Childhood HIV

A learning programme for professionals

Childhood HIV enables nurses and doctors to care for children with HIV infection. It covers an introduction to HIV in children, the clinical and immunological diagnosis of HIV infection, management of children with and without antiretroviral treatment, antiretroviral drugs, opportunistic infections and end-of-life care.

Keep up-to-date with the latest guidelines in HIV patient care for children

Complete the course with an online multiple-choice exam when you are ready

Practise what you learn, while you learn, without having to leave your workplace

ISBN 978 1 920218 21 8

“A superb manual which comprehensively covers HIV and its management.”

– Nonhlanhla P Khumalo, Editor

About the authors

A previous head of neonatal medicine at UCT, Dave Woods now consults to UNICEF and the WHO, and is developing distance-learning courses and innovative, power-free medical devices for health professionals in under-resourced countries.

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www.ebwhealthcare.com
Childhood HIV

A learning programme for professionals

Prof. David Woods and Prof. Brian Eley
VERY IMPORTANT

We have taken every care to ensure that drug dosages and related medical advice in this book are accurate. However, drug dosages can change and are updated often, so always double-check dosages and procedures against a reliable, up-to-date formulary and the given drug's documentation before administering it.

Childhood HIV:
A learning programme for professionals

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The aim of this book is to promote and improve the care of all HIV-infected children, especially in under-resourced communities in southern Africa. The learning material is presented in a way to enable groups of healthcare workers to take responsibility for their own continuing training.

We wish to gratefully acknowledge the contributions of Ms Patti Apolles, Dr Minette Coetzee, Prof Mark Cotton, Dr Teresa Edwards, Dr Beth Harley, Dr Steve Innes, Dr Karen Jennings, Dr James Nuttall, Ms Collette Mansfield, Dr Tammy Meyers and Prof David Power. When opinions differed between contributing colleagues, the simplest most practical choice was adopted. While every effort has been made to correct any errors in the text, the final decision and responsibility was ours alone.

Reference sources included the *Handbook of Paediatric AIDS in Africa* by the African Network for the Care of Children Affected by AIDS. Where possible, we attempted to comply with World Health Organisation, South African national and provincial, and Red Cross War Memorial Children’s Hospital HIV prevention, diagnostic and management protocols.

Our sincere thanks go to the publishers for their willingness to support this project and for their innovative vision of presenting the text in both book and web-based format. The question-and-answer layout is adapted from that of the highly successful Perinatal Education Programme.

Royalties from the sale of this book will go to Eduhealthcare, a not-for-profit organisation, which has the goal of improving the healthcare of children, especially in poor countries, through the education of nurses and doctors. We thank Eduhealthcare for generously funding this project.

*Prof David Woods and Prof Brian Eley*
About the EBW Healthcare Series

EBW Healthcare publishes an innovative series of distance-learning books for healthcare professionals, developed by the Perinatal Education Trust, Eduhealthcare, the Desmond Tutu HIV Foundation and the Desmond Tutu TB Centre, with contributions from numerous experts.

Our aim is to provide appropriate, affordable and up-to-date learning material for healthcare workers in under-resourced areas, so that they can manage their own continuing education courses which will enable them to learn, practise and deliver skillful, efficient patient care.

The EBW Healthcare series is built on the experience of the Perinatal Education Programme (PEP), which has provided learning opportunities to over 60 000 nurses and doctors in South Africa since 1992. Many of the educational methods developed by PEP are now being adopted by the World Health Organisation (WHO).

Why Decentralised Learning?

Continuing education for healthcare workers traditionally consists of courses and workshops run by formal trainers at large central hospitals. These teaching courses are expensive to attend, often far away from the healthcare workers’ families and places of work, and the content frequently fails to address the real healthcare requirements of the poor, rural communities who face the biggest healthcare challenges.

To help solve these many problems, a self-help decentralised learning method has been developed which addresses the needs of professional healthcare workers, especially those in poor, rural communities.

Books in the EBW Healthcare Series

Maternal Care addresses all the common and important problems that occur during pregnancy, labour, delivery and the puerperium. It covers the antenatal and postnatal care of healthy women with normal pregnancies, monitoring and managing the progress of labour, specific medical problems during pregnancy, labour and the puerperium, family planning and regionalised perinatal care. Skills workshops teach clinical examination in pregnancy and labour, routine screening tests, the use of an antenatal card and partogram, measuring blood pressure, detecting proteinurica and performing and repairing an episiotomy.

Maternal Care is aimed at healthcare workers in level 1 hospitals or clinics.
Primary Maternal Care addresses the needs of healthcare workers who provide antenatal and postnatal care, but do not conduct deliveries. It is adapted from theory chapters and skills workshops from Maternal Care. This book is ideal for midwives and doctors providing primary maternal care in level 1 district hospitals and clinics, and complements the national protocol of antenatal care in South Africa.

Intrapartum Care was developed for doctors and advanced midwives who care for women who deliver in district hospitals. It contains theory chapters and skills workshops adapted from the labour chapters of Maternal Care. Particular attention is given to the care of the mother, the management of labour and monitoring the wellbeing of the fetus. Intrapartum Care was written to support and complement the national protocol of intrapartum care in South Africa.

Newborn Care was written for healthcare workers providing special care for newborn infants in regional hospitals. It covers resuscitation at birth, assessing infant size and gestational age, routine care and feeding of both normal and high-risk infants, the prevention, diagnosis and management of hypothermia, hypoglycaemia, jaundice, respiratory distress, infection, trauma, bleeding and congenital abnormalities, as well as communication with parents. Skills workshops address resuscitation, size measurement, history, examination and clinical notes, nasogastric feeds, intravenous infusions, use of incubators, measuring blood glucose concentration, insertion of an umbilical vein catheter, phototherapy, apnoea monitors and oxygen therapy.

Primary Newborn Care was written specifically for nurses and doctors who provide primary care for newborn infants in level 1 clinics and hospitals. Primary Newborn Care addresses the care of infants at birth, care of normal infants, care of low-birth-weight infants, neonatal emergencies, and common minor problems in newborn infants.

Mother and Baby Friendly Care describes gentler, kinder, evidence-based ways of caring for women during pregnancy, labour and delivery. It also presents improved methods of providing infant care with an emphasis on kangaroo mother care and exclusive breastfeeding.

Saving Mothers and Babies was developed in response to the high maternal and perinatal mortality rates found in most developing countries. Learning material used in this book is based on the results of the annual confidential enquiries into maternal deaths and the Saving Mothers and Saving Babies reports published in South Africa. It addresses the basic principles of mortality audit, maternal mortality, perinatal mortality, managing mortality meetings and ways of reducing maternal and perinatal mortality rates. This book should be used together with the Perinatal Problem Identification Programme (PPIP).

Birth Defects was written for healthcare workers who look after individuals with birth defects, their families, and women who are at increased risk of giving birth to an infant with a birth defect. Special attention is given to modes of inheritance, medical genetic counselling, and birth defects due to chromosomal abnormalities, single gene defects, teratogens and multifactorial inheritance. This book is being used in the Genetics Education Programme which trains healthcare workers in genetic counselling in South Africa.

Perinatal HIV enables midwives, nurses and doctors to care for pregnant women and their infants in communities where HIV infection is common. Special emphasis has been placed on the prevention of mother-to-infant transmission of HIV. It covers the basics of HIV infection and screening, antenatal and intrapartum care of women with HIV infection, care of HIV-exposed newborn infants, and parent counselling.

Childhood HIV enables nurses and doctors to care for children with HIV infection. It addresses an introduction to HIV in children,
the clinical and immunological diagnosis of HIV infection, management of children with and without antiretroviral treatment, antiretroviral drugs, opportunistic infections and end-of-life care.

**Childhood TB** was written to enable healthcare workers to learn about the primary care of children with tuberculosis. The book covers an introduction to TB infection, and the clinical presentation, diagnosis, management and prevention of tuberculosis in children and HIV/TB co-infection. **Childhood TB** was developed by paediatricians with wide experience in the care of children with tuberculosis, through the auspices of the Desmond Tutu Tuberculosis Centre at the University of Stellenbosch.

**Child Healthcare** addresses all the common and important clinical problems in children, including immunisation, history and examination, growth and nutrition, acute and chronic infections, parasites, skin conditions, and difficulties in the home and society. **Child Healthcare** was developed for use in primary care settings.

**Adult HIV** covers an introduction to HIV infection, management of HIV-infected adults at primary-care clinics, preparing patients for antiretroviral (ARV) treatment, ARV drugs, starting and maintaining patients on ARV treatment and an approach to opportunistic infections. **Adult HIV** was developed by doctors and nurses with wide experience in the care of adults with HIV, through the auspices of the Desmond Tutu HIV Foundation at the University of Cape Town.

**FORMAT OF THE COURSES**

1. **Objectives**
   The learning objectives are clearly stated at the start of each chapter. They help the participant to identify and understand the important lessons to be learned.

2. **Pre- and post-tests**
   There is a multiple-choice test of 20 questions for each chapter at the end of the book. Participants are encouraged to take a pre-test before starting each chapter, to benchmark their current knowledge, and a post-test after each chapter, to assess what they have learned. Self-assessment allows participants to monitor their own progress through the course.

3. **Question-and-answer format**
   Theoretical knowledge is presented in a question-and-answer format, which encourages the learner to actively participate in the learning process. In this way, the participant is led step by step through the definitions, causes, diagnosis, prevention, dangers and management of a particular problem.

   Participants should cover the answer for a few minutes with a piece of paper while thinking about the correct reply to each question. This method helps learning.

   Simplified flow diagrams are also used, where necessary, to indicate the correct approach to diagnosing or managing a particular problem.

   Each question is written in bold, like this, and is identified with the number of the chapter, followed by the number of the question, e.g. 5-23.

4. **Important lessons**
   Important practical lessons are emphasised by placing them in a box like this.

5. **Notes**
   Additional, non-essential information is provided for interest and given in notes like this. These facts are not used in the case studies or included in the multiple-choice questions.
6. Case studies

Each chapter closes with a few case studies which encourage the participant to consolidate and apply what was learned earlier in the chapter. These studies give the participant an opportunity to see the problem as it usually presents itself in the clinic or hospital. The participant should attempt to answer each question in the case study before reading the correct answer.

7. Practical training

Certain chapters contain skills workshops, which need to be practised by the participants (preferably in groups). The skills workshops, which are often illustrated with line drawings, list essential equipment and present step-by-step instructions on how to perform each task. If participants aren’t familiar with a practical skill, they are encouraged to ask an appropriate medical or nursing colleague to demonstrate the clinical skill to them. In this way, senior personnel are encouraged to share their skills with their colleagues.

8. Final examination

On completion of each course, participants can take a 75-question multiple-choice examination on the EBW Healthcare website, when they are ready to.

All the exam questions will be taken from the multiple-choice tests from the book. The content of the skills workshops will not be included in the examination.

Participants need to achieve at least 80% in the examination in order to successfully complete the course. Successful candidates will be emailed a certificate which states that they have successfully completed that course. EBW Healthcare courses are not yet accredited for nurses, but South African doctors can earn CPD points on the successful completion of an examination.

Please contact info@ebwhealthcare.com or +27 021 44 88 336 when you are ready to take the exam.

CONTRIBUTORS

The developers of our learning materials are a multi-disciplinary team of nurses, midwives, obstetricians, neonatologists, and general paediatricians. The development and review of all course material is overseen by the Editor-in-Chief, emeritus Professor Dave Woods, a previous head of neonatal medicine at the University of Cape Town who now consults to UNICEF and the WHO.

Perinatal Education Trust

Books developed by the Perinatal Education Programme are provided as cheaply as possible. Writing and updating the programme is both funded and managed on a non-profit basis by the Perinatal Education Trust.

Eduhealthcare

Eduhealthcare is a non-profit organisation based in South Africa. It aims to improve health and wellbeing, especially in poor communities, through affordable education for healthcare workers. To this end it provides financial support for the development and publishing of the EBW Healthcare series.

The Desmond Tutu HIV Foundation

The Desmond Tutu HIV Foundation at the University of Cape Town, South Africa, is a centre of excellence in HIV medicine, building capacity through training and enhancing knowledge through research.

The Desmond Tutu Tuberculosis Centre

The Desmond Tutu Tuberculosis Centre at Stellenbosch University, South Africa, strives to improve the health of vulnerable groups through the education of healthcare workers and community members, and by influencing policy based on research into the epidemiology of childhood tuberculosis, multi-drug-resistant tuberculosis, HIV/TB co-infection and preventing the spread of TB and HIV in southern Africa.
UPDATING THE COURSE MATERIAL

EBW Healthcare learning materials are regularly updated to keep up with developments and changes in healthcare protocols. Course participants can make important contributions to the continual improvement of EBW Healthcare books by reporting factual or language errors, by identifying sections that are difficult to understand, and by suggesting additions or improvements to the contents. Details of alternative or better forms of management would be particularly appreciated. Please send any comments or suggestions to the Editor-in-Chief, Professor Dave Woods.

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Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you’ve worked through the unit, to evaluate what you have learned.

**Objectives**

When you have completed this unit you should be able to:
- Understand the meaning of HIV infection and AIDS.
- List the ways by which children can be infected with HIV.
- Appreciate the importance of HIV infection in the community.
- Reduce the risk of mother-to-child transmission of HIV.
- Advise mothers on their feeding options.
- Prevent HIV infection after sexual abuse of children.
- Prevent HIV infection after a needle-stick injury.

**INTRODUCTION TO HIV**

**1-1 What is HIV?**

HIV stands for the human immunodeficiency virus. Viruses are extremely small, very simple organisms which can only exist and multiply by invading and taking control of a plant or animal cell (the host cell). Viruses are responsible for many different diseases. Unlike bacteria, they are not killed by antibiotics.

**HIV is the human immunodeficiency virus.**

**NOTE** HIV was first identified in Paris in 1983. HIV is a new human virus which first appeared in the 1950s when it was probably transmitted to humans from chimpanzees in central Africa.

**1-2 What type of virus is HIV?**

Viruses may be divided into many different groups. HIV belongs to a group of viruses known as retroviruses. These viruses are unique in nature as they have a special enzyme called reverse transcriptase. This enzyme enables HIV to introduce its own genes into the nucleus of the host cell. The host cell is then instructed to produce millions of new copies of the virus each day. These are released into the bloodstream and can then infect other cells. Retroviruses usually cause long periods of silent infection before signs of disease appear.

**HIV is a retrovirus.**

**NOTE** Retroviruses contain an RNA genetic code. The viral enzyme reverse transcriptase
allows HIV to make double-strand DNA copies of its single-strand RNA. The viral DNA copy is then inserted into the DNA of the nucleus in the host cell. Only retroviruses have this ability to make a DNA copy of their RNA code.

1-3 What disease is caused by HIV?
HIV causes a chronic illness which is usually referred to as asymptomatic HIV infection or HIV disease. When HIV infection has reached an advanced, serious stage it is called AIDS (acquired immune deficiency syndrome). Unfortunately, the public often uses the term AIDS incorrectly to describe the illness in anyone who is infected with HIV. Without treatment with antiretroviral drugs, AIDS is a fatal disease. HIV is the only cause of AIDS.

1-4 What is the clinical presentation of HIV infection?
Symptomatic HIV infection may present in many different ways. The symptoms and signs of HIV infection are usually due to secondary infections caused by a wide range of organisms. While some of these organisms are the same as those that infect HIV-negative children, other infections are due to uncommon organisms not normally seen in children who are HIV negative.

1-5 How does HIV cause disease?
HIV infects, damages and finally destroys a special type of lymphocyte (white cell) called a CD4 cell. As the CD4 cells play a very important role in the functioning of the immune system, this destruction of CD4 cells damages the immune system, leading to immune deficiency.

The normal immune system protects the body against infection. By killing CD4 cells, HIV infection weakens the immune system which is then no longer able to prevent infection by many viruses, bacteria, fungi and parasites. As a result the person becomes ill.

HIV infection damages the immune system by killing CD4 cells.

A person who has HIV infection is said to be HIV positive, while someone without HIV infection is HIV negative.

1-6 Are there different types of HIV?
Two types of HIV are recognised: HIV1 and HIV2. Most HIV infection in southern Africa is caused by HIV1 which has many subtypes (clades). The important subtype in Africa is subtype C. Subtype B is the most common subtype in the developed world.

1-7 Is HIV infectious?
Yes. HIV infection can be spread from one person to another.

1-8 How is HIV transmitted from one person to another?
The virus may be transmitted from one person to another by:

1. Unprotected sexual contact (horizontal transmission). Body fluids such as vaginal and cervical secretions, semen and blood may contain large numbers of HIV. HIV is not present in urine or stool, while very little is present in saliva.
2. Crossing from a mother to her fetus or newborn infant (vertical transmission).
3. Intravenous drug abusers who use or share syringes and needles which are soiled with HIV-infected blood.
4. Health workers reusing disposable needles, blades or syringes, and using surgical instruments which are contaminated with HIV and have not been sterilised.
5. Using HIV-contaminated needles or blades in traditional rituals (e.g. circumcision).
6. Accidental needle-stick injuries.
7. A blood transfusion with HIV-infected blood or other HIV-infected blood products such as factor VIII in haemophiliacs. This is very rare in South Africa, where all blood products are screened for HIV.
8. Wet-nursing (feeding another woman’s infant) with HIV-contaminated breast milk.

There is no evidence that HIV can be spread by mosquitoes, lice or bed bugs. Neither can it be spread via food or water. In Africa HIV in adolescents and adults is most commonly spread by heterosexual intercourse.

1-9 How are children usually infected with HIV?

By the spread of HIV from a mother to her fetus or from a mother to her newly born or young infant. 95% of HIV-infected children are infected by their mother. Children may also be infected by sexual contact.

Children are usually infected with HIV by their mother.

1-10 What forms of sexual contact may transmit HIV?

1. HIV is almost always transmitted in adolescents and adults by penetrative sexual intercourse (heterosexual or homosexual). However, all forms of oral sexual contact (mouth to vagina or mouth to penis) can also result in infection, although the risk is much lower. Deep kissing may possibly transmit HIV, especially if mouth ulcers are present. HIV cannot penetrate intact skin but may infect open sores, cuts and abrasions, or mucous membranes. The transmission of HIV is more common in uncircumcised men as the mucous membrane under the foreskin is easily infected.
2. The thin, friable rectal mucosa is easily damaged during anal intercourse. This increases the risk of infection. The highest risk of sexual transmission for both men and women is during anal intercourse. The risk of HIV transmission from sexual intercourse is very high (up to 50%) in the first few months after one of the partners has become infected. The risk of infection is also raised if other sexually transmitted diseases are present.
3. Sexually abused children may be infected with HIV by penetrative sexual intercourse.

1-11 Can you become infected with HIV during normal social contact?

Family and friends of an HIV-infected person do not become infected except by sexual contact. HIV is not transmitted by close social contact such as touching, holding hands, hugging and social kissing. HIV is also not spread by coughing, sneezing, swimming pools, toilet seats, sharing cooking, drinking and eating utensils or by changing a nappy. However, any bleeding, such as nose bleeds, may spread HIV.

**Note** There are a few very rare but well-documented cases of horizontal HIV transmission between family members.

1-12 Can you have HIV infection and not be ill?

Yes. Adults are usually infected with HIV for years before becoming ill. Most children who are infected with HIV are clinically well (asymptomatic) for the first few months. However, the illness progresses rapidly in many children and by the age of 12 months almost 80% of HIV-infected children will have
symptomatic disease. In Africa, by two years of age more than 50% of HIV-infected children will die unless the correct treatment is available.

Note: Most children are ‘fast progressors’ as the asymptomatic HIV infection rapidly leads to clinical illness.

Many adults and some children with HIV infection are clinically well.

1-13 Can an HIV-infected person who is well transmit the virus?

Yes. HIV is frequently transmitted by people who appear to be clinically well but are infected with HIV. This is the great danger of HIV infection as most infected people do not know that they have been infected. They are also unaware that they may transmit HIV to another person.

HIV IN SOCIETY

1-14 How common is HIV infection in the general public?

Over 30 million people worldwide have HIV infection. It is estimated that six million South Africans are infected with HIV. In 2009, almost 30% of all pregnant women in South Africa were HIV-positive. The province of KwaZulu-Natal had the highest prevalence. In some antenatal clinics, over 50% of pregnant women were HIV positive.

Almost a third of pregnant women in South Africa are infected with HIV.

1-15 How can the sexual spread of HIV in the general public be reduced?

By practising the behavioural change of ‘ABC’:

- ‘A’ – Abstinence (no sex) and delay in sexual debut (first-time sex).
- ‘B’ – Be faithful to one partner (reduce the number of sexual partners).
- ‘C’ – Use a condom (especially when not being faithful to one partner).

A reduction in multiple sexual partners seems to have resulted in the declining HIV prevalence in countries such as Uganda and Zimbabwe. However, all three behavioural changes are important.

1-16 How common is HIV infection in children?

Over two million children under the age of 15 years are infected with HIV worldwide. At least 90% of these children live in sub-Saharan Africa. In 2009 there were about 300 000 children in South Africa with HIV infection.

1-17 How often does HIV infection cause death?

It is estimated that more than 850 people die of HIV infection each day in South Africa while more than 40% of childhood deaths are HIV related. Many of these deaths could be prevented with the correct management. However, without antiretroviral treatment most people with HIV infection will eventually die of AIDS. With antiretroviral treatment HIV infection is ‘a life sentence, not a death sentence’.

1-18 Is HIV infection a more serious disease in children?

Yes. Because they are still young and have immature immune systems. As a result, the progress of HIV infection to illness and death is faster in children than in adults.

1-19 Is the HIV epidemic in South Africa still expanding?

Hopefully the rapid increase in new cases will slow down. Since 1990 the rate of HIV infection in women attending state antenatal care clinics in South Africa has steadily climbed from less than 2% to reach about 30% in 2009. South Africa has one of the fastest-growing HIV epidemics in the world, with one to two thousand people infected every day.
South Africa has one of the fastest-growing HIV epidemics in the world.

1-20 What is the impact of HIV infection on society?

The epidemic of HIV infection is having a devastating impact on society in South Africa and other countries in sub-Saharan Africa. Since the start of the AIDS epidemic in South Africa, the average life expectancy has fallen from 60 to 45 years.

In Africa the majority of people with HIV infection are female and most are from poor communities. This has a massive effect on the whole family and increases the risk of childhood undernutrition and death, even in HIV-negative children. The number of children who have lost one or both parents to HIV in Africa already exceeds 12 million. As a result of the ever-increasing number of deaths, ill people and homeless children, HIV infection is having an enormous social and financial impact on all communities and placing a strain on the health services.

HIV infection is seriously affecting the lives of people in all communities in southern Africa.

**HIV TRANSMISSION FROM MOTHER TO CHILD**

1-21 When can HIV be transmitted from a mother to her infant?

Mother-to-child transmission of HIV (vertical transmission) may occur:

1. During pregnancy
2. During labour and delivery
3. During breastfeeding

Most children with HIV are infected by mother-to-child transmission (more than 95%).

Most children with HIV are infected by mother-to-child transmission.

1-22 What is the risk of HIV transmission during pregnancy?

If antiretroviral prophylaxis or treatment is not used, the risk of HIV crossing the placenta from a mother to her fetus during pregnancy is about 5%. Although transmission may take place at any time during pregnancy, the risk is probably greatest in the last trimester (28 to 40 weeks of gestation).

A number of factors will increase the risk of HIV transmission during pregnancy:

1. If the mother becomes infected with HIV during pregnancy
2. If the mother has advanced HIV infection (stage 3 or 4)
3. If the mother has a CD4 count below 350 cells/μl

These women have a large amount of virus (high viral load) in their blood and are, therefore, more infectious.

Other factors which increase the risk of HIV crossing the placenta are:

1. Chorioamnionitis (infection of the placental membranes)
2. Malaria
3. Amniocentesis (sampling amniotic fluid) or external cephalic version (manually turning a fetus in the breech position)
4. Maternal undernutrition, including vitamin A deficiency

1-23 What is the risk of HIV transmission during labour and delivery?

If antiretroviral prophylaxis or treatment is not used, the risk of HIV crossing the placenta from a mother to her fetus during labour and vaginal delivery is about 15%. As with pregnancy transmission, mothers with a high viral load have a greater risk of infecting their infant.

Other factors which increase the risk of infecting the infant during labour and vaginal delivery are:
1. Preterm labour
2. Prolonged labour and prolonged rupture of the membranes (more than four hours)
3. Episiotomy
4. Instrument delivery (forceps or vacuum)
5. The use of a scalp clip or fetal scalp pH monitoring
6. Suctioning the infant’s mouth and nose after delivery
7. Birth order. HIV infection is commoner in firstborn than second-born twins

The longer the infant is exposed to vaginal and cervical secretions during labour e.g. when there is a prolonged rupture of the membranes, the greater the risk of HIV infection.

**1-24 Can elective Caesarean section reduce the risk of HIV transmission during labour and delivery?**

Yes, provided it is performed before the onset of labour when the risk of HIV transmission during labour and delivery can be almost totally removed. However, the risk of post-operative bacterial infection is high in these mothers while Caesarean sections require additional staff, facilities and funds. Therefore, antiretroviral prophylaxis is the preferred method of reducing HIV transmission during labour and delivery.

**1-25 What is the risk of HIV transmission during breastfeeding?**

This depends on the method and duration of breastfeeding:

1. With mixed breastfeeding for 24 months (when the infant is breastfed and also receives additional fluids or food such as water and porridge) the risk of HIV transmission is about 15% if antiretroviral prophylaxis is not used. The approximate risk of transmission is 5% during the first six months, another 5% during the second six months and an additional 5% during the second year.
2. With exclusive breastfeeding (only breast milk with no additional fluid or food) the risk is much less.
3. The risk is very small if the mother is on antiretroviral treatment or the infant is on antiretroviral prophylaxis.
4. There is no risk of transmission during infant feeding if only formula is used (exclusive formula feeding).

Other factors which increase the risk of HIV transmission in the breast milk are oral candidiasis (moniliasis or thrush) in the infant and breast problems (cracked nipples, mastitis or abscess) in the mother. Mothers with a high viral load (either early or advanced HIV infection) are also at greater risk of transmitting HIV via their breast milk.

*Note* About 300 000 infants are infected via breast milk worldwide annually.

**1-26 What is the overall risk of HIV transmission from a mother to her infant?**

Without the use of antiretroviral drugs, the total risk after a vaginal delivery and two years of mixed breastfeeding is approximately 35% (i.e. 5% in pregnancy plus 15% at delivery plus 15% with mixed breastfeeding).

*The overall risk of mother-to-child transmission is 35% if steps are not taken to reduce the risk.*

**1-27 How can the risk of mother-to-child transmission be reduced during pregnancy and delivery?**

1. Avoid unplanned pregnancies. Many women would choose not to fall pregnant if they knew they were HIV positive.
2. Good antenatal care, including the early diagnosis and treatment of other sexually transmitted diseases.
3. Screen all pregnant women for HIV infection when they first book for antenatal care. If negative at booking, repeat the screen at 32 to 34 weeks of gestation.
4. Some HIV-positive women may decide to have their pregnancies terminated.
5. Avoid infection with HIV during pregnancy (‘ABC’).
6. Reduce the amount of virus in the mother’s blood and body secretions with antiretroviral drugs.
7. Intermittent preventative therapy for malaria in malaria areas.
8. Avoid episiotomy, scalp clips and instrument deliveries if possible.
9. Do not rupture the membranes unless there is a good obstetric indication.
10. Do not routinely suction infants at birth (suctioning meconium-stained infants or infants who need resuscitation remains important).

Every effort must be made to keep the community, especially women of childbearing age, HIV negative. Reduction in the number of unwanted pregnancies would significantly decrease the number of HIV-infected children.

1-28 How can antiretroviral drugs be used to reduce the risk of mother-to-child transmission?

The prevention of mother-to-child transmission (PMTCT) is usually achieved by the use of prophylactic antiretroviral drugs during pregnancy, labour and delivery, and for a few weeks after delivery. The aim of PMTCT is to reduce the amount of HIV in the mother’s blood and vaginal secretions and to protect the fetus and infant when exposed to HIV. This is also achieved if the mother is receiving antiretroviral treatment with three drugs for her HIV infection. PMTCT is given to protect the infant and not to treat the mother.

