrase* into the CD4 cell nucleus. 4) New viral components are then produced, using the cell's 'machinery'. These are assembled together using the enzyme *protease* & then released as new viruses. **Refer to Hand Outs 1: The Life Cycle of HIV.**

HIV Factory

- When HIV binds to a CD4 cell, it turns that cell in to an HIV Factory
- Billions of HIV viruses are produced, and the CD4 cell is eventually killed
- The new HIV viruses go on to infect other CD4 cells, and reproduce



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7. Use of the factory analogy may help trainees to understand how HIV works. HIV (blue, rounds cells in diagram) uses the CD4 cell like a factory. It needs the machinery inside the factory (CD4 cell) to replicate. So HIV enters the factory and starts replicating, using the CD4 cell's machinery. Millions of new viruses are released from the factory (CD4 cell). These new viruses then move on to infect other CD4 cells which become more factories for HIV.

A Losing Battle...

- The normal range for CD4 count is 600-- 1500 cells/mm³
- With HIV infection, every day more CD4 cells are made; and every day HIV uses CD4 cells to replicate itself
- In the long term, it's a losing battle for the CD4 cells...



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8. On average, an adult has between 600-1500 CD4 cells/mm³ in the body. If the person is infected with HIV, the virus gradually infects and destroys more and more CD4 cells. Over time, the number of CD4 cells in the body decreases.

Assessing the Damage

- The state of an HIV+ person's immune system is measured by counting the CD4 cells that remain ie CD4 count
- Over the years, HIV progressively weakens the body's immune system by decreasing the number of CD4 cells



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9. The number of CD4 cells can be counted in a small sample of blood. This is called the CD4 count and tells us how 'strong' the immune system is. A CD4 count between 600-1500 cells/mm³ indicates the immune system is coping well and managing to remain high in spite of HIV. However, over time, the CD4 cells are progressively destroyed and the CD4 count falls. A low CD4 count tells us the immune system is 'weak.'

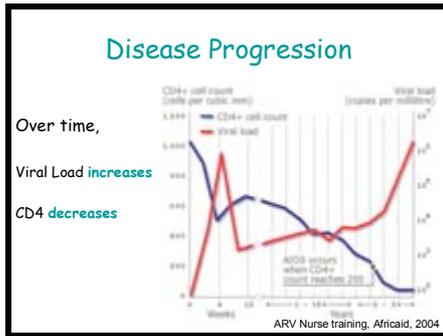
Assessing the Damage

- Viral Load is another useful blood test
- It tells us how much HIV virus is in the blood
- Over time, viral load increases as more and more virus is produced



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10. Another important blood test for people with HIV is the Viral Load test. This test measures how much virus is in the blood. As the virus replicates more and more, viral load will increase. The test is a useful indicator of disease progression.



11. The normal course of disease is shown in this graph. The viral load is very high within the first month of infection. This high level of virus means the CD4 count drops steeply as it is being attacked by HIV. Then, over the next few months, the immune system makes an attempt to fight the virus. Viral load drops steeply & CD4 count is able to rise slightly. After this initial stage, the HIV disease may then remain **latent** in the body during which a patient is **asymptomatic**. This asymptomatic phase varies but may last up to 15 years in some patients. Eventually however, the viral load starts increasing as replication continues. The CD4 cells are progressively overwhelmed and the patient becomes symptomatic. Towards the end, viral load gets extremely high as CD4 cell gets extremely low, dropping even as low as 0.

Opportunistic Infections

- HIV slowly destroys CD4 cells over years of infection
- As the CD4 count drops, infections take 'opportunity' of this weakened immune system, resulting in **opportunistic infections**

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12. Over time, HIV destroys the CD4 cells and the immune system becomes increasingly weakened. As CD4 count falls, the immune system is unable to fight off infections that it would usually be able to fight off, even with the help of medication. These infections therefore take the 'opportunity' of this weak immune system & are called *opportunistic infections*. These may be abbreviated to OIs.

Stages of HIV: Stage 1

- Usually asymptomatic (+/- persistent generalised lymphadenopathy)
- CD4 count 600-1500mm³
- Able to fight infection well
- CD4 drops slowly over time
- Possible to continue with normal daily life

Management

- ✓ Healthy Lifestyle (20 min walk/eating well)
- ✓ Regular check-ups, STI screening, PAP smears, influenza vaccines, Safer sex

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13. A system has been developed in which different 'stages' of disease from beginning to end are characterised by certain signs and symptoms. These give us an idea of the severity of disease and prognosis. Stage 1 is usually asymptomatic and may go on for many years. However, swollen lymph nodes are commonly seen as this is where more and more soldiers are produced in an attempt to fight against the HIV. Healthy lifestyle is important for maintaining good health for as long as possible.

Stages of HIV: Stage 2

- CD4 count drops below 350mm³
- Mild infections more often than usual, rashes, skin infections, fever, oral thrush, shingles, recurrent chest infections
- Weight loss common
- Possible to continue with normal daily life

Management

- ✓ Same as Stage 1 (Healthy Lifestyle, Check-ups, screening, safer sex, vaccines)
- ✓ Early treatment of infections
- ✓ Prophylaxis (co-trimoxazole - Bactrim)

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14. CD4 count falls below 350, indicating that the immune system is weakening. In turn, infections are seen more often than usual. Medication may help the patient to fight these and it is possible to continue with daily life. Weight loss is common. Maintaining health is essential. Prophylaxis against PCP & Toxoplasmosis is started, using Bactrim. Early treatment of infections is essential as they are normally much more difficult to treat and any infection weakens any remaining immune cells.

Stages of HIV: Stage 3

- CD4 count drops below 200mm³
- More serious OIs common (g pneumonia, meningitis)
- Chronic diarrhoea, prolonged fever, candida, TB, severe pneumonia
- Weight loss+
- Difficulty with daily activities

Management

- ✓ Same as Stage 1 (Healthy Lifestyle, Check-ups, screening, safer sex, vaccines)
- ✓ Early treatment of infections
- ✓ Antiretrovirals
- ✓ Prophylaxis (co-trimoxazole - Bactrim)

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15. As CD4 count drops further, more serious, debilitating Opportunistic Infections occur. Weight loss continues, along with a lack of energy and reduced ability to carry out daily activities. Again, primary health care, early treatment of infections and prophylaxis is all essential to promote health and preserve any remaining immune function for as long as possible. ARVs should be started now if available.

Stages of HIV: Stage 4

- CD4 count drops further, as low as 0mm³
- Often Very sick, bedridden
- More severe OIs eg PCP pneumonia, severe diarrhoea, lymphoma, extrapulmonary TB, toxoplasmosis, CMV, cryptococcal meningitis, Kaposi's sarcoma, HIV encephalopathy, oesophageal candidiasis
- Weight loss+++

Management

- ✓ Antiretrovirals
- ✓ Treatment of OIs
- ✓ Hospital or home-based care
- ✓ Prophylaxis (co-trimoxazole - Bactrim)

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16. CD4 count may reach 0. With next to no immune function left, patients are often extremely sick and very serious Opportunistic Infections occur. Weight loss is considerable. Treatment of infections and symptom management is of paramount importance. Patients may be cared for in the home or a hospice. The need for prophylaxis continues as does the need for ARVs. It must be stressed however, that some patients with very low CD4 counts are not so sick and continue to display reasonably good health.

Acquired Immune Deficiency Syndrome

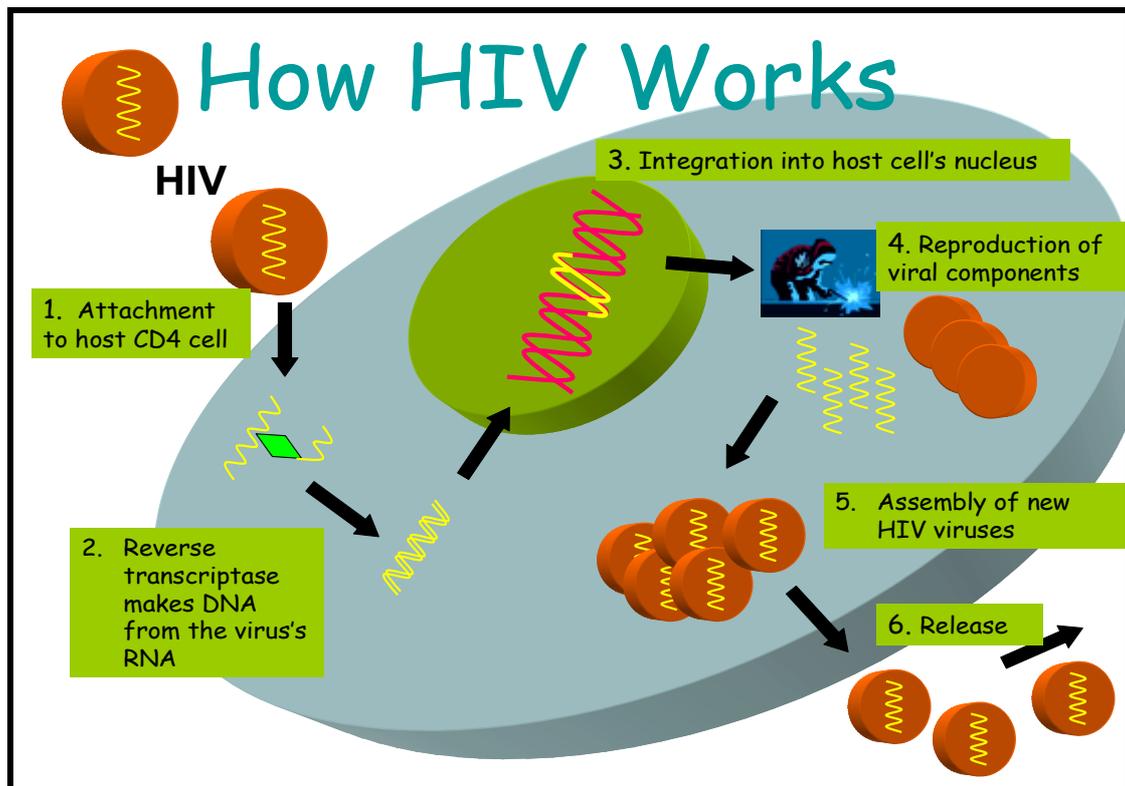
These opportunistic infections are the signs and symptoms associated with HIV infection

When an individual's immune system is damaged to the extent that these OIs occur, the individual is said to have AIDS

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17. HIV and AIDS are different! HIV is the virus that causes immune deficiency. This state of immune deficiency makes the body vulnerable to Opportunistic Infections. It is the collective presence of different Opportunistic Infections, as a result of immune deficiency, that is known as Acquired Immune Deficiency Syndrome. Someone may be infected with HIV for many years before their immune system is damaged sufficiently to cause Opportunistic Infections and hence AIDS.

Hand Out 1: **The Life Cycle of HIV** (diagram with kind permission of Dr J. Giddy)



1. HIV locates the CD4 cell and **attaches** to its surface. Having fused with the cell membrane, HIV releases its genetic material (viral RNA) and enzymes in to the CD4 cell.

2. A DNA copy of the viral RNA must now be made. The enzyme **Reverse Transcriptase** is essential for this process. It copies the viral RNA into viral DNA.

3. The viral DNA is now integrated in to the CD4 cell's nuclear material. This process is made possible by the enzyme *integrase*.

4. The individual components of HIV are then **produced** within the CD4 cell.

5. The individual components of HIV are then **assembled** together, to make new HIV viruses. This process depends on the enzyme *protease*.

6. New viruses are released from the CD4 cell. These infect other CD4 cells where the cycle repeats itself.

Remember the factory! During stages 1 to 6, HIV uses the CD4 cell like a factory. HIV needs the 'machinery' inside the CD4 cell in order to be able to replicate. By stage 6, new viruses are released from the factory.

Learning Exercises: 'Let's talk about HIV'

A. Questions

1. Which cells does HIV primarily target for replication?

CD4 cells, which are cells carrying a CD4 receptor on their surface. These are found on a variety of cells but primarily the T4 lymphocytes of the immune system.

2. Why does HIV 'need' CD4 cells?

Like all viruses, HIV cannot replicate on its own. It requires the 'machinery' of other cells. HIV must enter CD4 cells and use the cell to replicate, thus producing new HIV viruses.

3. What is the effect of HIV's attack on CD4 cells?

CD4 cells are essential in co-ordinating the immune system. When HIV uses CD4 cells for replication, it also destroys those CD4 cells. The immune system is therefore weakened and unable to fight off infections. Without medication to fight HIV, the immune system becomes weaker and weaker, opportunistic Infections occur and the patient develops AIDS. The eventual result is death.

4. What does 'latency' mean?

'Latency' refers to the period during which a patient is infected with HIV but is not experiencing signs and symptoms associated with HIV. This period varies greatly from one individual to the next. On average it lasts 8 – 10 years but it may be even longer in some people.

5. Using Handout 2: 'Life Cycle of HIV' below, write in the different stages of HIV replication from 1 – 10

Answers are on Hand Out 1: 'The Life Cycle of HIV'

6. What are the clinical signs and symptoms associated with early infection (Stage I & II)?

In Stage I, the patient is asymptomatic although may have swollen glands under the arms, in the neck or in the groin. CD4 count is usually high, between 600 and 1500 cells/mm³ and the patient can fight off infections and live a normal life. By Stage II, the CD4 count has dropped to below 350 and infections are more common e.g., shingles, rash, skin infections, oral thrush and recurrent chest infections. Weight loss commences. It is still possible to continue with normal daily life, with the help of treatment for infections.

7. What are the clinical signs and symptoms associated with the later stages of HIV infection (Stage III & IV)?

In Stage III, the CD4 count drop even further to below 200 and the patient is said to have AIDS. More serious Opportunistic infections are more common, e.g., pneumonia, TB (although this may be seen at any stage), meningitis, oesophageal candidiasis, chronic diarrhoea and prolonged fever. Weight loss continues and normal activities become more difficult. By Stage IV, the CD4 count is extremely low, even reaching zero. Severe Opportunistic infections occur e.g. PCP pneumonia, extra-pulmonary TB, lymphoma, severe diarrhoea, encephalopathy, Kaposi's sarcoma and CMV. The patient suffers extreme weight loss, is very sick and bedridden with death imminent.

B. Group Work

Patients look to nurses for explanations about their condition. If patients are to have confidence in their nurse and receive clear, accurate information, it is vital that nurses are able to answer their questions appropriately. These role plays have been designed to equip nurses with the skills to answer some common questions patients may have about their condition.

Divide the group in to groups of 2 - 4 and give each sub-group a question. Ask each group to discuss their question and to decide how best to respond to patients. Then ask each group to feedback to the whole group through role play, where one trainee is the patient asking the question and one is the nurse providing the answers.

Trainees may have their own way of explaining about HIV to patients but suggestions are included as example responses.

Typical Patient Questions:

1. What is the difference between HIV and AIDS?

*HIV is the **virus** which attacks your immune system. When HIV enters the body you are said to be 'HIV infected' or 'HIV positive'. It does not mean you have AIDS. You may be HIV positive for a long time before you become unwell. However, over time HIV **causes great damage** to your immune system so that you start to get infections that you could normally fight off. These are called **Opportunistic Infections**.*

When you start getting many of these Opportunistic Infections, you will have AIDS.

2. How does HIV make me sick?

When viruses enter the body, they are normally attacked by your immune system so that you do not become sick. HIV is also a virus, but unlike other viruses, HIV attacks the immune system itself. In other words, it destroys the very system that would usually fight against infection in the body.

HIV does this by using immune cells (tiny parts or building blocks of the immune system) known as CD4 cells, to replicate itself. HIV makes lots of new virus but destroys the CD4 cells in the process. This means the immune system becomes extremely weak and cannot protect you against infections.

3. What are these blood tests I have to have?

There are a variety of blood tests you may receive but there are two main tests which can show what the HIV is doing in your body.