**NOTE** The use of antiretroviral prophylaxis was first described in the USA in 1994.

Pregnant women with stage 3 or 4 disease, or a CD4 count of 350 cells/μl or less, should be fast-tracked onto antiretroviral treatment with three drugs. Usually TDF (tenofovir), 3TC (lamivudine) and nevirapine are used.

1-29 How successful is the prevention of mother-to-child transmission?

In women who deliver vaginally and do not breastfeed the risk of transmission can be reduced to less that 5% with PMTCT. The size of the reduction depends on the method of PMTCT being used. In developed countries mother-to-child transmission of HIV has been dramatically reduced due to successful PMTCT programmes.

If the mother is on antiretroviral treatment, the risk of HIV transmission is about 2%.

**Antiretroviral prophylaxis can reduce mother-to-child transmission of HIV.**

1-30 How is a prevention of mother-to-child transmission programme managed?

1. This is provided as part of the routine maternity care.
2. All pregnant women must book for antenatal care as soon as the pregnancy is confirmed.
3. All pregnant women must be offered HIV screening. Mothers are given information in groups before screening so that they can make an informed decision. In South Africa mothers are given the opportunity to ‘opt out’ of screening (as with syphilis screening). Women have the right not to be tested.
4. HIV-positive women must be individually counselled and offered PMTCT prophylaxis.
5. Prophylactic antiretroviral drugs are given to both the mother and newborn infant.
6. HIV-positive women must be counselled about feeding options.
7. All pregnant women must be encouraged to practise safer sex. HIV-negative women must be told about how to remain negative.
8. Certain healthcare practices may be altered (e.g. no unnecessary rupture of the membranes).
9. Elective Caesarean section because the mother is HIV-positive is rarely indicated now that antiretroviral prophylaxis is available.
It is important to determine the CD4 count in all HIV-positive women. Those with a low CD4 count (or clinical stage 3 or 4 disease) should be fast-tracked for antiretroviral treatment.

HIV in a family is often first detected because of HIV screening during pregnancy. This provides an opportunity to manage the whole family.

1-31 What regimen of antiretroviral prophylaxis is used?

The regimen currently used for prophylaxis in South Africa is:

1. For the mother, AZT during pregnancy plus nevirapine during labour. In addition, nevirapine is given to the infant. In some countries only nevirapine is used for prophylaxis.

1-32 How is nevirapine used alone to reduce the risk of vertical transmission of HIV?

1. A single oral dose of nevirapine is taken by the mother at the onset of labour. If possible, the dose should be taken more than two hours before delivery to allow time for the drug to cross the placenta to the fetus. The dose of nevirapine for the mother is 200 mg (a single tablet).

2. This is followed by a single dose to the infant within 72 hours after delivery. The dose of nevirapine to the infant is 0.6 ml (6 mg) for infants of 2000 g or more, and 0.2 ml/kg (2 mg/kg) for infants weighing less than 2000 g. Give the nevirapine to the infant as soon as possible after delivery if the mother did not receive her dose of nevirapine or if it was given less than two hours before delivery.

FEEEDING OPTIONS

1-35 What factors may increase the risk of HIV transmission via breast milk?

1. If the mother becomes infected with HIV while she is still breastfeeding, the risk of HIV transmission to the infant is as high
as 50%. Therefore, breastfeeding women who are HIV negative should not have unprotected intercourse.

2. The risk is also increased in women who have a low CD4 count, high viral load or clinical signs of advanced HIV infection.

3. Cracked or bleeding nipples and mastitis or breast abscess increase the risk of transmission. Good breast care is, therefore, important for HIV-positive women who breastfeed.

4. Sores in the infant’s mouth, such as oral candidiasis (thrush). HIV-positive mothers should take their infants to a clinic for early treatment if they notice oral candidiasis.

5. Mixed feeding, with breast milk plus formula feeds or solids, increases the risk of HIV transmission.

Good breast care and exclusive breastfeeding are important to reduce the risk of HIV transmission.

By preventing or treating these conditions the risk of transmission can be reduced.

In contrast, antiretroviral prophylaxis or treatment makes breastfeeding much safer.

**NOTE** With mixed feeding, the formula or solid food is believed to cause mild inflammation of the gut which allows entry of HIV from breast milk.

**1-36 Should all HIV-positive mothers formula feed their infants?**

Not necessarily. There are advantages and dangers of both breastfeeding and formula feeding infants who are born to HIV-positive women. The great danger of breastfeeding, especially mixed breastfeeding, is the additional risk of HIV transmission to the infant. However, the advantages of breastfeeding are the lower risk of gastroenteritis and undernutrition, especially in poor, rural communities. The advantages of breastfeeding (especially exclusive breastfeeding), may outweigh the dangers for many HIV-positive mothers from poor communities. In contrast, it would be safer for most HIV-positive women in urban areas to formula feed their infants.

Each HIV-positive mother should be counselled and informed of the risk and advantages so that they can make the best choice for their infant. While advice can be offered, women should not be instructed what to do. They should be encouraged to choose between exclusive breastfeeding and exclusive formula feeding. Once a woman has made her choice she should be supported in her decision by health workers. It is important that women decide on their chosen method of infant feeding before delivery. Mixed breastfeeding should be avoided if possible. Wet nursing (where the infant is breastfed by someone other than the mother) must be discouraged.

**1-37 Is exclusive breastfeeding easy?**

Unfortunately mothers need a lot of help and support from their family and healthcare workers to successfully breastfeed exclusively as this is not the traditional method of breastfeeding in most communities.

**1-38 When should HIV-positive women stop breastfeeding?**

If HIV-positive women choose to exclusively breastfeed, they should probably stop when their infant is between four and six months old. Ideally breastfeeding should be stopped over a month once formula and solid feeds are started, so that the period of mixed feeding is short. In practice it may be difficult for a mother to suddenly stop breastfeeding.

In very poor rural communities where severe childhood infections and undernutrition are common, mixed breastfeeding should be continued after the infant is six months old.

**1-39 How should HIV-negative women feed their infants?**

It is very important that HIV-negative women and women who do not know their status are not influenced to formula feed by advice being given to HIV-positive women. Exclusive
breastfeeding should be promoted among HIV-negative mothers.

1-40 How should a mother decide what feeding method to choose?

It is advisable that the following criteria should be met if a mother is to exclusively formula feed:

1. It should be acceptable to her family and friends. There are social and cultural barriers to formula feeding in many poor communities. In some communities women may be afraid of not breastfeeding.
2. It should be feasible to formula feed. The mother must have the knowledge and skills to make up formula correctly.
3. It must be affordable to formula feed. Formula is expensive. Free formula may be provided in some areas.
4. It should be sustainable. Formula must be available. Mothers often live far from shops in rural areas.
5. It should be safe. Clean water must be available. The mother should be able to prepare feeds hygienically and be able to clean the bottles, teats and cups. Access to primary healthcare is particularly important if infants are formula fed.

Formula feeding is only recommended in poor communities if all the above criteria are met. If not, it would be better for women to breastfeed unless the risk of HIV transmission in breast milk is greater than the dangers of formula feeding. Women who decide to formula feed must be taught how to prepare and give formula correctly. A cup rather than a bottle should be used as cups are easier to clean.

1-41 How can you tell whether an HIV-exposed infant has HIV infection?

Most HIV-infected infants appear normal and healthy at birth. Therefore clinical examination cannot be used to determine which newborn infants are infected with HIV and which are not (i.e. only HIV exposed). HIV does not cause congenital abnormalities (birth defects). The clinical signs of HIV infection often appear between three and six months of age.

The rapid test detects whether HIV antibodies are present. Therefore it will be positive in all infants born to women who are HIV positive as the maternal HIV antibodies (IgG) crosses the placenta to the fetus. All HIV-exposed infants (both HIV-infected and non-infected infants) may have a positive screening test (rapid test) up to 18 months of age as the maternal antibodies may remain in the infant until this time.

The only reliable method of telling whether an infant under the age of 18 months has been infected with HIV is to perform a PCR (polymerase chain reaction) blood test on the infant. This detects HIV genetic material. As the window period for the PCR test is six weeks, infants should only be tested six weeks after delivery or six weeks after the last feed of breast milk. A positive PCR test before six weeks will confirm HIV infection, but a negative test cannot reliably exclude infection.

Either a sample of venous blood can be taken or a few drops of capillary blood collected on filter paper (a dry blood spot) for PCR testing. Children found to be HIV infected must be referred to an HIV clinic for treatment.

Women should exclusively breastfeed unless the risk of HIV transmission via breast milk is greater than the dangers of formula feeding.

NOTE WHO uses the acronym AFASS for acceptable, feasible, affordable, sustainable and safe.

PCR testing at six weeks of age is important to identify infants infected with HIV before, during or soon after birth.

The ultra-sensitive p24 antigen test can be used instead of the PCR test.
Table 1-1: The standard dosing of prophylactic AZT and 3TC for children.

<table>
<thead>
<tr>
<th>Weight of child</th>
<th>AZT dose</th>
<th>3TC dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>7–15 kg</td>
<td>1 capsule (100 mg) twice daily</td>
<td>4 mg/kg oral solution twice daily</td>
</tr>
<tr>
<td>15–25 kg</td>
<td>2 capsules (200 mg) twice daily</td>
<td>½ tablet (75 mg) twice daily</td>
</tr>
<tr>
<td>25 kg or more</td>
<td>3 capsules (300 mg) twice daily</td>
<td>1 tablet (150 mg) twice daily</td>
</tr>
</tbody>
</table>

NOTE: The DNA-PCR test is used to diagnose HIV infection while the RNA-PCR test is used to measure viral load and confirm the DNA test.

1-42 How can HIV infection be prevented after a child is sexually assaulted?

Every effort must be made to prevent assault, especially sexual assault. However, should a child be sexually assaulted (rape or sodomy), post-exposure prophylaxis must be started within 72 hours to reduce the risk of HIV infection. The sooner the treatment is started the more likely it is to be effective. HIV can also be transmitted by human bites.

Usually three drugs are used for post-exposure prophylaxis.

1. 3TC
2. AZT
3. Lopinavir/ritonavir

The dose of lopinavir/ritonavir is given in 4-36.

Antiretroviral prophylaxis is given for 28 days. A rapid test (or PCR if the child is less than 18 months old) six weeks after the assault will indicate whether the child has become infected with HIV despite the prophylaxis. This is often repeated after a further six weeks. Usually an HIV screening test is done on the child to exclude previous infection before prophylaxis is started.

NOTE: Compliance with prophylaxis can be a problem, especially as AZT causes side effects such as nausea, vomiting and lethargy. Nausea is less of a problem in children than adults. An antiemetic, such as oral cyclizine (Valoid) to prevent nausea may be helpful in older children.

1-43 Are nurses and doctors at risk of infection when caring for HIV-positive children at a clinic?

Yes, as most body fluids, especially blood, may contain HIV. Therefore, healthcare workers can become infected by HIV through needle-stick injuries or by cutting one’s finger during minor surgery. It is also possible to become infected with HIV through sores or abrasions of the skin when handling body fluids, especially blood.

1-44 How can healthcare workers reduce the risk of HIV infection?

By adopting standard (universal) precautions. This means that all body fluids should be regarded as potentially infectious in all patients. Precautions should always be taken to prevent exposure to HIV, especially when taking a blood sample.

1-45 What are the standard precautions to prevent HIV infection when caring for children?

All adults and children should be regarded as being potentially HIV positive. Therefore, standard precautions should be taken with all children. These precautions are especially important in children known to be HIV positive.

1. Wash your hands, or spray them with disinfectant, after touching a patient or after handling body fluids. Wash your hands with soap and water immediately should they become contaminated with blood. Any cuts or sores on your skin should be covered.
2. If possible, gloves should be used when taking a blood sample, especially if the patient is known to be infected with HIV.

3. All spilt blood must be cleaned up immediately and the surface wiped with a hypochlorite solution (Biocide, Milton or Jik mixed 2:1 with water). Use paper towels, which should then be placed in an approved disposal bag for incineration.

4. All blood specimens for the laboratory must be placed in a leak-proof packet or container.

5. Be very careful when handling ‘sharps’ (needles, blades, lancets).

6. Bedding, clothing or nappies contaminated with blood should always be safely disposed of in an appropriate bag or container.

**Standard precautions should be adopted when managing all patients.**

1-46 How should sharps be handled?

1. Whenever sharps (needles, blades, lancets) are used, great care must be taken not to puncture or injure your skin.

2. Handling of sharps should be reduced to a minimum.

3. Needles must **not** be resheathed.

4. Once used, always keep the sharp end of a needle, blade or lancet pointing away from you. Be careful not to stick anyone accidentally.

5. After withdrawing the sharp from the skin, immediately place it in the sharps container. The container must be within easy reach before starting the procedure. Failure to do this is the commonest way healthcare workers are infected with HIV while on duty.

6. Never place a used sharp on the bed or work top.

7. Correctly designed sharps containers must always be available. Do not allow them to become overfilled. They should be collected and be disposed of in a safe manner.

Always use a sharps container for the disposal of lancets or needles and never resheath a needle.

1-47 What is the risk of HIV infection after an accidental needle-stick injury?

If the patient is infected with HIV, the overall risk is 1 in 300. Therefore, of every 300 healthcare workers who prick or cut themselves with an instrument covered with HIV-positive blood, one person will become infected with HIV. With the correct use of antiretroviral prophylaxis this risk is reduced by 80%. The risk of infection is greatest if the child has AIDS or has recently been infected with HIV (because the child will have a high viral load). It is also higher if prophylaxis is not given correctly.

1-48 What antiretroviral prophylaxis should be given to a healthcare worker accidentally exposed to HIV?

Every effort must be made to start prophylaxis within two hours of exposure. If possible, start prophylaxis as soon as possible. Treatment is given orally for 28 days.

1. AZT 300 mg 12-hourly
2. 3TC 150 mg 12-hourly
3. Lopinavir/ritonavir three capsules 12-hourly

Unfortunately AZT often makes the healthcare worker feel nauseous and unwell. It is important to take the full course of drugs. Usually an HIV screening test is done on the healthcare worker to exclude previous infection before prophylaxis is started. An HIV screening test six weeks after exposure will indicate whether the prophylaxis has been effective or not. This is often repeated after a further six weeks.

1-49 What is the correct procedure after a needle-stick injury?

After a needle-stick (‘sharps’) injury the following procedure should be followed:

1. Do not panic. Encourage bleeding from the puncture site and wash with soap and water.
The mouth or eyes should immediately be washed with water after a blood splash.

2. Notify the correct hospital or clinic authority. Every hospital and clinic must have a clear management policy for accidental HIV exposure. This should be available to all staff. Everyone must know who the correct person is to contact should an accidental HIV exposure occur.

3. Start prophylactic antiretroviral treatment as soon as possible. These drugs must be readily available in all hospitals and clinics both day and night. Do not wait for the screening results.

4. Obtain consent and collect blood samples from the child for an HIV screen. If consent is refused, assume that the child is HIV positive.

5. An HIV test on the healthcare worker is recommended if the patient tests positive. This is done to make sure that the healthcare worker is not already HIV positive. If so, prophylaxis is not indicated.

6. Notify the laboratory that two urgent HIV tests are needed for screening. The screening test must be done as soon as possible.

7. If the HIV test on the child’s blood is negative, stop treatment. If the test is positive, continue treatment for 28 days.

8. Repeat the HIV test on the healthcare worker after six weeks to determine whether or not he/she has become HIV positive. If the test is negative, repeat after another six weeks.

9. Counselling is recommended for all healthcare workers exposed to HIV-contaminated blood.

All hospitals and clinics must keep emergency packs of prophylactic antiretrovirals for staff with accidental exposure to HIV.

CASE STUDY 1

A mother brings her 20-month-old son to a local clinic as he is unwell. On examination the child has clinical signs of HIV infection and the mother’s screening test for HIV is positive. She is very upset as she did not know her positive HIV status. She is clinically well.

1. **How is HIV infection usually spread between adults?**

By unprotected sexual intercourse.

2. **Could this mother have been infected with HIV during normal social contact?**

No, as HIV is not transmitted during normal social contact such as touching, holding hands, hugging and social kissing. HIV is also not spread by toilet seats, shared cooking, drinking or eating utensils.

3. **How can this mother be infected with HIV and not be ill?**

Most HIV-infected adults are not ill as HIV infection usually takes years before it causes illness in adults.

4. **How is HIV infection commonly spread to young children?**

Most are infected from their mothers during pregnancy, labour or delivery, or through breast milk (vertical or mother-to-child transmission).

5. **What is the risk of HIV infecting the unborn infant during pregnancy?**

About 5% if antiretroviral prophylaxis is not used. This risk is increased if the mother is infected with HIV during pregnancy or has advanced (stage 4) HIV disease. Other risk factors during pregnancy include malaria and malnutrition, especially vitamin A deficiency.

6. **Is the risk of HIV transmission higher during labour and delivery?**

Yes. During normal labour and vaginal delivery without antiretroviral prophylaxis the risk of mother-to-child transmission is about 15%. The overall risk of transmission during pregnancy, labour and delivery is, therefore, about 20%.
CASE STUDY 2

Parents bring their three-year-old daughter to a general practitioner for a second opinion. The child has been diagnosed with HIV infection at the local hospital. The parents have very little knowledge about HIV infection and AIDS.

1. How common is HIV infection in South Africa?

It is estimated that six million South Africans are infected with HIV. Almost a third of pregnant women in South Africa are infected with HIV.

2. How many children are infected with HIV in South Africa?

About 300 000 in 2009. HIV infection is one of the major causes of death in both children and adults in most developing countries.

3. What is the impact of the HIV epidemic on children in society?

Not only does HIV infection cause illness and death of children but also loss of parents. This may result in many homeless and orphaned children. Everyone in society is affected by the HIV epidemic.

4. How does HIV infection cause illness?

By damaging the body’s immune system and making one more susceptible to a wide range of other infections.

5. Why is HIV infection more serious in children than adults?

Because children have an immature immune system, the illness caused by HIV progresses more rapidly.

6. How soon can you tell whether a child has been infected with HIV?

If a mother does not breastfeed at all, a PCR test on the infant at six weeks of age will indicate whether the infant is infected or not.

If the mother breastfeeds, the test should be done and if negative it should be repeated again six weeks after she stops breastfeeding. An HIV antibody screening test (rapid test) can reliably exclude HIV infection in children only at or beyond 18 months of age.

CASE STUDY 3

The superintendent and his staff of a small hospital plan to start a programme of antiretroviral prophylaxis in the maternity service. They are looking at various options and have asked for guidelines. The hospital is poorly staffed and not able to manage a lot of extra work for the nurses.

1. What antiretroviral drugs are usually used for antiretroviral prophylaxis to prevent mother-to-child transmission?

AZT (zidovudine) and nevirapine.

2. What is the simplest regimen of drug prophylaxis?

A single oral dose of 200 mg nevirapine to the mother at the onset of labour plus a single oral dose of 0.6 ml (6 mg) nevirapine to the infant within three days of delivery.

3. How is dual drug prophylaxis given?

In addition to the nevirapine, the mother is given 300 mg AZT orally twice daily from 14 weeks and then 300 mg orally every three hours during labour. The infant is given a daily dose of nevirapine for six weeks after birth.

4. What would you advise this superintendent to do?

It may be best to start with nevirapine alone as they are very short-staffed. They should then try to find the extra staff needed for a full prophylaxis programme with both AZT and nevirapine.
5. What drug prophylaxis should be offered to staff members who prick their finger while taking blood from an HIV patient?

Therapy with AZT, 3TC and lopinavir/ritonavir for 28 days.

CASE STUDY 4

An HIV-positive pregnant woman is being counselled at an antenatal clinic. She asks the midwife whether she should plan to breastfeed her infant. This mother lives in a rural community with poor facilities. She has come to town to deliver her infant and wants to return home as soon as possible after the birth.

1. How should you help this mother to make a wise feeding choice?

You should give her the necessary information so that she can make the best choice for herself and her infant. Do not simply push her into doing what you think is best.

2. Is there a risk to her infant if she decides to breastfeed?

Yes, as HIV is present in breast milk. With mixed breastfeeding (breast milk plus other liquids or solids) for two years there is a 15% chance of the HIV in her breast milk infecting her infant. The risk is much less with exclusive breastfeeding for six months followed by rapid weaning off breast milk.

3. Could formula feeding be dangerous for her infant?

Probably not if she remained in town for the first few years. However, she plans to return to a rural area where formula milk may not be available, affordable or safe. It may also not be acceptable to her family and community. The result may be malnutrition and gastroenteritis in her infant.

4. What problems with her breasts could increase the risk of HIV transmission to her infant?

Mastitis or breast abscess. These can be avoided with good breastfeeding practices. Therefore it is important to teach this mother how to breastfeed correctly.

5. What do you think would be her best feeding option?

Probably to exclusively breastfeed for six months unless she is able to safely formula feed at her rural home. Antiretroviral treatment for the mother or prophylaxis for the infant will greatly reduce the risk of HIV transmission.
Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you’ve worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- Understand the natural history of HIV infection.
- Describe the clinical presentation of HIV infection.
- Explain the clinical staging of HIV infection.
- Immunologically confirm the diagnosis of HIV infection.
- Explain the immunological staging of HIV infection.
- Address the question of consent for testing in children.

2-1 What is the natural history of HIV infection in children?

1. Once HIV enters the body at the time of infection, it starts to multiply rapidly in CD4 cells. These HIV-infected CD4 cells then release large amounts of virus into the bloodstream so that HIV can infect other CD4 cells. For a short while the number of CD4 cells may drop.

2. The body responds after a few weeks by producing antibodies in an attempt to control the virus. As a result of this immune response, the amount of HIV in the body decreases and the number of CD4 cells increases after a few months.

3. However, the CD4 cells continue to be infected and killed. The number of CD4 cells eventually starts to fall and the function of the immune system begins to fail. As a result, the rate of HIV multiplication rises again and the amount of virus in the blood slowly increases once more.

Therefore the amount of virus in the blood is high early and late in the course of HIV infection. The number of CD4 cells in the blood slowly falls as the HIV infection progresses and the body is no longer able to replace the killed CD4 cells. The infection progresses much more rapidly in children than in adults. The increase in HIV and decrease in CD4 cells result in the children becoming progressively more ill.
HIV infects CD4 cells and slowly damages the immune system.

2-2 Do children become ill as soon as they are infected with HIV?
No. They do not become ill at the time of HIV infection. However, they may develop acute seroconversion illness soon after infection. Acute seroconversion illness is relatively common in infants, older children, adolescents and adults.

Infection with HIV may cause acute seroconversion illness.

ACUTE SEROCONVERSION ILLNESS

2-3 What is acute seroconversion illness?
At the time that HIV antibodies appear in the blood (seroconversion) about 50% of infected people develop a flu-like illness which lasts a few days or weeks. This illness occurs two to four weeks after infection with HIV and is called acute seroconversion illness.

During acute seroconversion illness (acute retroviral syndrome or acute HIV disease) the amount of virus in the blood is very high but the amount of antibody still very low. Therefore, the screening tests for HIV (which depend on the presence of HIV antibodies) may still be negative at the time of acute seroconversion illness, i.e. may still be the ‘window period’ (the period of time from infection to when the HIV tests become positive).

Acute seroconversion illness is often the first clinical sign of HIV infection in adults and older children.

During acute seroconversion illness the CD4 count may be temporarily depressed.

2-4 What are the common clinical features of acute seroconversion illness?
The common clinical features of acute seroconversion illness are:

![Figure 2-1: The changes in viral load, CD4 count and clinical features of HIV infection in adults](image-url)
1. Fever and sweating
2. General tiredness
3. Headache
4. Cough or sore throat (pharyngitis)
5. Muscle or joint pains
6. Nausea, vomiting or diarrhoea
7. Enlarged lymph nodes (generalised lymphadenopathy)
8. A measles-like rash
9. Oral or genital ulcers

The above symptoms and signs are similar to those found in glandular fever (infectious mononucleosis). Many people with acute seroconversion illness think they have severe 'flu. During infancy lymphadenopathy, rash and failure to thrive are common signs of acute seroconversion illness.

2-5 How are patients with acute seroconversion illness managed?

Patients with acute seroconversion illness are managed symptomatically with antipyretics (e.g. paracetamol) for fever. There is no role for antiretroviral treatment.

During the first few weeks of HIV infection, especially if the person develops seroconversion illness, large amounts of virus are present in the blood and other body fluids. As a result, the person is very infectious to others. It is therefore of particular importance in adults to abstain from sexual intercourse during this time. Unfortunately most are not aware that they have been recently infected with HIV.

2-6 What is the latent phase of HIV infection?

Following the primary HIV infection (and acute seroconversion illness) there is a latent phase before chronic HIV illness develops.

2-7 What are the clinical features of the latent phase of HIV infection?

HIV infection and seroconversion are followed by a latent period when the child looks and feels well. During this phase it is not obvious that the child has HIV infection. There may be no clinical signs at all or only persistent, painless, generalised lymphadenopathy during the latent phase.

During the latent phase the viral load is low and the CD4 count is normal or only mildly depressed.

2-8 How long does the latent phase last?

In adults this silent, asymptomatic period usually lasts five to 10 years. However, in children it is much shorter. Owing to their immature immune system, HIV infection progresses much faster from the latent phase to the symptomatic phase.

2-9 Is the length of the latent phase of HIV infection the same in all children?

No. In some children the progression to symptomatic infection is much faster ('fast progressors') than in other children ('slow progressors'). As a result their latent phase is shorter in 'fast progressors'. The most important factor indicating how fast the HIV infection will progress is the timing of the infection:

1. Children who are infected before, during or soon after delivery usually progress fast. In many the latent phase is only a few months long. Most infants with perinatal infection will have symptoms and signs of HIV infection by six months of age. Without appropriate management, including antiretroviral treatment, 35% of these children will die before one year of age and more than 50% will die by their second birthday.
2. Children who are infected later, usually via breast milk, tend to progress much more slowly. Most will die by five years but some may survive beyond 10 years without treatment.

The earlier the HIV infection, the shorter the asymptomatic latent phase.
2-10 What is symptomatic HIV infection?
When patients who have been clinically well during the latent (asymptomatic) phase of HIV infection become ill, they are said to have symptomatic HIV infection (HIV disease). The symptoms and signs of symptomatic chronic HIV infection only present when the damaged immune system is no longer able to protect the person from serious infections.

2-11 What are the common clinical presentations of HIV infection in children?
Chronic HIV infection can present with a very wide range of clinical symptoms and signs. These are usually due to secondary viral, bacterial, fungal or parasitic infections.

Common ways that HIV infection can present include:

1. Weight loss or failure to thrive
2. Severe or persistent oral thrush beyond the first two months of life
3. Enlarged lymph nodes, liver, spleen or parotid glands
4. Severe rash
5. Serious, repeated or chronic bacterial infections such as pneumonia
6. Severe forms of common viral infections which often respond slowly to treatment such as severe oral herpes
7. Chronic diarrhoea
8. Tuberculosis
9. Infections which do not usually affect children with a healthy immune system, such as oesophageal candidiasis
10. Delayed developmental milestones

CLINICAL STAGING OF HIV INFECTION

2-12 What are the clinical stages of HIV infection?
The WHO clinical criteria divide HIV infection into four stages: an asymptomatic, latent stage (stage 1) followed by three symptomatic stages (stages 2, 3 and 4). As the HIV infection progresses and the illness becomes more severe, the clinical stage progresses from 2 to 4.

HIV infection can be divided into four clinical stages.

2-13 What is the value of knowing the clinical stage?
Knowing the clinical stage is a valuable way of predicting what the prognosis will be, especially if the child is not given antiretroviral treatment. Therefore the clinical stage can be used to estimate how long the child is likely to survive without treatment.

The clinical stage helps to predict the likely course of the illness.

2-14 What is advanced HIV disease?
The World Health Organisation defines advanced HIV disease as stage 3 or 4 HIV infection. AIDS (acquired human immunodeficiency syndrome) refers to stage 4 disease. Infants with AIDS are at high risk of dying within weeks or months unless correctly treated. With antiretroviral treatment AIDS is a manageable chronic condition.

AIDS is the most advanced form of HIV infection.

NOTE The term AIDS is confusing to the public as it is often used incorrectly to describe any person with symptomatic HIV infection. Many experts regard both stage 3 and 4 as AIDS in children. Previously the Centre for Disease Control (CDC) in the USA defined AIDS as clinical category C disease. Therefore it is best not to use the term AIDS.

2-15 What are the features of stage 1 HIV infection?
These children are clinically well. However, they may have persistent, generalised lymphadenopathy on clinical examination.
Although acute seroconversion illness is part of the primary HIV infection, it is formally included in stage 1.

2-16 What are the clinical features of stage 2 HIV infection?

These children are moderately symptomatic and may present with any of the following clinical features:

1. Unexplained persistent hepatosplenomegaly (enlarged liver and spleen)
2. Unexplained chronically enlarged painless parotid glands
3. Repeated or chronic upper respiratory tract infections (e.g. otitis media, tonsillitis, pharyngitis and sinusitis)
4. Skin rashes (‘itchy bump disease’, warts, molluscum) and fungal nail infections
5. Recurrent mouth ulcers (aphthous ulcers) and inflamed gums
6. Herpes zoster

Stage 2 presents with many common mild childhood infections.

2-17 What are the clinical features of stage 3 HIV infection?

These children are more ill than children with stage 2 HIV infection. They have advanced signs and may present with any of the following:

1. Unexplained moderate malnutrition
2. Persistent fever (intermittently or persistently above 37.5 °C for longer than a month)
3. Persistent diarrhoea (14 days or more)
4. Oral candidiasis (thrush) after two months of age
5. Oral hairy leucoplakia (white lines on the edge of the tongue)
6. Severe ulceration and bleeding of the gums
7. Pulmonary tuberculosis (TB) or lymph node TB
8. Severe, recurrent bacterial pneumonia
9. Symptomatic lymphoid interstitial pneumonitis (LIP)

Stage 3 presents with common severe infections.

2-18 What are the clinical features of stage 4 HIV infection?

These children are severely symptomatic and are seriously ill with any of the following:

1. Unexplained severe malnutrition with wasting that does not respond to feeding
2. Recurrent severe bacterial infections other than pneumonia, e.g. meningitis or osteitis
3. Pneumocystis pneumonia
4. Oesophageal candidiasis
5. Severe chronic herpes simplex infection
6. Extrapulmonary disseminated TB
7. HIV-associated disseminated TB
8. HIV encephalopathy
9. Chronic lung disease including bronchiectasis
10. Unexplained anaemia, neutropenia (low white cells) or thrombocytopenia (low platelets)

Stage 4 presents with uncommon severe infections.

CMV retinitis, cryptococcal meningitis, disseminated fungal infections, disseminated non-tuberculous mycobacterial infection and chronic cryptosporidiosis or isosporiasis are also included as stage 4 conditions. However, these infections are not common in children with advanced HIV disease. HIV-associated cardiomyopathy, nephropathy and rectovaginal fistula are now also classified as stage 4 conditions.

NOTE The new WHO classification defines moderate malnutrition as a z-score below 2 (2 SD below the mean weight for age) and severe malnutrition as a z-score below 3.

2-19 What rashes are common in children with stage 2 HIV infection?

1. Pruritic papular eruption
2. Seborrhoeic dermatitis
3. Extensive molluscum contagiosum
4. Extensive warts

Note: Although acute seroconversion illness is part of the primary HIV infection, it is formally included in stage 1.

Stage 3 presents with common severe infections.

Stage 4 presents with uncommon severe infections.

NOTE: Although acute seroconversion illness is part of the primary HIV infection, it is formally included in stage 1.
5. Herpes zoster (especially if widespread)
6. Fungal nail infections
7. Severe scabies

Other non-specific skin rashes are also common in children with HIV infection.

Skin rashes are common in children with HIV infection.

2-20 What is pruritic papular eruption?
This is very common in children with HIV infection and presents with a persistent severe itch and scattered pigmented papules, especially on the trunk and limbs ('itchy bump disease'). It responds to topical steroids.

2-21 Which malignancies are common in HIV-infected infants?
1. Lymphomas, which usually occur in the lung or brain. They are especially common in East Africa.
2. Kaposi’s sarcoma, which usually presents with multiple painless purple or brown patches or nodules (bumps) on the skin, especially the face, trunk and legs. The mouth may also be involved, especially the hard palate. In advanced cases other organs such as the gut, lungs and lymph nodes can be affected. Kaposi’s sarcoma is usually not life threatening and the patches and nodules often improve with antiretroviral treatment.

2-22 How is the clinical diagnosis of HIV infection confirmed?

By testing for the presence of antibodies to HIV (antibody tests) or the presence of HIV itself (viral tests). In adults the diagnosis of HIV infection is usually based on finding antibodies to HIV in the blood or other body fluids (e.g. saliva). However, in young children it is often necessary to show that the virus (HIV) itself is present.

Screening for HIV infection should be seriously considered in all sick children in countries where AIDS is common.

2-23 When is antibody testing helpful in diagnosing HIV infection in children?

Only in older children (18 month of age or more) if the mother is HIV positive. Mothers who are infected with HIV produce antibodies to HIV and these antibodies pass across the placenta to their fetus. Therefore, if the mother has antibodies to HIV, her newborn infant will also have HIV antibodies whether the infant is infected with HIV or not. These maternal antibodies slowly disappear from the infant's blood during the months after birth but may remain up to the age of 18 months. As a result, positive antibody screening tests for HIV antibody (ELISA test and rapid test) cannot be used to diagnose HIV infection in children before the age of 18 months. However, if the antibody test is negative, the child has not been infected with HIV from the mother.

Many HIV-exposed but uninfected children will already have a negative HIV antibody screening test by nine months of age when the child attends clinic for the first measles immunisation. Most, but not all, uninfected children will have a negative antibody screening test by 12 months. All uninfected children will get an HIV-negative result by 18 months.

A screening HIV test is useful if the mother’s HIV status is unknown or cannot be obtained, e.g. for orphans or abandoned children. However, HIV screening of all children is encouraged to establish their HIV-exposure status.
2-24 What tests detect whether HIV is present?

1. DNA (genetic material) from the HIV can be detected, using the polymerase chain reaction (or PCR) test. If the PCR test for HIV is positive, the child is definitely infected with HIV. However, the PCR test takes up to six weeks to become positive after the child has been infected with HIV. Therefore, it can only be used with confidence to make or exclude a diagnosis of HIV infection in children who have never been breastfed once they reach the age of six weeks. In breastfed infants, a negative test result is only reliable if done from six weeks after breastfeeding has been completely stopped.

2. The ultra-sensitive p24 antigen test can be used to detect HIV proteins in children. A positive ultrasensitive p24 antigen test, therefore, confirms HIV infection even in children less than 18 months. The ultrasensitive p24 antigen tests are as reliable as PCR for diagnosing HIV infection in children. Like the PCR test, it is important to wait for six weeks.

Where PCR testing is not available, clinical features and antibody screening should be used to make a probable diagnosis on HIV infection until testing at 18 months.

2-25 What is the window period?

This is the time after infection with HIV when the blood tests may still be negative. For both the antibody tests and the viral tests the window period may last up to six weeks.

During the six-week window period the tests for HIV infection may be negative, even if the child is infected with HIV.

IMMUNOLOGICAL STAGING OF HIV INFECTION

2-26 How is HIV infection staged immunologically?

In addition to the clinical staging of HIV infection, patients should also be staged immunologically. This is based on the number of CD4 cells (helper or CD4+ T cells) in the blood. As HIV destroys more and more CD4 cells the body’s immune system becomes weaker and weaker. The number of CD4 cells in the blood is therefore a direct measure of the degree of damage to the immune system and the risk of HIV-associated infections.

The number of CD4 cells indicates whether the immune system has been damaged.

2-27 What is the CD4 count?

This is the number of CD4 cells in one µl of serum (i.e. a 1000th of a ml). In normal healthy adults who are HIV negative, the CD4 count is above 500 cells/µl (usually about 1000 cells/µl). In children the normal range is higher, especially in younger children who have an immature immune system. As the CD4 count varies according to the child’s age, it is preferable to use the CD4 percentage rather than the absolute CD4 count in younger children (under the age of five years). The CD4 percentage is the per cent of lymphocytes in the blood that are CD4 cells.
2-28 What is the normal percentage of CD4 cells in children?

In normal healthy children, more than 25% of the lymphocytes in their blood should be CD4 cells. This indicates that there is no immunosuppression (no damage to the immune system). If the immune system of children with HIV infection is suppressed, their percentage of CD4 cells will be less than 25%.

Normal children have a CD4 percentage of 25 or more.

2-29 How can the percentage of CD4 cells be used to grade the degree of immune suppression in children?

1. A CD4 percentage between 15 and 24 indicates moderate immune suppression.
2. A CD4 percentage of less than 15 indicates severe immune suppression.

A CD4 percentage below 15% indicates severe immunosuppression.

2-30 What is the value of knowing the CD4 percentage?

The lower the CD4 percentage, the greater the risk of severe illness and death.

NOTE The CD4 percentage is not as accurate a predictor of death as the CD4 count is in adults.

2-31 Should both the clinical and immunological staging be used together?

Yes. It is best if both systems of staging are used together, especially when deciding whether a child needs to be started on antiretroviral treatment. While the immunological staging indicates the degree of immunosuppression, the clinical staging indicates the effect of the immunosuppression. Both are important.

CONSENT FOR 
HIV TESTING

2-32 Is consent for HIV testing always necessary?

Yes. It is very important that informed consent is always obtained before any form of HIV testing is done. This means that counselling must be provided before obtaining consent.

Consent must be obtained before testing a child for HIV.

2-33 Who should give consent for HIV testing in children?

When children need to be tested, consent is usually obtained from a responsible adult, such as the parent or guardian (caretaker). Adolescents of 12 years or more can give their own consent, although it is always preferable to get consent from a parent or legal guardian as well. Children who give consent must receive pretest counselling which they can understand. If a child is not able to give consent, the person providing consent must receive appropriate counselling.

NOTE The new South African Children’s Bill recognises certain rights of children, including the right to consent to medical treatment if they are 12 years old and are sufficiently mature and capable of understanding the benefits, risks and social implications of the test. Therefore, the age of consent is 12 years in the new bill.

2-34 Who can give consent if there are no parents?

Abandoned or orphaned children have the same legal rights as other children. Adoptive or foster parents are legal guardians and can give consent. If there is no available guardian, the provincial minister for social services should be approached for consent. This is often needed when abandoned children who are ill are admitted to hospital.
The High Court may also be approached for consent. However, this is seldom necessary as the option only arises if a dispute occurs between legal guardians and doctors when treatment is considered to be lifesaving.

2-35 Can children be tested without their parents knowing?

Confidentiality is important and children of 12 years or more can be tested and keep the result of their HIV test from their parents if they so wish. Consent for the clinic or hospital staff to disclose the result of the HIV test to the parents must first be obtained from these children. Therefore, older children should be tested without their parents knowledge or permission if this is their wish.

2-36 What counselling is needed before HIV testing?

As a diagnosis of HIV infection in a child has important implications for the parents and whole family, the parents should be counselled before they give consent for the child to be tested. In most children a positive diagnosis in the child implies HIV infection in the mother and often the father. The parents need to understand what HIV infection is, how a child becomes infected with HIV and the clinical presentation and course of HIV infection.

CASE STUDY 1

A 15-year-old adolescent presents with a fever, sore throat, headache and general feeling of tiredness. On examination she has pharyngitis and a measles-like rash. When questioned she gives a history of recent sexual relations with an older man.

1. What is the probable diagnosis?

Acute seroconversion illness. This presents in some people two to four weeks after infection with HIV. The symptoms and signs usually disappear after a few weeks. Acute seroconversion illness is uncommon in young children.

2. How can the diagnosis be confirmed?

Usually an HIV screening test (rapid test) is done. However, the test may still be negative even though the person is infected with HIV because they are still in the window period.

3. What is the latent period?

This is the time between infection and the first appearance of symptoms and signs due to chronic HIV infection (i.e. symptomatic HIV infection).

4. How long is the latent period in children?

It is shorter than in adults where the latent period is usually a number of years. In children who are infected around the time of birth, the latent period is usually weeks or months (‘fast progressors’). It is longer in children who are infected via breast milk (‘slow progressors’).

5. What is often the first clinical sign of chronic HIV infection?

Persistent, painless, generalised lymphadenopathy.

6. Can she be tested for HIV infection without her parents’ consent?

Yes. At the age of 15 years she can give consent for the test. However, it is always preferable to also obtain the parents’ consent.

CASE STUDY 2

A two-year-old child is brought to a clinic by a woman who was HIV positive when screened during her pregnancy. The infant was never breastfed. She reports that the child has had an itchy skin rash for the past few days. On examination he also has an enlarged liver and spleen, as well as a chronic otitis media.
1. Do you think this child has HIV infection?
Yes. The hepatosplenomegaly, skin rash and chronic otitis media all suggest symptomatic HIV infection, especially if the mother is HIV positive. A positive rapid test would confirm the HIV infection.

2. What rash do you think this child has?
Pruritic papular eruption or ‘itchy bump disease’. It responds to topical steroids.

3. What other itchy skin rash is common in HIV-positive children?
Severe scabies.

4. How would you stage the infection?
The child has some features of stage 2 infection (a typical rash, hepatosplenomegaly and chronic upper respiratory tract infection).

5. What other clinical signs may be present in a child with stage 2 HIV infection?
Enlarged painless parotid glands, other skin rashes such as warts and molluscum, fungal nail infections, mouth ulcers and inflamed gums, other upper respiratory tract infections and Herpes zoster.

6. Can the child be tested for HIV without getting consent?
Consent must always be obtained first before testing anyone for HIV infection.

1. How would you stage this child’s HIV infection?
Stage 3, as he has oral candidiasis. He is probably malnourished as well.

2. What is the likely cause of his cough?
Pulmonary tuberculosis. However, he should be fully investigated as there are many other causes of chronic cough and lung infection in children with HIV infection.

3. What other lung diseases are seen in children with stage 3 HIV infection?
Severe recurrent bacterial pneumonia, symptomatic lymphoid interstitial pneumonitis and chronic lung disease.

4. Is Kaposi’s sarcoma a feature of stage 3 HIV infection?
No. This is a feature of stage 4 HIV infection.

5. Can the CD4 percentage be used to stage the clinical progress of HIV infection?
No. The CD4 percentage is used to immunologically stage the illness. Both the clinical and the immunological staging are important as they are used to decide when to start antiretroviral treatment.

6. Does this child have advanced HIV disease?
Yes. Advanced HIV disease in children is defined as stage 3 or 4 HIV infection.

CASE STUDY 3

A six-month-old child with known HIV infection presents at the outpatients department of the local hospital. His mother says that he has lost weight recently, has a sore mouth and a chronic cough. On examination the child has oral candidiasis (thrush).

CASE STUDY 4

A woman with asymptomatic HIV infection delivers a preterm infant who is clinically healthy. The infant is not breastfed. She wants to know whether her infant is also infected with HIV. The mother has a normal CD4 count.
1. Can a rapid test be used to determine whether this infant is infected with HIV?

No. In an HIV-exposed infant, these tests can only be used to diagnose HIV infection after 18 months. The rapid test will be positive even if the infant is not infected with HIV.

2. What test can be used to decide whether this child has HIV infection?

Once this infant is six weeks old, the PCR test for HIV or the ultra-sensitive p24 antigen can be used. A negative test at six weeks or more would indicate that the infant has not been infected with HIV while a positive test would indicate HIV infection. If the infant had been breastfed the PCR should only be done six weeks after the last feed of breast milk.

3. What is a CD4 count?

This is a test to determine whether the immune system has been damaged. The CD4 percentage rather than the CD4 count is used in children.

4. What is a normal CD4 percentage in children?

More than 25%. A CD4 percentage of 15 to 24% indicates moderate immune suppression while a CD4 percentage below 15% indicates severe immunosuppression.

5. What is the value of knowing a child’s CD4 percentage?

It helps to predict how fast the HIV infection will progress. Children with a low CD4 percentage will reach stage 3 or 4 sooner than children with a higher CD4 percentage.
Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you’ve worked through the unit, to evaluate what you have learned.

3 Management of children with HIV infection

FAMILY-CENTRED CARE

3-1 What is the management of children with HIV infection?

All aspects of the health and emotional wellbeing of an HIV-positive child must be addressed, whether or not the child is receiving antiretroviral treatment. An enormous amount can be done for an HIV-infected child even if antiretroviral treatment is not available. The general management of all HIV-infected children is the same.

If HIV infection is excluded in an HIV-exposed child, the child should be referred to a well-child clinic and requires no further follow up for HIV infection. With the use of antiretroviral prophylaxis perinatally, most HIV-exposed infants will not be infected.

3-2 Where should children with HIV infection be managed?

Every effort must be made to keep HIV-infected children at home with their family and to manage them at a local primary-care clinic. They should only be referred to a special HIV clinic or hospital if there are clear indications.

Objectives

When you have completed this unit you should be able to:

- Describe family-centred care.
- Plan routine clinical care.
- Provide immunisation.
- Provide co-trimoxazole prophylaxis.
- Monitor and support growth and nutrition.
- Monitor neurodevelopment.
- Screen for HIV-associated infections.
- Monitor clinical and immunological staging.
- Manage adolescents with HIV infection.
- Advise on disclosing HIV status to children.
- Decide when to start antiretroviral treatment.
HIV-infected children should be managed at home if at all possible.

Ideally the community-based primary-care clinic should meet the needs of most HIV-positive children. This requires the integration of many different services (a ‘one-stop shop’). Care at a primary health clinic is usually provided by nurses and not doctors.

3-3 What is family-centred care?
Children should always be seen as a member of a ‘family’ and not simply as an individual. Many of the health problems of children are a direct result of problems within the family (poverty, neglect, abuse, poor education). Therefore the management of any child must take into consideration the family and home environment. Family-centred care (or family-oriented care) is the care of a child as a member of a family. ‘Do not forget the family!’

Ideally the whole family should be cared for by the same staff at the same clinic.

ROUTINE CLINICAL CARE

3-4 What are the main steps in managing children with HIV infection?
1. Routine clinical care.
2. Provide immunisation.
3. Provide co-trimoxazole prophylaxis.
4. Monitor and support growth and nutrition.
5. Monitor neurodevelopment.
7. Diagnose and manage HIV-associated infections.
8. Provide counselling and support.
9. Support and monitor good adherence.
10. Provide and monitor antiretroviral treatment when indicated.
11. Help access social grants and other support structures.
12. Conduct home visits if needed.

3-5 What routine clinical care is needed?
Both HIV-positive and negative children should receive routine clinical care. This is provided at a local primary-care clinic. The ‘well-baby clinics’ and ‘under-5 clinics’ must be integrated into other health services such as maternal care, immunisation and managing sick children.

Routine care includes:
- Immunisation
- Growth and neurodevelopmental monitoring
- Nutritional support
- Vitamin supplementation
- Regular deworming
- Treatment of common minor illnesses
- Health education

3-6 What special care is needed by HIV-exposed infants?
All infants born to HIV-positive mothers are at risk of being infected themselves with HIV. It is important to determine whether these HIV-exposed infants are HIV infected or not as soon as possible after birth. This is possible with PCR testing from six weeks onwards, in infants who have never been breastfed. Infants who have received breast milk should also be tested after six weeks. If the result is negative the test should be repeated at six weeks after their last feed of breast milk.

If PCR testing is not available, clinical features should be used to make a probable diagnosis. A rapid test should then be done at 18 months. Often rapid testing is also done at nine or 12 months as many uninfected children will already have a negative test by this time.

Once HIV infection has been excluded, these infants require only routine care at a well-baby clinic. However, until HIV infection has been excluded, HIV-exposed infants should be followed-up together with the HIV-infected infants.
When should HIV-exposed infants be followed up?

Until HIV infection has been excluded, HIV-exposed infants must be closely followed:

1. At six weeks for immunisation. The PCR should be done at this visit. Co-trimoxazole should be started if HIV infection has not yet been excluded.
2. Again at 10 and 14 weeks for immunisation.
3. Monthly until six months.
4. Every three months from six to 12 months.
5. Every six months from one year.
6. A rapid screen should be done at 18 months (and possibly nine or 12 months) if PCR testing is not available.
7. At every visit the child must be weighed and the weight plotted on the Road-to-Health card. In addition, the child's clinical wellbeing should be assessed and the mother given counselling and support. Infants who are not well should be seen more frequently.
8. If a diagnosis of HIV infection is made for an infant under 12 months of age, the infant must be started on antiretroviral treatment.

3-8 Is it safe to give routine immunisations to infants who may be infected with HIV?

It is safe to give most routine immunisations (Expanded Programme on Immunisation) to well HIV-exposed infants in the first months of life. Ideally, BCG should not be given to children with clinical signs of HIV infection. However, giving BCG to all infants after delivery, irrespective of their HIV status, is still recommended in countries where tuberculosis is common.

Other routine immunisations should be given to all HIV-infected children even if they have signs of HIV disease.

3-9 What additional immunisation may be useful?

Routine pneumococcal and rotavirus immunisation is being introduced in many countries where HIV infection is common, to reduce the frequency and severity of pneumonia and gastroenteritis in HIV-infected children.

Additional immunisations with pneumococcal, chickenpox and influenza vaccines may help to prevent infections which can be serious in children with HIV.

**PRIMARY PROPHYLAXIS**

3-10 What is primary prophylaxis?

Most of the morbidity and mortality in HIV-infected children are due to HIV-associated infections. Primary prophylaxis is the use of antibiotics to prevent some of these infections. Therefore primary prophylaxis is an important part of healthcare during the asymptomatic phase of HIV infection.

Secondary prophylaxis is the use of antibiotics to prevent recurrences of HIV-associated infections, i.e. in children who have previously had that HIV-associated infection.

**Primary prophylaxis is the use of antibiotics to prevent HIV-associated infections.**

3-11 What primary prophylaxis should be provided?

Co-trimoxazole. This broad-spectrum antibiotic helps prevent:
1. Pneumocystis jiroveci pneumonia (PJP – previously known as PCP)
2. Common bacterial infections such as pneumococcal pneumonia
3. Infection with non-typhoid Salmonella
4. Diarrhoeal disease due to Isospora and Cyclospora
5. Co-trimoxazole also reduces the risk of infection with falciparum malaria and Toxoplasmosis.

Isoniazid (INH) may also be used to prevent tuberculosis in children under five years at high risk of infection due to exposure to an adult with sputum-positive (‘open’) pulmonary TB. However, it is not used routinely for prophylaxis in all children with HIV.

**NOTE** Co-trimoxazole consists of a combination of sulfamethoxazole and trimethoprim.

### 3.12 How effective is primary prophylaxis with co-trimoxazole?

It is very effective in reducing illness and deaths due to Pneumocystis pneumonia and common bacterial infections. Pneumocystis pneumonia is the main cause of death in HIV-infected infants, especially infants under six months of age. Pneumocystis infection is particularly common in Africa.

The prophylactic use of co-trimoxazole is simple, cheap, well tolerated and lifesaving. It forms a very important part of the management of HIV-infected children and can halve the mortality from HIV-associated infections.

### 3.13 Which children should receive co-trimoxazole?

1. All HIV-exposed infants should be given prophylactic co-trimoxazole, starting at six weeks. It is most convenient to start co-trimoxazole prophylaxis at six weeks in infants born to HIV-positive women as this is the time when the routine immunisations are begun.

### 3.14 When should co-trimoxazole prophylaxis be stopped?

1. It can be stopped if HIV infection is excluded by PCR testing. If the PCR is negative six weeks after the birth of an HIV-exposed infant, who has not been breastfed, prophylaxis need not be started at all.
2. All children with proven HIV infection should receive co-trimoxazole prophylaxis until one year of age, regardless of their CD4 percentage. The risk of Pneumocystis pneumonia is much less after one year.

Prophylaxis should be continued beyond one year until their CD4 percentage returns to normal for six months.

**All HIV-infected infants should receive co-trimoxazole prophylaxis.**

Children who have already had Pneumocystis pneumonia should remain on secondary co-trimoxazole prophylaxis until they are five years old.

### 3.15 How should co-trimoxazole prophylaxis be given?

Infants should be given co-trimoxazole syrup. Older children may be given single-strength tablets. WHO recommends a daily dose. The daily dose depends on the child’s weight.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 kg</td>
<td>2.5 ml paediatric suspension</td>
</tr>
<tr>
<td>5–14 kg</td>
<td>5 ml paediatric suspension or 1/2 regular strength tablet</td>
</tr>
<tr>
<td>15–29 kg</td>
<td>10 ml paediatric suspension or 1 regular strength tablet</td>
</tr>
<tr>
<td>30 kg or more</td>
<td>2 regular strength tablets</td>
</tr>
</tbody>
</table>

Co-trimoxazole prophylaxis forms a very important part of the management of HIV-infected children.
Several alternative co-trimoxazole regimens are effective. However, the above regimen is preferred.

3-16 How common are side effects to co-trimoxazole?

Side effects are uncommon in children. The commonest side effects are skin rashes, which usually occur in the first few weeks of treatment. These are usually mild erythematous rashes. However, they can be serious. Parents must stop the co-trimoxazole and bring the child to the clinic if the child develops a generalised, maculopapular rash, skin blisters or mouth ulcers, as these are the signs of serious hypersensitivity to the drug.

Note Co-trimoxazole may rarely cause hepatotoxicity and bone marrow suppression. Children with G6PD deficiency should not be given co-trimoxazole or dapsone as these drugs can cause acute haemolysis.

3-17 Should children receiving co-trimoxazole be routinely monitored for side effects?

A careful watch should be made for a rash. Routine laboratory tests are not needed.

3-18 What can be done if children cannot receive co-trimoxazole?

Children who have developed side effects to co-trimoxazole should be given dapsone instead. The dose of oral dapsone is 2 mg/kg daily up to an adult dose of 100 mg daily. Crushed tablets are used. Unfortunately dapsone is not as effective as co-trimoxazole in preventing Pneumocystis pneumonia and it does not provide prophylaxis against other organisms.

If the side effects to co-trimoxazole are only moderate or severe (grade 2 or 3) the child can be referred to an antiretroviral centre for desensitisation with low doses of co-trimoxazole. Co-trimoxazole should never be given again after a potentially fatal (grade 4) reaction.

**NUTRITION AND GROWTH**

3-19 Why is good nutrition so important in children with HIV infection?

In all children, good nutrition plays an important role in helping to maintain the normal functioning of the immune system. In contrast, malnutrition (undernutrition) weakens the immune system. Therefore, poor nutrition is especially dangerous in HIV-infected children, placing them at even greater risk of HIV-associated infections. Unfortunately, children with HIV infection are often undernourished.

Good nutrition is an important part of managing children with HIV infection.

3-20 Why is undernutrition common in children with HIV?

1. A poor appetite is common in ill children.
2. They may have a sore mouth or swallowing difficulties due to candidiasis.
3. Loss of nutrients due to chronic diarrhoea.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td></td>
<td>diffuse maculopapular rash or dry desquamation</td>
<td>vesicles or ulcers</td>
<td>Stevens-Johnson or erythema</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>multifforme or moist desquamation</td>
</tr>
</tbody>
</table>
4. Increased nutritional needs due to infections, especially tuberculosis.
5. Inadequate care and feeding at home, especially if the mother has AIDS.

3-21 How is the nutritional state routinely monitored?

1. By regularly weighing the child at each clinic visit. Good weight gain on the Road-to-Health card is the best indicator that the child is well nourished. A careful nutritional and social history must be taken of children who fail to thrive or who lose weight. Supplementary feeds should be given to children with a weight below the 3rd centile. This can usually be obtained from the nutrition clinic.
2. Head circumference and height (length until the child can stand) are important to measure in children who do not have a normal weight gain.
3. The haemoglobin concentration must be determined to screen for anaemia in children who appear pale.

Always look carefully for missed infections in undernourished children (especially tuberculosis). Infections often lead to a rapid deterioration in the child’s nutritional state.

3-22 How can parents improve their child’s nutrition?