- *CD4 count which measures the number of CD4 cells in your blood. This tells you how strong your immune system is. The higher the CD4 count the better.*
- *Viral Load measures the amount of HIV in your blood. The lower the Viral Load the better.*

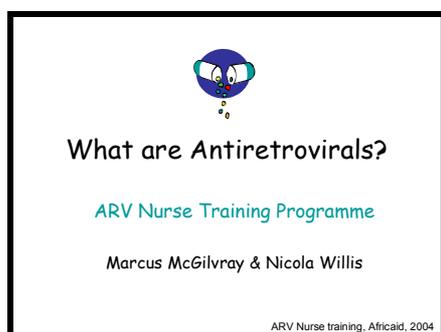
4. What will happen to me now that I have HIV?

Everybody is different. Many people stay well for a very long time while others may become sick with different infections more quickly. What is important is to try and stay healthy for as long as possible. Various things are very important and include good nutrition, exercise, being immunised, having regular checks at the clinic, and having safe sex. You may also be given medication to prevent you from getting certain infections. ARV drugs will be given to you when you need them.

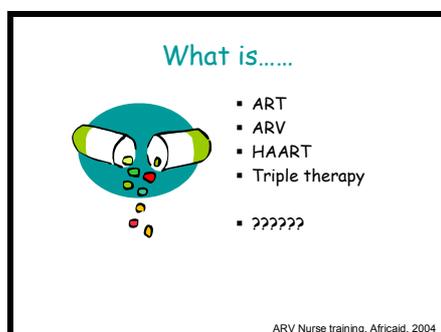
Module Objectives

- To equip nurses with an understanding of how ARV drugs work
 - To demonstrate the impact of ARV drugs and triple therapy on HIV disease
 - To provide nurses with a basic understanding of the criteria for commencing ARV therapy
 - To introduce nurses to the ARV drug combinations most commonly used
 - To equip nurses with the skills required to explain about ARV drugs to their patients
 - To introduce the immense challenges associated with ARV administration
-

Slide Presentation: Let's Talk About ARVs



1. Welcome trainees and introduce yourself, including a brief background of your area of practice, role & experience in the provision of care for patients taking ARVs. If there is time, trainees may be asked to share with one another their own experiences of ARVs, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage nurses to feel free to interrupt with questions at any time.



2. There are various terms and abbreviations used when referring to 'anti-HIV drugs'. **Ask the group if they have heard of any of these and if they know what they mean.**

Confusing terminology....!

- ART = AntiRetroviral Treatment
- ARV = AntiRetroVirals
- HAART = Highly Active AntiRetroviral Treatment
- Triple Therapy = Three Antiretrovirals

Basically it all means the same thing!

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3. All these different terms are confusing but they all refer to the same thing – the use of antiretroviral drugs. People use different abbreviations - that's all!

But what are Antiretrovirals?

Medicines that are used to fight the HIV virus directly

Versus

Medicines used to treat OIs
Immune Boosters
Herbal Remedies

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4. It is important to differentiate between ARVs and other medication commonly taken by people with HIV. Treatments for OIs are used to fight individual infections that occur due to the person's weakened immune system. These include antibiotics and antifungal drugs for example. They are extremely important, but they do not fight the virus directly. Neither do immune boosters or herbal remedies.

What do ARVs do....?

ARVs change HIV from a terminal (fatal) disease to a "chronic disease".

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5. ARVs have a dramatic effect on HIV infection. Without ARVs, HIV is a terminal disease, commonly associated with progressive deterioration of the patient's health once OIs start occurring. With ARVs, although HIV will not be cured, HIV is no longer a progressive deterioration to death but instead a stable chronic disease.

What is a Chronic Disease??

An illness which cannot be "cured" but can be controlled

Examples of chronic diseases:

- Diabetes
- High Blood pressure
- Asthma
- Schizophrenia



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6. Discuss examples of chronic disease to illustrate that there are many diseases for which there is no cure but with which people live long, normal lives as long as the disease is kept under control through medication. HIV is the same – ARVs are able to control the virus, allowing people to live longer normal lives.

How do they control HIV?

- ARVs reduce the ability of the HIV virus to replicate
- In turn, this increases the ability of the body to fight disease

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7. Remember, as HIV replicates inside CD4 cells, it destroys those CD4 cells and gradually weakens the immune system. Therefore, by reducing the ability of HIV to replicate, ARVs 'control' HIV infection and therefore protect the immune system which would otherwise be destroyed. With the immune system restored and protected, the body is then able to fight infections as in uninfected individuals.

Primary Goal of ARVs

to decrease or reverse immune system damage associated with HIV infection,

thus improving quality of life and reducing HIV-related morbidity and mortality

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8. The primary goal of ARVs is to decrease or reverse immune system damage associated with HIV infection. In turn, the number of infections is reduced, general health improves, quality of life is restored and the length of life is increased.

How HIV Works

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9. To understand how ARVs work we must think back to the 6 stages of the HIV Life Cycle. **Ask the trainees to refer to Hand Out 1 from Module 1. Ask if anyone is able to talk through the different stages of the Life Cycle of HIV.**

ARVs at Work....

- Remember - HIV uses the CD4 cell as an HIV factory.....
- ARVs get inside the factory, and at different places, reduce the ability of the virus to replicate
- So, less virus can be made

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10. ARVs inhibit replication in the CD4 cell. Use of the factory analogy may help trainees to understand this. Normally, HIV uses the CD4 cell like a factory. It needs the machinery inside the factory (CD4 cell) to replicate. So it enters the factory and starts replicating, using the CD4 cell's machinery. Millions of new viruses are released from the factory (CD4 cell). ARVs prevent process from occurring in the CD4 cell, so that new viruses are no longer produced. There is therefore less virus around to infect and destroy other CD4 cells

3 Main Classes of ARVs

NRTIs - "nukes" eg AZT, 3TC, DDI, D4T

NNRTIs - "non nukes" eg EFV, NVP (Nevirapine)

PIs - protease inhibitors eg lopinavir, ritonavir

Each class acts at a different stage and in a different way, to prevent HIV replicating within the CD4 cell

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11. There are three main classes of ARV drugs including Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) and Protease Inhibitors (PIs). All three work in different ways to inhibit the replication of HIV inside the CD4 cells. **Refer to Hand Out 3: Antiretroviral Drugs & Doses.**

ARVs at Work.....

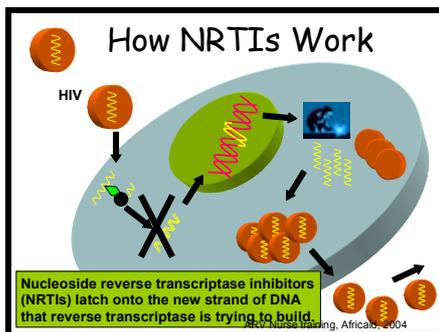
Remember the enzymes involved in HIV replication....?

- **Reverse Transcriptase** (essential for copying RNA into DNA in the **early stages** of replication)
- **Protease** (required for assembly and maturation of fully-infectious new virus in **final stages** of replication)

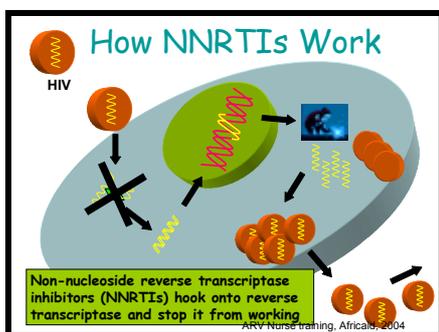
ARVs **INHIBIT** these enzymes, thus slowing down the replication cycle

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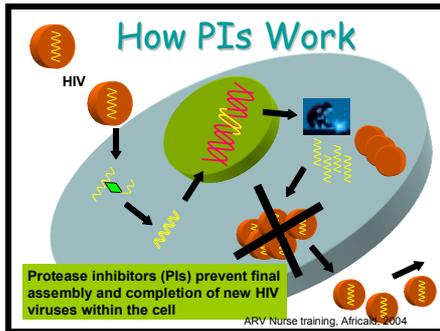
12. Remember there are three enzymes involved in replication. Without them replication cannot occur. The first, *Reverse Transcriptase*, is needed at the beginning in order to make DNA copies of viral RNA. *Protease* is essential at the end, for assembling new viral particles in to new viruses. ARVs stop these enzymes from working, thus slowing down the process of replication



13. Talk the group through the life cycle again, indicating where *Reverse Transcriptase* is normally involved in making a DNA copy of the viral RNA. The black cross indicates inhibition (blocking) of this enzyme, so that this DNA copy cannot be made. NRTIs attach to the new strand of DNA being made. In this way, viral RNA cannot be copied into viral DNA and the whole life cycle breaks down. **Refer to Hand Out 4: How do ARVs work?**



14. NNRTIS also work at the beginning, inhibiting *Reverse Transcriptase*, but stress to the group that they work in a *different way* to NRTIs. They hook on to the actual enzyme which stops it from working. The result is the same though, as the DNA copy of viral RNA cannot be made and therefore cannot be integrated in to the nucleus. Again, the life cycle breaks down. **Refer to Hand Out 4: How do ARVs work?**



15. Continue to talk through the life cycle, indicating where the enzyme *protease* operates. Protease is essential for assembly of new viral particles. Without it, new viruses cannot be assembled. PIs prevent *protease* from assembling new virus in the final stages of the life cycle. **Refer to Hand Out 4: How do ARVs work?**

Does everyone with HIV need ARVs ?

NO

It depends on the 'Stage' of HIV Infection

Which depends on.....

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16. The group may be asked their thoughts on this question. Many misunderstandings and preconceptions commonly exist. A common question is "Why did the doctor wait to give ARVs to this patient when they can help so much?" The need for ARVs depends on the Stage of HIV and the CD4 count. Remind the group of the Stages 1 - 4, discussed in Module 1.

Who needs ARVs.....?

The 'Stage' of HIV depends upon:

- Immunological markers (CD4 count)
- Clinical symptoms (Opportunistic infections)

It also depends greatly on whether the patient is ready to start

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17. The patient's stage of HIV is assessed by looking at their CD4 count & Clinical symptoms. CD4 count provides an indication of the damage to the immune system and how strong the immune system is as a result. Clinical symptoms show the extent to which the damaged immune system is able to fight off infections. Opportunistic Infections indicate that the immune system is NOT coping. Patient readiness is also very important.

WHO Guidelines (2002)

HIV infected adults and adolescents should start ARV therapy when they have:

- WHO stage IV of HIV disease, regardless of CD4 count
- WHO stages I, II, III of HIV disease, with a CD4 count below 200/mm³

(where CD4 testing available!)

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18. Numerous trials are being run all over the world to decide the best time to start ARVs. Years of experience with people on ARVs in other countries, have enabled the World Health Organisation to confirm these guidelines for Rolling Out in South Africa. All patients in Stage IV should start ARVs. Patients in stages I, II and III should start ONLY if their CD4 count is below 200/mm³. This is the time when they are at most risk of developing OIs.

Starting ARVs in Children (WHO 2002)

NB: Children differ in their immunology and virological response to HIV
And are managed differently!

<18 months:
Paediatric Stage III, irrespective of CD4 cell %
Paediatric Stage I or II with CD4 <20%

18+ months:
Paediatric Stage III, irrespective of CD4 cell %
Paediatric Stage I or II with CD4 <15%

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19. Whilst HIV works in the same way in children as in adults, CD4 counts and viral load in children respond slightly differently. **See Module 6 for more information.** ALL children with Paediatric Stage III of infection should start ARVs. For children in Stages I, II and III, CD4% must be considered: If the child is less than 18mths old, <20% indicates ARVs. If the child is older than 18mths, <15% indicates ARVs.

What to Start.....?

- The most effective regimens utilise drugs from **different classes**
- This promotes maximum viral suppression by inhibiting replication in **different ways, at different places** in the life cycle

NRTIs:
AZT, D4T, 3TC, ddI

NNRTIs:
NVP, EFV

PIs:
NFV, IDV, LPV, SQV

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20. Remind the group that each class of ARVs inhibits HIV replication in either different places or in a different way. Therefore, if a patient takes a combination of drugs from different classes, HIV replication is blocked at different stages in the life cycle. This has a much greater impact on suppressing (reducing) overall HIV replication. For example, use of 2NRTIs and 1PI means HIV is fought at the beginning (by inhibiting Reverse Transcriptase) AND at the end (by inhibiting protease) of the life cycle.

So....

Examples of drug regimens commonly used in ARV combinations

d4T + 3TC	+	NVP
d4T + 3TC	+	EFV
AZT + ddI	+	Lopinavir/Ritonavir

NB AZT + D4T should NEVER be used together!

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21. These ARV drug combinations have been carefully considered in order to ensure maximum benefit to patients. Over time, more drug choices will become available but the initial first-line therapy will contain 2NRTIs and 1NNRTI **or** 2NRTIs and a combination of 2 PIs. These regimens have been heavily investigated and shown to have dramatic effects on viral suppression

What to expect!

Treatment success =

- Decline in VL of at least 1.0 log from pre-treatment levels by 6-8 weeks after initiating ARVs
- A decline in VL to <400 RNA copies/mL by 24 weeks after commencing ARVs

Undetectable viral load = ultimate goal!

(A sustained viral load of <50 RNA copies/mL is associated with the most durable virological benefit)

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22. Patients starting ARVs may expect a reduction in their viral load to less than 400 copies/ml, within 6 months of treatment. The ultimate goal of treatment is to reduce viral load to undetectable levels. This DOES NOT mean HIV is no longer present, but that it is in such small quantities that it cannot be found under a microscope. The best long-term results with ARVs are seen in patients whose viral load remains below 50 copies/ml for as long as possible.

Achievable.....?

YES

ARVs are able to significantly reduce viral load, allowing immune reconstitution followed by an increase in quality of life and reduction in morbidity and mortality

BUT

they are not perfect.....

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23. Years of experience with ARVs in other countries have demonstrated that ARVs can have a dramatic effect on viral load, reducing it to low levels so that the immune system can re-build again and be protected from damage by HIV. This is followed by a reduction in infections and an increase in quality and length of life

Not perfect!

Unfortunately, 'treatment failure' may occur for some people, where:

- A sustained increase in VL >5000 copies/mL
- A decline in VL of less than 1 log within 6-8 weeks after commencing ARVs
- A sustained increase in VL of >0.6 log from its lowest point or a return to 50% of pre-treatment value

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24. A balanced view **MUST** be given. In spite of the dramatic effects of ARVs, they are not perfect and treatment failure can occur. This is where ARVs are taken but viral load continues to rise to >5000 copies/ml; OR viral load only drops slightly once ARVs have been commenced OR viral load starts to increase again, having initially dropped when ARVs were started.

"It is not like just giving 2 aspirins..."

(National AIDS conference, RSA, August 2003)

This is true

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25. A realistic picture is essential. ARVs are not like most drugs. They have significant challenges which nurses must understand in order to support their patients effectively. Whilst they can work very well, they are often difficult to manage.

And.....



Everybody is different

What may work for one, may not work for another

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26. Whenever we talk about HIV and ARVs with the patient, we must make it clear that ARVs are often good but are not perfect. Whilst these drugs may help one person, they may not fully support another. We must be realistic with patients, in order that they do not have unrealistic expectations!

Why is HIV so hard to treat?

It's a cheeky little devil!

10 billion copies of the virus are made every day

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27. HIV is exceptionally clever. Not only does it attack the very system that would usually destroy it, but it replicates so rapidly that it is extremely difficult to control.

And...

- The problem of **resistance** (a biological issue)
- The challenge of **adherence** (a human issue)
- Side effects.....

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28. Three main issues provide great challenges to controlling HIV with ARVs. HIV may quickly become resistant to ARVs. Strict adherence is required for life. Side Effects sometimes make it difficult for people taking the drugs, both in the short-term and the long-term. All these will be explored further in Modules 3, 4, & 5.