It is important that parents are aware of the importance of good nutrition and have the knowledge to give their children the correct foods. The nutritional value of meals can be improved by:

1. Using starchy foods as the basis of most meals to provide calories, e.g porridge, samp (mielies), rice or potatoes.
2. Adding 1–2 teaspoons of vegetable oil, margarine or peanut butter to provide added calories.
3. Using wholewheat or brown bread rather than white bread.
4. Providing protein with fish, eggs and meat (expensive) or beans, peas, lentils or soya products (cheaper). Milk (breast milk or formula) usually is the main source of protein during the first year of life. Skimmed milk powder or fresh cows’ milk can be used after one year to add protein to the diet.
5. Using only a little fat and salt.
6. Buying fruit in season (expensive) or fresh vegetables (cheaper). Do not overcook vegetables as this damages vitamins.
7. Use a variety of foods, mixing starch, protein, vegetables and fruit. Cultivating a vegetable garden can save costs.
8. Avoid sweets, potato chips, cool drinks and ‘junk’ foods which are often expensive and of little nutritional value.
9. Access food supplements if needed and available.

A balanced, mixed diet need not be expensive.

3-23 What vitamin supplements are necessary?

Vitamin A is important in maintaining a healthy immune system. All children with HIV infection should be given oral vitamin A supplements.

1. 50 000 iu once if under six months (best at six weeks), then:
2. 100 000 iu once if six to 12 months, then:
3. 200 000 iu every six months between 12 months and five years.

Although a standard paediatric multivitamin supplement 5 ml daily is often recommended, this has not been shown to be necessary unless the child is undernourished.

Zinc supplements (10 mg elemental zinc as zinc sulphate daily) from six months of age reduces morbidity from diarrhoea.

3-24 Is regular deworming important?

Yes. It is important to regularly deworm all young children, but especially children with HIV. Deworming every six months is recommended for children between the ages of two and five years in communities with poor hygiene and inadequate sanitation (poor
toilet facilities). This should be done even if there is no history of roundworms in the stool. Medication is usually given at the local primary-care clinic or in schools. Deworming has been found to improve the learning capacity and growth of school children.

Mebendazole is the drug of choice. Albendazole is more expensive. Both these drugs are highly effective for roundworms. The dose for deworming is:

1. Mebendazole orally 100 mg (i.e. one tablet) twice a day for three days if below two years old and 500 mg as a single dose if two years or older
2. Albendazole as a single dose 200 mg (two tablets) for children below two years old and 400 mg for children of two years or older

3-25 What is the importance of teeth care?

Dental care is important as dental caries are very common in children with HIV. Bad teeth may also reduce nutrition intake. Daily brushing of the teeth and restriction of sweetened food and drinks helps to keep the teeth healthy. Most children cannot brush their own teeth adequately until the age of seven years. Therefore, the caregiver should do the brushing with a gentle action, using a soft toothbrush. If the caregiver cannot afford toothpaste, salt may be used. Children with dental caries should be referred to a dentist for treatment.

3-26 What should be done if a child is failing to thrive?

1. Carefully weigh the child and plot the weight on a growth chart.
2. A careful family and nutritional history must be taken. It is important to determine whether the child is receiving a good diet. A poor diet as a result of poverty, ignorance or ill parents is a common cause of failing to thrive with poor weight gain or actual weight loss.
3. The child should have a full clinical examination to look for signs of malnutrition, clinically stage the HIV, and check for HIV-associated infections. Malnutrition usually presents with wasting of muscles and subcutaneous fat.
4. TB should be excluded.
5. If a poor diet is the cause of the failure to thrive, the child needs nutritional support and the parents need education and support.
6. The child will need appropriate medical management if the HIV staging is 2 to 4 or an HIV-associated infection is present.

3-27 How can nutrition be supported?

Children who fail to thrive despite optimal medical treatment may require additional nutritional support. Ideally they should be assessed by a dietician. Additional protein and calorie intake should be considered up to 150% of the daily recommended allowance.

3-28 Why is regular exercise important?

Although rest is important, children also need regular exercise to grow and develop normally. Most well HIV children can play sport normally. Play is important for all children. It is essential that children with HIV mix with other children in play groups and at school. They should attend normal schools as they are not a risk to HIV-negative children.

MONITORING NEURODEVELOPMENT

3-29 How should neurodevelopment be monitored?

Neurodevelopment as well as physical growth should be routinely monitored in all children, but especially children with HIV infection. Developmental milestones are used for the routine monitoring of neurodevelopment.
3-30 Why are delayed milestones important to detect?

One of the first and most important clinical features of symptomatic HIV infection in children is a delay in developmental milestones. Children with advanced HIV disease may also have a slowing of head growth (head circumference).

3-31 Why do children with HIV infection often have delayed milestones?

1. They may have HIV-associated infections.
2. They may be malnourished.
3. They may have HIV encephalopathy.
4. They may have little stimulation because of poverty, ill or depressed parents, and frequent or long periods of hospitalisation.

3-32 Where should clinical staging be monitored?

All HIV-infected children who are not already on antiretroviral treatment must be seen regularly at the local primary-care clinic in order to monitor their clinical condition and staging. This is an important part of monitoring the progress of the disease. It is not practical to follow all HIV-positive children at a special HIV clinic.

3-33 How often should children be clinically assessed?

All clinically well children who are HIV infected (or where HIV infection has not yet been excluded) should be followed every six months.

Children who have clinical signs of symptomatic HIV infection (stage 2 or more) must be seen more frequently, depending on the severity of their illness.

3-34 How is clinical staging performed?

This is based on general examination. Specific signs of HIV infection and HIV-associated infections must be looked for. A history of infection is also important. Usually special investigations are not needed to assess the clinical stage.

Clinical staging is an important part of routine follow up.

MONITORING IMMUNE FUNCTION

3-35 What test is used to monitor the immune system in HIV-infected children?

The CD4 percentage. The aim is to keep the CD4 percentage within the normal range (above 25%) for as long as possible. Capillary or venous blood has to be sampled for the CD4 measurement.

NOTE Capillary blood collection as a dry spot on filter paper is very useful to measure the CD4 percentage.

The CD4 percentage is used to monitor the child’s immune function.

3-36 How often should the CD4 percentage be measured?

In children who are well, and not yet on antiretroviral treatment, the CD4 percentage should be measured every six months to assess the condition of the immune system. Once the CD4 count falls to 25% or below, the child should be followed more closely.

3-37 What are the immunological indications to start antiretroviral treatment?

- All HIV-infected children below one year of age should be started on antiretroviral
management of children with HIV infection

treatment, irrespective of their clinical stage or CD4 percentage.
- Children between 12 months and five years with a CD4 percentage of 25% or less, or a CD4 count of 750 cells/µl or less.
- Older children with a CD4 count of 350 cells/µl or less.

3-38 Should the viral load be monitored in well patients?

There is no need to routinely measure the viral load in older children with HIV infection who are not yet on antiretroviral treatment.

SCREENING FOR HIV-ASSOCIATED INFECTIONS

3-39 Why is it so important to screen for HIV-associated infections?

Because HIV-infected children usually present clinically with an HIV-associated infection. These infections are often the final cause of death. Therefore it is vitally important that HIV-associated infections are detected and diagnosed as soon as possible so that early treatment can be started.

3-40 How should you screen for HIV-associated infections?

By taking a careful history and performing a good clinical examination at every follow-up visit. Important questions to ask (‘red flags’) are:

1. Has the child become unwell recently?
2. Does the child have a poor appetite?
3. Does the child have a sore mouth or difficulty swallowing?
4. Does it look as if the child has lost weight?
5. Does the child have loose stools?
6. Does anyone in the family have tuberculosis?
7. Does the child cough?

Important clinical signs are:
1. Weight loss
2. Fever
3. Oral thrush or mouth sores
4. Skin rash
5. Enlarged lymph nodes, parotid glands, liver or spleen
6. Signs of upper or lower respiratory tract infection

Any child with a suspected or obvious HIV-associated infection should be treated or referred immediately.

CARE OF ADOLESCENTS WITH HIV INFECTION

3-41 What is an adolescent?

The WHO defines adolescence as young people between the ages of 10 and 19 years. Adolescence is the time of physical, emotional and psychosocial change from childhood to adulthood. Adolescents require special care as their needs are different from those of both children and adults. The first signs of puberty (breast buds, testicular enlargement and pubic hair) usually indicate that the child should be regarded as an adolescent.

Adolescence is the time of physical, emotional and psychosocial change from childhood to adulthood.

3-42 Why are the needs of adolescents different?

Because they are growing rapidly, becoming sexually mature, and undergoing major emotional, psychological and social changes.

1. During early adolescence (10 to 13 years) their self-image is changing as they are experiencing the start of puberty, they have intense feelings and mood swings, they feel a need for privacy, and have close relationships with friends of the same sex.
2. During middle adolescence (14 to 16 years) they are reaching the end of puberty, conflict with family is common and they identify strongly with their peers of both sexes. Many feel invincible (‘it can’t happen to me’). Rebelling, rejecting parents’ values and high-risk behaviour is common.

3. During late adolescence (17 to 19 years) they are more responsible, consider the feelings of others, develop mature long-term sexual relationships with less risk-taking. Some adolescents are physically but not emotionally mature.

The WHO recommends the use of paediatric clinical staging charts and criteria for starting antiretroviral treatment for adolescents younger than 15 years of age and adult clinical staging charts and starting criteria for adolescents who are 15 years of age or older. Paediatric doses of antiretroviral drugs are usually recommended for adolescents in early puberty (Tanner stages 1 to 3) and adult doses for adolescents in late puberty with full physical maturation (Tanner stage 4 and 5).

NOTE Tanner stages 1 to 3 includes growth spurt, but only early signs of breast and genital development, while stages 4 and 5 are almost complete sexual maturation.

3-43 Why do adolescents have greater health risks?

1. High-risk behaviour is common. Sexual promiscuity, smoking, drinking and drug abuse are problems. Due to their insecurity and lack of experience, adolescents are sexually vulnerable.

2. They often give in to peer pressure and are unable to set limits. Parents have less control and antisocial behaviour is common.

3. They often distrust health workers.

4. Depression is common in HIV-infected adolescents.

5. They may not have parents. Some are ‘AIDS orphans’. Others may be the head of the household or have ill parents.

6. They may deny that they have HIV infection.

7. Adherence is often poor. It is not ‘cool’ to take medication.

8. Disclosure is difficult and stigma causes fear and anxiety. Shame, anger and guilt are common reactions.

3-44 Which adolescents may have HIV infection?

1. Adolescents who were perinatally infected and have had HIV infection since birth or the first months of life. Many HIV-infected infants are now surviving into adolescence. Most will already be on antiretroviral treatment. They may have retarded growth and development, delayed puberty or signs of chronic illness. Schooling may have been interrupted due to illness. They may also have lost one or both parents from HIV infection.

2. Adolescents who have been infected recently via sexual intercourse. This might be with or without consent. It is estimated that 20% of young women below 20 years of age in South Africa have HIV infection. This makes up about a third of all new HIV infections each year.

3-45 Which adolescents are most sexually vulnerable?

Boys usually have an earlier sexual debut (first experience) than girls. However, the prevalence of HIV infection is much higher in adolescent girls than boys, as young girls usually have older male partners. Girls, especially homeless or orphaned girls, may also be sexually abused or sell/swap sex for financial or other favours. The immature cervix is easily infected by HIV.

During adolescence girls are at higher risk of HIV infection than boys.

3-46 What is a youth-centred approach to HIV counselling?

Every effort should be made to meet the special needs of adolescence. This is best done at a youth centre. This is a clinic where the facilities,
staffing and care are designed to make it user-friendly to both HIV-positive and negative adolescents. The features of a youth centre are:

1. Adolescent-friendly staff who are warm, non-judgemental and respect and understand the common problems. They need to be able to openly discuss sensitive issues. Some adolescents do not want their parents to know that they have become HIV positive. In South Africa children of 12 years or older do not need parental consent for care. Afternoon clinics will not interfere with schooling.
2. An informal atmosphere where adolescents feel at ease. If possible, the adolescent should always see the same health worker who they should know by name.
3. Peer support groups.
4. Meet all the health needs of adolescents.
5. The ability to counsel and screen for HIV. Language and cultural differences should be respected.
6. The ability to manage an HIV-infected adolescent. The staff need skills to handle issues of disclosure, stigma, depression and adherence. Adolescents need to learn to manage their own treatment.
7. Provide condoms and family planning support.
8. Treat other sexually transmitted infections.

If there is no youth centre, general HIV clinics should at least be adolescent friendly. The staff usually consists of nurses, doctors, counsellors, social workers and psychologists who work together as a multidisciplinary team.

**An adolescent-friendly approach with peer support is very important.**

**3-47 How can adolescents protect themselves from HIV infection?**

1. Delay sexual debut for as long as possible. Adolescents need to learn how to overcome the peer pressure to become sexually active.
2. Always use a condom. Girls need to learn how to negotiate safer sex.
3. Limit the number of sexual partners.
4. Schools must provide healthy lifestyle education.
5. Avoid dropping out of school early.
6. They should be encouraged to know their HIV status.
7. They should have any sexually transmitted infection diagnosed and treated early.

All adolescents must have sex education and be given the life skills to protect themselves and others from HIV infection. This should be taught in the home, schools, peer groups and health services. They need to become confident and have the knowledge to take responsibility for their lives.

**DISCLOSURE**

**3-48 Should HIV-infected children be told their HIV status?**

Yes, but only when they have reached an age and stage of maturity when they can understand and handle this information. Revealing a child’s HIV status is a process over a number of years and not a once-off event. It can be compared to telling an adopted child the details of their parents and the adoption, or providing a child with sex education. They are provided with a little information at a time in a step-wise fashion. This is best done by simply and honestly answering their questions. It can be frightening and confusing to give too much detailed information too soon.

Parents often find this difficult and need the advice and support of health professionals. Failure of full disclosure by the time adolescence is reached can result in emotional difficulties, a lack of trust in the parents and health workers, and poor adherence. Every effort should be made to get the parents to agree to the disclosure.

**It is important to give children information about their HIV status when they reach an appropriate age to accept the facts.**
3-49 At what age should children be given information about their HIV status?

1. Very young children (below five years):
   Disclosure usually is not necessary. Comfort, support and security are most important. They need to feel loved and cared for. Children can be present during consultations with health workers and they should be congratulated for taking their medicine. They need confidence in the health workers and accept taking medicine every day.

2. Young children (five to seven years):
   Disclosure can be started by linking medicines and diet to good health. Often the idea of ‘goodies’ (the blood cells which are ‘soldiers’) and the ‘baddies’ (which are the viruses) is used. They need to understand that taking medicine will keep them well. They should never be made to feel guilty. HIV infection is not their fault.

3. Older children (eight to 11 years):
   Partial disclosure with a better understanding of viruses and immunity. The word 'HIV' can be used. They should restrict this private information to their parents and carers. Older children have rights to both know their diagnosis and take part in treatment decisions. Always be honest.

4. Young adolescence (12 years and older):
   Full disclosure is now needed. They need to know the cause, clinical problems, management and prognosis of HIV infection. It is very important that they are educated about ‘safer sex’. They also need to learn how to disclose their HIV status to their close friends. Teenagers need support and counselling as they become independent of their parents. Written information is useful.

HIV-infected children often have a developmental age below their age in years. This should always be taken into consideration when counselling. Be led by the child’s questions and use language that the child can understand.

3-50 Who should tell children about their HIV status?

Usually parents are afraid but still prefer to provide this information themselves. They may need advice, encouragement and support from health workers. Some parents have difficulty with guilt and denial about their own infection and transferring HIV to their children.

**CASE STUDY 1**

An HIV-positive mother is told at the local clinic that it will be dangerous to immunise her six-week-old infant. She is asked to come back when the infant is three months old. No medications are given as the infant appears healthy.

1. **Should all children born to HIV-positive mothers receive routine immunisations?**
   Yes, they can be fully immunised, including BCG immunisation.

2. **What medications should this child have received?**
   Prophylactic co-trimoxazole from six weeks. This can be stopped if HIV infection is excluded with a negative PCR test.

3. **Why is this prophylaxis given?**
   Because it reduces the risk of Pneumocystis pneumonia. It also reduces the risk of some serious bacterial infections.

4. **For how long should primary prophylaxis be continued in young children with HIV infection?**
   Usually for the first year of life. The risk of Pneumocystis pneumonia is less in older children.
5. What is the important side effect of co-trimoxazole?

Rash. This is usually mild but can be severe and even life threatening, especially in adults. Therefore parents should be warned to return to the clinic immediately if the child develops a rash.

**CASE STUDY 2**

A mother and her two HIV-infected children attend a primary-care clinic for a routine follow-up appointment. The clinic practises family-centred care. She is concerned as her four-year-old daughter has lost weight recently. A neighbour said that the child may have worms.

**1. What is family-centred care?**

With family-centred care the whole family is taken into consideration when the child is seen. Many of the health problems in children are a direct result of family problems such as poverty, neglect and abuse. Therefore the family cannot be ignored.

**2. Name some of the main steps in the routine follow up of well children who are HIV infected?**

- Immunisation
- Co-trimoxazole prophylaxis
- Monitoring growth and development
- Monitoring clinical and immunological staging
- Providing counselling and support
- Assessing for antiretroviral treatment

**3. How should growth be monitored?**

By plotting the child’s weight on the Road-to-Health card. It is particularly important to chart this child’s weight as there is some concern that she has lost weight recently.

4. Why may an HIV-infected child lose weight?

- Because of a poor appetite
- As a result of a sore mouth and painful swallowing caused by candidiasis
- Due to chronic diarrhoea, TB or an HIV-associated infection
- Due to problems in the family such as poverty or an ill mother

5. Can worms be a problem in HIV-infected children?

Yes. Therefore they should be regularly dewormed every six months. Usually mebendazole is used.

6. What vitamin supplements should this child receive?

Vitamin A.

**CASE STUDY 3**

An adolescent is seen by a general practitioner as she is embarrassed to attend the local clinic. The doctor diagnoses primary syphilis and is concerned that she is not practising safer sex. After counselling her, he performs a rapid test for HIV and this is positive.

**1. When does a child become an adolescent?**

The WHO defines adolescence as young people between the ages of 10 and 19 years. Adolescence is the time of physical, emotional and psychosocial change from childhood to adulthood. The first signs of puberty usually indicate that the child should be regarded as an adolescent.

**2. Why do you think the patient is unhappy to attend the local clinic?**

Because the clinic does not have a ‘youth-centred’ approach.
3. What could the clinic do to be more user-friendly to adolescents?
Train their staff to be adolescent-friendly by being welcoming, non-judgemental and to respect and understand the concerns of young people. Adolescents prefer an informal atmosphere and appreciate peer support groups.

4. How do you think this adolescent became HIV infected?
Almost certainly by sexual intercourse as she has another sexually transmitted infection. However, some perinatally HIV-infected children are now reaching adolescence.

5. Why are young women sexually vulnerable?
Because they often are still emotionally immature and inexperienced. Therefore they are at risk of abuse and may sell sex to older men for financial or other favours.

6. How can adolescents protect themselves from HIV infection?
By delaying sexual debut, limiting the number of sexual partners and always using a condom. In order to achieve this they need education about how to live a healthy lifestyle.

CASE STUDY 4
An HIV-infected woman asks a nursing friend how she should tell her young son that he also has HIV infection. He is starting to show the first signs of puberty.

1. Should children be told their HIV status?
Yes, but only when they have reached a stage of maturity when they are old enough to understand what this means and to emotionally handle the information. It is not helpful to provide too much information too soon. Older children have the right to know their status.

2. At what age should their HIV status be disclosed?
This should be a slow process starting when the child is young. As they grow older they can be given more information. Very young children need security and encouragement to take their medication. By the age of five most children can understand that they have a chronic illness and why they have to take regular medication. Older children can be given information about HIV and the implication this has in their lives. As this child is entering puberty he should be able to accept and understand the cause, clinical symptoms and prognosis of HIV infection.

3. Who should provide this information to children?
Their parents or carers if possible. Parents often find this difficult and need the advice and support of health workers.

4. What is the best way of providing HIV information to children?
By answering their questions simply and honestly.

5. Should this child have sex education?
Yes. This is very important so that he can prevent spreading HIV to others.

6. Who should be told that he is HIV positive?
At this age only family and close friends. Children may need help and support in disclosing their HIV status.
Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you’ve worked through the unit, to evaluate what you have learned.

**Objectives**

When you have completed this unit you should be able to:
- List the goals of antiretroviral treatment.
- Give the classes of antiretroviral drugs.
- Describe the standard regimens of antiretroviral treatment.
- Describe the use of antiretroviral medication.
- Recognise important side effects of antiretroviral drugs.

**INTRODUCTION TO ANTIRETROVIRAL TREATMENT**

**4-1 What is antiretroviral treatment?**

Antiretroviral treatment is the use of a combination of drugs (i.e. medicines) to treat people who are clinically ill due to an infection with the human immunodeficiency virus (HIV). This differs from the prophylactic use of antiretroviral drugs to prevent the transmission of HIV from mother to infant.

Antiretroviral treatment is also known as HAART (highly active antiretroviral treatment) or ART (antiretroviral therapy).

**NOTE** In 1996 Dr David Ho of New York presented the results of a landmark study showing that multi-drug antiretroviral treatment was successful in stopping viral replication and controlling the immune damage of HIV. Earlier results with single-drug treatment had been disappointing.

**4-2 How does antiretroviral treatment work?**

Antiretroviral drugs prevent HIV from multiplying in CD4 lymphocytes. This reduces the number of viruses in the body and allows the damaged immune system to slowly recover. Therefore, antiretroviral treatment results in an improvement of the clinical disease. Unfortunately, antiretroviral drugs cannot cure HIV infection as the virus is able to ‘hide’ in some cells.

Antiretroviral treatment stops HIV from multiplying in the body and damaging the immune system.
4-3 What are the goals of antiretroviral treatment?

The goals of antiretroviral treatment are to:

1. Prevent the multiplication (replication) of HIV and thereby suppress the viral load and keep it suppressed. This will stop the progression of the disease.
2. Protect (preserve or restore) immune function by increasing the CD4 count. This will improve the quality of life and general health.
3. Promote normal growth and development.
4. Reduce the occurrence of HIV-associated infections.
5. Prolong survival and reduce the risk of death due to AIDS.
6. Minimise side effects to the drugs.

The main goals of antiretroviral treatment are to improve the quality of life and reduce mortality due to AIDS.

4-4 What are the classes of antiretroviral drugs?

There are three main classes of antiretroviral drugs:

1. ‘Nucs’: These drugs block an important enzyme (called reverse transcriptase) and this prevents HIV taking control over the CD4 cells.
2. ‘Non-nucs’: These drugs also block the same enzyme. However, their method of action is different from that of ‘nucs’.
3. ‘PIs’: They prevent the HIV-infected CD4 lymphocytes from building and releasing new mature viruses.

‘Nucs’ is pronounced ‘nukes’.

There are three main classes of antiretroviral drugs.
NOTE ‘Nucs’ (nucleoside antagonists) are known as nucleoside reverse transcriptase inhibitors (NRTIs) while ‘non-nucs’ (non-nucleoside antagonists) are known as non-nucleoside reverse transcriptase inhibitors (NNRTIs). They both act by blocking the formation of viral DNA by the reverse transcriptase enzyme. NRTIs bind directly to the viral DNA while NNRTIs bind to the reverse transcriptase enzyme. ‘PIs’ (protease inhibitors) block the protease enzyme responsible for the release of intact viruses from infected CD4 cells. New drugs include nucleotide (phosphorylated nucleosides) blockers (such as TDF), as well as drugs that block HIV attachment to CD4 cells and drugs that block the entry of HIV into cells (entry inhibitors).

See Figure 4-1, which shows the multiplication of HIV.

4-5 What are common examples of ‘nucs’?

1. ABC (or abacavir)
2. 3TC (or lamivudine)
3. AZT (or zidovudine)
4. ddI (or didanosine)
5. d4T (or stavudine)

These are the generic (common) names of the drugs. For each generic drug there are one or more different trade names for the same drug manufactured by different companies. This makes it difficult to remember all the trade names. Therefore, it is best to remember the generic name and only the commonly used trade names of the frequently used antiretroviral drugs. If possible use the generic names rather than the trade names. However, patients often use the trade names as they are shown on the drug containers.

4-6 Can different ‘nucs’ be used together?

‘Nucs’ are generally used in pairs, e.g. ABC and 3TC or 3TC and AZT or AZT and ddI. However, AZT and d4T should not be used together as they compete with each other. The combination of d4T and ddI must also be avoided because this combination is associated with a higher risk for peripheral neuropathy and lactic acidosis.

Some medication contains a combination of two or three different drugs, e.g. AZT and 3TC can be combined as Combivir. This makes taking medication easier.

AZT and TDF should not be used together as they compete with one another.

A pair of ‘nucs’ form the basis of most antiretroviral drug combinations.

4-7 What are common trade names for the ‘nucs’?

Common ‘nucs’ are:
1. ABC is sold as Ziagen.
2. 3TC is simply called 3TC.
3. AZT is sold as Retrovir.
4. ddI is sold as Videx.
5. d4T is sold as Zerit.

4-8 What are examples of ‘non-nucs’?

The two common ‘non-nucs’ are:
1. Nevirapine
2. Efavirenz

‘Non-nucs’ are particularly powerful inhibitors of HIV multiplication. However, HIV rapidly becomes resistant to ‘non-nucs’ if they are used alone. Therefore, for antiretroviral treatment they are used in combination with a pair of ‘nucs’.

4-9 What are common trade names for the ‘non-nucs’?

1. Nevirapine is called Viramune.
2. Efavirenz is called Stocrin.

4-10 What are examples of commonly used ‘PIs’?

1. Ritonavir (Norvir)
2. Lopinavir

Ritonavir and lopinavir are used together in a single preparation such as Aluvia (a trade name). Using two ‘PIs’ together in a special combination allows a lower dose of both drugs with greater effectiveness and fewer side
effects. ‘PIs’, like ‘non-nucs’, are usually used together with a pair of ‘nucs’.

**NOTE** There are a large number of other ‘PIs’. They are easy to recognise as their generic names all end in ‘avir’ such as ritonavir. A low dose of ritonavir blocks the breakdown of lopinavir. This increases the serum concentration of lopinavir and enhances its effect.

### 4-11 Can antiretroviral drugs be taken by mouth?

Yes. The common antiretroviral drugs in all three classes are taken by mouth. Antiretroviral drugs can be taken as capsules, tablets or as an oral suspension. It is important that drugs for children be changed from an oral suspension to capsules or tablets as soon as they are big enough as the oral suspension is not always stable, often tastes unpleasant and is more difficult to make up and give. Unfortunately there are only a few ‘child-friendly’ formulations of antiretroviral drugs.

**Change from an oral suspension to tablets or capsules as soon as possible.**

### 4-12 Should a number of antiretroviral drugs be used together?

Yes. When giving antiretroviral treatment it is best to use three drugs together. This is called triple combination or multi-drug treatment. It is important to use multi-drug treatment as it is more effective and also reduces the chance of the HIV becoming resistant to the drugs. The same advantages of multi-drug therapy apply to the treatment of TB. If possible, single- or double-drug treatment of HIV infection should never be used except for mother-to-child HIV prophylaxis.

**Triple-drug combinations should be used to treat HIV.**

### 4-13 What is HAART?

Highly active antiretroviral treatment (HAART) is another term for antiretroviral treatment (ART) with three drugs. Therefore HAART is the use of multiple drugs to treat HIV infection.

A combination of three antiretroviral drugs are usually used to provide antiretroviral treatment.

### 4-14 Can antiretroviral treatment cure HIV infection?

Unfortunately it cannot. However, antiretroviral treatment can dramatically improve the symptoms and clinical signs of HIV infection and allow the patient to remain healthy for many years. Antiretroviral treatment is the most important advance in the management of HIV infection and has changed the outcome of HIV infection from a rapidly fatal disease into a manageable chronic illness. To be effective, antiretroviral treatment must be taken every day for life.

**Antiretroviral treatment is the most important advance in the management of HIV infection and has changed the course from a rapidly fatal disease into a manageable chronic illness.**

**NOTE** In November 2003 the South African government agreed to the widespread introduction of antiretroviral treatment in the management of patients with HIV infection.

### STANDARDISED TREATMENT REGIMENS

#### 4-15 What approaches can be used for treating HIV infection?

The choice of which combination of antiretroviral drugs to use can be based on either an individualised or a standardised approach:
Initially an individualised approach was used where the most appropriate drugs were chosen to meet the needs of each patient. More recently a standardised approach has been used where all patients are started on the same drug combination, as is done with TB treatment.

4-16 What are the advantages of using a standardised regimen?

1. The standardised approach is safer, easier and simpler, with few serious side effects.
2. It is also affordable and effective.
3. Both healthcare workers and patients can learn how to use these drugs correctly and which side effects to be aware of. The education and training of healthcare workers and patients is much easier.
4. It limits the number of drugs that are used and makes it possible to monitor patterns of drug use and resistance. Monitoring for side effects is also simplified.
5. It is easier to buy and distribute a limited range of drugs.
6. Fixed-dose formulations (single tablets containing two or three antiretroviral drugs) may be used in the standardised approach.

A standardised regimen consists of a specific combination of antiretroviral drugs where the risk of drug interactions and side effects are low. The drug combination should target at least two sites in the life-cycle of HIV (i.e. important stages in the viral replication).

4-17 What are the disadvantages of an individualised approach?

Using different combinations of antiretroviral drugs is very complicated as each combination has its own risk of drug interactions. Some drugs counteract each other (block the function of the other drug). Some drug combinations have a higher risk of serious side effects. Therefore, a wide knowledge and experience of these drugs is essential if the individual approach is to be used. This ability is usually only available at antiretroviral clinics where particularly difficult management problems are referred.

4-18 What is a first-line combination?

This is the combination of three antiretroviral drugs which are routinely used when patients first start antiretroviral treatment. In South Africa the starting combination of antiretroviral drugs consists of two ‘nucs’ plus either a ‘non-nuc’ or a ‘PI’.

The first-line combination is the combination of three antiretroviral drugs which is used to start treatment in most children with HIV infection.

4-19 What is a first-line combination commonly used for children in South Africa?

This depends on the child’s age, body weight and whether there was exposure to nevirapine at birth:

1. For children younger than three years or weighing less than 10 kg in South Africa, the first-line combination is two ‘nucs’ together with a ‘PI’. Therefore the common combination for young children is ABC and 3TC plus lopinavir/ritonavir. Unless contraindicated, all these younger patients should be started on this regimen. This combination is chosen for its effectiveness and availability, few serious side effects and low cost. It also avoids nevirapine which is widely used in antiretroviral prophylaxis at birth. Children on d4T, without side effects, can be continued on d4T. Change to ABC if lipodystrophy is suspected.

In South Africa antiretroviral treatment for young children is usually started with a combination of ABC and 3TC plus lopinavir/ritonavir.

2. For children three years and older or weighing more than 10 kg, the first-line combination is two ‘nucs’ together with a
A combination of ABC, 3TC and efavirenz is used.

**Antiretroviral treatment for older children is usually started with a combination of ABC and 3TC plus efavirenz.**

_Note_ It is currently not known how long the nevirapine-resistant HIV remains after prophylaxis at birth. At present there is little information on the use of efavirenz in small children.

### 4-20 What is a second-line combination?

Patients who fail to respond to the first-line combination, despite good adherence, are changed to a second-line combination of antiretroviral drugs.

### 4-21 What common second-line combination is used for children in South Africa?

1. When treating children with HIV infection in South Africa, the second-line combination for those who have had ABC, 3TC and efavirenz is to change to AZT, ddi and lopinavir/ritonavir.
2. Children under three years old or children on a drug combination including lopinavir/ritonavir should be referred to a treatment expert.

**In South Africa the usual second-line combination for most children is AZT and ddi plus either nevirapine or efavirenz.**

Therefore both the first- and second-line combinations include two ‘nucs’. The choice of ‘nucs’ is changed from the first- to the second-line combinations. In addition, the choice of ‘non-nucs’ and ‘PIs’ are swapped around. All three drugs are changed. This ensures that there is the best chance that the child will respond to the new combination.

### 4-22 When are other combinations of antiretroviral drugs used?

Sometimes changes to the first- or second-line combinations are made when there are serious side effects to only one drug in a standardised regimen.

These changes (‘swaps’) should only be made by an experienced doctor at an antiretroviral clinic. Using individualised combinations reduces the future options of treatment.

Patients who have failed to respond to both first- and second-line combinations, despite good adherence, may be offered ‘salvage treatment’ with new drugs. Again, this decision must be made by an experienced doctor at an antiretroviral clinic.

### 4-23 What first-line antiretroviral drugs should be used if nevirapine is given after delivery?

If nevirapine is used alone, or in combination with AZT, for the prevention of mother-to-child transmission of HIV, the infant may be resistant to nevirapine and efavirenz for months after delivery. Therefore, these nevirapine-exposed infants should be given a first-line combination of ABC, 3TC and lopinavir/ritonavir. This is the current practice for all children under three years in South Africa as many HIV-exposed infants would have been given nevirapine after birth.

### ANTIRETROVIRAL MEDICATION

### 4-24 What are the practical implications of taking antiretroviral treatment?

The following questions must be considered:

1. Which medications are taken?
2. How much medication is taken at a time?
3. Is the medication taken as tablets, capsules or an oral suspension?
4. When and how often is the medication taken?
5. Should the medication be taken with or without food?
6. Can all the drugs be taken together at the same time?
7. Is the drug stable at room temperature?

4-25 How should antiretroviral drugs be given?

1. Children prefer to take the medication in a small volume of pleasant-tasting liquid. Otherwise pills which can be crushed or dissolved in water can be given with something sweet, such as jam, to hide any bitter taste. Unfortunately, many antiretroviral drugs are not child-friendly as they have been designed for adults.
2. The correct dose of each drug must be calculated. The most accurate method is to use body surface area (which is expressed as m²). Unfortunately this requires accurate weight and height measurements and a calculator to determine the dosage. Therefore weight bands are preferred from 3 kg upwards. For children below 3 kg, body weight is used to calculate the dose of most antiretroviral drugs.
3. The dose of each drug must be increased as the child grows and gains weight (however, the dose per kg or m² will stay the same).

4-26 How should abacavir be taken?

Abacavir (generic name ABC) is a ‘nuc’ (trade name is Ziagen). ABC can be taken with or without food. The dose is 8 mg/kg/dose twice daily. The oral solution contains 20 mg/ml.

ABC is replacing d4T, which has many serious side effects.

4-27 What are the weight bands for abacavir?

<table>
<thead>
<tr>
<th>Weight</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–6.9 kg</td>
<td>3 ml</td>
</tr>
<tr>
<td>7–9.9 kg</td>
<td>4 ml</td>
</tr>
<tr>
<td>10–13.9 kg</td>
<td>6 ml</td>
</tr>
<tr>
<td>14–16.9 kg</td>
<td>7 ml</td>
</tr>
<tr>
<td>17–19.9 kg</td>
<td>8 ml</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>10 ml</td>
</tr>
<tr>
<td>25 + kg</td>
<td>1 tablet</td>
</tr>
</tbody>
</table>

4-28 How should 3TC be taken?

3TC (generic name lamivudine) is also a ‘nuc’. 3TC is well tolerated and has very few side effects. Mild nausea, headache and diarrhoea may occur. 3TC can be taken with or without food. The dose is 4 mg/kg/dose twice a day.

1. An oral suspension is available for children weighing less than 14 kg. The concentration of the oral suspension is 10 mg/ml. The oral suspension is stable at room temperature.
2. For heavier children:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>14–19.9 kg</td>
<td>Half a tablet twice daily</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>1 tablet in the morning and half a tablet in the evening.</td>
</tr>
<tr>
<td>25 + kg</td>
<td>1 tablet twice daily.</td>
</tr>
</tbody>
</table>

3TC is well tolerated with few side effects.

4-29 How should an oral suspension of 3TC be given?

The oral suspension is usually made up by the clinic. The correct dose is as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–5.9 kg</td>
<td>3 ml</td>
</tr>
<tr>
<td>6–9.9 kg</td>
<td>4 ml</td>
</tr>
<tr>
<td>10–13.9 kg</td>
<td>6 ml</td>
</tr>
</tbody>
</table>
4-30 How should AZT be taken?

AZT (generic name zidovudine) is a ‘nuc’ (trade name is Retrovir). AZT has many short-term minor side effects such as fatigue, nausea and vomiting, headache, muscle pains and altered taste. These are common at the start of treatment but become less after a few weeks. The most important side effect of AZT is anaemia.

AZT can be taken with or without food. However, the risk of nausea may be less if taken with food.

**AZT may cause anaemia.**

The dose of AZT is 240 mg/m²/dose twice daily. However, a recent study has shown that the dose of AZT can be calculated per kg body weight. AZT is available in capsules and tablets.

An oral suspension has to be made for small children weighing less than 14 kg. As an AZT solution is stable, this is usually done by the clinic.

The standard dosing of AZT is as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–5.9 kg</td>
<td>6 ml (60 mg) twice daily</td>
</tr>
<tr>
<td>6–9.9 kg</td>
<td>9 ml (90 mg) twice daily</td>
</tr>
<tr>
<td>10–13.9 kg</td>
<td>12 ml (120 mg) twice daily or 1 capsule 100 mg twice daily</td>
</tr>
<tr>
<td>14–19.9 kg</td>
<td>2 capsules in the morning and 1 tablet in the evening</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>2 capsules twice daily</td>
</tr>
<tr>
<td>25+ kg</td>
<td>1 tablet twice daily</td>
</tr>
</tbody>
</table>

**Note:** For young children, capsules can be used to make an oral suspension which is stable at room temperature. If the contents of one capsule (100 mg) is added to 10 ml water, the oral suspension contains 10 mg AZT per ml.

4-31 How should ddI be taken?

ddi (generic name didanosine) is a ‘nuc’ (trade name is Videx). The correct dose is 120 mg/m²/dose twice daily but dosage is usually given by weight band. ddI is available as 25 mg, 50 mg and 100 mg tablets, which can be chewed or crushed. It is important to take at least two tablets at a time to ensure that there is enough antacid in the tablets to buffer the drug.

Unlike other antiretroviral drugs, ddI should not be taken with meals as food reduces the absorption of the drug. ddI should be taken at least 30 minutes before eating or two hours after eating. Therefore, ddI is usually not given at the same time as other antiretrovirals. To ensure good compliance it is important that parents be given a detailed explanation of why ddI needs to be taken on an empty stomach.

The standard doses of ddI in older children are as follows:

1. Children weighing 17 to 19.9 kg take two 50 mg tablets twice a day.
2. Children weighing 20 kg or more should take one 100 mg plus one 25 mg tablet twice daily.

Using ddI for smaller children is problematic as the dose is less than two tablets at a time. An oral suspension of ddI is available. However, this is not stable at room temperature but can be kept for 30 days in a fridge.

The standard doses of ddI in young children are:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–9.9 kg</td>
<td>2 x 25 mg tablets twice a day</td>
</tr>
<tr>
<td>10–10.9 kg</td>
<td>3 x 25 mg tablets in the morning and 2 x 25 mg tablets in the evening</td>
</tr>
<tr>
<td>11–13.9 kg</td>
<td>3 x 25 mg tablets twice daily</td>
</tr>
<tr>
<td>14–16.9 kg</td>
<td>2 x 50 mg tablets in the morning and 3 x 25 mg tablets in the evening</td>
</tr>
</tbody>
</table>

**Note:** The ddI suspension contains 10 mg/ml. An antacid or buffering agent is included in the suspension. When administering ddI tablets to children each dose MUST be made up of at least two tablets to ensure adequate buffering.
**ddI should not be taken with meals.**

**4-32 How should nevirapine be taken?**
Nevirapine (trade name Viramune) is a ‘non-nuc’. An introduction dose of nevirapine is given once daily in the evening for 14 days. This may cause a mild erythematous (pink) or measles-like rash. If no rash occurs, a maintenance dose is given twice daily.

Consult an antiretroviral clinic and do not increase the dose to twice daily if a mild rash is present. The drug must be stopped immediately if a severe rash appears as this can be dangerous. A severe rash is usually due to a hypersensitivity reaction and presents with blisters or target lesions on the skin, mouth ulcers, fever or being generally unwell.

**4-33 How should the introduction doses of nevirapine be given?**
The introduction dose is the same as the maintenance dose, but is given only once daily, not twice daily.

**4-34 How should the maintenance doses of nevirapine be given?**
1. For smaller children an oral suspension is used (10 mg/ml) daily. This is stable and need not be kept in a fridge. For children weighing less than 14 kg, the twice-daily dose is as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–5.9 kg</td>
<td>5 ml</td>
</tr>
<tr>
<td>6–9.9 kg</td>
<td>8 ml</td>
</tr>
<tr>
<td>10–13.9 kg</td>
<td>10 ml</td>
</tr>
<tr>
<td>14 to 24.9 kg</td>
<td>1 x 200 mg tablet in the morning and half a 200 mg tablet (i.e. 100 mg) in the evening</td>
</tr>
</tbody>
</table>

2. For older children tablets are used. The tablets can be snapped in half easily.
   - Children weighing between 14 and 24.9 kg should have half a 200 mg tablet (i.e. 100 mg) in the morning.

**4-35 How should efavirenz be taken?**
Efavirenz (trade name Stocrin) is also a ‘non-nuc’ and is very similar to nevirapine. Efavirenz, rather than nevirapine, is used in children as it has fewer severe side effects. Efavirenz also has the advantage of only needing a single daily dose, which is taken in the evenings. Like nevirapine, it is not used in children under three years old, especially those that have had nevirapine at birth. Efavirenz is available in 50 mg, 200 mg and 600 mg capsules.

The standard once-daily dose of efavirenz is as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–13.9 kg</td>
<td>1 x 200 mg capsule</td>
</tr>
<tr>
<td>14–19.9 kg</td>
<td>1 x 200 mg capsule plus 1 x 50 mg capsule</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>1 x 200 mg capsule plus 2 x 50 mg capsules</td>
</tr>
<tr>
<td>25–29.9 kg</td>
<td>1 x 200 mg plus 3 x 50 mg capsules</td>
</tr>
<tr>
<td>30–39.9 kg</td>
<td>2 x 200 mg capsules</td>
</tr>
<tr>
<td>40+ kg</td>
<td>1 x 600 mg capsule</td>
</tr>
</tbody>
</table>

**NOTE** There are no 100 mg capsules available.

A rash may occur. However, this side effect is less common and not as severe as with nevirapine. Efavirenz commonly causes mild emotional symptoms (mood changes, abnormal dreams, insomnia and dizziness) for the first few weeks. These are reduced if efavirenz is taken on an empty stomach in the evening, which slows down the absorption. When side effects have cleared, efavirenz should be taken with meals.

**Efavirenz is taken once a day.**
4-36 How should ‘PIs’ be taken?

Usually lopinavir and ritonavir are taken in combination as Aluvia (a trade name). Lopinavir/ritonavir is taken twice a day. The oral suspension should be kept in a cool place. The tablet is stable at room temperature. Lopinavir/ritonavir should be taken with food as this reduces the risk of nausea and diarrhoea which are common for the first few weeks. Lopinavir/ritonavir has a very unpleasant taste and is sometimes spat out or vomited by children. It may help to give the medication with fruit juice, milk, chocolate, jam or a banana. Repeat the dose if it is vomited within an hour.

Note: Tablets contain 200 mg of lopinavir and 50 mg ritonavir while the liquid formulation contains 80 mg of lopinavir and 20 mg ritonavir per 1 ml. A paediatric tablet containing 100 mg of lopinavir and 25 mg of ritonavir is currently being licensed. This will allow dosing with paediatric tablets from 10 kg.

The standard doses of lopinavir/ritonavir twice a day are as follows:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–3.9 kg</td>
<td>1 ml of oral suspension</td>
</tr>
<tr>
<td>4–9.9 kg</td>
<td>1.5 ml of oral suspension</td>
</tr>
<tr>
<td>10–13.9 kg</td>
<td>2 ml of oral suspension</td>
</tr>
<tr>
<td>14–19.9 kg</td>
<td>2.5 ml of oral suspension or 2 tablets (100/25 mg tablets)</td>
</tr>
<tr>
<td>20–24.9 kg</td>
<td>3 ml of oral suspension or 3 morning tablets and 2 evening tablets (100/25 mg tablets)</td>
</tr>
<tr>
<td>25–29.9 kg</td>
<td>3.5 ml of oral suspension or 2 morning tablets and 1 evening tablet (200/50 mg tablets)</td>
</tr>
<tr>
<td>30–34.9 kg</td>
<td>4 ml of oral suspension or 2 morning and 1 evening tablet (200/50 mg tablets)</td>
</tr>
<tr>
<td>35 kg and above</td>
<td>5 ml of oral suspension or 2 tablets twice daily (200/50 mg tablets)</td>
</tr>
</tbody>
</table>

4-37 Which antiretroviral drugs should be taken with meals?

Most antiretroviral drugs should be taken twice a day with meals. However, it is important that ddI is taken on an empty stomach, as food decreases the absorption of the drug. Parents need to understand this. The side effects of efavirenz are less if the drug is taken on an empty stomach in the evenings. Therefore it is best if efavirenz is taken without food for the first few weeks.

ddI should be taken on an empty stomach.

4-38 Should drugs be kept cool?

Most drugs can be kept at room temperature.

4-39 How should antiretroviral drug doses be calculated for very young children?

Sometimes children with a weight below 3 kg need antiretroviral treatment. These young children should be referred to a paediatric specialist who manages HIV-infected children. Drug doses must be increased with weight gain and therefore frequently need to be adjusted.

4-40 Do all antiretroviral drugs have side effects?

All antiretroviral drugs may have side effects (adverse effects or toxicity). However, some antiretroviral drugs have a lower risk of side effects than others. 3TC has the least side effects.

Remember that drugs used to treat HIV-associated infections may cause similar side effects, e.g. hepatitis with isoniazid and rash with co-trimoxazole.

Some of the clinical symptoms and signs of HIV infection or HIV-associated infections
Antiretroviral drugs may also be similar to the side effects to antiretroviral treatment. Other diseases may also mimic side effects, e.g. viral hepatitis may mimic liver toxicity.

All antiretroviral drugs may have side effects.

4-41 Do children have more side effects than adults?

No. Side effects are less common in children. Fortunately, most children do not have side effects to antiretroviral treatment.

Most children have no side effects to antiretroviral treatment.

While most side effects are mild, some may be severe. Side effects are graded into mild, moderate, severe and life threatening.

4-42 Should children and their parents be warned about side effects?

It is very important that both children and their families know the common side effects of the antiretroviral drugs that are being taken. It is also important that they know which side effects to look out for, especially the severe side effects. Educating children and parents about side effects is an important part of care. Parents should be able to monitor their children for side effects.

Children and parents should be educated about side effects.

Monitoring for side effects of antiretroviral drugs depends on the early detection of clinical signs and symptoms rather than routine blood tests.

4-43 What are the common mild side effects of antiretroviral drugs?

Tiredness, headaches, nausea and vomiting, abdominal pain and diarrhoea are common and may be caused by all classes of antiretroviral drugs. These side effects are usually mild and settle after the first few days or weeks. Taking antiretroviral treatment with food often helps reduce the common side effects.

However, side effects must always be reported to the staff at the HIV clinic. Usually children can continue with their antiretroviral drugs in spite of mild side effects. Sometimes other medication can be taken to help relieve these symptoms (e.g. paracetamol for headache and antiemetics for nausea and vomiting).

It is very important that patients with mild side effects are supported and understand that the side effects will disappear. Patients

---

**Table 4-1: Details of antiretroviral drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Generic name</th>
<th>Trade name</th>
<th>Frequency</th>
<th>With meals</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>abacavir</td>
<td>Ziagen</td>
<td>Twice daily</td>
<td>Yes</td>
</tr>
<tr>
<td>3TC</td>
<td>lamivudine</td>
<td>3TC</td>
<td>Twice daily</td>
<td>Yes</td>
</tr>
<tr>
<td>AZT</td>
<td>zidovudine</td>
<td>Retrovir</td>
<td>Twice daily</td>
<td>Yes</td>
</tr>
<tr>
<td>ddi</td>
<td>didanosine</td>
<td>Videx</td>
<td>Twice daily</td>
<td>No</td>
</tr>
<tr>
<td>d4T</td>
<td>stavudine</td>
<td>Zerit</td>
<td>Twice daily</td>
<td>Yes</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>nevirapine</td>
<td>Viramune</td>
<td>Twice daily*</td>
<td>Yes</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>efavirenz</td>
<td>Stocrin</td>
<td>Daily</td>
<td>Yes**</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>lopinavir/ritonavir</td>
<td>Aluvia</td>
<td>Twice daily</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Nevirapine should be taken daily for the first 14 days.
** Efavirenz is best taken on an empty stomach for the first few weeks.
must not stop antiretroviral treatment or fail to take their medication correctly because of mild side effects.

**NOTE** Severe vomiting or diarrhoea may cause dehydration as well as reduce absorption of medication.

### 4-44 When do most side effects occur?

Most side effects occur in the first six weeks of starting antiretroviral treatment. They usually get better on their own after a few days or weeks. However, some serious side effects may occur at any time that antiretroviral drugs are taken. Side effects that occur for the first time after months on treatment are often serious.

### 4-45 What serious side effects may occur with antiretroviral drugs?

1. Severe rash
2. Acute hypersensitivity
3. Hepatitis
4. Anaemia
5. Peripheral neuropathy
6. Wasting and accumulation of fat (lipodystrophy) often with raised serum lipid and glucose levels
7. Pancreatitits
8. Lactic (metabolic) acidosis
9. Severe vomiting or diarrhoea

Severe side effects should be reported immediately to the clinic.

### 4-46 What rashes occur commonly with antiretroviral drugs?

1. Mild rashes are common and include a localised or generalised erythematous (pink), maculopapular (measles-like) or urticarial rash with no other symptoms.
2. Severe rashes include any rash with blistering, peeling or involvement of the mucous membranes of the mouth and conjunctiva. These children are usually ill with a fever. Severe rashes can be fatal and, therefore, must be taken seriously.

Rashes are usually caused by ‘non-nucs’ especially nevirapine. These rashes almost always occur in the first six weeks of treatment. They are due to a hypersensitivity reaction.

**Nevirapine can cause a severe skin rash.**

Remember that HIV infection itself and drugs used to treat HIV-associated infections (especially co-trimoxazole) also commonly causes rashes. Therefore the rash may not be due to the antiretroviral drugs.

**NOTE** Severe rashes may progress to Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Constitutional symptoms such as fever are also present and warn of a dangerous side effect. Always look for hepatitis with severe side effect.

### 4-47 How should skin rashes be managed?

Nevirapine is started at a daily dose only for the first 14 days as this reduces the risk of a rash. Continue treatment if the rash is mild. However, do not increase the dose to twice a day until any rash has settled.

All patients with a severe rash must be referred to hospital urgently. Stop all three antiretroviral drugs immediately. Usually nevirapine is swapped for lopinavir/ritonavir if a severe rash develops. These patients must never be given a ‘non-nuc’ again.

**All drugs should be stopped immediately if a severe rash occurs.**

**NOTE** Steroids and antihistamines do not help most hypersensitivity rashes caused by nevirapine.

### 4-48 What is acute hypersensitivity?

Acute hypersensitivity is a severe reaction to a drug. Features of acute hypersensitivity include fever, muscle pain (myalgia), joint pain (arthralgia), flu-like symptoms, abdominal symptoms and hepatitis with or without a maculopapular rash. Acute hypersensitivity reactions can be fatal and are an indication for immediately stopping all drugs and urgent referral to hospital. Although uncommon,
nevirapine and ABC are the main causes of acute hypersensitivity reactions.

4-49 Which antiretroviral drugs cause hepatitis?

All classes of antiretroviral drugs can cause hepatitis. However, nevirapine is the drug which is usually associated with severe hepatitis. Like a severe rash, this is due to a hypersensitivity reaction. Efavirenz, the 'nucs' and 'PIs' rarely cause hepatitis.

Liver function tests (ALT) should be done on all patients when nevirapine is started and then repeated at two, four and eight weeks and then every six months as hepatitis usually occurs during the first few weeks of treatment.

Hepatitis is usually caused by nevirapine.

**Note** Nevirapine causes asymptomatic hepatitis in 10% and clinical hepatitis in 1% of adults. Nevirapine plus TB treatment increases the risk of severe rash and hepatitis. Co-trimoxazole may rarely cause hepatitis. 'Nucs' may cause a fatty liver (steatosis).

4-50 What are the clinical signs of hepatitis?

Hepatitis is usually asymptomatic when it is diagnosed by finding raised liver enzymes in the blood without any clinical signs. It may, however, present with typical clinical features of hepatitis (nausea, loss of appetite, jaundice, enlarged tender liver, itching and abdominal pain), usually in the first eight weeks of treatment.

Patients with asymptomatic hepatitis and mildly or moderately raised liver enzymes (up to five times the upper limit of normal) can be followed clinically without stopping the drugs. Their liver functions should be monitored regularly. The hepatitis usually resolves. Using a low dose of nevirapine for the first two weeks lowers the risk of hepatitis (and rash).

Patients with clinical hepatitis or asymptomatic hepatitis with markedly raised liver enzymes should be urgently referred to hospital. Stopping all treatment may be considered.

Pancreatitis (inflammation of the pancreas) may also present with abdominal pain and vomiting. It is a severe complication of d4T and ddi, especially when they are used together. Pancreatitis is less common in children than in adults on antiretroviral treatment.

4-51 Is anaemia a common problem with antiretroviral drugs?

Anaemia (Hb below 10 g/dl) is only seen in some children receiving AZT. With severe anaemia, these children may appear pale and feel weak and dizzy. However, anaemia is usually mild and the AZT need not be stopped.

A full blood count should be done when AZT is started and then be repeated at four, eight and 12 weeks and then every six months. Patients with a haemoglobin concentration (Hb) below 8 g/dl due to AZT should be referred to an HIV specialist. It is important to monitor the Hb in patients receiving AZT.

Anaemia is an important side effect of AZT.

**Note** With severe anaemia (haemoglobin less than 6.5 g/dl) it is important to stop AZT. A blood transfusion may be needed. Patients with a Hb between 6.5 and 8 g/dl should be closely followed. AZT also causes neutropenia but does not lower the platelet count.

4-52 What is peripheral neuropathy?

This is a problem which affects the peripheral nerves, especially in the legs. It presents with pain, numbness and abnormal sensation in a 'glove and stocking' distribution. Most patients with peripheral neuropathy present with painful feet at night.

Like pancreatitis, peripheral neuropathy is usually caused by 'nucs' which have a 'd' in their names, e.g. ddi and d4T. These drugs should not be used together as this increases the risk of peripheral neuropathy. Children with signs or symptoms of peripheral neuropathy must be referred to an HIV specialist. Other drugs, such as INH, may also cause peripheral neuropathy.
d4T and ddI are associated with both pancreatitis and peripheral neuropathy, especially if they are used together.

4-53 Which drugs may cause lactic acidosis?

Lactic acidosis is a rare but serious and potentially fatal side effect caused by ‘nucs’, particularly d4T and ddI (again ‘nucs’ with a ‘d’ in their names). Therefore these drugs must never be used together, and d4T is being phased out. It usually only occurs more than six months after antiretroviral treatment has been started. Patients with lactic acidosis present with a gradual onset of weight loss, tiredness, weakness and abdominal complaints (nausea, vomiting, abdominal pain or discomfort). Muscle pain (myalgia), respiratory distress (increased respiratory rate) and liver dysfunction (enlarged liver, liver tenderness and jaundice) may also develop. If lactic acidosis is suspected, the patient must be urgently referred to hospital for blood tests to confirm the diagnosis.

If symptomatic lactic acidosis is confirmed, all antiretroviral drugs should be stopped immediately. Always suspect lactic acidosis if patients who have been well, taking their medications correctly and been gaining weight for months, suddenly start to lose weight.