What can we do.....?

Understanding the way in which ARVs work and the challenges our patients face, helps us to help them!



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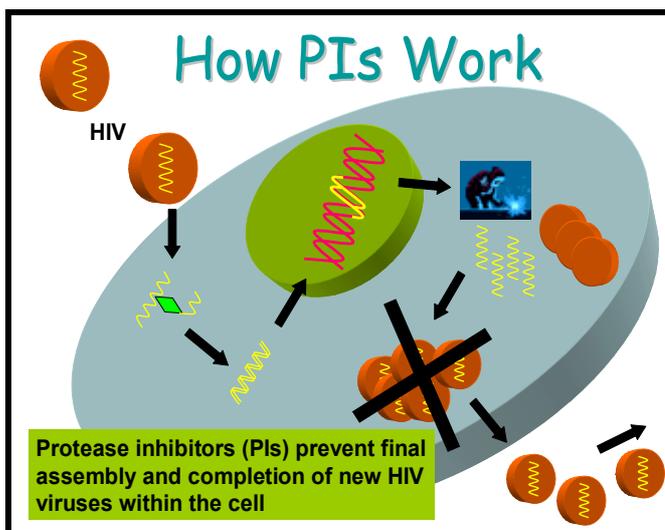
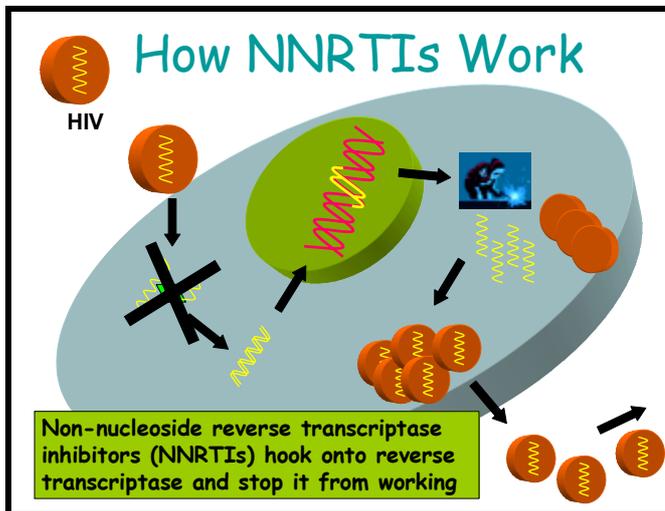
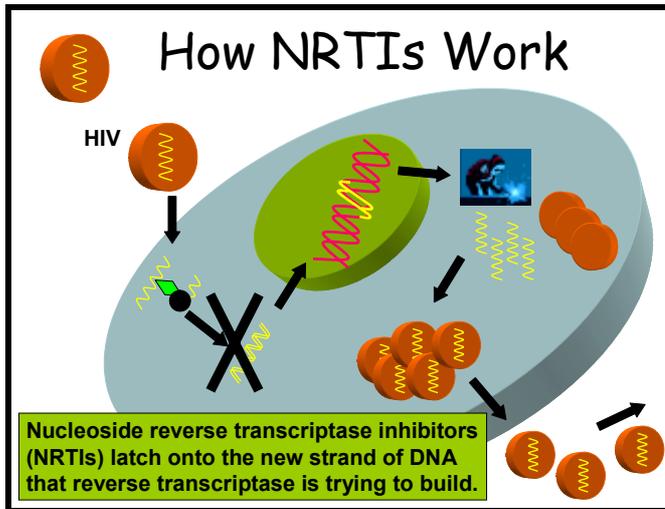
29. Patients taking ARVs face immense challenges. We can only truly understand these if we have taken ARVs ourselves. However, an understanding of the way in which these drugs work and how they affect patients can help us to meet their needs in the overall goal of reducing viral load, thus promoting immune responses and improved quality and length of life.

Handout 3: Antiretroviral Drugs & Doses

Name	Brand & other name	Dosing	Total daily pills	Food restrictions
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs, 'NUKES')				
D4T	Zerit, stavudine	1 capsule, twice daily	2	none
AZT	Retrovir, zidovudine	1 capsule, twice daily	2	none
ddl 100mg ddl 200mg ddl/EC	Videx, didanosine 'reduced mass' ddl 'enteric coated'	4 tabs, once daily 2 tabs, once daily 1 capsule, once daily	4 2 1	do not eat for 2 hours before & 1 hour after (2 hours after for EC)
3TC(150mg) 3TC (300mg)	Epivir, lamivudine Epivir, lamivudine	1 tab, twice daily 1 tab, once daily	2 1	none none
abacavir	Ziagen, 1592	1 tab, twice daily	2	None
Combivir	(AZT/3TC)	1 tab, twice daily	2	None
Trizivir	(AZT/3TC/abacavir)	1 tab, twice daily	2	None
Tenofovir	Viread	1 tab, once daily	1	take with food
FTC*	Emtracitabine	1 capsule, once daily	1	None
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs, 'NON-NUKES')				
efavirenz	Sustiva Stocrin	1 tab(600mg) once daily	1	not with high-fat meal
nevirapine	Viramune	1 tab, twice daily	2	None
delavirdine*	Rescriptor	6 tabs, twice daily	12	None
DUAL & BOOSTED PROTEASE COMBINATIONS				
lopinavir/r	Kaletra, ABT-378/r	3 capsules, twice daily	6	take with food
Indinavir/ritonavir	400mg/400mg	1xIDV/4xRTV twice daily	10	none
	800mg/200mg	2xIDV/2xRTV twice daily	8	none
	800mg/100mg	2xIDV/1xRTV twice daily	6	none
saquinavir/ritonavir	400mg/400mg	2xSQV/4xRTV twice daily	12	food side effects
saquinavir,ritonavir	1000mg/100mg	5xSQV/1xRTV twice daily	12	food side effects
Fosamprenavir*/ritonavir	700mg/100mg	1xFosAPV/1xRTV twice daily (once daily possible)		None
Atazanavir*/ritonavir	300mg/100mg	2xATV/1xRTV twice daily	3	None
SINGLE PROTEASE INHIBITORS (PIs)				
indinavir	Crixivan	2 capsules, 3 times daily	6	2 hours after or 1hour before food
nelfinavir	Viracept-film coated	5 tabs, twice daily	10	take with meal
atazanavir	Reyataz	2 capsules, once daily	2	take with food
ENTRY INHIBITORS (Fusion inhibitors)				
enfuvirtide	T-20, Fuzeon	Sub-cut inj, twice daily		None

The above table is a reference for different names of drugs, doses, total pill count & brief details of food restrictions. The drugs and associated information highlighted in **BLUE** indicate ARVs most commonly used in resource-limited settings. Other drugs listed are purely for the interest of the nurse. An asterisk * is for a drug which may be available on an expanded access programme and/or which is expected to be licensed shortly.

Handout 4: **How do ARVs Work?** (With kind permission from Dr J. Giddy)



Learning Exercises: 'How do ARVs work?'

A. Questions

1. How do ARV drugs affect HIV disease?

ARV drugs **control** HIV disease, turning it from a progressive, terminal diagnosis to a long-term, manageable chronic illness. They do this by reducing the replication of HIV in the CD4 cells so that new viruses cannot be made. In this way, CD4 cells are protected and the immune system remains strong to fight infections.

2. Name the three main classes of ARV drugs

- NRTIs – nucleoside reverse transcriptase inhibitors
- NNRTIs – non-nucleoside reverse transcriptase inhibitors
- PIs – protease inhibitors

3. Where do ARVs work in the HIV Life Cycle?

Use **Hand Out 2: The Life Cycle of HIV**, to mark the different places where ARV drugs work.

4. What are the two main enzymes which current ARV drugs inhibit?

- Reverse Transcriptase, at the beginning of the Life Cycle
- Protease, at the end of the life cycle

5. What is the main goal of ARV therapy?

To decrease or reverse immune system damage associated with HIV

6. What are the main advantages of ARV drugs?

Improved quality of life, reduced sickness and prolonged life

7. When should ARV drugs be started?

Any patient with Stage IV disease OR any patient with Stage I, II or III and a CD4 count less than 200 cells/mm³.

8. What are the three main challenges of ARV drugs?

Resistance, Adherence & Side Effects

9. What three main factors are taken in to consideration before starting patients on ARV drugs?

CD4 count, Clinical Symptoms & Patient Readiness

B. Group Work

1. How do ARV drugs work?

Divide the group into pairs and then ask each pair to take it in turns to describe to each other where ARVs work, using Hand Out 1: **The Life Cycle of HIV**. Allow 15 minutes for this exercise before bringing the group back for discussion.

2. Why should I take ARVs?

Patients need to know the benefits of taking ARV drugs. Nurses must be able to explain to patients the effect of ARV drugs on HIV disease. Divide the group in to pairs and ask each pair to discuss how they could explain this to a patient. Ask the

groups to feedback through role play, where one is the patient asking the question “Why should I take ARVs?” and the other is the nurse, providing the response.

ARV drugs ‘control’ HIV disease. Without them, HIV gradually destroys your immune system, making it more and more difficult for you to fight infections. Although everyone is different and some people will remain well for a long time, there WILL come a time when your immune system becomes weaker and weaker, you will get increasingly severe infections and eventually not be able to survive these.

However, ARV drugs control HIV by slowing down the damage it does to the immune system. When HIV replicates (reproduces), it damages the immune system. It also produces more and more virus. By preventing the virus from reproducing, ARVs protect the immune system, making you stronger and more able to fight infections.

Although everybody is different and it is not possible to say that ARVs will definitely help you live much longer with a better quality of life, people with HIV all over the world, including South Africa, are now living for years longer than they had expected, with far fewer sicknesses and living normal lives.

The ARV drugs will NOT remove HIV from the body so it is NOT a cure. But they are providing new hope and a new lease of life for many, many people.

3. Case Scenario

Divide the group in to smaller groups then read out the following case scenario.

Nkosnati is a 25 year old, HIV positive man. 7 months ago, his CD4 count was 50 cells/mm³ and his viral load was 200,000 copies. He was bedridden and extremely sick with cryptococcal meningitis, severe weight loss and chronic diarrhoea. As well as being treated for cryptococcal meningitis, Nkosnati commenced ARV therapy. He started taking AZT, 3TC and Efavirenz. After 3 months, Nkosnati’s general health was much improved. The cryptococcal meningitis had been treated, his appetite had improved considerably and he was gaining weight. The diarrhoea continued but had improved dramatically. His blood tests revealed his viral load was now undetectable and his CD4 count had increased to 120 cells/mm³.

Now ask the groups to discuss the following question before feeding back their thoughts to the whole group.

How have the ARVs helped Nkosnati?

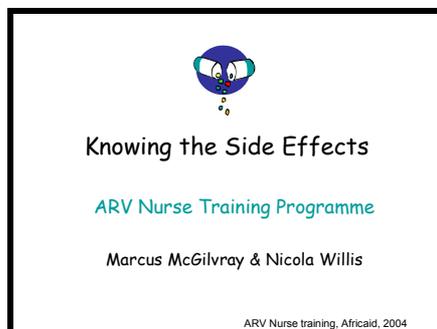
Prior to commencing ARVs, Nkosnati’s viral load was extremely high and his CD4 count extremely low. This showed that HIV was overwhelming his immune system and had destroyed most of his CD4 cells, leaving him with very little defence against severe Opportunistic Infections like Cryptococcal meningitis.

When he started ARVs, HIV replication was slowed down considerably. By taking 2NRTIs (AZT and 3TC) and 1NNRTI (Efavirenz), the replication of HIV was inhibited in the early stages of its life cycle in two different ways. AZT and 3TC inhibited the enzyme Reverse Transcriptase in one way whilst Efavirenz inhibited it another. The result was a strong suppression of HIV replication. In turn, the number of viruses dropped dramatically. So, with fewer viruses around to infect and destroy CD4 cells, CD4 cells were able to build up again, providing an improved immune system for Nkosnati. He is now much stronger as a result.

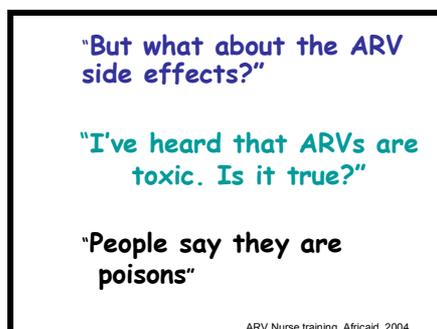
Module Objectives

- To ensure nurses have the skills and knowledge required to recognise common side effects associated with ARVs
 - To equip nurses with an understanding of the impact of these side effects on patients taking ARVs
 - To differentiate between more common, manageable side effects and severe side effects requiring immediate referral by the nurse
 - To provide nurses with the knowledge and skills required to manage common side effects
 - To demonstrate the importance of support and encouragement for patients experiencing side effects
-

Slide Presentation: Side Effects



1. Welcome trainees and introduce yourself, including a brief background in to your area of practice, role & experience in the supporting patients experiencing side effects of ARVs. If there is time, trainees may be asked to share with one another their own experiences of ARV side effects, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage trainees to feel free to interrupt and ask questions at any time



2. There are many myths circulating the world about ARV drugs. The majority of these relate to the side effects of ARV drugs. This has contributed to wide spread fear of ARVs or misunderstanding about them.

Side Effects

It is true ARVs do have side effects

BUT.....

Many other drugs also have side effects - even common antibiotics and painkillers



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3. And it is true. ARVs do have side effects but it should not be forgotten that many other drugs also have side effects. However, because those drugs are more common, these are not so heavily discussed. *Ask trainees to suggest other drugs that they have used and which have known side effects*

What are the Side Effects?

These depend on

- the drugs used
- the person



Not all drugs affect all people in the same way

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4. So what are the potential side effects of ARVs? *Ask trainees whether they know any of the side effects?* They depend very much on the particular drugs used and the individual person. It must always be stressed that everyone is different. Not all drugs affect people in the same way. **Refer to Hand Out 5: ARVs and Side Effects**

Different types

'Acceptable' (transient)

Versus

'Unacceptable' (severe, unsafe)

.....but, **ALL** must be reported so that they can be managed appropriately!



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5. The side effects experienced differ in severity. The majority are transient, commonly resolving after a few weeks/months of taking ARVs. Other side effects may be much more concerning. Stress to trainees that ALL side effects must be reported to the Doctor in order that he/she can decide how to manage them appropriately.

Transient Side Effects

- Many are transient in the first few weeks
eg headache, nausea, diarrhoea, vomiting
- Other medication can be used to manage/alleviate these symptoms
- Patients need **IMMENSE SUPPORT** and **ENCOURAGEMENT** to continue with regimen

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6. Many patients experience side effects when starting ARVs. These may resolve after a few weeks. In most cases, the Doctor will decide that the patient should continue the drugs whilst receiving careful management of symptoms (e.g. analgesia, anti-emetics). This period is extremely important as patients may get 'put off' ARVs and stop taking them.

Severe Side Effects

- Some side effects may be severe
eg rash, hepatitis, lactic acidosis, pancreatitis, hyperlipidaemia, peripheral neuropathy
- The Doctor may need to change the ARVs being taken by the patient
- Early identification and prompt, appropriate management is **essential!**

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7. There is a chance of more severe side effects but these should be detected by the routine laboratory monitoring that all patients should have. For example, blood tests will show raised levels of U&Es or LFTs. Alternatively, rashes, jaundice or numb limbs may be visually observed or verbally reported. ARV drugs may be stopped but **ONLY** by the doctor! **NEVER** stop a patient's drugs yourself but get the patient seen immediately if you are concerned.

Side Effects of NRTIs

- AZT (Retrovir):** headache, nausea, diarrhoea, anaemia, neutropenia, thrombocytopenia, liver toxicity
- 3TC (Epivir):** nausea, diarrhoea, headache, fatigue, skin rash, abdominal pain, increase LFTs
- D4T (Zerit):** headache, nausea, vomiting, diarrhoea, rash, increase LFTs, peripheral neuropathy, pancreatitis
- DDI (Videx):** nausea, vomiting, diarrhoea, abdo pain, peripheral neuropathy, increase LFTs, pancreatitis

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8. The side effects vary according to the drug. This table does not mean a patient will experience all of the side effects commonly seen in that drug! NRTIs are very commonly associated with nausea, diarrhoea & vomiting. As all your patients will usually be on one or more NRTI, you may expect to see that a lot of your patients experience some nausea, diarrhoea and vomiting at some point.

Side Effects of NNRTIs

- Efavirenz (Stocrin):** rash, sedative effects, headache, nausea, diarrhoea, vivid dreams, insomnia, 'drunk feeling', increase LFTs, hepatitis, liver failure
- Nevirapine (Viramune):** headache, nausea, rash, diarrhoea, increase LFTs, hepatitis, liver failure

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9. Efavirenz is particularly known for its effect on the Central Nervous System (e.g. sleep disturbance, mood changes). Many patients find it best taken before bed. Symptoms usually resolve but patients still need encouragement and support. Efavirenz must never be used in children under 3 years. Both Efavirenz and Nevirapine can cause rash and liver toxicity which can be serious and occasionally fatal. Rashes must be reported immediately. Liver damage should be detected by regular monitoring.

Side Effects of PIs

- Nelfinavir (Viracept):** nausea, vomiting, diarrhoea, headache, asthenia, abdo pain, rash, hyperglycaemia, lipodystrophy
- Ritonavir (Norvir):** nausea, vomiting, diarrhoea, abdominal pain, anorexia, increase LFTs, pancreatitis, hyperlipidemia, hyperglycemia, circumoral paresthesia, lipodystrophy

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10. The Protease Inhibitors are particularly known for increasing blood lipid levels and fat redistribution (lipodystrophy). Again, careful monitoring of blood levels will provide warning about increasing lipid levels.

Diarrhoea

Possible causes:

- OIs (e.g. cryptosporidium, CMV, giardia, salmonella, shigella)
- Antibiotics
- ARVs (e.g. PIs, ddI, Abacavir)

i.e. not necessarily ARV-related but it is common



Severity and duration variable
Dependent on person and drug

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11. It must be stressed that diarrhoea can certainly be caused by ARVs but may also be the result of an OI or Antibiotic. If it is ARV related, everyone is different. The severity and duration of diarrhoea will very much depend on the person and the drug being taken.

Management of Diarrhoea

- **Identify cause:** stool sample to exclude OI
- **Rehydration:** encourage fluids >3L/day
- **Replace potassium:** bananas, potatoes, chicken, fish
- **Soluble fibres:** pulses, oats, bananas, apples, pears
- **Anti-diarrhoea drugs:** e.g. loperamide



Support & Encouragement to promote Adherence!

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12. Firstly, an OI or other cause must be excluded and treated appropriately before deciding diarrhoea is the result of ARVs. Nursing care must involve rehydration or prevention of dehydration. Fluids **MUST** be continued and diet must be slowly re-introduced, as tolerated. Anti-diarrhoeal drugs are commonly used for symptom management. Support and encouragement is essential as people may well get 'put off' ARVs.

Nausea and Vomiting

Possible causes:

- OIs (e.g. acute diarrhoeal infections)
- ARVs (eg 3TC, ddI, D4T, EFV, NVP & PIs)

i.e. not necessarily ARV-related but it is common



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13. Again, whilst nausea and vomiting are commonly associated with ARVs, this may not be the only cause. OIs, other sicknesses or pregnancy may also be the cause.

Management of Nausea & Vomiting

- **Exclude other cause:** eg OI, diarrhoeal disease, pregnancy
- **Investigation:** eg U&Es
- **Anti-emetic drugs:** e.g. Maxalon
- **Dietary Advice:** adhere to dietary requirements of ARV drugs
- **Other:** eg small, frequent meals; space intake of fluids/solids; avoid fatty, fried food; salty, dry foods; cold foods; remain elevated; herbal teas
- **Change Regimen:** ?? Reduce dosage or frequency; stop drug

Support & Encouragement to promote Adherence!

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14. Firstly, other causes must be excluded and treated appropriately. Nursing care may involve blood tests for U&Es, hydration, dietary advice and anti-emetic drugs for control of symptoms. Fluids and diet must be slowly reintroduced as tolerated. Support and encouragement is essential as people may well get 'put off' ARVs. Occasionally, the ARV drugs may need to be changed, but **ONLY** by a Doctor.

Skin Problems

Possible causes:

- Interaction between immune system and HIV (eg seroconversion illness, pruritic rash)
- Infections (eg bacterial, viral, fungal)
- ARVs (eg NVP, 3TC, D4T, EFV, NFV)

Severity and duration variable
Most are mild and can be treated

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15. Whilst skin problems are very common with ARVs, they may also be the direct result of HIV on the immune system or skin infections in their own right. The severity and duration may be variable. Most ARV-related skin problems are mild and can be treated.

Management of Skin Problems

- **Mild skin rash:** treatment can be continued; treat with prednisone, antihistamines; advice on not using soaps & deodorants
- **Severe rash:** discontinue and do not take again!
- **Nevirapine:** rash experienced in 20-30% of patients; 2% experience life-threatening Stevens Johnsons Syndrome. Nevirapine is commenced in low doses, increasing to full dose over 2 weeks

Support & Encouragement to promote Adherence

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16. Mild skin rashes must be managed symptomatically whilst the patient continues with ARVs. Patients must be supported at all times otherwise they may be 'put off' ARVs. 20-30% patients taking Nevirapine, will experience mild skin rash. 2% will experience a severe rash which is dangerous. In these severe cases, the patient must be seen by the Doctor immediately who will stop the Nevirapine. Patients on Nevirapine must always be told that if they experience a rash, they must inform the clinic immediately.

Anaemia

Possible causes:

- Common with AZT
- OIs eg MAI
- Maybe HIV related (Rare in CD4 >200mL)

Management:

- Routine monitoring of FBC
- Reduce dose / change drug eg ddI

Support & Encouragement to promote Adherence

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17. Anaemia is common with AZT and should be detected with regular monitoring of blood tests. Importantly, nurses may identify signs of anaemia too (pallor, fatigue). Again, other causes do exist e.g. HIV-related or an OI. The doctor will want regular blood tests and may change the dose or the drug, where possible. Iron tablets are also a possibility, as is transfusion in extremely severe cases, although regular monitoring should prevent this.

Other toxicities.....

Regular monitoring of blood levels is essential to identify ARV toxicities

Appropriate intervention can then be made



FBC

LFTs

U&Es

Cholesterol

Glucose

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18. As shown on the slides earlier, there are other toxicities associated with ARVs which can be identified by blood tests. Patients must be informed of the importance of regular blood tests in order that problems can be identified as early as possible.

Our Role.....

As nurses, we have a vital role to play in ensuring side effects are

identified, managed and treated

appropriately and effectively



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19. Side effects **MUST** be identified, managed and treated effectively. If not, depending on their severity, patients' quality of life will deteriorate or they may become severely unwell. Importantly, patients may start to question why they are taking ARVs and lose confidence in the health professionals supporting them, including you! Nurses have a central role to play through ensuring all this is prevented as far as possible.

How do we do this?.....

- Educating patients
- Prompt recognition and referral
- Understanding lab tests and results
- Explaining lab tests to patients
- Therapeutic intervention
- Providing support and counselling for patient and family
- Ensuring follow up of patients
- Educating the general public

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20. Nurses have a diverse role to play. Educating patients in what to expect and when to come to clinic is of paramount importance in detecting side effects early and ensuring patients are not left struggling with side effects and questioning ARVs. Awareness of side effects helps us to understand the importance of the blood tests we take and the significance of the results. Support, counselling & management of side effects are vital. Follow up is often forgotten, particularly when we get busy. But it is essential to ensure that patients' side effects are alleviated and ARVs continue to be taken.

In turn.....

- We are able to ensure **safety** of our patients
- Enhance **quality of life** for people taking ARVs through therapeutic intervention
- Promote **adherence**, through understanding of side effects
- Dispel **myths** and **misconceptions** about ARVs

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21. We can play a central role in protecting our patients from harm and promoting quality of life. Side effects are a significant threat to the improved quality of life that patients hope to achieve with ARVs. They may become non-adherent very quickly if they are not supported. Effective management of side effects can alleviate symptoms in order that patients may enjoy the benefits of ARVs. Educating the general public helps to dispel myths and misconceptions about ARVs.

Patients taking ARVs face a very difficult challenge

BUT

together,

we **CAN** make a big difference



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22. It is extremely important that you familiarise yourself with the type of side effects commonly seen in the drugs used in your clinic. That way you can educate patients about what to expect and recognise them if they occur. The need for you to support and encourage your patients cannot be underestimated.

Hand Out 5: ARVs and Side Effects

Generic Name	Trade Name	How Supplied	Notes	Side Effects
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Didanosine (ddl)	Videx	Chew Tab (white; round) 25mg, 50mg, 100mg, 150mg; Powder for oral solution in packets & bulk bottles	ddl liquid: mixed with antacids, Shake well; refrigerate; stable for 30 days. Take on empty stomach	Common: nausea/vomiting/diarrhoea (N/V/D), abdominal pain. Severe: peripheral neuropathy; electrolyte abnormalities; hyperuricemia. Uncommon: pancreatitis; increase liver function tests (LFTS); retinal depigmentation.
Lamivudine (3TC)	Epivir	150mg white tab; Oral solution:10mg/ml (strawberry,banana)	With or without food Active against Hep B Store oral solution at room temp	Common: nausea/diarrhoea (N/D); headache (HA); fatigue; skin rash; abdominal pain. Severe: pancreatitis.
Stavudine (d4T)	Zerit	Cap: 15mg, 20mg,30mg,40mg. Oral powder for solution: 1mg/ml	With or without food Oral solution: shake, refrigerate, stable for 30 days	Common: HA; N/V/D; skin rash; increased LFTs. Severe: peripheral neuropathy; pancreatitis.
Zidovudine (AZT) & (ZDV)	Retrovir	Cap: 100mg (white with blue stripe); tab: 300mg (white, round, biconvex); Syrup 10mg/ml; IV 10mg/ml	Take with food Hematologic toxicity: interrupt therapy or decrease dose, or use erythropoietin	Common: Hematologic toxicity; HA Other: myopathy; myositis; liver toxicity.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Efavirenz (Stocrin)	Sustiva	Cap: 50mg,100mg,200mg	With or without food avoid high fat	Common: Rash; sedative effects; HA; N/D Other: Increase LFTs; rare-hepatitis.
Nevirapine (NVP)	Viramune	Tabs: 200mg (oblong, white scored); Oral liquid: 10mg/ml sweet tasting off-white liquid)	With or without food Don't crush tabs because of salt form	Common: Rash; sedative effects; HA; N/D Other: Increase LFTs; rare-hepatitis.

Table courtesy of Baylor College of Medicine (2001). Adapted for Nurse Training Manual.

Learning Exercises: 'Side Effects'

A. Questions

1. Name some of the more common side effects associated with ARVs

Nausea, diarrhoea, vomiting, headache, abdominal pain, skin rash

2. Why is regular monitoring of Full Blood Count, U&Es and LFTs so important for patients taking ARVs?

ARVs can be toxic to the liver, kidneys and blood cells. Any damage may be detected by taking regular blood tests to identify changes in blood levels from the normal range as early as possible. There is then plenty of time for the medical team to decide what to do for the patient.

3. What must a patient be told when starting Nevirapine?

If they experience a rash when starting Nevirapine, they must come to the clinic immediately.

4. How can a nurse best help patients when they first start ARVs?

Patients need to know that they may experience side effects, how to recognise them and what to do if they occur. This requires that the nurse takes the time to ensure patients have correct, clear information about their drugs and are confident what to do if they experience any side effects.

5. If a patient arrives at clinic with yellow eyes, what may be the cause and what should you do as a nurse?

ARVs may be toxic to the liver. The patient may have jaundice and must be referred immediately to a doctor for appropriate management.

6. Whilst taking vital signs from a patient taking ARVs, you ask the patient how she is managing with them. The patient becomes very distressed and informs you she is finding it very difficult indeed, due to the diarrhoea she experiences on a daily basis. What should you do for your patient?

First and foremost, she must be praised highly for doing so well by continuing with her ARVs. She must be reassured that she is not alone and has lots of people in the clinic to support her. Explain to her that although the diarrhoea may be due to the ARVs, it is necessary to take some stool specimens in case she has an infection. Then, ensure she is seen by the Doctor for further investigation. The Doctor may prescribe anti-diarrhoeal medication to help alleviate the symptoms. Encourage her that diarrhoea is a very common side effect of ARVs and often passes. Remind her again of the importance of adherence, offering support at all times.

B. Group Work

1. Nurses' experiences of ARV Side Effects

Give out Hand Out 5: *ARVs and Common Side Effects*. Ask the group to share and discuss any experiences they have of ARV side effects experienced by patients in their care.

2. Recognising and Managing Side Effects

Divide the group into subgroups. Give each group one ARV drug used in their clinic. Ask each sub-group to find out the more common side effects associated with that drug using Hand Out 5: *ARVs and Common Side Effects*. Then ask each sub-group

to feedback to the main group about the common side effects of their drug and how they would manage these side effects

3. Case Scenario

Read the following case scenario then ask the group the questions below.

Nothando is a 34 year old lady, diagnosed with HIV 18months ago. For the first 14 months, Nothando was fairly well with a CD4 count between 350 and 500 cells/mm³. She had occasional chest infections and skin rashes. However, with treatment for these infections, good nutrition and exercise and regular visits to the clinic, she was able to lead a normal life. However, 4 months ago, her health started deteriorating rapidly. Nothando had come to clinic with chronic diarrhoea, recurrent fever and shingles. She also had symptoms of TB. Blood tests revealed Nothando's CD4 count had dropped to 200 cells/mm³. TB was confirmed and she commenced on TB treatment. The doctor explained that after the intensive phase of TB, Nothando could commence ARV drugs to help control the HIV. Nothando was very reluctant however as she had heard many stories about ARVs making people even sicker.

When Nothando returned to clinic at the end of the intensive phase of TB treatment, the Doctor raised the issue of ARVs again. Still Nothando was worried about taking them in case they made her feel worse than without them. However, she trusted the doctor and the nurses who had explained to her the benefits of ARVs.

Nothando left the clinic having been told by the doctor, nurse, counsellor and pharmacist how important it is to take ARVs exactly as prescribed. Nothando was given a chart explaining which drugs to take and when, which she understood. That evening, Nothando took her first dose of ARVs. The following night, Nothando woke in the night having had extremely vivid dreams. She was afraid what the ARVs were doing to her. The next night, she experienced these dreams again and also started feeling nauseous.

After a week, Nothando was exhausted and frightened. The dreams continued and she was now vomiting. Any improvement in her health that they had talked about at the clinic seemed to be a lie. Nothando felt she had been right all along and should never have trusted them at the clinic. The rumours were true and she must stop the ARVs immediately.

1) Should Nothando stop taking the ARVs?

No, she should not stop them herself. If she does, the virus will be able to start replicating again and she may even develop strains of HIV that are resistant to the drugs. However, she should be seen by a Doctor who will decide on appropriate action.

2) What should Nothando have done when she started feeling unwell?

She should have gone to the clinic to tell the clinic staff that she was experiencing side effects. Then she could be supported with explanations that these side effects are quite common and should pass. She could have been given drugs to help reduce the vomiting and given advice about fluid intake and diet. She could be given a great deal of encouragement for taking the drugs so well and the benefits of ARVs stressed again. The side effects would hopefully be alleviated and Nothando could continue to take the ARVs and start feeling a lot better.