Table 4-2: Summary of side effects of antiretroviral drugs

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>‘Nucs’</strong></td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td>Few side effects. Uncommonly headache and nausea</td>
</tr>
<tr>
<td>AZT</td>
<td>Commonly headache, nausea and vomiting, anaemia and neutropenia Rarely muscle pain and lactic acidosis</td>
</tr>
<tr>
<td>ABC</td>
<td>Uncommonly rash, fever, respiratory and abdominal symptoms</td>
</tr>
<tr>
<td>ddI</td>
<td>Commonly nausea, vomiting, abdominal pain Uncommonly peripheral neuropathy, pancreatitis and lactic acidosis</td>
</tr>
<tr>
<td>d4T</td>
<td>Commonly headache, rash and nausea Rarely peripheral neuropathy, pancreatitis and lactic acidosis</td>
</tr>
<tr>
<td><strong>‘Non-nucs’</strong></td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Commonly mild rash, headache, nausea, vomiting and diarrhoea Uncommonly severe rash and hepatitis</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Commonly mild skin rash, sleep and emotional disturbances or psychiatric symptoms</td>
</tr>
<tr>
<td><strong>‘PIs’</strong></td>
<td></td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>Commonly nausea, vomiting, diarrhoea, hypercholesterolaemia and triglyceridaemia Rarely pancreatitis, hyperglycaemia and lipodystrophy</td>
</tr>
</tbody>
</table>
deposits) with hepatomegaly is commonly seen with lactic acidosis. Hyperlactaemia is defined as a serum lactate above 2 mmol/l.

4-54 What is lipodystrophy?

Lipodystrophy is an abnormal distribution of subcutaneous fat resulting in a change in body shape. Fat is lost (fat atrophy) from the face and limbs and gained (fat accumulation) over the abdomen, back of the neck and breasts. Unfortunately lipodystrophy usually does not recover when the antiretroviral drugs are stopped. Lipodystrophy is usually associated with ‘PIs’ and was also seen with d4T. Patients with lipodystrophy should be referred to an HIV specialist for management.

**Note** Lipodystrophy may be caused by ‘PIs’ but other antiretrovirals and genetic factors may also contribute. Children between the ages of 10 and 15 years are at a greater risk for lipodystrophy, suggesting that physiological changes during puberty may also contribute.

4-55 Should antiretroviral drugs be stopped if there are severe side effects?

It may be necessary to stop an antiretroviral drug if severe side effects occur, e.g. severe rash with nevirapine. If this is done all drugs must be stopped together. Stopping just one drug may lead to resistance of the remaining two drugs.

The drug combination must now be carefully examined as the problem drug may have to be swapped for another drug (e.g. swap nevirapine for lopinavir/ritonavir) or a totally different combination may be needed. Changing drugs must always be done by an HIV expert. HIV infection must never be treated with only one or two drugs. A full combination of three drugs is always needed.

**Never stop one drug and only give antiretroviral treatment with two drugs.**

**Case Study 1**

A one-year-old child with stage 3 HIV infection and a very low CD4 percentage is started on first-line antiretroviral treatment with ABC, 3TC and lopinavir/ritonavir. The mother asks how these drugs should be taken and whether they cause side effects.

1. What is first-line treatment?

This is a standardised combination of antiretroviral drugs which are used when antiretroviral treatment is first started. It is safer, easier, simpler and cheaper than individualised treatment. Patients and staff can be taught to understand and manage this drug combination.

2. What class of drugs are ABC and 3TC?

They are both ‘nucs’. These drugs prevent HIV from taking control of CD4 cells. The generic name for ABC is abacavir while that for 3TC is lamivudine. The trade name for ABC is Ziagen.

3. What class of drugs are lopinavir and ritonavir?

These are both ‘PIs’ which act together to prevent the infected CD4 cells from releasing new copies of HIV into the blood.

4. How should these three drugs be taken?

They should be taken twice daily (12-hourly) by mouth. It is best if they are taken with food.

5. What drug preparations are available?

A suspension for small children and capsules or tablets for older children and adults.
6. Are there common mild side effects of antiretroviral drugs?

There is a risk of side effects with all antiretroviral drugs. These are usually mild and settle after a few weeks. Nausea, vomiting, abdominal discomfort and diarrhoea are not uncommon with most drugs. These side effects are less if the medication is taken with food.

**CASE STUDY 2**

A five-year-old child is started on antiretroviral treatment with ABC, 3TC and nevirapine. After two weeks of treatment she develops a mild erythematous rash but is otherwise well.

1. **What class of drug is nevirapine?**
   Nevirapine and efavirenz are both ‘non-nucs’.

2. **Is a mild skin rash common with nevirapine?**
   Yes. This is a common side effect. It can often be prevented by giving nevirapine only once a day for the first 14 days. If there is no rash after two weeks of treatment, the dose can be increased to twice daily. Do not increase the dose until any rash has cleared.

3. **Can nevirapine cause a severe skin rash?**
   Yes. This is an important and potentially dangerous side effect. A severe rash presents with blistering, peeling or involvement of the mucous membranes. These children are usually ill with a fever and must be urgently referred to hospital. Nevirapine can also cause hepatitis. Both these severe side effects are less common with efavirenz.

4. **How is the diagnosis of hepatitis made?**
   The clinical signs and symptoms of hepatitis are nausea, loss of appetite, itching, jaundice and an enlarged tender liver. Hepatitis may be asymptomatic. The diagnosis can be confirmed by finding a raised serum concentration of liver enzymes (e.g. ALT).

5. **How should children with drug-induced hepatitis be managed?**
   The antiretroviral treatment can be continued in children with asymptomatic hepatitis and only mildly raised ALT (up to five times the upper limit of normal). They should be followed clinically and the hepatitis usually resolves. Children with symptomatic hepatitis or a markedly raised ALT must be urgently referred to hospital.

**CASE STUDY 3**

After failing first-line treatment despite good adherence, a young boy is started on second-line treatment with AZT, ddI and lopinavir/ritonavir. The treatment is well tolerated and after a month he is gaining weight.

1. **What important side effect is seen with AZT?**
   Anaemia.

2. **Should ddI be taken with food?**
   No, as this reduces absorption of the drug. ddI should be taken at least 30 minutes before food or two hours after food.

3. **Do children have more side effects than adults to antiretroviral drugs?**
   No. Most children have few or no side effects. However, it is important that parents are aware of the important side effects so that they can be detected as soon as possible.

4. **When do most side effects occur?**
   In the first six weeks of treatment. However, some severe side effects can occur much later.

5. **What is lipodystrophy?**
   This is an abnormal distribution of fat with change in body shape. Fat is lost from the face and limbs and gained over the abdomen, back and breasts. The ‘PIs’ such as lopinavir/
ritonavir contribute to the development of lipodystrophy.

**CASE STUDY 4**

A child of eight years with symptomatic HIV infection is placed on individualised treatment with ABC, ddi and lopinavir/ritonavir in private practice. His weight is 27 kg. Initially he responds well to treatment. However, after four months he starts to lose weight, complains of abdominal pain, nausea and vomiting. The ddi is stopped and the ABC and lopinavir/ritonavir continued.

1. **What important side effect may present with these symptoms?**
   Lactic acidosis. This is a rare but serious and potentially fatal side effect.

2. **Which drugs are usually the cause?**
   ‘Nucs’, especially ddi. Lactic acidosis is most common if ddi and d4T are used together. Therefore this is a combination that must not be used, and d4T is best avoided. An incorrect mix of drugs is one of the risks of using individualised rather than standard combinations of antiretroviral drugs.

3. **Why has this side effect presented so late?**
   Lactic acidosis typically appears many months after treatment has started when patients, who have been well and gaining weight, suddenly start to lose weight.

4. **What mistake has been made in the management of this side effect?**
   All drugs should have been stopped and the child should have been transferred urgently to hospital. One drug alone should not be stopped as drug resistance can develop to the two remaining drugs. Either the problem drug should be swapped for another drug or the whole combination should be changed. This decision must be made by an HIV expert.

5. **What dangerous side effects may be due to ‘nucs’?**
   - Peripheral neuropathy
   - Pancreatitis
   - Lactic acidosis

6. **How is the dose of antiretroviral drugs calculated?**
   The dose depends on the child’s weight. Usually a fixed dose is given for each weight range (weight bands). For example, the dose of 3TC in a child weighing 25 kg or more is one tablet (150 mg) twice a day.
Management of children with antiretroviral treatment

Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you’ve worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:
- Understand the importance of antiretroviral treatment.
- List the criteria for starting antiretroviral treatment.
- Prepare a child and family for antiretroviral treatment.
- Describe what is done at the first few treatment visits.
- Care for a child on antiretroviral treatment.
- Monitor the clinical and immunological response to treatment.
- Promote excellent adherence.
- Detect and manage problems with treatment.

5-1 What are the benefits of antiretroviral treatment?

Once the immune system has been severely damaged by HIV infection, and the disease has reached stage 3 or 4, only antiretroviral treatment can control and reverse the disease process. Without antiretroviral treatment most of these children will die within a few months.

Antiretroviral treatment (highly active antiretroviral treatment or HAART) can change HIV infection from a rapidly fatal disease to a manageable, chronic illness.

Only antiretroviral treatment can change AIDS from a rapidly fatal disease to a manageable chronic illness.

5-2 What can antiretroviral treatment achieve?

1. The child should feel well again and have few HIV-related illnesses. Growth and mental development should improve or be normal.
2. The CD4 percentage should increase and remain above the baseline level.
3. The viral load should become undetectable and remain undetectable.
With antiretroviral treatment the child should feel well again.

5-3 For how long will these children need to remain on antiretroviral treatment?
For life. Antiretroviral treatment can control HIV infection but not cure it.

**CRITERIA FOR ANTIRETROVIRAL TREATMENT**

5-4 What are the criteria for starting antiretroviral treatment?
All children under 12 months of age with confirmed HIV infection should be started on antiretroviral treatment irrespective of their clinical or immunological stage, as they are at high risk of rapid progress of their disease and early death.

All HIV-infected children below 12 months should be started on antiretroviral treatment.

The criteria for starting older children on antiretroviral treatment are:

1. Clinical (clinical staging)
2. Immunological (CD4 count)
3. Social (home and family circumstances)

Either the clinical or immunological criteria must be met before starting antiretroviral treatment in children of 12 months or more. Every effort should also be made to meet the social criteria. If the clinical or immunological criteria are not yet met, the child should be carefully followed up with regular monitoring of the clinical stage and CD4 count.

Either clinical or immunological criteria can be used to indicate the need for antiretroviral treatment in children aged one year or older.

In children with HIV infection it is better to start antiretroviral treatment earlier than later.

5-5 What are the clinical criteria?
All children with stage 3 or stage 4 disease should be started on antiretroviral treatment even if their CD4 count is not severely depressed or if a CD4 count is not available. Recurrent hospital admissions (more than two per year) or prolonged hospital admissions (more than four weeks) strongly suggest that the child needs antiretroviral treatment. It is important to follow the current national protocol for starting antiretroviral treatment.

Clinical stage 3 or 4 HIV infection alone is an indication for antiretroviral treatment.

**NOTE** In children with stage 1 or 2 disease the decision to start antiretroviral therapy should be based on their CD4 percentage or count. In resource-poor areas, all HIV-infected children needing antiretroviral treatment on medical criteria should be considered even if immunological tests are not available.

5-6 What are the immunological criteria?
The development of age-related severe immunodeficiency i.e.:

1. All children under 12 months should be started on antiretroviral treatment even if the CD4 percentage is normal.
2. Children aged 12 to 59 months: CD4 percentage on or below 25% or CD4 count on or below 750 cells/μl.
3. Children aged five years and older: a CD4 count on or below 350 cells/μl.

The immunological criteria indicate how severely the immune system has been damaged by HIV. Therefore, it is a very useful measure of when best to start antiretroviral treatment.

To simplify the immunological criteria, CD4 percentage is usually used under the age of five years. From five and older a CD4 count should be used to decide when to start antiretroviral treatment.
5-7 What are the social criteria?

1. It is essential that there is at least one responsible adult (parent or care giver) who can administer the antiretroviral medication.
2. The responsible parent or care giver must be ‘treatment ready’.
3. It is strongly recommended that the responsible parent or caregiver reveal the child’s HIV status to at least one other family member or friend who can give support. It is best to have a treatment supporter in the home.
4. The child and responsible parent or care giver must be able to attend an antiretroviral centre on a regular basis. It may be necessary to arrange transport.

The social criteria should be met before starting antiretroviral treatment.

If the social criteria are not met, there is little chance that medication will be given regularly. As a result antiretroviral treatment is likely to fail. A social worker should help if the social criteria cannot be met.

PATIENT READINESS

5-8 Who usually refers a child for antiretroviral treatment?

The staff at a primary-care clinic or HIV clinic where the child has been followed up. The child should be referred when the criteria for antiretroviral treatment have been met. Many children with HIV infection are admitted to hospital with HIV-associated infections such as diarrhoea and pneumonia. These children should be assessed and, if necessary, also referred for antiretroviral treatment.

5-9 Where should antiretroviral treatment be started?

Ideally at a local antiretroviral clinic. However, some children who have been admitted to hospital need to start antiretroviral therapy during their admission. Children should be referred to an antiretroviral clinic when they are ready for discharge from hospital. An antiretroviral clinic is staffed by nurses and doctors who have had special training in the correct use of antiretroviral drugs and the correct management of children receiving these drugs.

NOTE Children below the age of six months, or with a weight below 3 kg should ideally be started on antiretroviral therapy by an experienced doctor or nurse.

5-10 What is patient readiness?

Patient readiness means that the child’s parent or caregiver has been fully prepared for antiretroviral treatment to start. If this preparation is not correctly planned and done properly, then antiretroviral treatment is unlikely to be successful due to poor adherence (compliance). Therefore, patient readiness is very important and is needed before antiretroviral treatment can be started. With a family-oriented approach to HIV infection, the whole family should become involved with patient readiness.

5-11 What are the aims of preparing for antiretroviral treatment?

1. The parent (or care giver) must have a good understanding of HIV infection.
2. The importance of excellent adherence must be understood and accepted.
3. The names, dosing and timing of the antiretroviral agents must be learned.
4. The risk and symptoms of possible side effects must be known.
5. Disclosure to a family member or friend is needed.
6. The importance of regular follow-up care must be accepted.
5-12 How long does it usually take to prepare for antiretroviral treatment?

It usually takes about four weeks. If the parents are not yet 'treatment ready' the start of antiretroviral treatment may have to be postponed.

5-13 What visits are needed before antiretroviral treatment is started?

Usually two visits to the antiretroviral clinic are needed before treatment can be started:

1. **The first screening visit** (often called the week –4 visit). This visit is usually the parent and child's first contact with the staff of the antiretroviral clinic.
2. **The second screening visit** (often called the week –2 visit). The first and second visits are used to prepare and assess whether the parent/care giver is ready for the treatment to start.

Following the two screening visits, the 'start of treatment' visit can be planned (often called the week 0 visit).

### PREPARATION FOR ANTIRETROVIRAL TREATMENT

#### 5-14 What should be done at the first screening visit?

The child and parents (or caregiver) are usually referred to the antiretroviral clinic with a referral letter from the primary-care clinic. They should be seen by a doctor at the first screening visit.

1. Check that the diagnosis of HIV infection is correct by measuring the viral load.
2. Make sure that the clinical and immunological criteria for antiretroviral treatment have been met.
3. Take a careful history and perform a physical examination of the child.
4. Measure and plot the child's weight, height (or length) and head circumference, and assess the developmental level.
5. Complete the information record form.
6. Speak to the parents or the person who will be responsible for giving the medicine and bringing the child for follow-up visits.
7. Arrange for readiness education and counselling. This is often done in a group session. Ideally the parents and child should meet the multidisciplinary team of doctors, nurses and counsellors.
8. Exclude tuberculosis. This requires a careful history including TB contacts, a sputum examination and Mantoux skin test.
9. Assess whether there has been good adherence with co-trimoxazole prophylaxis. Count the tablets or measure the volume of medication remaining in the bottle.
10. Take blood for baseline investigations: a full blood count or Hb, and ALT if nevirapine is to be used.
11. Make an appointment for the second screening visit.
12. Following the first screening visit, a home visit by a counsellor is recommended before starting antiretroviral treatment. Unfortunately this may not be possible due to limited counsellor support. Home visits may be difficult if hospital-based programmes are far from the child's home.

#### 5-15 What should be looked for during the physical examination?

1. Assess the child's general health.
2. Determine the nutritional status.
3. Confirm the clinical stage.
4. Look for signs of HIV-associated conditions, especially tuberculosis.

#### 5-16 What is the importance of a home visit?

If possible, a home visit by a counsellor should be done to:

1. Make sure that the contact address is correct.
2. Assess the home circumstances.
3. Determine what support there is at home and whether there has been disclosure.
4. Find out where the medicines will be stored.

**A home visit is an important part of preparing for antiretroviral treatment.**

### 5-17 What education is needed?

It is essential that the parents (or guardians) fully understand HIV infection as well as why the child needs treatment and how the treatment should be correctly given. The same applies to older children.

The parent needs to:

1. Understand what HIV infection is.
2. Understand what antiretroviral treatment is.
3. Know the names and appearance of the antiretroviral drugs to be used.
4. Know the dose and how to give these drugs correctly.
5. Know the symptoms and signs of the possible side effects.
6. Know about the common HIV-associated infections.
7. Know that a good diet is important.
8. Know to store the drugs safely in a place where young children cannot reach.

It is particularly important that the parents accept that excellent adherence is essential, resistance is dangerous, and that failure of treatment and development of resistance are usually due to poor adherence.

**Parents need to know about the drugs that their child will be taking.**

### 5-18 How is education provided?

1. During individual counselling sessions
2. In group education classes
3. With pamphlets on HIV infection and antiretroviral treatment
4. Posters and videos are helpful
5. A treatment chart illustrating the drugs, timing of doses and possible side effects

**Usually two education classes are attended before the second screening visit**

### 5-19 What counselling is needed?

Counselling is important so that parents (and older children) are emotionally ready for antiretroviral treatment and have the home and social support needed for successful management. The parents may need help in accepting the family’s HIV status and the importance of antiretroviral treatment. They may also have difficulty disclosing the HIV status and finding someone who can support them. All parents preparing for antiretroviral treatment should be encouraged to join a support group. They often need an opportunity to talk about their fears and concerns.

Counselling empowers parents to make the best decisions for themselves and their child. It helps them understand, accept and make choices. Trained lay counsellors are very important members of the treatment team and play an important role in parent counselling.

**Disclosure and support are needed for successful treatment.**

### 5-20 What baseline blood tests are needed?

1. The baseline CD4 percentage is usually done before the patient is referred for treatment consideration and, therefore, need not be repeated. If the CD4 percentage was not measured, this should be done.
2. A baseline viral load should also be done.
3. Blood should be taken for baseline full blood count. Serum ALT (alanine transaminase) should also be measured if nevirapine is to be used.

**A baseline CD4 count and viral load is needed before antiretroviral treatment is started.**

### 5-21 What should be done at the second screening visit?

1. The clinical assessment should be repeated.
2. Get the baseline blood results and
the screenings tests for TB (sputum
examination and Mantoux skin test).
3. Consider the counsellor’s feedback report
plus the report of the home visit, if these
have been done.
4. The important of adherence and regular
attendance is stressed.
5. Assess whether the co-trimoxazole
medication has been taken correctly.
6. Make sure that education has been
provided.

Following the second visit the details
of the child should be discussed by the
multidisciplinary team to decide whether
treatment readiness has been achieved.

MANAGING ANTI-
RETROVIRAL TREATMENT

5-22 Who are the members of the multi-
disciplinary team at the antiretroviral clinic?

1. The doctor or nurse practitioner, who
should take a history and perform a
general examination at the first treatment
visit and again at the follow-up visits.
2. The nurse, who should see the patient to
complete the treatment register and take
the necessary blood samples. The nurse
should also check adherence at every visit.
3. The counsellor/educator, who should see the
patient at every visit. Trained lay educators
and counsellors often help at the clinic.
4. The pharmacist, who should provide the
antiretroviral drugs and advise the patient
on how to take them every time medicines
are dispensed.

The role of each member of the multi-
disciplinary team may vary between different
clinics.

5-23 What should be done
at the starting visit?

This is the visit when antiretroviral treatment
is started (i.e. the starting or commencement
visit). The child and parents (or carer) should
already have been prepared for antiretroviral
treatment at two screening visits. A decision
would already have been made that the child
and parents are ‘treatment ready’ and baseline
blood tests done. A final check is made that
the parents are fully prepared for treatment. At
the starting visit the following should be done:

1. An assessment of the co-trimoxazole
medication is done once more to assess
adherence (compliance).
2. The importance of excellent adherence is
again stressed by the counsellor.
3. The child and parent see the doctor
or nurse for the final instructions and
support. A detailed description of the
drugs and their doses are given by the
doctor or nurse using a treatment chart. A
graphic treatment chart is very useful and
should be given to the parents.
4. The child’s details are entered into the
antiretroviral treatment register.
5. An HIV summary record is started which
will be kept by the clinic and updated on
the child’s notes at each visit. Examination
notes from the two screening visits should
be included.
6. The instructions and dosing are reinforced
by the nurse. The instructions must be
clearly written on the pill container or
medicine bottle with a permanent marker.
7. The parent is given a two-week supply of
drugs by the pharmacist.

Each person in the team makes sure that the
parents understand which medicines are to
be given, how much and when. They also
check that the parent knows the side effects of
the drugs to be taken and the importance of
excellent adherence.

In some services, parents or caregivers are
given a patient-carried HIV treatment card.

5-24 When should the first
follow-up visit be planned?

The child should be brought back after two
weeks. If there are any problems the child
should be brought back earlier.
5-25 What should be done at the first follow-up visit?

The most important reasons for the child attending this visit are to assess adherence and check for side effects.

1. Repeat the history and examination. Be aware of symptoms and signs of side effects of the medication.
2. Measure and plot the child’s weight.
3. Check the drug doses and assess how much medication has been taken. This is important to determine adherence. Make sure that the medication schedule is understood and that all the drugs are being given in the correct dose and at the correct time.
4. The importance of excellent adherence must be stressed.
5. Treat any infections or other medical problems.
6. Provide medication and make an appointment for four weeks later.

5-26 What should be done at the second follow-up visit?

The second follow-up visit should take place four weeks after starting antiretroviral treatment. Again adherence and side effects must be assessed.

1. Repeat the history and examination. Be aware of symptoms and signs of side effects of the medication.
2. Measure and plot the child’s weight.
3. Check the drug doses and assess how much medication has been taken.
4. Stress the importance of excellent adherence.
5. Manage any new medical problem.
6. Take blood for a full blood count (if on AZT) and ALT (if on nevirapine). These results must be reviewed and the child recalled if they are abnormal.

5-27 What further follow-up visits are needed?

1. The child should be seen again at eight weeks (two months) and then 12 weeks (three months) after starting treatment.
2. The next visit usually is at six months after starting treatment. However, more frequent visits (monthly or every three months) may be needed for some children who are still unwell.
3. A full blood count should be done at one, two and three months, and then annually, for children on AZT.
4. Repeat ALT in children on nevirapine only if rash or jaundice appears.

Parents must be able to bring their child back at any time if they are concerned or if a new problem appears. They must not wait until the next scheduled visit.

5-28 How often should medication be collected?

Medicines still need to be collected every month. A careful record in the antiretroviral treatment register must be kept of all medication given. Excellent adherence must be stressed every time medication is collected. It is important to check how much medication has been returned and not taken. A missed medication visit suggests poor adherence.

5-29 What should be done at the six month visit?

In addition to the routine checks (history, examination, weight), it is very important to make a formal assessment of treatment success or failure.

1. Assess growth by measuring and plotting weight, height and head circumference.
2. Grade the clinical stage of HIV infection and assess whether the child is clinically well.
3. Take blood for CD4 percentage or count and viral load.
5-30 What is the expected clinical response to antiretroviral treatment?

With successful treatment children should start to feel and look well again. Most children will develop a good appetite and gain weight. Associated infections such as thrush and diarrhoea disappear and skin rashes clear up. The clinical response follows the gradual recovery of the immune system. By three months there should be a big difference in their general health.

5-31 What change should take place in the CD4 percentage by six months?

The CD4 percentage usually increases above the baseline level.

5-32 What should the viral load be by six months?

If the response to antiretroviral treatment is good, the viral load is usually less than 400 copies/ml (i.e. an undetectable viral load) by six months.

NOTE Some infants will respond well both clinically and immunologically without full suppression of the viral load. In these children the viral load at the start of treatment is often very high and the fall in viral load is slow. However, the drop in viral load should be at least 1 log value (a factor of 10).

5-33 What is the best indicator of treatment success?

An undetectable viral load.

An undetectable viral load is the best indicator of successful treatment.

NOTE An undetectable viral load is less than 400 cells/ml on the sensitive and less than 50 cells/ml on the more expensive (supersensitive) assay.

5-34 When can the child be transferred to the local community clinic?

If the child is relatively well, antiretroviral treatment can usually be managed at a clinic in the community in which the child lives. Sick children who are started on antiretroviral treatment in hospital should be referred to their community clinic for ongoing care as soon as they are clinically stable, usually within six months after starting treatment. A small proportion of children have complex problems or severe HIV-related complications. These children are best managed by an experienced paediatrician, usually at a hospital-based antiretroviral clinic.

Antiretroviral management is being offered at more and more community clinics as the ‘roll-out’ programme continues. Most of the children can be managed by nurses trained in antiretroviral care.

5-35 For how long can treatment remain successful?

Children who achieve an undetectable viral load and who maintain excellent adherence should remain well for many years. However, the average time before treatment fails has not yet been established in resource-poor settings.

NOTE Clinical trials in children have shown that between 63 and 87% achieve undetectable viral loads under optimal care conditions. Therefore, some children will never become fully virologically suppressed and they are likely to fail antiretroviral treatment much sooner.

Antiretroviral treatment can be successful for many years.

5-36 What additional visits are needed?

The child should be seen at nine and 12 months (one year) after starting treatment. If the child is well and the blood tests are normal, the child can be seen every three months.

1. At the one year visit a CD4 percentage or count and viral load should be measured.
2. The random lipid profile should also be done if the child is receiving lopinavir/ritonavir. This must be repeated annually. If the random lipid profile is abnormal, a fasting lipid profile should be done.
Abnormalities on a fasting lipid profile should be discussed with a doctor experienced in the care of children on antiretroviral therapy.

3. Measure a full blood count if the child is receiving AZT.
4. A neurodevelopmental assessment must be done at one year and then repeated annually.

**5-37 When can co-trimoxazole prophylaxis be stopped?**

The prophylaxis in children on antiretroviral treatment should only be stopped when there is good evidence that the immune function is recovering well. It is suggested that co-trimoxazole in children be stopped when antiretroviral treatment has provided the following improvement in CD4 percentage:

1. Children aged one to five years have a sustained CD4 percentage of 25% or more.
2. Children aged six years or more have a sustained CD4 percentage of 25% or more or a CD4 count of 250 cells/µl.
3. Children started on antiretroviral treatment soon after birth should remain on co-trimoxazole prophylaxis.

**ADHERENCE**

**5-39 What is adherence?**

Adherence (or compliance) is the degree to which patients take their antiretroviral drugs correctly.

**5-40 What is excellent adherence?**

Excellent adherence is taking all the medication correctly every day. With excellent adherence, 95% of all doses must be taken (i.e. 19 out of 20 doses). This means that not more than three doses can be missed in a month. It is also important that the doses are taken at the same time each day. Taking all the drugs at the correct dose and at the correct time each day is very important if antiretroviral treatment is going to be successful. Antiretroviral treatment can suppress the viral load reliably only if adherence is excellent.

**5-41 What is poor adherence?**

Poor adherence is missing doses or taking doses at the wrong time. Any adherence of less than 95% is not good enough (i.e. poor). Even adherence of 80 to 95% may be inadequate.
5-42 What are the dangers of poor adherence?

1. Drug resistance
2. Treatment failure
3. Increased morbidity and mortality

Every effort must be made to ensure excellent adherence. Without excellent adherence the progression of HIV will not be stopped.

Poor adherence increases the risk of drug resistance and treatment failure.

5-43 How is adherence measured?

The history given by the parent or guardian may be an unreliable method of assessing adherence. Better methods include:

1. Counting tablets that have not been taken (pill count) or measuring the amount of medication remaining in the bottle. Parents should be asked to bring all the medication back to the clinic at every visit.
2. Daily record cards or dosing diaries.
3. Unannounced home visits with pill counts.

A simple card for recording each dose on a daily basis helps promote and assess excellent adherence.

A home record card of medication is important to maintain excellent adherence.

5-44 What factors are associated with poor adherence?

2. Inadequate home support. This is often due to non-disclosure of the child’s HIV status.
3. Poor relationship with the clinic staff.
4. Alcohol, drug abuse, depression or other emotional problems in the care giver or among other household members.
5. Side effects to antiretroviral treatment.

Note that excellent adherence is not related to the race, gender, education level, socioeconomic class or cultural background of the parent. Adherence can be excellent even in poor, underdeveloped communities.

5-45 How can adherence be improved?

Excellent adherence must be promoted before treatment is started and then promoted continually during treatment. Discuss excellent adherence at every clinic visit. Parents and older children must be encouraged to take an active and responsible role in the treatment.

1. Before starting antiretroviral treatment, parents and older children must make a firm decision to take medication at the correct time every day for life. A clearly understood treatment plan must be negotiated with the parents.
2. Parents must understand why adherence is important and know about the dangers of poor adherence. Education and counselling about adherence should be provided in the parents’ home language. A supportive and non-judgemental approach is needed.
3. It is important to make sure that the adherence with co-trimoxazole treatment is excellent before starting antiretroviral treatment.
4. The clinic should check on adherence at every visit. A pill or medication count should be done. If adherence is poor, ask the parent why doses have been missed and re-educate them about the importance of adhering to treatment.
5. Suggest practical reminders such as an alarm clock, or link the time of taking medication to a particular radio or TV programme or cleaning teeth. A cell phone message or pager call can be arranged. Get the parent to use a pill box where tablets for the day can be counted out beforehand in children and adolescents who are receiving capsules or tablets. Counsellors who know the community well can often
offer the best adherence advice that will be suitable to the family’s lifestyle.
6. Regular support groups of other parents with children on antiretroviral treatment are very helpful.
7. Side effects must be promptly and correctly managed.
8. Provide a more caring service.

Parents often need constant monitoring, education, encouragement and support. Good preparation and long-term support are essential for excellent adherence.

5-46 How can health workers provide a more caring service?
1. Healthcare providers must make every effort to establish a trusting relationship with each patient. If possible the parents should see the same dedicated carer at each visit.
2. Parents should feel they are welcome to come to the clinic with a problem on any day, not just on their appointment day.
3. Remember that acceptance and emotional support by the clinic staff are very important parts of good care. Regular updating of education and an evaluation of the quality of advice being given by health workers are important.
4. A patient should never be without the required medication. It is unacceptable for the clinic to run out of drugs.

It is very important to find out why doses have been missed. Reasons for missing doses must be addressed by the clinic staff.

5-48 Can a dose be taken late?
If a dose is not taken at the correct time, it can still be safely taken up to six hours late. It is better to take the dose late than not at all.

5-49 What should be done if adherence remains poor?
If adherence remains very poor (below 80%), it may be necessary to attempt directly observed therapy (DOT) using a community clinic counsellor or a treatment buddy, i.e. an adult who can support the primary caregiver. In exceptional circumstances it may be necessary to discontinue the child’s antiretroviral therapy temporarily until such time that the caregiver is re-counselling and prepared to administer the medication optimally.

5-50 What are the dangers of inadequate dosage?
Besides poor adherence, prescribing lower than the recommended doses of antiretroviral drugs may also lead to treatment failure. The dosing requirements increase as the child grows. Therefore doctors and nurses treating HIV-infected children must check the doses of all antiretroviral drugs at each clinic appointment to ensure that the doses remain adequate.

The use of weight bands has made it easier to decide on the correct dose of antiretroviral drug.

Drug doses must be increased as the child grows.
5-51 Does it matter if the medication is vomited?

Yes. If the child vomits up the medication, the dose should be given again immediately. Vomiting a few hours after the medication is probably not important.

5-52 What factor may cause poor absorption of drugs?

Taking ddI with meals results in poor absorption. Therefore ddI is always taken well before or well after a meal. Drug absorption may be low with chronic diarrhoea.

NOTE Measuring serum levels of antiretroviral drugs is rarely done in developing countries. However, in resource-rich settings drug levels are part of standard clinical practice.

5-53 What is drug resistance?

Drug resistance in HIV develops when the multiplication of HIV is not blocked by a particular triple antiretroviral combination. Drug resistance will lead to treatment failure. The development of resistance to one or more antiretroviral drugs is important as it will reduce the chance of successful treatment and shorten the effectiveness of antiretroviral therapy.

Drug resistance may be due to:

1. Infection with HIV that is already resistant to one or more drugs (primary drug resistance). This is still uncommon in South Africa.
2. Resistance only developing some time after treatment had started (secondary drug resistance). Every effort must be made to avoid this form of drug resistance, which is mainly caused by poor adherence.

NOTE Resistance is most common with ‘non-nucs’ and 3TC as resistance occurs after a single mutation. Resistance only develops slowly with AZT and d4T. Resistance to lopinavir/ritonavir and ddI is uncommon.

5-54 How can the development of drug resistance be avoided?

1. By always using a combination of three drugs from two different drug classes to treat patients. This is the basis of standardised regimens. If one drug runs out, all drugs should be stopped until a new supply is obtained.
2. By excellent adherence. The more frequently doses are missed, the greater is the risk of resistance to those drugs.
3. By making sure that the weight and length of the child are measured, and the doses of the antiretroviral drugs are checked at each clinic visit.

Excellent adherence to antiretroviral treatment is the best way of avoiding the development of drug resistance.

5-55 May resistance be caused by previous drug exposure?

1. There is concern that nevirapine used in the prevention of mother-to-child transmission (PMTCT) may cause drug resistance to both nevirapine and efavirenz in mother or infant. This may limit the success of future antiretroviral treatment. Children who have previously been given antiretroviral drugs (‘non-naive patients’) must be carefully assessed by an antiretroviral expert before one of the standard drug combinations is started.

5-56 What is cross-resistance?

If HIV becomes resistant to one drug in a class it is often also resistant to some or all the drugs in the same class. This is called cross-resistance (i.e. HIV is resistant to drugs within a drug class). This is particularly common for ‘non-nucs’. If patients are resistant to
nevirapine there is a high chance that they will also be resistant to efavirenz. Drug resistance between classes is uncommon.

**NOTE** Genotyping can be done to identify mutations associated with drug resistance. It is expensive.

### TREATMENT FAILURE

**5-57 What is treatment failure?**

The features of treatment failure on antiretroviral therapy are:

1. The development of new signs or recurrent signs of stage 3 or 4 HIV infection.
2. Development of immunodeficiency after initial improvement of the CD4 percentage or CD4 count. An abnormal CD4 percentage or count should always be confirmed by a repeat measurement.
3. The presence of a detectable or increasing viral load suggests that the HIV infection is not being controlled. This is the most accurate measure of treatment failure.

**NOTE** The criteria for treatment failure in children is a viral load above 1000 copies/ml despite good adherence for six months. It is important to obtain a local expert opinion. Within the first six months after starting antiretroviral treatment, clinical deterioration may be caused by the Immune Reconstitution Inflammatory Syndrome which does not mean treatment failure and should not be an indication to consider changing treatment.

**5-58 How is treatment failure confirmed?**

Before diagnosing treatment failure on a viral load measurement it is important to repeat the viral load after a month. The diagnosis of treatment failure is confirmed if the viral load remains high or increases further. Sometimes the viral load will be increased at the time of the first measurement but falls with the second measurement. Transient rises in the viral load are called ‘blips’. They are not uncommon and may be caused by a recent viral or bacterial infection, or an immunisation. Therefore, always repeat the viral load after a month before diagnosing treatment failure.

**5-59 What are the causes of treatment failure?**

There are a number of causes:

1. Poor adherence
2. Poor absorption
3. Adverse drug interactions
4. Drug resistance (infection with a drug-resistant HI virus causes treatment failure from the start)
5. Incorrect dosing

Poor adherence is the commonest cause of treatment failure. These children usually respond to treatment at the beginning but later fail. Excellent adherence must be stressed at every visit to the HIV clinic.

**Poor adherence is the commonest cause of treatment failure.**

**5-60 How should treatment failure be managed?**

Further care, including decisions about second-line treatment and the selection of subsequent regimens should be guided by an experienced clinician. The cause of the treatment failure must be determined as far as possible. It is important that the treatment regimen should not be changed until a careful assessment is done and all the options considered. Remember that a second measurement of the viral load must be done before diagnosing treatment failure.

**The treatment regimen should not be changed in haste.**

If adherence has been poor, every effort must be made to improve adherence. If adherence has been good, a change to the second-line treatment regime should be considered.
5-61 Can previous exposure to antiretrovirals lead to treatment failure?

Yes. If first-line treatment including nevirapine has failed, despite excellent adherence, make sure that the child was not given nevirapine for the prevention of mother-to-child transmission of HIV. In many countries, previous exposure to nevirapine is not considered a contraindication to standardised first-line treatment which includes nevirapine. However, treatment of children previously exposed to any antiretroviral drugs should be discussed with an antiretroviral expert before starting a new treatment regimen.

**NOTE** Children who have previously been exposed to one or more antiretroviral drugs are no longer ‘antiretroviral naive’ and may already be resistant to one or more of these drugs.

5-62 What should be done if first-line treatment has failed despite excellent adherence?

Change from first-line to second-line treatment. This decision must always be made by an expert in antiretroviral treatment as it is an important step. Do not rush into second-line therapy. Re-counsel the parent or caregiver.

Treatment is changed to three new drugs, from at least two antiretroviral classes. The second-line combination in children is usually AZT, ddI and lopinavir/ritonavir. Review all other medication for possible drug reactions.

5-63 What should be done if the second-line of treatment fails?

If adherence is excellent and the patient becomes clinically worse on the second combination, a decision may be made to stop all antiretroviral treatment and start supportive care only. If failure is due to poor adherence every effort must be made to improve adherence.

**NOTE** Additional antiretroviral drugs can be used in new combinations in an attempt to control viral replication in patients who have failed on both first- and second-line treatment. This is a complex problem that must only be addressed by an ART specialist.

### DRUG INTERACTIONS

5-64 What is a drug interaction?

This is the interference of one drug with another drug. Common examples of drug interaction are:

1. Two similar drugs compete with each other at their site of action. For example, nevirapine and efavirenz should not be used together.
2. One drug alters the rate at which another drug is broken down in the body. This may result in the blood level of either the drug being too high or too low. For example rifampicin can decrease the blood concentrations of some antiretroviral drugs.
3. If two drugs have similar side effects, these side effects are more likely to occur and be severe if the two drugs are used together. For example, both nevirapine and co-trimoxazole may cause skin rashes.

5-65 Which antiretroviral agents should not be used together?

Using either the first- or second-line combinations for antiretroviral treatment avoids drug combinations which compete with each other.

**NOTE** AZT should not be used together with d4T due to their competing sites of action while ddI and d4T should not be combined if possible, due to additive toxicities.

5-66 What is the effect of rifampicin on antiretroviral drugs?

Rifampicin, used in the treatment of TB, increases the rate at which some antiretroviral drugs are broken down by the liver. As a result these drugs may not act adequately because their blood levels are too low:

1. Rifampicin causes no problems with ‘nucs’.
2. Rifampicin causes some problems with ‘non-nucs’ and lowers blood level of these drugs, especially nevirapine. Efavirenz is less affected than nevirapine, therefore nevirapine is often changed to efavirenz when first-line antiretroviral treatment is being given at the same time as anti-TB treatment. The dose of efavirenz need not be changed.

3. Rifampicin causes serious problems with ‘PIs’ as it lowers blood levels of most of these drugs by about 80%. Therefore higher doses of ‘PIs’ are needed when they are used with rifampicin. Ritonavir is least affected by rifampicin. Therefore a good approach is to boost the normal daily dose of lopinavir/ritonavir with additional ritonavir. This has been shown to maintain blood concentrations of lopinavir, the active antiviral, in children treated with rifampicin-based TB treatment.

4. Because rifampicin does not affect the blood levels of the ‘nucs’, an alternative approach during TB treatment is to switch to an antiretroviral regimen containing three ‘nucs’.

**NOTE** Boosted lopinavir/ritonavir means that the total amount (dose) of lopinavir in mg is equivalent to the total amount (dose) of ritonavir in mg administered to the patient.

**DRUG INTERRUPTIONS**

5-68 What is a drug interruption?

This is when antiretroviral treatment is stopped for a short period (a temporary interruption). Drug interruptions must be avoided. The cause of drug interruptions may be intolerable side effects or poor adherence. These children should be reviewed by an experienced clinician and the cause for the interruption established. If the cause is intolerable side effects then further investigation and/or treatment modification may be required. Lack of drugs at the clinic should never be the cause of a drug interruption.

5-69 What is the danger of drug interruption?

If only one antiretroviral drug is stopped for a while there is a danger that resistance may develop to the remaining drugs. Therefore, it is best to stop all the antiretroviral drugs if drug interruption cannot be avoided.

**It is better to stop all drugs rather than the one drug believed to be causing a problem.**

**NOTE** Planned drug interruptions at regular intervals are not being used in the treatment of HIV.

**SIDE EFFECTS OF ANTIRETROVIRAL AGENTS**

5-70 What should be done if the patient has a severe drug reaction to a drug?

All drugs must be stopped immediately. **Never** only stop one drug. The whole drug combination must be assessed by an expert. A common and important side effect of d4T and lopinavir/ritonavir is wasting of the face (lipoatrophy). This should be recognised early, as the wasting may be permanent.
5-71 What is the immune reconstitution inflammatory syndrome?

This is an unexpected clinical deterioration which occurs soon (usually within four to 12 weeks) after antiretroviral treatment is begun. After initially improving, the child becomes ill once again.

Functional immune recovery starts within weeks of beginning antiretroviral treatment. An inflammatory response to an HIV-associated infection (such as BCG vaccination or TB) was not possible before antiretroviral treatment was started as the immune system was too suppressed. As the immune system recovers, the body may develop an inflammatory response to any of the following:

1. Hidden or mild infections which have been missed clinically. An example would be silent TB.
2. Worsen existing infections. An example would be TB which has only been treated for a few weeks.

BCG-associated lymphadenitis is the commonest form of IRIS in children in South Africa. TB is another important cause.

**NOTE** During the initial stages of antiretroviral therapy many children with advanced HIV infection are still severely immunosuppressed and are thus susceptible to new opportunistic infections. Therefore differentiating classic IRIS from new infection associated with ongoing immune suppression during the first six months of antiretroviral treatment may be difficult.

TB may present for the first time (previously missed clinically) or partially treated TB (dead bacteria still present) may flare up with an acute inflammatory reaction such as suddenly enlarged paratracheal nodes, pleural effusions or parenchymal lung disease which may be seen on chest X-ray.

5-72 How many patients develop the immune reconstitution inflammatory syndrome?

About a third of adults starting antiretroviral treatment develop mild IRIS. The frequency has not been established in children, but at least 20% of children with advanced HIV infection experience serious infections during the first six months of antiretroviral treatment, requiring admission. Many of these infections may be due to IRIS, which can be serious, but rarely life threatening. Children who start antiretroviral treatment with a very low CD4 percentage have the greatest risk of developing IRIS.

5-73 How does the immune reconstitutinal inflammatory syndrome present clinically?

It usually presents with fever and a worsening of the patient’s symptoms after starting antiretroviral treatment. The clinical features vary and depend on the anatomical site. For example, children may develop a reaction at their BCG site or axillary adenitis with or without the formation of a fistula as a result of previous BCG vaccination. Lymphadenopathy or the appearance of the chest X-ray may become worse in children whose lungs are colonised with the TB organism. Children whose liver is colonised with hepatitis B or C will present with features of acute hepatitis or liver failure. All children with possible IRIS must be referred to an experienced clinician for assessment and appropriate investigations. Consider IRIS in anyone who is not improving within the first few months of antiretroviral treatment.

The immune reconstitution inflammatory syndrome presents suddenly and unexpectedly with the clinical deterioration soon after antiretroviral treatment is started.

**CASE STUDY 1**

An 18-month-old child is referred for antiretroviral treatment. His HIV infection
is graded at stage 2 and his CD4 percentage is 18%. He is brought by a neighbour as his mother died a year before.

1. **Does this child meet the clinical criteria for antiretroviral treatment?**

No, as he is assessed as only stage 2. Stage 3 and 4 are current clinical indicators for treatment in children over one year of age.

2. **Does he meet the immunological criteria?**

Yes, as his CD4 percentage is below 25%. This is the indication for treatment in children between 12 months and five years of age.

3. **Would he meet the treatment criteria if he were six years old?**

The CD4 count, rather than CD4 percentage, is used for children aged five years or older.

4. **Do both clinical and immunological criteria have to be met before treatment is started?**

No. Either clinical or immunological criteria can be used on their own. However, both are often present in a child.

5. **What are the social criteria for treatment?**

At least one adult must be responsible for giving the treatment, they should be ‘treatment ready’, and they should be able to bring the child to the clinic for the scheduled visits. Treatment is unlikely to succeed if all these criteria are not met.

6. **Does this child meet the social criteria?**

No. A home visit is needed to identify the best person to take responsibility for giving this child’s antiretroviral treatment.

7. **What are the criteria for antiretroviral treatment in children below one year?**

All HIV-infected children under one year of age should be treated.

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**CASE STUDY 2**

The parents of an eight-year-old child with stage 4 HIV infection are referred for education and counselling in preparation for the child’s antiretroviral treatment. They are anxious that the treatment is started as soon as possible and are willing to be actively involved in the care needed.

1. **What parent education is needed?**

The parents need to understand what HIV infection is and what treatment is needed. They must be able to recognise the drugs to be used and know how to give them correctly. They should also know what side effects to look for and what common HIV-associated infections may occur. They must understand the importance of excellent adherence.

2. **Who should provide this education?**

Usually a counsellor in individual sessions or in group education classes. Often trained lay counsellors are used to provide the education needed. Pamphlets, videos and posters are also useful.

3. **What parent counselling is needed?**

It is important that the parents are able to accept the child’s HIV status (and often that of the family), are able to disclose the status to close family members and friends, and are emotionally ready for the start of the child’s antiretroviral treatment.

4. **How may the parents be emotionally supported?**

It is important that their family and close friends support them. It is often very helpful if they join a support group.

5. **How long does it take to become ‘treatment ready’?**

Usually four weeks. It is very important that the parents are well prepared before treatment is started.
6. Should the child be involved in the education and counselling?
Yes. Older children should be involved in the decisions and management of their illness.

**CASE STUDY 3**

A mother brings her daughter to the first screening visit. She is examined by the doctor who says that she has the criteria for starting antiretroviral treatment.

1. **What needs to be done at the first screening visit other than checking the criteria for antiretroviral treatment?**
   1. A history is taken and general examination done.
   2. The child is weighed and measured.
   3. Readiness education and counselling are arranged.
   4. A home visit is planned if possible.
   5. The management is discussed with the parents.

2. **What infection should be screened for?**
Tuberculosis. A history of TB in the family is taken, sputum sample collected for examination and Mantoux skin test performed. It is very important to exclude TB before starting antiretroviral treatment.

3. **Can adherence to treatment be assessed at the first visit?**
Yes, if the child is receiving co-trimoxazole prophylaxis. Good adherence to prophylaxis suggests that there will be excellent adherence to antiretroviral treatment.

4. **Why is a home visit important?**
It is important to confirm the correct home address and assess the home circumstances where support and disclosure can be determined.

5. **What baseline blood tests should be done at the first screening visit?**
Usually a CD4 percentage has already been done for staging. A full blood count, and ALT if nevirapine is to be used, should be taken.

6. **When is it decided whether the parents are ‘treatment ready’?**
This decision is made by the multidisciplinary team at the second screening visit.

**CASE STUDY 4**

A child who is started on antiretroviral treatment attends the first follow-up visit. His father asks what the chances of drug failure are. He has read about antiretroviral treatment and wants to know about ‘IRIS’.

1. **What is the schedule of visits once antiretroviral treatment is started?**
The child is usually seen at two, four, eight and 12 weeks after starting treatment. Thereafter visits are at three- or six-month intervals if progress is satisfactory.

2. **What is the expected response to antiretroviral treatment?**
The child gradually feels better and gains weight. HIV-associated infections become less frequent and severe. By six months the CD4 percentage should be above baseline. In most children the viral load is undetectable. This is the best indicator of successful treatment.

3. **What is the main cause of drug failure?**
Poor adherence. With excellent adherence this child has a good chance of steady improvement. Excellent adherence means that no more than one in 20 doses should be missed. That is one mistake in 10 days.
4. What are a few ways of improving adherence?

1. The parents must be well prepared before treatment is started. They must understand the importance of excellent adherence.
2. Practical reminders are important. An alarm clock, radio or TV programme or cell phone message may be helpful.
3. Side effects must be correctly managed.

5. Can previous exposure to antiretroviral drugs lead to treatment failure?

Yes. The commonest cause is exposure to prophylactic nevirapine at the time of delivery. Therefore nevirapine is usually not used for first-line antiretroviral treatment in children younger than three years.

6. What is ‘IRIS’?

The immune reconstitution inflammatory syndrome (IRIS) is an unexpected clinical deterioration after starting antiretroviral treatment. It is due to an immune response to an HIV-associated infection, usually TB.
Before you begin this unit, please take the corresponding test at the end of the book to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

**Objectives**

When you have completed this unit you should be able to:
- Define an HIV-associated infection.
- Define an AIDS-defining infection.
- List the common childhood HIV-associated infections.
- Diagnose and manage the common HIV-associated infections.
- Diagnose and manage tuberculosis co-infection.
- Provide palliative and terminal care.

**HIV-ASSOCIATED INFECTIONS**

**6-1 What are HIV-associated infections?**

HIV-associated infections are infections which are common in HIV-infected people. They may be caused by a wide range of organisms such as bacteria, viruses, fungi or protozoa. These infections occur when the immune system becomes damaged. The first clinical sign to suggest that a child has a weakened immune system is often the appearance of an HIV-associated infection.

**HIV-associated infections are common in people with a weakened immune system.**

**6-2 Which are the common HIV-associated infections in children?**

1. Infections which are also seen in children who are not infected with HIV:
   - Skin infections
   - Mild oral candidiasis (thrush)
   - Bacterial pneumonia
   - Otitis media or sinusitis
   - Pulmonary tuberculosis (TB)
   - Diarrhoeal disease
   - Septicaemia

2. Infections which are uncommon in children who are not infected with HIV:
   - Recurrent or chronic oral candidiasis
   - Recurrent bacterial pneumonia
   - Shingles (Herpes zoster)
   - Severe, recurrent mouth ulcers
   - Lymphoid interstitial pneumonitis
   - Extra-pulmonary TB

3. Infections which are rare in children who are not infected with HIV.
6-3 Which infections are common in HIV-infected children but rare in children without HIV infection?

1. Oesophageal candidiasis
2. Pneumocystis pneumonia
3. Cryptococcal meningitis
4. Cerebral toxoplasmosis
5. Cytomegalovirus (CMV) retinitis

**Note** Less common HIV-associated infections include Hepatitis B and C, non-tuberculosis mycobacteria or disseminated fungal infections and chronic diarrhoea due to Isospora or Cryptosporidium. Other HIV-associated infections seen in adults are rare in children.

6-4 Do HIV-associated infections always indicate that the child has advanced disease?

No, as some HIV-associated infections such as pulmonary TB or shingles may also be found in HIV-negative children and children with stage 1 to 3 HIV infection. These infections, however, should always alert one to the fact that the child may be HIV infected. HIV-associated infections are therefore an important indicator for HIV screening.

6-5 What are the AIDS-defining infections?

These are clinical infections which only occur in children who have a severely damaged immune system due to HIV infection. Therefore they are called ‘AIDS-defining infections’. They include conditions which are rare in HIV-negative children, such as oesophageal candidiasis and Pneumocystis pneumonia.

The term ‘AIDS-defining illnesses’ also includes conditions such as unexplained wasting, stunting or severe malnutrition, HIV encephalopathy, non-Hodgkin’s lymphoma, and Kaposi’s sarcoma.

Children with an AIDS-defining illness are classified as having stage 4 HIV infection.

**Note** A number of malignancies associated with AIDS have a viral cause, e.g. Kaposi’s sarcoma is caused by the herpes virus.

6-6 What are opportunistic infections?

Opportunistic infections or ‘OIs’ are infections which should not occur in children with a healthy immune system. These organisms ‘take the opportunity’ of infecting and causing illness in children with a weakened immune system. Unfortunately this is a confusing term as some experts use the term opportunistic infections only for AIDS-defining infections while others use the term for all infections seen in HIV-infected children.

6-7 Which children are at high risk for HIV-associated infections?

1. All children with HIV infection are at an increased risk for HIV-associated infections.
2. The lower the CD4 percentage, the greater the risk for HIV-associated infections. Therefore, children with a CD4 percentage below 15% are at the greatest risk.
3. Unlike in HIV-infected adults, where there is a clear relation between the CD4 count and specific HIV-associated infections, in children the relation between CD4 percentage and specific infections is less predictable. For example, HIV-infected adults with a CD4 count below 200 cells/µl are at a high risk for Pneumocystis pneumonia. In HIV-infected children, particularly those less than one year of age, Pneumocystis pneumonia can occur at any CD4 percentage even in those children with a CD4 percentage greater than 25%. Therefore, all HIV-exposed children must be started on co-trimoxazole prophylaxis from the age of four to six weeks to prevent this life-threatening HIV-associated infection.

Both infections and malignancies can be AIDS-defining illnesses.

The lower the CD4 percentage or count the higher the risk of an HIV-associated infection.
6-8 Can HIV-associated infections be prevented?

The best way of preventing most severe HIV-associated infections is to start antiretroviral treatment (HAART) in HIV patients when their CD4 percentage (or count) falls below the critical level. The risk of HIV-associated infections can also be reduced by:

1. Primary prophylaxis that prevents the HIV-associated infection from occurring. This is done for Pneumocystis and TB.
2. Secondary prophylaxis that prevents recurrences of HIV-associated infections which have already occurred. This is done for cryptococcal meningitis and Pneumocystis pneumonia.

6-9 Which HIV-associated infections are the most important in children?

Severe or repeated bacterial infections as these are very common and can be fatal in HIV-positive children. Important bacterial infections include pneumonia, septicaemia, meningitis, urinary tract infection, osteitis, skin sepsis and otitis media. They often run a complicated course and respond slowly to treatment.

6-10 What skin infections are common in children with HIV infection?

Many common skin infections occur in children who are HIV-infected. However, they are more severe, and often take longer to respond to treatment, than in children who are not immunosuppressed. Common skin infections in children with HIV infection are:

1. Severe molluscum contagiosum
2. Severe candidiasis nappy rash, which may ulcerate
3. Widespread warts
4. Severe chicken pox or shingles due to Herpes zoster virus
5. Severe scabies, which may involve the whole body
6. Severe tinea capitis (ringworm of the scalp)
7. Severe impetigo
8. Severe seborrhoeic dermatitis

Any of these severe skin conditions, especially shingles, suggests that the child is infected with HIV. Shingles is a very painful vesicular rash which usually only affects one part of the body. Molluscum contagiosum and warts are often extensive and do not recover spontaneously. Severe tinea capitis and impetigo often need systemic therapy and do not respond to local treatment.

6-11 What gastrointestinal problems are common in children with HIV infection?

1. Severe, persistent or recurrent oral candidiasis (moniliasis or thrush). Severe oral candidiasis after two months of age is uncommon in children who are not HIV infected.
2. Oesophageal candidiasis: Infants who have severe oral candidiasis, pain and difficulty with swallowing and drool saliva, probably have oesophageal candidiasis as well. These children refuse feeds and are very irritable due to hunger and thirst. This rapidly results in dehydration.
3. Herpes stomatitis: This is often severe in children with HIV infection, resulting in dehydration. Aphthous ulcers and gum infections (necrotising ulcerative gingivitis) are also common.
4. Acute diarrhoea: This is usually due to viruses and bacteria which also cause diarrhoea in children who are not infected with HIV.
5. Chronic diarrhoea: This may complicate acute diarrhoea or be due to unusual organism such as Cryptosporidium or Isospora. Lactose intolerance may complicate chronic diarrhoea.

Except for children with mild, acute diarrhoea, most of these children should be referred
to hospital for further investigation and management.