3) Why did Nothando not go to the clinic?

Nothando was let down as she had not been made aware of the particular side effects that may occur. So the side effects she experienced were a great shock to her and confirmed all her fears about ARVs. She therefore lost faith in those that should be supporting her. Also, she had not been told what to do if she did experience any side effects.

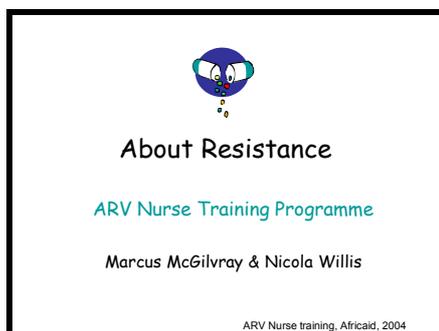
4) What should have happened?

Nothando should have been warned of the possible common side effects associated with her drugs. She should have been told what to expect and then been reassured that these are quite common but do usually pass. She should know that, in the meantime, the clinic staff will always be there to support her in order that she can continue with ARVs and gain from their full benefits.

Module Objectives

- To explain resistance in the context of Antiretroviral Drugs
 - To equip nurses with a basic understanding of how resistance occurs
 - To describe the impact of resistance on HIV disease at an individual and public health level
 - To distinguish between 'monotherapy', 'dual therapy' and 'triple therapy' and their role in the development of resistance
 - To discuss optimal strategies for preventing resistance
 - To discuss the role of the nurse in preventing resistance
-

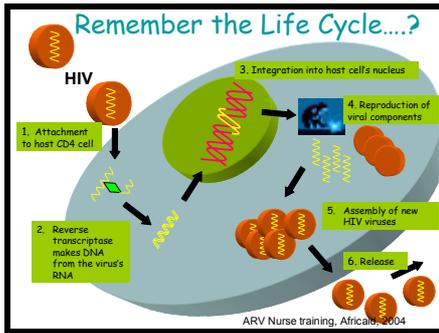
Slide Presentation: Resistance



1. Welcome trainees and introduce yourself, including a brief background in to your area of practice, role & experience in addressing ARV resistance. If there is time, trainees may be asked to share with one another their own ideas and experiences of ARV resistance, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage trainees to feel free to interrupt and ask questions at any time.



2. HIV is very clever – it manages to destroy the very system that would usually destroy it. However, it is not perfect as mistakes are made when HIV replicates itself.



3. Think back to the life cycle. HIV attaches to the CD4 cell & releases RNA & enzymes. The enzyme *Reverse Transcriptase* makes DNA from the viral RNA. New viral DNA is integrated using *integrase* into the CD4 cell's nuclear material. New viral components are then produced, using the cell's 'machinery'. These are assembled together using the enzyme *protease* and released as new viruses.

What is resistance?

Basically.....

- Reverse transcriptase works so hard and so fast that it makes a lot of mistakes
- Sometimes these mistakes turn into mutant forms of the virus that the ARVs can no longer kill

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4. HIV replicates extremely rapidly. It is thought to produce 10 billion copies of virus a day! Sometimes, when Reverse Transcriptase copies viral RNA in to viral DNA at the beginning of the cycle, mistakes are made. These can become mutant forms of HIV, which are not sensitive to ARVs. In other words, the ARVs are no longer able to control HIV.

To explain more....

- Left alone, HIV grows and multiplies inside the body.
- As it grows, HIV can change itself. This is called **mutating**.
- What will happen when we give one antiretroviral drug? (**monotherapy**)

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5. Normally, HIV will continue to replicate within the CD4 cells. The viruses (green in this diagram) are all original virus, becoming more and more in number as they replicate. Over time, as mistakes are made during replication, mutant forms of virus arise (purple in this diagram), a process known as mutating. What will be the effect of giving one ARV drug?

- With **monotherapy**, the antiretroviral drug is able to kill all of the original (unmutated) HIV

BUT

- the mutated virus is **RESISTANT** to the antiretroviral being used.

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6. If one ARV drug is given, it may be able to kill off all the original (green) virus - BUT...the ARV drug will have no effect on the mutant (purple) virus. This mutant (purple) virus is said to be resistant to that ARV drug being used.

Then.....!

- The mutated HIV grows and multiplies, even in the presence of the antiretroviral.
- This virus is now **RESISTANT** and will continue to attack the immune system unless a different drug is used.

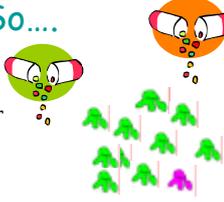


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7. The mutated virus then multiplies rapidly, untouched by the ARV drug being taken. This mutated virus will continue to infect CD4 cells, destroying them in the process and slowly weakening the immune system even though an ARV drug is being taken.

So....

- Now we need another strategy
- Two drugs together (**dual therapy**) can keep all HIV from multiplying, even if it has mutated
- So if the purple virus is resistant to one drug (purple), it can be destroyed by the second drug

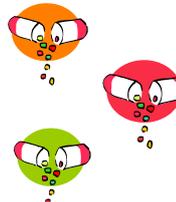


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8. But if you add in another, different ARV drug, a 'double-pronged' attack on both the original virus and any mutant viruses occurs. Even if the virus is resistant to one drug, the second drug is able to destroy that virus. This is far more effective in controlling HIV reproduction and any subsequent attack on the immune system.

Triple Therapy

- Now we understand why **triple therapy** works
- Two drugs together can keep all HIV from multiplying, even if it has mutated
- BUT, three drugs can work even better!

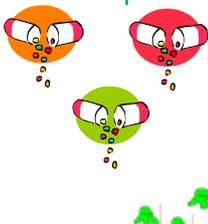


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9. In the early days of ARVs, monotherapy was used and whilst people's health improved, it was short-lived due to emerging resistance. We now know that triple therapy, the use of three different drugs, is the most powerful way to stop HIV replicating and allowing mutant viruses to proliferate.

If only it were that simple...

- Unfortunately, triple therapy is **NOT** able to cure HIV.
- HIV is a very tricky virus. While most of it is getting killed by triple therapy, a few viruses find places to hide where they are safe from triple therapy.



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10. Triple therapy may have a powerful effect on reducing the number of viruses in the blood to a very low level but unfortunately, it will never remove HIV from the body completely. Levels of virus in the blood may drop and even be 'undetectable' (they cannot be found with the usual blood tests) but the virus is still there somewhere. It gets in to many different parts of the body, hiding away, only to re-emerge at a later date.

A big concern!

If resistance develops:

- Drugs start failing as virus is able to replicate
- As virus replicates, immune system is damaged
- OIs occur, progressing to AIDS
- Also, there are only **limited drug options** available!

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11. The threat of resistance and its role in treatment failure cannot be underestimated. If resistance occurs, people who have initially responded well to ARVs will become unwell again as the ARVs can no longer control the new mutant viruses. In turn, the mutant virus replicates, damages the immune system and OIs commence again. Also, if drugs fail, there are not many others to try after that.

Cross Resistance

Resistance to a drug in **one class** of ARV

commonly results in

Resistance to other drugs
within that **same class**

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12. Importantly, if an individual becomes resistant to one ARV drug, they may well be resistant to other drugs in that same class. For example, if resistance occurs to D4T, the individual may also be resistant to AZT, having never even had taken AZT. AZT can therefore not be taken either and drug options are limited for that patient.

Everyone is different!

NB!! people respond differently to these drugs

Whilst one regimen may suppress viral replication well in one person, another may develop resistance

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13. Whenever we talk about HIV & ARVs, it must always be stressed that everybody is different. What may be true for one person, may not be true for another. One person may develop resistance very quickly and rapidly deteriorate, whilst another may not develop resistance and stays well for a long time.

Reducing Resistance....

The BEST way to reduce the development of resistance is:

to ensure maximum viral suppression using **three** drugs, taken as the **correct dose**, at the **correct time**, in the **correct way**

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14. If maximum suppression of the virus is maintained at all times, the chance of mutant viruses occurring is small indeed. The best way to get maximum suppression of the virus is through 100% adherence! If doses are missed or not taken properly, mutant virus will take the opportunity of this 'gap' in ARV circulating in the blood and start replicating. Before long, those mutant viruses become plenty in number and resistant to the ARVs.

Public Health

- Resistant HIV may be transmitted to someone else
- If someone is infected with resistant HIV, they will be resistant to one or more ARVs, even though they have never taken them before
- Potentially, ARVs could become less help for people across South Africa due to resistance, as already being seen in Europe & the States.
- Abstinence and Safer Sex is the best way to prevent this occurring

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15. The importance of resistance does not stop at an individual level. ARV-resistant HIV may be transmitted to other people. So if someone has developed resistance to one or more ARV drugs, and transmits HIV to someone, that person will also have HIV that is resistant to those drugs. He/she will be unable to take those drugs when he needs to, even though he has never had them before. This could mean ARVs may become less help for lots of people across South Africa in the future. The best way to prevent this is through abstinence or safer sex.

Our role.....

Nurses have an essential role to play in reducing resistance through:

- Educating patients about resistance
- Recognising non-adherence
- Promoting adherence
- Laboratory testing for resistance
- Explaining to patients re resistance testing



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16. Patients need to know about the importance of resistance. They have a responsibility to take ARVs properly. Educating about adherence is the most important thing you can do to help prevent resistance occurring. You will also be involved in taking blood tests to measure resistance and explaining this test to patients. This is a highly specialised blood test which can identify whether the HIV in the patient's blood is resistant or not to the ARVs being taken.

Finally,

Resistance is one of the biggest challenges and threats to the success of ARVs, both at an individual level and at broader, public health level

Nurses CAN make a big difference!

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17. At an individual level, resistance contributes to ARV failure and thus deterioration in health. At a public health level, resistant virus can be transmitted. The spread of ARV-resistant virus would be a disaster, bringing us back to the days before ARVs. You have a key role to play in educating about resistance and promoting adherence.

Learning Exercises – ‘Resistance’

A. Questions

1. What is ‘resistance’?

Resistance is where HIV becomes ‘resistant to’ or ‘unaffected by’ ARV drugs. The ARV drugs being taken are no longer able to suppress replication of HIV.

2. How does resistance occur?

Resistance begins when Reverse Transcriptase makes mistakes as it copies the viral RNA to make viral DNA. Any viral DNA copied with ‘mistakes’ goes on to make mutant forms of virus which are not affected by the ARVs being taken. If given the opportunity, they will replicate quickly and become plenty in number. The ARVs are unable to control these mutated viruses and are said to be resistant to the ARVs.

3. What is the advantage of triple ARV therapy over monotherapy?

Monotherapy, one ARV drug alone, is unable to suppress HIV enough and resistant virus emerges. However, if three drugs are used (i.e. triple therapy), when the virus becomes resistant to one drug, there are two other drugs in the system to destroy it. Triple therapy therefore has a much greater effect on inhibiting HIV replication. This is particularly so when different classes of drugs are used. Resistance is much less likely to emerge.

4. Why may a patient who has developed resistance to D4T also be said to be resistant to AZT when he has never taken AZT before?

This is known as ‘cross resistance’. When HIV becomes resistant to an ARV drug being taken, HIV may also be resistant to other drugs within that same class, even if they have never been taken. D4T and AZT are both NRTIs.

5. What is the best way to prevent resistance?

Strict adherence is the best way to prevent resistance occurring. If drugs are taken exactly as prescribed, this limits the possibility of viral replication and that resistant virus may emerge.

6. What is the effect of resistance at an individual level?

If a patient becomes resistant to the ARVs being taken, HIV will start replicating again as the ARVs are unable to control it. Viral Load will increase again and CD4 count will decline as CD4 cells are destroyed by rapidly replicating virus. That particular regimen will no longer be effective for that patient. Future treatment options are limited as there are finite drug options available, particularly where cross resistance occurs.

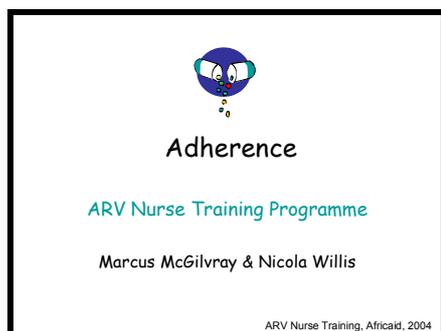
7. What is the effect of resistance at a public health level?

Millions of people around the world could benefit from ARV drugs. However, ARV resistant HIV may be transmitted. In other words, if an individual is resistant to ARVs, he may infect someone else with this resistant virus. They will also be resistant to those ARVs and unable to take them when they need them. Like Multi drug resistant TB, the potential for widespread ARV-resistant HIV is a great concern as it could render ARVs useless.

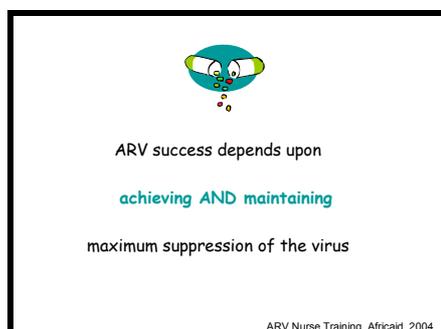
Module Objectives

- To define adherence
 - To demonstrate the importance of adherence to ARV drugs, both at an individual level and at a public health level
 - To provide nurses with an understanding of the immense challenges faced by patients on ARV drugs
 - To instil nurses with a sense of responsibility and significance in the promotion of adherence
 - To equip nurses with strategies for supporting their patients and promoting adherence
-

Slide Presentation: Adherence

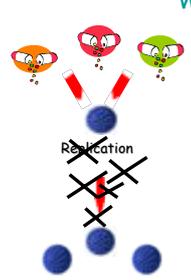


1. Welcome trainees and introduce yourself, including a brief background in to your area of practice, role & experience in promoting adherence to ARVs. If there is time, trainees may be asked to share with one another their own ideas and experiences of promoting adherence, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage nurses to feel free to interrupt with questions at any time.



2. The success of ARV therapy depends on maximal suppression of the virus AT ALL TIMES. No opportunities must be created whereby the virus can 'get away' and start reproducing. This means not only 'achieving' maximal suppression initially, but maintaining it long term.

Why?



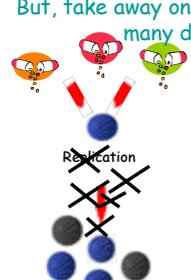
- Viral Load Decreases
- CD4 Increases
- Decreased morbidity and mortality

TREATMENT SUCCESS

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3. Left alone, HIV will reproduce freely, producing billions of new viruses. But, if three ARV drugs are added, the replication of new virus is prevented. In turn, the level of virus in the blood decreases, the CD4 cells begin to build up again and the immune system becomes stronger again. This is treatment success.

But, take away one drug, or miss too many doses.....



- Viral Replication continues
- CD4 Decreases
- OIs occur
- Resistance emerges

TREATMENT FAILURE

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4. But, if this maximum suppression of the virus is reduced (e.g. one drug is not taken or too many doses are missed), then HIV is not fully suppressed and can replicate once more. The level of virus increases again, the CD4 cells continue to be destroyed and Opportunistic Infections occur. Resistance occurs and treatment fails.

But.....

..... treatment success is largely dependent on the patient's ability to take the drugs **exactly as prescribed**



This is known as ADHERENCE

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5. There are many factors involved in ARV success. However, adherence is the single most important factor in achieving success. Adherence is the term used to describe the patient's ability to take the drugs **EXACTLY** as prescribed.

Adherence is.....

- The right drugs
- In the right way
- At the right time



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6. Adherence is multi-faceted. Taking the drugs exactly as prescribed means taking the right drugs, at the right time, in the right way. Patients **MUST** understand that they can not just take them as and when they feel like it! The nurse must ensure that all patients understand this before starting treatment.

Taking the right drugs....

Each drug is carefully investigated in the laboratory to ensure maximum potency against the virus



The **right drugs** and the **right doses** (ie number of tablets) **MUST** be taken

Or.....sub-optimal suppression of the virus will allow viral replication and resistance to develop

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7. Scientists have spent years investigating each drug and the dose of each drug in order to ensure maximum suppression of HIV. The combination of the three different drugs is the result of numerous trials. The right drugs, in the right doses, **MUST** be taken to prevent viral replication & resistance from occurring.

The right time.....

- Taking ARVs **exactly on time** is very important
- There is usually a window period of approximately one hour but this varies with drugs and people
- **SO** - better to stick to exact same time, or **viral load will increase and resistant virus may emerge!**



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8. The timing of the drug doses is also extremely important. If drug levels in the blood are allowed to fall, HIV suppression is reduced, allowing reproduction. Trials have demonstrated that a one hour window period is allowed (i.e. taking ARVs one hour later than normal) but this varies with drugs and people. So stress exact times only!

The right way

- Some drugs have **dietary restrictions** (ie taken with or without food)
- Ignoring these can be like only taking half a dose - you will not absorb enough of the drug for it to work properly
- **Viral load will increase & Resistance is more likely to occur**



with or without



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9. In addition to getting the times, doses and drugs right, some drugs have dietary restrictions. If these are not adhered to, the amount of drug absorbed may be insufficient, meaning viral suppression is reduced. Not all drugs have dietary requirements, but those that do must be adhered to!

Dietary restrictions

With!



Nelfinavir
Ritonavir

(EFV - avoid fatty food)

Without!



ddI
Indinavir (or light meal)

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10. The Protease Inhibitors usually need to be eaten with food. ddI **MUST** be taken without food, which means 1 hour before or two hours after food. Patients need lots of help in planning when to take their drugs if there are dietary restrictions

How much adherence is good enough?

50%

100%

20%

95%

60%

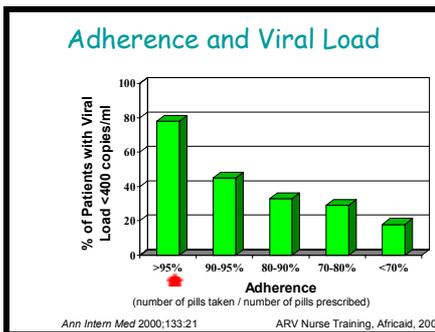


75%

90%

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11. Ask the group their perceptions of the level of adherence required by patients on ARVs and their justifications for this. Encourage trainees to call out which level of adherence they believe to be the correct answer.



12. This graph demonstrates the results of one study. Different groups had different levels of adherence. In the group with >95% adherence, almost 80% had Viral Load less than 400 copies/ml. If adherence dropped to 90-95%, only 41% of patients had Viral Loads less than 400copies/mL. This is a significant drop where the difference of >95% and 90-95% adherence equates to only a few doses more being missed



Many studies have shown that even missing **one** or **two doses a week** can have a big impact on the chance of successful treatment

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13. So, in line with the previous slide and numerous other studies, it is now widely accepted that missing even one or two doses a month can have a significant impact on viral load. As doses are missed, HIV starts to replicate again, and levels of virus in the blood increase.

So.....

Unfortunately, the answer is

100%

Adherence

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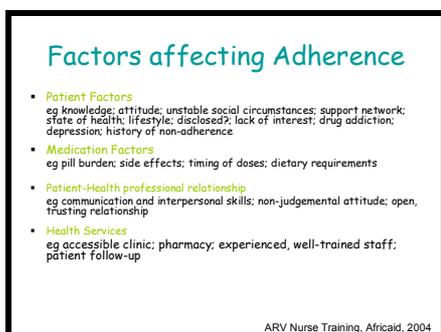
14. 100% adherence means every single drug being taken at the right dose, in the right time, in the right way. For life!



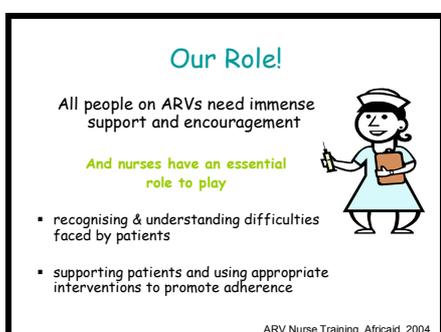
15. The challenge of adherence cannot be underestimated. Whilst ARVs have dramatic results, patients are faced with a multitude of difficulties which they have to cope with in order to achieve these results. Patients with HIV have significant challenges in their life already. These are then added to with the need for adherence



16. We must always remember how difficult adherence is. It is not just about remembering to take them. There may be many factors making adherence difficult, some of which may be beyond the control of the individual yet they are forced to cope with.



17. Many factors affect adherence. Does the patient understand them? Is he supported? Is he concealing the drugs? Does he want to take them? Is he too ill to remember? Are side effects worse than not taking ARVs? Is he struggling with so many tablets and fitting them in to daily life? Is he 'judged' at clinic for not taking them properly? Does he feel able to ask for help at the clinic? How easy is it to collect the drugs? Do the clinic staff know how best to help him?



18. Nurses play an essential role in supporting the patient. Nurses must use their time wisely with patients to discuss any problems the patient may be experiencing whilst developing with the patient ways to overcome difficulties. The nurse must endeavour to create a close bond with the patient so that the patient is more likely to talk freely and openly about any difficulties or concerns.

Promoting Adherence

....requires a
multidimensional, multidisciplinary,
continuous approach

where the patient is supported &
counselled
at every opportunity

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19. Stress again the importance of adherence. It's not just the responsibility of the nurse but the responsibility of the WHOLE multidisciplinary team when they come into contact with the patient to discuss and encourage 100% adherence.

....from the start!

**Promoting adherence
must start
from the very beginning,
prior to treatment
being commenced!!**

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20. Promoting adherence begins prior to the patient starting treatment. If difficulties and challenges are discussed beforehand then the patient is given more time to consider any life style changes, interventions and strategies needed that may assist in his/her adherence. This way, patients are involved in their treatment from the very beginning and know what to expect.

Ready for ARVs....?

- Has patient disclosed to anyone?
- Is there support at home or through friends?
- Is there a treatment supporter?
- Is there a stable living situation?
- Does the patient understand ARVs, expected outcomes and side effects?
- Does patient understand need for intensive follow-up?

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21. There are various factors we know to effect adherence. If these exist, we can anticipate adherence to be poor. An assessment of ARV readiness prior to starting is therefore essential in order to establish pre existing problems that may make adherence more difficult.

- Does the patient have a plan how to take ARVs and not miss a dose?
- Does the patient understand the need to take treatment for life, even if there are no symptoms or he/she feels better?
- Does the patient understand the impact of non-adherence?
- Is the patient committed to participating in on-going care?

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22. These questions should be worked through with the patient when considering whether to start the patient on treatment or not. Nurses are ideally placed to work through such as assessment making sure that liaison with the multidisciplinary team is incorporated.

Take-home messages!

- How many tablets should I take?
- What do they look like?
- How often do I need to take them?
- How exact do I have to be with timing?
- Are there any food or storage restrictions?
- What will happen if I miss doses?
- How can I fit these in to my daily routine?
- What should I do if I feel unwell on these drugs?



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23. Before a patient goes home with the drugs for the first time a check list must be completed by the nurse to determine whether the patient has all the correct information. And it doesn't stop there. Every member of the team should be checking that patients know how and when to take their drugs.

Practical Ideas

- Alarm clock
- Mobile phone
- Treatment supporter
- 'Normalise' in to daily life (eg TV programme, radio, meals)
- Pill box
- Colour-coded cards



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24. Various strategies may be suggested to help patient remember their drugs. Everybody is different and people must be helped in ways that is most suited to them. All efforts must be made to help patients maintain a normal life as possible incorporating drug regimens into daily life.

Remember.....

These drugs are not easy!

Patients must feel able to tell us that they are having difficulties or have missed doses.

Only then can we support and assist them

We must listen, empathise & support!

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25. Unless we have been on ARVs ourselves we cannot possibly begin to know what it means to take these drugs! Patients need all the support you can give every time you see them. If we do not support them in an open non-judgemental manner they will not disclose problems with you and are subsequently more likely to fail treatment.

Learning Exercises: 'Adherence'

A. Questions

1. What do we mean by adherence?

Adherence means taking ARVs exactly as prescribed, that is, the right drugs, at the right time, in the right way. Any difference is non-adherence.

2. For how long must patients remain adherent to ARVs?

Strict adherence must be maintained for as long as they are taking them.

3. How many doses of ARVs is it safe for a patient to miss in a month?

None! 100% adherence is the ideal for maximum benefit.

4. What happens if a patient is non-adherent to ARVs?

HIV will no longer be fully suppressed so will be able to start replicating again. Resistant viruses may also emerge.

5. What signs may indicate that a patient is non-adherent?

- *Viral Load starts increasing again*
- *CD4 count starts dropping again*
- *The patient's health starts deteriorating and Opportunistic Infections occur.*
- *The patient is unsure about the names, doses or timings of his drugs when asked*
- *The patient has not brought pill boxes for re-filling for a long time*

(It must be stressed that these signs do not **always** mean someone is non-adherent)

6. List 5 factors which make adherence difficult

Possible answers:

- *Pills must be taken every day for life*
- *Medicine must be taken in spite of unpleasant side effects*
- *Tablets may be difficult to swallow*
- *Tablets sometimes taste bad*
- *Patients may get confused about which drugs to take, when and how to take them*
- *Patients often have to take many tablets, several times a day*
- *Patients must fit them in to their lives (daily activities, visiting friends, work)*
- *Patients may be concealing the drugs from friends and family*
- *Some ARVs have dietary restrictions, complicating daily routine*
- *Patients may be too unwell to take them correctly*
- *Patients must make sure that they have their drugs with them if they travel*

B. Group Work

1. Barriers to Adherence

Divide the group into small groups of 2-4 people and ask them to discuss issues that prevent good patient adherence.

2. Nurses Role in Promoting Adherence

Now ask the group to discuss ways of overcoming these issues.

3. Case Scenario

Read the case scenario to the group then ask them to answer the questions below.

Bongani is 29 years old and is HIV positive. He has been taking ARVS for 6 months. At his last clinic appointment, his blood results showed that the ARVs were working well for Bongani. His viral load had dropped to undetectable levels and his CD4 count had increased to 250 cells/mm³. He was in very good health. However, at his next clinic appointment, his blood results were not so good. His viral load was increasing again and was no longer undetectable. His CD4 count had dropped to 200 cells/mm³.

Whilst talking with Bongani, you sense how disappointed he is with his blood results, particularly as he had been doing so well.

1) Why may Bongani's blood results have changed in this way?

There are two main possibilities:

a) Bongani may be very unlucky in that he has been taking his ARVs exactly as prescribed BUT the virus has managed to fight around them. In turn, HIV has started replicating again (increasing viral load) and started to infect and destroy CD4 cells once more (decreasing CD4 count).

b) Bongani may be non-adherent to his ARVs. This could mean a number of things, such as:

- He may be missing just a few doses every now and then*
- He may be taking them at different times each day*
- He may have stopped taking them completely*
- He may be taking it with fatty meals (Ideally, Efavirenz should not be taken with fatty foods if maximum absorption is to occur)*
- He may be taking the wrong number of tablets for one or all three drugs*

2) How can you help Bongani?

Above all, Bongani needs a great deal of support and encouragement. He will only feel able to discuss any problems he may be having with adherence if he feels he can trust and confide in a supportive and non-judgmental nurse. Always remember, adherence is an immense challenge and you are there to identify any problems he may be having with adherence and to help him overcome them. Only then, can he hope for achieving undetectable viral load and improved CD4 count again.

Firstly, you must try to identify whether Bongani is adherent to his ARVs. This does not just mean asking him whether he is taking his drugs. You must be sure he knows what adherence means – that he must take the right drugs, at the right time, in the right way, every single time. You may quickly realize that Bongani has started taking doses late or even missing some. For example, may be he has started a new job and this has made it difficult to take drugs exactly on time as he gets home late? Or maybe he has become confused about which drugs to take when?

All this can be identified through gentle, sensitive questions about when Bongani takes his medicines, what he takes and when.

Alternatively, Bongani may have started experiencing unpleasant side effects associated with his ARVs which may be putting him off taking them. Again, a sensitive, open-approach can facilitate conversation about these difficulties.

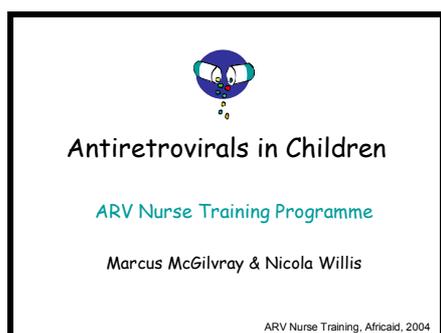
Once problems have been identified, Bongani may be helped and supported with appropriate intervention. This may involve reinforcement about the need for strict timing, practical ideas about how to take the drugs on time or further investigation of side effects and drugs to alleviate symptoms.

A combination of approaches may be required but the overall effect is the same – you will be able to help Bongani to adhere to the ARVs in order that he can hopefully achieve an undetectable viral load once more.

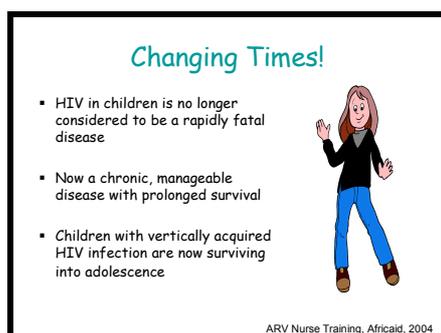
Module Objectives

- To review the use of ARVs in children and their impact on disease progression
- To provide nurses with a general understanding of the differences in ARV use in children
- To ensure nurses have a good understanding of the challenges associated with the use of ARVs in children
- To equip nurses with the skills required for supporting children and their families taking ARVs

Slide Presentation: ARVs in Children



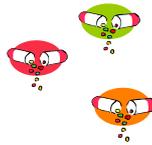
1. Welcome trainees and introduce yourself, including a brief background in to your area of practice, role & experience in providing ARVs to children. If there is time, trainees may be asked to share with one another their own ideas and experiences of ARVs in children, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage trainees to feel free to interrupt and ask questions at any time.



2. In some countries like the States, the UK & other parts of Europe, children infected with HIV at birth are now surviving in to adolescence. HIV is no longer the rapidly fatal disease seen in other parts of the world. Whilst it remains a terminal diagnosis, children and their families are learning to live with a chronic disease, which can be managed in order to improve quality and length of life.

What's changed?.....

- 1996-1997: paediatric dual ARV therapy started
- 1997-1998: protease inhibitor-based triple ARV therapy started
- 1998-2003: a dramatic improvement in the health of HIV + children on triple ARV therapy!



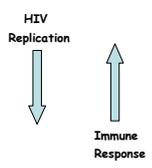
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3. The use of ARV drugs in children got off to a slower start than their use in adults. Drug options and doses had to be checked for safety in children. The combined use of two drugs commenced in 1996-1997. This was shortly followed by much improved responses with triple therapy, once protease inhibitors had been approved in children. Children are doing extremely well on Triple ARV therapy.

Response in Children.....

Most children treated with ARVs have excellent immune repopulation

morbidity and mortality is significantly reduced



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4. The majority of children respond well to ARV drugs, experiencing a reduction in viral replication and a corresponding increase in CD4 cells. Immune repopulation refers to the regeneration of immune system cells. The result is a significant reduction in opportunistic infections, improved general health and quality of life, and increased length of life.

But.....

Like adults.....

suppressing the virus and preserving the immune system is associated with numerous challenges!

And... many of these challenges are exacerbated in children!



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5. However, like adults, if children are to achieve viral suppression and the subsequent increase in immune response, they also have to face numerous challenges associated with ARVs. While adults commonly find these exceptionally difficult, they are often exacerbated further in children.

.....not just little adults!

- Children have unique needs
- They are physically, developmentally and psychologically different to adults
- They should be managed and treated differently



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6. It has long been understood that children are not just little adults. They have unique needs and an understanding of their physical, developmental and psychological make-up is essential in order to understand the different principles of ARV use in children.

CD4 counts

- Infants and children normally have **higher CD4 counts**
- As CD4 cell count varies with age, **CD4 percentage** is considered a more reliable marker of immunological status in children
- An understanding of this is essential in order to accurately assess disease progression



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7. Infants and young children usually have higher CD4 counts than adults. The normal count varies with age but is equal to the adult value by the time the child is 6 years old. CD4 percentages are therefore considered to be more reliable markers prior to this age. If this is not understood, blood results may be misleading which could be dangerous for the child.

Viral Load

- After starting ARVs, Viral load may **decrease more slowly** in children cf adults
- Infants may take **longer to reach an undetectable viral load**
- Only 40% of children may experience a reduction in Viral Load to <500copies



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8. The reduction in viral load is often slower in children commencing ARVs than is seen in adults. Each child is different but in comparison to adults, children may take longer to reach undetectable viral load or may even never reach it. This is particularly so if the child is born with a very high viral load.

Aim of therapy

To maintain the child's immunological status at a level that prevents disease progression



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9. The overall aim of therapy in children is to maintain the child's immune system at a level that protects them from developing opportunistic infections and disease progression. Like adults, ARV drugs will not cure HIV in children but help to 'control' the virus by reducing viral replication thus preserving the immune system.

ARV Drug Options

- ↓range of available/licensed drugs for children compared with adults
eg EFV: cannot be used <3 years
- Most of usual NRTIs & NRTIs are available
eg AZT, 3TC, ddI, d4T, NVP
- ? NVP Resistance following exposure in MTCT programme



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10. Great progress is being made in terms of drug choices for children. Due to the smaller population to recruit in to studies and the ethics of testing drugs in children, it is usually more difficult to secure new drugs for children. Fortunately, most of the main drugs are now available. However, one concern for the future is that children exposed to Nevirapine before birth may be resistant to it in the future.

Paediatric Drug Options

- Paediatric formulations not always available
eg **NFV: only available in tablets**
PIs: extremely unpalatable
- ARV syrups more expensive than tablets
- Relatively little research on ARVs & pharmacokinetic data due to the smaller population of potential subjects

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11. Again, things are improving but many of the ARV drugs started off as (and continue to be!) big, chalky tablets that were difficult to swallow for adults. ARVs are slowly becoming available in syrup form but are unfortunately more expensive and often taste terrible!

Paediatric Doses



- children have different metabolism from adults
- higher doses of ARVs are usually necessary
- drug distribution and metabolism/elimination varies with growth and development
- Older children: surface area more accurately reflects drug metabolism and clearance than body weight (but over estimates doses for infants)

$$\text{Surface area (m}^2\text{)} = \sqrt{\frac{\text{weight (kg)} \times \text{height (cm)}}{3600}}$$

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12. Doses are very different for children. Children usually need higher doses of ARVs. The way in which drugs are distributed and metabolised in children is different to adults and varies with growth. In this case, an adult dose would provide insufficient viral suppression. This formula is used by pharmacists and doctors to calculate the dose required for children

Side Effects

Toxicities are of great concern and increasingly problematic for children and families

...particularly as:

- children's bodies are still developing
- children may well be exposed to these drugs for much longer than adults



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13. Like adults, children experience side effects (toxicities) to ARVs. Unfortunately however, these toxicities may cause more harm in children as their bodies are still developing and it is very early days in the world of ARVs for us to know the long term side effects on the body. Many long term studies are being carried out to investigate this

Mild side effects

Children commonly experience side effects

They are often transient and manageable with appropriate therapeutic intervention

Support and encouragement for the child and family is essential

- nausea
- vomiting
- diarrhoea
- abdominal pain
- skin rashes
- headaches

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14. The more common side effects seen in children are similar to those seen in adults. They are commonly short-term and resolve after a few months of starting the drugs. It is essential that symptoms are controlled as early as possible and that the child and care giver are supported. Adherence must be promoted at all times. The care giver must not be 'put off' the ARVs due to side effects which could be managed

Severe side effects

Unfortunately, children on ARVs may also experience worrying long-term side effects

- lipodystrophy
- mitochondrial toxicity (NRTIs)
- bone density changes (PIs)
- lipidaemias with accelerated atherosclerosis (PIs)
- carcinogenicity (NRTIs)

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15. We are also seeing worrying long-term side effects in children including fat redistribution, disorders related to mitochondrial damage, changes in bone density, high lipids & cholesterol and even cancers. More and more studies are providing information on the side effects of different drugs and are directing doctors in deciding which drugs to use in the future

Monitoring

- Regular blood tests are essential to identify toxicities and to ensure appropriate intervention and management
- This presents another challenge:

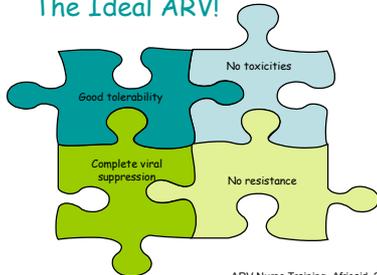
Few children willingly give their blood!



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16. Whilst many side effects can be assessed by listening to the child and the care giver, or by examining the child, any effect of the ARVs on different organs can be assessed with various blood tests. Regular FBC, U&Es, LFTs should be taken to monitor potential toxicity. Blood tests are an immense ordeal for children who are afraid and do not understand what is happening

The Ideal ARV!



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17. ARVs are good but far from perfect. We know them to dramatically improve people's health but they may simultaneously cause side effects. Adherence is extremely difficult, they never remove the virus completely and resistance is a huge problem. In an ideal world....

If this ideal were available.....

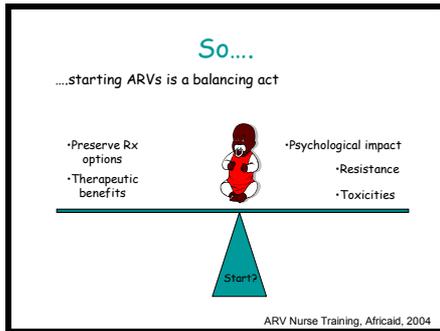
...ARVs should be started as soon as a child is diagnosed!

BUT

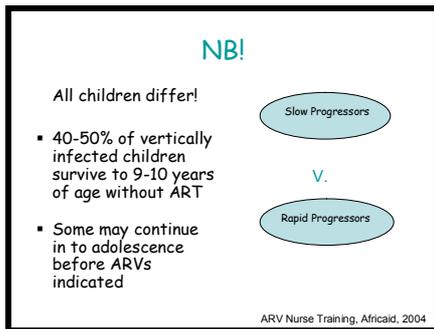
It is still not clear whether the potential virological and immunological benefits of starting therapy early outweigh the problems with adherence, resistance and toxicity

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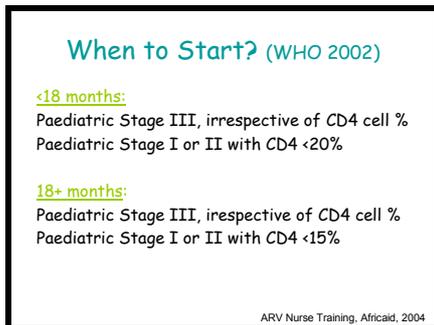
18. Should this ideal ARV drug be available, children would be started on ARVs immediately. However, we still don't know whether the early use of ARVs in children will result in such a dramatic reduction in viral load and improvement in immune response that outweighs the immense problems of adherence, resistance and toxicity.



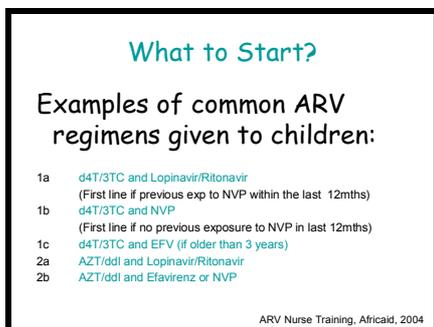
19. So the decision to start children on ARVs is an extremely carefully thought out process. The pros and cons are weighed up. Clinical trials are being conducted all over the world, (including KZN!) to investigate the optimal time to start ARVs in children. This conundrum must be explained to care givers, who may wonder why doctors are delaying treatment for the child



20. It must be remembered that all children are different. Some children with HIV will deteriorate rapidly within a few months or years. Others will remain relatively well for some years and their immune system may be sufficiently strong for up to 10 years. This may be less so in areas of extreme poverty where health is compromised further



21. The Center for Disease Control has set out these guidelines for commencement of ARVs in children. ALL children with Paediatric Stage III disease should be started on ARVs, irrespective of CD4%. For children with Stage I or II, if they are <18months, a CD4 <20% indicates treatment. If they are >18months, a CD4 <15% indicates treatment. If CD4 testing is not available, clinical symptoms must form the basis of the decision



22. Common regimens used in children usually involve five different drug options but specific combinations will depend on locally available drugs. Exposure to NVP during Prevention of Mother-To-Child Transmission programmes may influence drug choice (in which case Lopinavir/Ritonavir will be used). The age of the child also influences the use of EFV or NVP (if the child is younger than three EFV should not be used). Abacavir may be used in some areas and has been shown to be extremely effective.

Adherence

Is a HUGE challenge for adults.....

It is even more difficult with children!



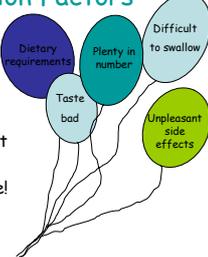
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23. If you thought it was hard for adults, it can be even harder for children! Ask the group why it may be harder for children to adhere to ARV drugs.

Medication Factors

All children dislike medicine!

But ARVs are difficult **AND** must be taken for life!



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24. The drugs themselves present numerous challenges for children. All children dislike medicine. Now they have been started on something they have to take for life. Improvements are being made but it often tastes bad, there are lots of them, they are often difficult to swallow, they may be dietary requirements AND they may make the child sick with side effects.

Child/Family Factors

- Child's lifestyle
Fitting ARVs around school & friends
- Child's lack of understanding
Why do I need medicine?
- Children are usually reliant on their parent or carer for ARVs
*Is the parent sick/unable to administer ARVs?
Has the parent had any negative experiences of ARVs?
Is the parent adherent?
How is the parent coping with own diagnosis AND child's?
What is the parent's perception of the child's illness?*



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25. It is usually extremely difficult for a child to understand why he has to put up with all this! He is usually dependent on a care giver to receive them. Are they actually given? Or he may refuse to take them, draining the energies of a care giver, particularly if they are sick themselves. The carer has an enormous amount to deal with and may be unable to cope

Promoting adherence

- Assessment of child & family prior to child commencing ARVs
- Assist families in developing routine for ARVs. ARVs should NOT dictate every aspect of daily life
- Open, supportive approach
- Age-appropriate explanations to child re need for medication
- Continuing support and re-assessment of each child and family's situation
- Support from other parents and children

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26. Promoting adherence is multi-faceted and must be a continuous process. This is highly skilled, addressing both the child's needs and issues and those of the care giver. The child **MUST** be involved. Children cope far better when they are able to understand what is happening to them and have a sense of control. Use child-sensitive, age-appropriate explanations of the need for medicine 'to keep you strong and prevent infections'.

Promoting adherence

- Trial runs
- Play therapy
- Sticker charts
- Art therapy
- Taking medication with parent
- Support groups



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27. A variety of strategies may be used to help encourage the child to take ARVs and to assist and support the care giver. Remember, a child's work is to play. Use art and fun games to provide incorporate some fun and provide the child with a sense of control in the process of taking ARVs. Taking ARVs at the same time as a parent or sibling can also help as the child wants to be like them. Games with other children in support groups help too

Remember.....

- ARVs cause great distress, anxiety and confusion for children
- It is equally difficult for parents, who are commonly under enormous strain with their own diagnosis and ARVs
- The child and family **MUST** be considered as a whole
- **They require immense support and encouragement**



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28. A child with HIV has significant challenges to cope with. Their parent or carer has potentially even greater concerns, as they cope with their own illness or concerns about the child's future and face worry or guilt over the child's HIV infection. On top of all that, ARVs may add to their problems if they are not supported and encouraged at all times. You have a significant role to play!!

Learning Exercises

A. Group Work

1. Case Scenario

Read the following case scenario to the group, before answering the following questions.

Faith is a 29 year old mother. Both Faith and her two year old daughter, Gracie, are HIV positive. Faith has been very unwell over the past six months. After treatment for toxoplasmosis, she started ARVs. Unfortunately, whilst she has recovered from toxoplasmosis, her overall health has remained poor. She gets recurrent chest infections. At clinic, Faith reveals that she frequently forgets to take her ARVs. In further discussion, she informs you that her husband died 8 months ago and she is feeling very depressed.

At the same clinic appointment, Gracie is also seen by the doctor. The doctor informs Faith that Gracie also requires ARV treatment now as her CD4 count has fallen below 200 cells/mm³. Gracie has also been unwell with recurrent chest infections, severe weight loss and now shingles.

a) What concerns are there over Gracie stating ARV treatment?

Gracie is a two year old child and therefore dependent on her mother for everything. This includes ARV drugs. If Faith forgets to take her own drugs, it is likely that she will forget to give Gracie her drugs.

Faith has an enormous amount to cope with in her life including her own diagnosis and sicknesses, grief for her husband, her daughter's diagnosis and how she was infected and worry for her daughter's future in the event of Faith's death.

The need for Gracie to commence ARV drugs is an overwhelming challenge for a mother already struggling to cope. If Faith cannot remember Gracie's drugs, Gracie will become increasingly unwell. Even if Faith is able to remember Gracie's drugs, 2 year old children can be extremely reluctant to take medicines. Faith would need to be giving Gracie syrups at least twice a day, every day. This could be an exhausting struggle and strain on both Faith and Gracie at a period when quality time together is of enormous importance. In addition, Gracie may experience side effects to the ARVs and she will require additional support and care from her mother. This will also contribute further to Faith's concerns.

b) What measures are required to ensure that Gracie receives the drugs she requires?

Both Faith and Gracie have significant needs. Gracie needs ARVs and she must receive them. Every effort must therefore be made to ensure that this is achieved. Her mother requires a great deal of support in her own right. However, her needs are exacerbated by Gracie's need for ARVs.

A multi disciplinary approach is required with particular emphasis on the social workers and counsellors. Faith requires a great deal of psychosocial support in order to help her cope with her own circumstances before she can start to think about coping with Gracie. Support groups can have a profound effect on individuals' ability

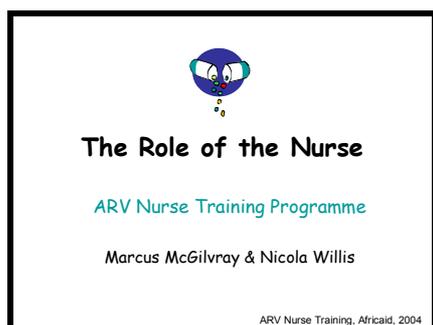
to cope. Meeting with other people in her situation may help Faith greatly, if she is willing to attend the group. With appropriate intervention, she may be helped to cope more which will, in turn, help Gracie. A treatment supporter may be of great benefit as he/she could supervise and ensure that both Faith and Gracie receive their medication.

Faith and Gracie will require close follow up and a continuing supportive, non-judgmental approach if they are to receive the care and support they desperately need. Only then can they both receive optimal ARV treatment and achieve increased quality of life and prolonged life.

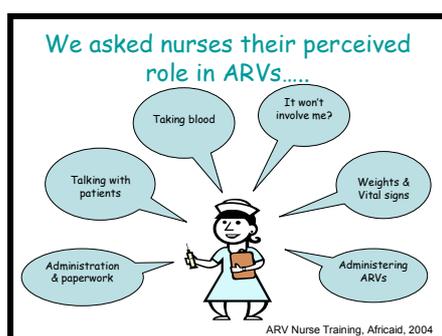
Module Objectives

- To describe the dynamic role of the nurse in the holistic care of a patient receiving ARV treatment
- To equip nurses with a sense of importance and belief in their role in the overall success of ARV treatment.
- To encourage nurses to consider the diversity of their role in the management of patients taking ARV drugs.

Slide Presentation: The Role of the Nurse



1. Welcome trainees and introduce yourself, including a brief background in to your area of practice, role & experience in the care of patients with HIV and the provision of ARVs. If there is time, trainees may be asked to share with one another their own ideas and experiences of ARVs, what they personally hope to take away from the training session and how it may help them in their nursing role. Encourage trainees to feel free to interrupt and ask questions at any time.



2. Since the Government agreed in principal to the ARV roll out, nurses have been anticipating the arrival of ARVs across South Africa. Prior to the development of this manual, in October 2003 we asked nurses what they perceived their training needs to be to meet this roll-out. They ALL expressed the need to know more about ARVs. However, with regard to their role, they envisaged it to be very practical and task orientated.

These may be true

BUT.....

they underestimate the immense importance of the dynamic role nurses have to play

And this is why!

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3. Indeed, the nurse has an essential role to play in blood taking, measurement of vital signs and documentation. However, the nurse's role, in no way stops there!!! We have an immense part to play, a role that is very dynamic and tackles every aspect of ARV administration.

ARVs

The Goal!

To decrease or reverse immune system damage associated with HIV infection,

thus improving quality of life and reducing HIV-related morbidity and mortality



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4. The goal of ARV therapy is primarily to decrease or reverse immune system damage associated with HIV infection. This results in an improvement of the patient's quality of life through the reduction of infections and an increase in length of life.

The role of the nurse is.....

.....to ensure that this goal is achieved!

that quality of life is improved for patients with HIV

by decreasing or reversing immune system damage with Antiretroviral drugs



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5. With this goal in mind, the role of the nurse is to ensure that this goal is achieved, i.e. that the patients quality of life is improved by suppressing HIV and allowing an improvement in the patients immune system.

How?

Historically, nurses have provided holistic care for their patients, attending to their physical, psychological and social needs in order to promote quality of life

Patients requiring ARVs are no different and require our whole range of skills and expertise, right from the beginning and from then onwards.....

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6. This is nothing new for nurses! Since the days of Florence Nightingale, nurses have been providing holistic care. ARVs represent an immense challenge for patients, placing huge physical, psychological and social demands on them. Through recognition of these needs plus a sensitive, supportive approach to our patients we may dramatically influence their quality of life. ***If you can - give an example, based on your own experience as nurse, of good holistic care provided to a patient and the positive effects it had on that person.***

Starting ARVs

Early days are EXTREMELY influential in ARV success

Why?

- Patient is **not ready?** – he/she may be non-adherent
- Patient **doesn't understand** the drugs? – he/she may take them incorrectly
- Patient **doesn't expect** side effects? – he/she may be shocked and get 'put off' ARVs or not report any problems
- Patient **feels alone** and unsupported? – he/she may be frightened, reluctant to take drugs or to report any problems

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7. If a patient is not properly prepared before starting ARVs, adherence may be poor. If factors known to make adherence difficult already exist for that patient, adherence may also be poor. Assessing ARV readiness helps us to assess whether the patient is ready to start treatment and ensures that all the issues involved in ARV therapy have been discussed. If a patient hasn't been informed about what to expect when starting ARVs then the patient is likely to feel stressed and anxious and may even stop treatment.

Starting ARVs

Our diverse nursing role!

- Blood collection (baseline results eg CD4, VL, U&Es, FBC)
- Education for patient re ARVs (What are they?, Side effects)
- Counselling re starting ARVs
- Assessing ARV Readiness
- Liaising with MDT re ARV readiness
- Adherence support

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8. When a patient starts ARVs, our role is extremely diverse. Let's think further than simply the blood we have been asked to collect. This is a time for educating the patient about ARVs, on issues such as adherence and resistance; that ARVs are a treatment and not a cure which bring with them their own unique problems such as side effect; identifying whether the patient is really ready to start ARVs; liaising with the Multidisciplinary team to discuss any patient issues that may have arisen.

Monitoring ARVs

ARV success depends on regular monitoring of their **efficacy & safety**

This is assessed using a combination of:

- **Verbal Reporting:** "I feel much stronger now"
"I keep getting headaches"
"My appetite is much better"
"I am having bad dreams"
- **Clinical Examination:** eg weight gain; 'looks better'; rash; jaundice
- **Laboratory Testing:** CD4, Viral Load, U&Es, FBC, Resistance testing

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9. Monitoring ARV efficacy and safety tells us how well the drugs are working and whether they are causing any problems. A three-pronged approach is involved: A report from the patient as to how they are feeling, Clinical examination and Laboratory tests all give vital information. They inform us both of improvements which are extremely encouraging and warn us of potential problems. Don't forget correct documentation of all these reports!

Nurses role in Monitoring

Verbal Reporting

- Nurses are often the first point of contact
- Patients often feel more comfortable raising issues with nurses
- Nursing activities (eg vital signs) provides opportunity for informal conversation re problems/issues

Assessment: Is patient experiencing any side effects? How are they feeling? Any problems?

Follow up: Referral of concerns to Doctor; Recognising urgent referrals; Good MDT communication

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10. Nurses are the key to monitoring patients' progress on ARVs. Verbal reporting allows the nurse to identify whether the patient is experiencing any problems, or has any questions? Nurses are ideally placed for this as they are usually the first point of contact & patients often feel reluctant to raise issues with the Doctor. Nursing tasks provide many informal opportunities for talking. Any concerns that may arise must ALWAYS be referred and discussed with the Multidisciplinary team.

Nurses Role in Monitoring

Clinical Examination

- Again, nurses are often the first point of contact
- Clinical examination can take place during other activities eg blood taking

Assessment: Recognising ARV side effects (eg jaundice, rash) or improved patient health

Referral: Prompt, appropriate intervention

Counselling: reassurance for patient

Encouragement for patient doing well!!!

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11. Clinical Examination provides the next method of monitoring. Again, nurses are often the first point of contact, enabling us to identify a problem immediately and ensure prompt referral, particularly in an emergency. Counselling is vital for patients, whether they are doing well or experiencing problems. Always support and encourage! **Ask the group to discuss some of the conditions patients present with, i.e. rash, nausea, headaches and the nurse intervention.**

Laboratory testing

A variety of different blood tests are used to measure the efficacy and safety of ARVs

The results provide essential information re:

- Disease progression
- Is patient safe to continue taking regimen?
- Is the patient resistant to the ARV regimen?
- Is the patient at risk of OIs and in need of prophylaxis?
- Psychological support & encouragement for patient



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12. Laboratory tests provide invaluable information that cannot be assessed verbally or visually. Doctors use the results to make clinical decisions about the safety of the drugs for that patient, how well they are working for the patient, is there resistance? Is prophylaxis needed for any impending OIs? **Also**, (a point often forgotten) - good results provide encouragement, psychological support for patients taking ARVs

And who takes the blood?

Nurses!!

....and we have a direct responsibility to ensure that accurate results are obtained which may inform appropriate clinical decisions



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13. Blood tests can and do play a very important role in monitoring the patient's health. Accurate results are essential as they often dictate appropriate health intervention. It is our responsibility to ensure that bloods are taken correctly

(other factors also play a part e.g. correct laboratory techniques)

Getting it right!

Correct clinical decisions depend on meaningful clinical laboratory information

This depends on **proper specimen collection!**

Common blood tests:

- CD4 Count
- Viral Load
- Safety Labs (FBC, LFTs, U&Es)
- Resistance Testing



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14. Correct blood taking is vital if we are to know the 'correct' health of our patient. Common bloods taken include CD4 - this simply measures the CD4 (normal range is between 600-1200 mls) allowing us to determine the state of the patients immune system. Viral load measures the amount of HIV in the blood. Other tests including FBC, LFT & U&Es allow us to monitor the health of the patient, i.e. the liver, kidneys, red blood cells etc. Finally, a resistance test indicates any mutations of the HIV virus that lead to an ARV drug resistance. (this test is uncommon in most parts of the world because it is VERY expensive).

Getting it wrong....

Improper technique may lead to danger signs being over-looked and/or mismanaged

Case scenario A

A patient is in his third month of ARVs. The wrong name is put on his blood sample so the results are lost. The doctor is therefore not aware that his LFTs are dangerously high.

Case scenario B

An urgent CD4 count is required for a patient. The blood bottle is insufficiently filled and the lab cannot get an accurate reading.

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15. Labelling errors are a common occurrence in nurse practice. Busy clinics with many patients often lead the nurse to neglect the job in hand. It's essential that we all practise good blood taking techniques and focus on the patient in front of us. Correct blood taking is not a job that can be carried out at the same time as others – however busy we may feel we are! Incorrect blood tests lead to poor patient care and can directly affect the patient's health.

When taking blood.....

- Correct patient labeling!
- Correct tube for test
- Correct volume for test
- Correct request form
- Securely attached label to bottle
- Clear, legible writing on bottle/form
- Secure, designated container for blood bottles

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16. Concentrate on one patient at a time. Check patient details are correct, label blood bottles and request forms clearly prior to taking blood. Ensure the blood bottles are adequately filled and then double check that the patient details match those recorded on the bottle. Ask the group to discuss the issues of **universal precautions** in respect to blood taking.

And don't forget.....

- Check patient details are correct!
- Label blood bottles before collection
- Always wear gloves for collection of specimens!
- NEVER re-sheath a needle
- Dispose of used needle in near by sharps bin
- Then wash your hands
- Wear NEW gloves for the next patient!
- Take your time! A few moments longer may prevent needle sticks!

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17. Compare issues of universal precautions raised by the group with those listed on this slide. Emphasize any points missed.

Nurses and Adherence

- Educate, educate, educate.....
- Support, support, support.....
- Counsel, counsel, counsel.....

You can never do this enough!!!

It is the single most important thing you can do for your patients

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18. Good patient adherence to ARVs is the MOST important role of the nurse. Whenever you see patients, educate, support and counsel about the need for adherence. This alone will dramatically affect the outcome of your patients ARV.

Don't forget Safer Sex!

Safer Sex is essential to prevent:

- **Transmission:** someone on ARVs can still transmit HIV, even if their viral load is undetectable
- **Re-infection:** someone on ARVs may be re-infected with a different strain of HIV, making treatment success more difficult

Nurses should take every opportunity to counsel about safer sex practices



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19. This is all too frequently forgotten or overlooked. Many people prefer not to discuss sex! However, nurses are ideally placed to meet this challenge. Patients on ARVs MUST be told that they can still transmit the virus and that they themselves can be re-infected with different strains through sex. We know that people are reluctant to disclose their status to sexual partners but even so, we must continually advocate safe sex for the good of the patient's health and also for the good of public health!

Variety of Roles

- Educating
- Counselling
- Assessing
- Managing
- Referring
- Administrating



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20. Nurses have a broad range of roles to play. These roles already make up the unique skills and characteristics of the modern nurse – they just need applying now to ARV treatment. We now have an understanding of ARV drugs, so let's do what we're good at:-

- Educating patients, other nurses, health professionals and the general public.
- Counselling patients.
- Assessing and Managing the patient's needs.
- Recognising our own limitations and Referring patients to the doctor where required.

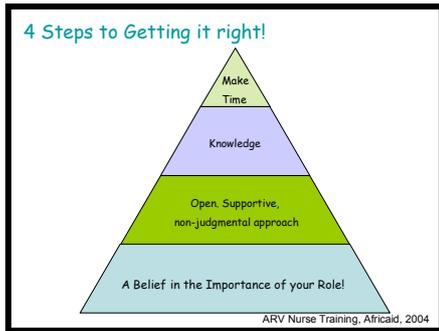
Fulfilling these roles

- **Knowledge!** Know your drugs, side effects, doses & dietary requirements
- **Understanding:** Be aware of the challenges and the psycho-social needs of YOUR patient
- **Confidence:** Your patient will look to you for advice, information and support

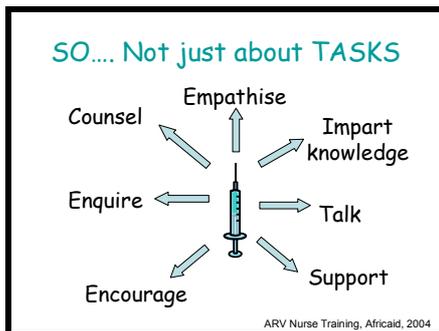
THESE ALL ENHANCE NURSING CARE!

ARV Nurse Training, Africaid, 2004

21. The ability to fulfil these roles depends upon our knowledge, our character and our confidence. Do not be daunted or put off! We are all learning and there are plenty of people around to discuss issues with, clarify points and answer questions. Above all, the aim is to provide comprehensive care that supports and encourages patients on ARV treatment.



22. This pyramid represents four building blocks designed to successfully care for our patients. Firstly a belief in the importance of our role is paramount and will encourage us to achieve the following three. An open, supportive, non-judgmental approach encourages patients to adhere to ARV treatment and to seek support and advice from us. This requires knowledge. If you don't know – ask someone in your team. Finally, if you don't make time to talk and find out your patients needs and concerns, how can you possibly nurse them!



23. So our role is not just about completing tasks. Instead, one task provides a multitude of opportunities to meet the needs of our patient on ARVs. For example, if vital signs are to be taken, use the opportunity to build trust and to identify patient's needs. We are then able to identify any areas requiring intervention or, just as importantly, to encourage the patient doing well with no problems!

In summary...

Patients on ARVs face an immense challenge

Yours is an extremely exciting role, where you **CAN** and **WILL** have a huge influence on the success of ARV treatment for your patients

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24. The challenges of ARVs are immense. Effective ARV programmes depend on enthusiastic, committed nurses who believe in the influence they may have on treatment success. Increasing access to ARVs is an extremely exciting opportunity for nurses to deliver the holistic care they are trained to provide, and for being directly involved in promoting quality of life and length of life for people with HIV.

Learning Exercises: 'The Role of the Nurse'

A. Group Work

Divide the group into pairs. Give each pair one of the following nursing roles, as discussed in the slide presentation:

- Educating
- Counselling
- Assessing
- Managing
- Administrating
- Referring

Ask each pair to discuss the following questions with reference to the role they have been given:

1) **When** does the nurse engage in that role during the overall care of a patient on/considering ARVs?

Trainers prompt: *Encourage trainees to think of all the occasions that they would be involved in that particular role when working with patients.*

For example:

i) Nurses are **assessing** patients at different times: assessing vital signs, assessing adherence and assessing side-effects.

ii) Patients require **educating** in not just one issue but many different issues: safer sex, drug resistance, adherence and drug side effects.

2) **Why** is this important in the overall success of ARV therapy?

Trainers prompt: *Encourage trainees to think of a variety of different reasons why that role is so significant in ensuring ARV success.*

For example:

i) Assessing adherence is vital to ensure patients are taking their ARVs as prescribed because adherence is one of the most important factors in treatment success.

ii) Educating patients about drug resistance is important in order to help them understand the importance of adherence whilst educating about drug side effects is important if patients are to recognise and report them.

3) **What** knowledge and skills do nurses require to fulfil the role effectively?

Allow 15 – 20 minutes for this exercise and then allow trainees to feedback their responses to the group.

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