**Oesophageal candidiasis presents with painful swallowing.**

**Note** Other conditions which may cause oesophagitis are Herpes simplex, CMV infection or severe gastro-oesophageal reflux. Endoscopy may be needed to confirm the diagnosis.

**6-12 How should a child with severe oral or oesophageal candidiasis be managed?**

Oral candidiasis (thrush) can usually be successfully treated with mycostatin drops 1 ml or miconazole gel six-hourly after a feed or meal. If the response is poor, oral fluconazole 3 mg/kg daily can be used for seven days.

Oesophageal candidiasis is treated with oral fluconazole 5 mg/kg daily for 21 days. Intravenous treatment may be needed for a few days if the child cannot swallow. Local treatment with topical drugs is not adequate. These patients must be referred to hospital as they may need intravenous rehydration or nasogastric feeding. Analgesia should be given as this condition is painful.

**6-13 What is the management of mouth ulcers in children with HIV infection?**

1. Severe, recurrent aphthous ulcers. These are very painful ulcers that can occur anywhere in the mouth. They may be single or multiple, small or large. Manage with paracetamol (Panado) for pain, and chlorhexidine mouthwashes to prevent secondary bacterial infection. Local (topical) steroids (e.g. Kenalog in Orabase) or spraying a beclomethasone inhaler directly onto the ulcer is helpful in severe cases.
2. Herpes infections. These multiple, shallow ulcers often are recurrent or become chronic. Topical gentian violet or 0.1% povidone-iodine (Betadine mouthwash) may be used while oral acyclovir (20 mg/kg three times per day for five days) is indicated for large or extensive ulcers.
3. Necrotising ulcerative gingivitis. This causes bleeding and ulceration along the gum margins of the teeth. Mouth washes with 0.2% chlorhexidine gluconate helps while oral metronidazole (Flagyl) is indicated in severe cases. Severe cases should be referred to a dental hygienist.

It is important that children with a sore mouth take adequate amounts of fluids and do not become dehydrated. Intravenous or nasogastric fluids may be required.

**Note** Oral hairy leucoplakia with white marks on the sides of the tongue is not painful.

**6-14 What are important respiratory infections in children with HIV infection?**

1. Bacterial ear infections (otitis media), bronchitis and sinusitis are common.
2. Severe, recurrent or chronic pneumonia caused by bacteria that also cause pneumonia in children who do not have HIV infection, e.g. Streptococcal pneumonia (Pneumococcus) and *Haemophilus influenza* B.
3. Viral pneumonias and bronchiolitis.
4. Chronic lung disease especially bronchiectasis.
5. Pneumocystis pneumonia.
7. Tuberculosis.

**6-15 What is Pneumocystis pneumonia?**

Pneumocystis pneumonia is a severe lung infection caused by a fungus called *Pneumocystis jiroveci*. This fungus does not cause pneumonia in children with a healthy immune system. Therefore, a diagnosis of Pneumocystis pneumonia usually indicates that the child has AIDS. Pneumocystis pneumonia commonly presents in the first year of life with high fever, a cough and marked respiratory distress often with hypoxia. The onset of illness is sudden. It is a fatal infection if not treated.
The risk of Pneumocystis pneumonia can be greatly reduced with co-trimoxazole prophylaxis from four to six weeks in all HIV-exposed infants (i.e. infants born to HIV-positive women).

Chest X-ray shows non-specific changes.

**Pneumocystis pneumonia is an important cause of respiratory distress in infants with HIV infection.**

**NOTE** Previously Pneumocystis jiroveci was called Pneumocystis carinii, hence PCP or Pneumocystis carinii pneumonia. The diagnosis can be confirmed by finding cysts of Pneumocystis in the sputum using a special stain.

6-17 What is lymphoid interstitial pneumonia?

Lymphoid interstitial pneumonitis (LIP) is a common type of chronic lung disease in children with HIV infection, especially children older than two years. While rare in HIV-infected adults, it occurs in at least 30% of African children with stage 3 or 4 HIV infection. The cause of LIP remains uncertain but it may be caused by a viral infection.

LIP is a slowly progressive condition which usually presents with a chronic cough and shortness of breath (dyspnoea). These children are usually not generally ill other than their respiratory symptoms. They may even have no symptoms at all. However, enlarged parotid glands, lymph nodes, liver and spleen with finger clubbing are common. Advanced LIP causes central cyanosis and severe respiratory distress. It can be fatal. An oxygen saturation of less than 90% confirms hypoxia.

**Lymphoid interstitial pneumonitis is an important cause of respiratory distress in older children with HIV infection.**

**NOTE** LIP is the only stage 3 condition that is regarded as an AIDS-defining illness.

6-18 How is the clinical diagnosis of lymphoid interstitial pneumonitis confirmed?

By taking an X-ray of the child's chest. This looks like miliary tuberculosis. It is important to exclude other pulmonary conditions such as bacterial or viral pneumonia, tuberculosis and bronchiectasis.

6-19 How should you manage a child with lymphoid interstitial pneumonitis?

If the condition is symptomatic (respiratory distress or hypoxia) these children should be admitted to hospital. Oxygen should be given for hypoxia if cyanosis is present or the oxygen saturation is low. A course of antibiotics is often given to treat a suspected bacterial
infection. LIP does not respond to antibiotics. Children with severe respiratory distress improve dramatically with oral steroids.

**TUBERCULOSIS**

6-20 **How common is tuberculosis in children with HIV infection?**

Tuberculosis is one of the commonest serious bacterial infections seen in children with HIV infection. The clinical pattern of tuberculosis is similar in both HIV-positive and negative children. The risk of tuberculosis is increased even in children with stage 1 and 2 HIV disease.

**Tuberculosis is common in children with HIV infection.**

6-21 **What forms of tuberculosis are common in children with HIV infection?**

Pulmonary TB due to Mycobacterium tuberculosis is the commonest form of TB in both HIV-infected and non-infected children. However, tuberculosis of other organs (extrapulmonary TB, i.e. lymph node TB, TB meningitis, abdominal TB, TB osteitis, TB arthritis and miliary TB) is far more common in children who are infected with HIV.

A combination of HIV and TB infection leads to rapid immunosuppression with progression of both diseases. As a result, TB is more common and more severe in children with HIV infection.

TB in HIV-infected children usually responds well to treatment. However, multi-drug-resistant TB (MDR TB) and extensively drug resistant TB (XDR TB) are becoming a problem with HIV-infected children in South Africa. It is often the result of inadequate or incomplete TB treatment or spread from adults with multi-drug-resistant TB.

**Note** Infection with Mycobacterium avium complex (MAC) is rare in children with AIDS.

6-22 **How is pulmonary tuberculosis diagnosed in children with HIV infection?**

1. A high index of suspicion is most important. Usually there is an adult with ‘open’ pulmonary tuberculosis in the home. Tuberculosis is most common in undernourished children from poor, overcrowded communities.

2. General symptoms and signs of tuberculosis include poor appetite, weight loss, fatigue and malaise, and fever with night sweats.

3. Signs of pulmonary tuberculosis include a persistent cough lasting three weeks or more. The cough may be dry or productive. Shortness of breath, fast breathing and chest pain may also be present. Unlike adults, blood-stained sputum is uncommon in children with pulmonary tuberculosis. Enlarged hilar nodes may press on a bronchus causing wheezing or stridor.

4. The Mantoux skin test is usually positive. However, it may be negative, especially in children with malnutrition. The Mantoux skin test may take three months to become positive after TB infection.

5. Chest X-ray will usually show bronchopneumonia, enlarged lymph nodes, a pleural effusion or miliary TB. However, the chest X-ray may appear normal. Other pulmonary infections, such as bacterial and viral pneumonias, may be confused with tuberculosis.

6. A stained smear of sputum or gastric aspirate may show TB bacilli. However, the smear may be negative. Induced coughing is the best method of obtaining a sputum sample.

7. TB culture of the sputum or gastric aspirate is usually positive with widespread pulmonary TB. However, cultures may be negative.

8. The child improves clinically on anti-TB treatment. Sometimes this is the only way of confirming the clinical diagnosis.

**Note** A useful method of inducing coughing and sputum collection in a child can be performed before a meal. A puff of inhaled bronchodilator is given using a spacer followed 10 minutes later by 5 ml hypertonic saline (5% saline) also by
nebuliser. This is followed by chest physiotherapy to loosen the mucus and promote coughing.

**TREATING TUBERCULOSIS CO-INFECTION**

6-23 Can HIV infection and tuberculosis be treated at the same time?

If TB is diagnosed at the time that antiretroviral treatment is being considered then, if possible, the TB should be fully treated first before antiretroviral treatment is started. However, in some children with advanced HIV disease it may be necessary to start antiretroviral treatment soon after starting the TB treatment. When using anti-TB and antiretroviral treatments together, ALT should be monitored monthly, as drug-induced hepatitis is common.

6-24 What problems are common when treating tuberculosis and HIV at the same time?

1. A large number of different drugs have to be taken which complicates the drug administration. This may confuse care givers, increase the chances of mistakes when giving the medicines and lead to poor adherence.
2. The immune reconstitution inflammatory syndrome may occur. This is particularly common if antiretroviral therapy is started during the first two months of TB treatment, especially if the CD4 count is below 15%.
3. Drug interactions between antiretroviral and anti-TB drugs are common.
4. Drug side effects are more frequent and may be severe as anti-TB drugs and antiretroviral drugs often have similar side effects. This may further affect adherence.

Treatment of HIV is difficult if TB treatment is also being given at the same time. Therefore, children with a co-infection of TB and HIV should be managed by an experienced clinician.

6-25 What drugs are usually used to treat pulmonary tuberculosis in children with HIV infection?

Most children can be treated with combination tablets, i.e. rifampicin, INH and pyrazinamide for two months (intensive phase) followed by rifampicin and INH only for the remaining four months (maintenance phase). Therefore the full course is for six months. The anti-TB drugs are given daily. Compliance is better with daily treatment than only five days a week.

Children older than eight years or children weighing more than 35 kg are treated with four drugs (ethambutol added) in the initial phase as with the adult anti-TB treatment regimen.

6-26 When should antiretroviral treatment be started in children who have tuberculosis?

1. If the CD4 count is above 25% and the HIV infection has not reached stage 3 there is no need for antiretroviral treatment yet. The TB should be fully treated before considering the start of antiretroviral treatment.
2. If the CD4 count is between 15 and 25%, treat the TB for two months before starting antiretroviral treatment.
3. If the CD4 count is below 15% or the child is very ill, treat TB for two weeks before starting antiretroviral treatment. These
children have a high risk of dying and therefore the introduction of antiretroviral therapy should not be delayed any further.

6-27 What may happen if anti-TB and antiretroviral treatment are started together?

Unless the TB has been treated for at least two months, large numbers of TB bacilli may still remain in the body. Once antiretroviral treatment is begun the child’s immune system will begin to recover and may start to respond to the dead TB bacilli. This results in the immune reconstitution inflammatory syndrome (IRIS) with worsening of the signs of TB. Children with marked immune suppression are at greatest risk of this complication.

**Note** Even the protein remaining in dead TB bacilli may cause the immune reconstitution inflammatory syndrome.

6-28 What should be done if a child on antiretroviral treatment develops tuberculosis?

The antiretroviral treatment must be continued and anti-TB treatment started. However, the child should be carefully monitored for signs of drug interactions and side effects. It is important to exclude TB before starting antiretroviral treatment.

6-29 How do drugs used to treat tuberculosis and HIV interact with each other?

Rifampicin is the usual cause of adverse drug interactions. Rifampicin affects the blood levels of many antiretroviral drugs, especially the ‘non-nucs’ and PIs. Rifampicin stimulates liver enzymes which, as a result, increase the rate of breakdown of these antiretroviral drugs. This leads to low blood levels of these antiretroviral drugs which may prevent them killing HIV. Therefore the choice of antiretroviral drugs and their doses may need to be changed.

The choice and dose of antiretroviral drugs may have to be changed if rifampicin is used to treat tuberculosis.

6-30 What antiretroviral drug changes may be needed if rifampicin is given?

1. If nevirapine is being used, it should be replaced with efavirenz, which is less affected by rifampicin.
2. If lopinavir/ritonavir is being used, it should be boosted with additional ritonavir to maintain adequate blood levels.

These decisions should be made by an experienced clinician. Not making these changes may lead to drug resistance and failure of antiretroviral treatment.

6-31 What are the shared side effects of the drugs used to treat tuberculosis and HIV?

Nausea, rash, hepatitis and peripheral neuropathy. As a result these side effects are commoner and may be more serious if the two drug regimens are used together. This may result in a change in the choice of antiretroviral drugs. Careful monitoring is needed for these side effects.

Drug side effects are more frequent and may be severe if anti-tuberculous and antiretroviral treatments are given together.

6-32 How may taking many tablets cause problems?

Adherence may be poor when so many medicines need to be taken. There may also be confusion about the dosing instructions of the many different medicines. Patients should be told they will have to take a large number of medicines and be counselled about these possible problems. A clearly written plan for both anti-TB and antiretroviral treatment is essential. Additional support may be necessary to ensure adherence such as additional counselling and education sessions, more
frequent clinic visits, or using a ‘treatment buddy’ or DOTS advocate.

6-33 What is the role of TB prophylaxis?
HIV-positive children who are at high risk of TB should be considered for prophylaxis with INH.

6-34 When are anti-tuberculous drugs given prophylactically to HIV-infected children?
Clinically well children under five years of age who have been in contact with someone who has smear-positive pulmonary TB should be given prophylactic treatment. These young children are at very high risk of developing TB. Children under five years who are clinically well but have a positive Mantoux skin test (10 mm or more) should also be started on anti-TB treatment. Currently, prophylaxis consists of isoniazid for six months. The treatment is given daily for seven days a week using the same dose as for short-course treatment. It is important to exclude active TB before starting prophylaxis.

6-35 What neurological infections are common in HIV-positive children?
1. The most important neurological complication is HIV encephalopathy. The cause is uncertain but it is probably due to an infection.
2. Bacterial and tuberculous meningitis are also common.
3. Cerebral toxoplasmosis, cryptococcal meningitis, CMV retinitis and progressive multifocal leucoencephalopathy (PML) are uncommon in children.

6-36 What are the clinical features of HIV encephalopathy?
These children present with delayed milestones and develop neurological signs such as weakness, brisk reflexes, increased tone and gait disturbance. The expected growth in head circumference may slow down. The diagnosis is confirmed by CT brain scan.

6-37 What is palliative care?
Palliative care is the care of patients who have an incurable disease (such as AIDS). It also addresses the needs of the family. It aims at reducing suffering and improving the quality of life in these patients so that they can still have a good life for as long as possible. Palliative care starts at the time of the diagnosis and addresses all the patient’s physical, emotional, social and spiritual needs. Although HIV infection cannot be cured, most of the HIV-associated conditions can be prevented or adequately treated and controlled. HIV infection has now become a chronic, manageable condition.

6-38 What is terminal care?
In contrast, terminal care (or end-of-life care) is the active care of patients whose disease no longer responds to treatment. Terminal care is not the same as no care or poor care. Patients who are dying of AIDS need terminal care. Care should never be withdrawn because there is no longer any hope for cure.
Terminal care is the supportive care of patients who have a serious illness that no longer responds to treatment.

6-39 Do children with advanced HIV infection need terminal care?
Yes. As with adults dying of AIDS, there is an enormous need for terminal care for these children. Terminal care is most needed for children who are likely to die within months or weeks. Their families and carers also need support.

6-40 Where should terminal care be provided?
Home care is the basis of terminal care. If at all possible these children should be cared for in their own home where they are comfortable in their own surroundings and with their family and friends. Only if this is impossible should they be given care in an institution, preferably in a hospice. Hospital admission should be avoided if possible. Community helpers can be trained to provide basic nursing and provide extra help in the home (shopping, cooking, cleaning).

6-41 What is a hospice?
This is a place where terminally ill patients can be cared for. Management is aimed at compassionate care and support rather than cure. Members of a hospice team also help to care for patients who are at home.

6-42 Who should provide terminal care?
As there are so many aspects to terminal care, it is best provided by a team of people who are trained in this special type of care. A multidisciplinary approach is needed to meet the many different physical, psychosocial and spiritual needs of terminally ill children. Patients, family and friends also have a very important role in terminal care. However, they need professional support to enable them to play their role in helping the child.

6-43 What are the goals of terminal care?
To improve the quality of care of children, and their families, who are facing death. The goal of terminal care is not necessarily to prolong life, but to offer prevention and relief of suffering.

The goal of terminal care is to prevent and relieve suffering.

6-44 What does terminal care involve?
1. Controlling unpleasant symptoms, especially pain
2. Reducing the side effects of drugs used
3. Treating HIV-associated infections
4. Supporting the patient, family and friends
5. Giving patients and families control over the management

6-45 What physical problems need to be addressed with terminal care?
1. Nutrition
2. Pain
3. Discomfort

6-46 What are the nutritional needs in children with terminal HIV infection?
These children are often wasted and very underweight. They may also have a poor appetite, nausea and difficulty swallowing. As a result it is often difficult for them to eat or drink.

High calorie and protein foods are important. It is important that these children are able to choose whichever foods they prefer. If possible, intravenous fluids or nasogastric feeds should be avoided. Soft or liquid foods are best.

6-47 Is pain a common problem in patients with advanced HIV infection?
Yes, severe pain is very common in children who are dying of AIDS. It is likely to be
underdiagnosed and undertreated. Pain significantly reduces the quality of life and results in fear and despair. Pain also causes distress to the family.

**Severe pain is a major problem in children who are dying of AIDS.**

### 6-48 What are the principles of pain relief?

1. The correct choice and dose of analgesia (pain relief) is important.
2. Analgesics (drugs to relieve pain) should be given regularly (‘by the clock’) to both prevent and treat pain.
3. Oral analgesia should be used whenever possible.
4. Give clear written instructions.
5. Assess the amount of pain and review the pain management frequently.
6. Manage factors which aggravate pain such as fear.

The aim of pain management is to control pain by giving analgesia regularly so that pain can be prevented.

**The aim of pain management is to prevent pain.**

### 6-49 How is pain assessed in children?

Older children can say when they have pain. The assessment of pain in young children is dependent on observing the child’s behaviour and looking at their facial expression. Family and carers are usually good at assessing the degree of pain.

### 6-50 How is the severity of pain graded?

Into mild, moderate and severe. This is important, as the choice of analgesic is dependent on the severity of the pain.

### 6-51 What common analgesics are used to control pain?

1. For mild pain: Paracetamol (Panado) and ibuprofen (Brufen). The dose of paracetamol is 60 to 120 mg for children under one year, 120 to 250 mg to children from one to five years and 250 to 500 mg for older children. Syrup contains 120 mg/5 ml while tablets are 500 mg each. The dose of ibuprofen is 20 mg/kg/day in divided doses. Paracetamol and ibuprofen should be given every four to six hours as required. Aspirin must be avoided.

2. For moderate pain: Codeine phosphate 30 to 60 mg every four hours. Often paracetamol or ibuprofen are used in addition.

3. For severe pain: Oral morphine solution starting at 5 to 10 mg every four hours.

The choice of analgesics in an individual depends on their degree of pain. As pain increases one moves up the ‘treatment ladder’ from step 1 (non-opioids such as paracetamol and ibuprofen) to step 2 (weak opioids such as codeine phosphate) to step 3 (strong opioids such as morphine).

### 6-52 How is morphine used?

If possible it should be given orally. A dose must be given every four hours as the action of morphine is short. Give an extra dose equivalent to the four-hourly dose if the pain is not controlled. Giving extra doses for ‘breakthrough’ pain is very important. The starting four-hourly dose is 2.5 to 5 mg for children of one to five years and 5 to 10 mg for older children. Add up the total amount of morphine given in 24 hours (four-hourly dose plus any extra doses) to calculate the four-hourly dose for the next day. There is no maximum dose. The correct dose is the dose which is effective in controlling the pain. Therefore the dose of morphine should be titrated against the degree of pain.

Morphine can also be given intravenously or intramuscularly, but preferably by continuous subcutaneous infusion with a syringe driver.

**Frequent doses of oral morphine are the most effective form of pain relief.**
6-53 What common problems occur with morphine?

1. All patients on morphine develop constipation. Fruit, bran and extra fluids are helpful. Laxatives such as liquid paraffin 5 to 10 ml daily and senna (Senokot) 5 to 20 mg daily should be used. Constipation does not improve with continued use of morphine and is the major side effect. Morphine may be useful in controlling chronic diarrhoea.

2. Nausea and drowsiness. This improves with time (tolerance) and responds to a lower dose.

Addiction is not of concern when morphine is used to control pain in terminally ill patients. Do not stop morphine suddenly, however, as this may result in withdrawal symptoms. Respiratory depression is uncommon when morphine is used to control pain.

6-54 What common mistakes are made in treating pain?

1. Morphine is used too late.
2. The dose of analgesic is too low.
3. Medication is not given frequently or regularly enough.
4. Medication is only used to treat rather than prevent pain.

6-55 What other forms of discomfort are common in severe HIV infection?

1. Anorexia, nausea and vomiting
2. Diarrhoea
3. Constipation
4. Cough and shortness of breath
5. Itchy or dry skin
6. Fatigue and weakness
7. Lack of sleep
8. Bed sores
9. Incontinence

A syndromic approach is often used in terminal care when the symptoms are managed even if the underlying cause cannot be treated. Help from hospice staff is very useful in preventing and managing most of these problems.

6-56 What can be used to treat nausea?

Nausea is a common problem, especially when treatment with morphine is started. Metoclopramide (Maxolon) 1 to 5 mg (for children of two to 10 years) orally eight-hourly is helpful.

6-57 How can treating HIV-associated infections improve the quality of life in a patient dying of AIDS?

Improving the symptoms caused by HIV-associated infections can greatly improve the quality of the last weeks of life. For example, treating painful mouth ulcers or improving painful swallowing by managing fungal oesophagitis.

Relief of symptoms is often best achieved by treating HIV-associated infections.

6-58 Is it worthwhile treating children who are dying?

This is often a very difficult question to answer. Sometimes it may be realistic not to treat terminally ill children if the treatment will only prolong their suffering. However, pain, discomfort and distress must always be aggressively managed. Both children and their parents should never be allowed to feel abandoned by their health carers.

The question that must always be asked is: 'Will this make a difference to the quality of the child’s life?'

6-59 What are the psychological aspects of terminal care?

Anxiety and depression are common in terminally ill children and are often not recognised. It is important to manage anxiety and depression as they both aggravate pain. Children need comfort and love and should never feel abandoned or isolated. Physical touch (holding, stroking, cuddling) and emotional closeness are very important.
Anxiety and depression make pain worse.

6-60 Do children understand the concept of dying?

Young children think that dying is like falling asleep and do not understand that dead people do not wake up again. Older children are afraid of being separated from their parents. Children are often more accepting of death than adults and do not understand all that death means. Their questions should be answered simply and honestly.

6-61 How do children manage the death of a parent?

Unfortunately many children are losing parents to AIDS. They may even lose both parents. This is very traumatic and these children need an enormous amount of help and support. This is best provided by family and close friends. Siblings of dying children must not be forgotten as they also need help to talk about and accept the death. Dying parents need help to say farewell to their children.

6-62 What is a memory box?

This is a simple box that parents can store mementos in for their children. Photographs, letters and cards are kept in the box which is given to the children when they are older, to help them remember a parent who has died of AIDS. A memory box is one of the many ways that a parent can prepare themselves before death separates them from their children.

6-63 Do the carers need care themselves?

Yes. This is often forgotten or not realised. Care of the carers (both family and health workers) is a very important part of terminal care. It is physically and emotionally exhausting to care for a terminally ill patient. Signs of depression are often missed.

CASE STUDY 1

A three-year-old child is brought to a primary-care clinic with failure to thrive, dehydration, oral candidiasis and a one-week history of pain and difficulty in swallowing. It is noted that she has extensive severe scabies. A rapid HIV test is positive.

1. Is oral candidiasis common in children with HIV infection?

Yes. It is one of the first presentations in children with HIV infection. It is uncommon to get oral candidiasis (thrush) in children older than two months who have a healthy immune system. Oral candidiasis can usually be successfully treated with mycostatin drops 1 ml or miconazole gel six-hourly after a feed or meal.

2. What is an HIV-associated infection?

This is any infection which is more common in children who have a suppressed immune system due to HIV infection. Therefore, oral candidiasis is an HIV-associated infection.

3. Why do you think this child is having difficulties with swallowing?

She almost certainly has oesophageal candidiasis. These children have pain and difficulty with swallowing and may drool saliva. They are hungry and thirsty but unable to swallow liquids or food. It is very important to look for signs of dehydration.

4. How should oesophageal candidiasis be treated?

This child must be given fluids intravenously or via a nasogastric tube. Usually oesophageal candidiasis is treated with oral fluconazole for 14 days. It may be necessary to give intravenous fluconazole for a few days until the child can swallow the medication. Treating the oral candidiasis alone will not help. Analgesia should be given as the condition is painful.
5. Is oesophageal candidiasis an AIDS-defining infection?
Yes, as it would be graded as stage 4 HIV infection.

6. Why does this child have extensive scabies?
Extensive scabies is common in HIV-infected children because of their weakened immune system. Many other skin infections, such as molluscum, warts, chickenpox, herpes, tinea and impetigo may also be severe and respond poorly to standard treatment.

**CASE STUDY 2**

A nine-month-old child is brought to a local hospital with an acute onset of cough, high fever and shortness of breath. The mother was found to be HIV positive when screened during pregnancy but was not given prophylactic antiretroviral treatment. On clinical examination the child had clinical signs of pneumonia. There were also many small, painful ulcers on his mouth.

1. What is the likely cause of the pneumonia?
He may have a viral or bacterial pneumonia. However, he is most likely to have Pneumocystis pneumonia which is common in young infants who are HIV infected. TB pneumonia usually does not have an acute onset while lymphoid interstitial pneumonia is usually seen in older children. A chest X-ray will confirm the pneumonia but often does not help to identify the cause.

2. What would be the correct treatment of this child?
Pneumocystis pneumonia is usually treated with intravenous co-trimoxazole for 21 days. If drip access becomes difficult the antibiotic course may be completed with oral co-trimoxazole. Oral treatment can be used from the start if intravenous co-trimoxazole cannot be started. Additional antibiotics may be added to treat bacterial pneumonia (e.g. ampicillin). The selection of antibiotics is dependent on the suspected organism. Steroids are also given with severe pneumonia.

3. Which HIV-infected children develop Pneumocystis pneumonia?
Children with stage 4 disease as Pneumocystis pneumonia is an AIDS-defining infection.

4. How can this condition be prevented?
By starting all HIV-exposed children on prophylactic co-trimoxazole from six weeks of life. It should be continued unless the diagnosis of HIV infection is excluded.

5. What is the most likely cause of the mouth ulcers?
Probably Herpes simplex causing severe stomatitis. Severe aphthous ulcers, necrotising ulcerative gingivitis and oral candidiasis can also cause a sore mouth.

6. What is the treatment of Herpes stomatitis?
Topical gentian violet or 0.1% povidone-iodine (Betadine mouth wash) may be used while oral acyclovir is indicated for large ulcers. Paracetamol can be given for pain. It is important to make sure that these children take enough liquids and do not become dehydrated.

**CASE STUDY 3**

While being prepared for antiretroviral treatment, a five-year-old child has a positive Mantoux skin test and signs of TB on his chest X-ray. The sputum smear is negative for TB bacilli but sputum is sent off for culture. The CD4 count is 20%. His mother asked when antiretroviral treatment will be started.
1. Should this child be started on antiretroviral treatment now?

If possible, the TB should be fully treated first. If the CD4 percentage is between 15 and 25%, the TB should be treated for two months before starting antiretroviral treatment. In ill children with a CD4 percentage below 15%, antiretroviral treatment should be started after two weeks of TB treatment for this child. It is important to screen all children for TB before starting antiretroviral treatment.

2. Why is it a problem to start TB and HIV treatment at the same time?

Because of the risk of immune reconstruction inflammatory syndrome (IRIS). When the immune system starts to recover with antiretroviral treatment, there may be a severe inflammatory response to TB bacilli. The risk of IRIS is much less after two months of anti-TB treatment.

3. Why is the TB smear negative in this child?

This is not uncommon in children with TB. In children with HIV infection and TB, the Mantoux skin test may also be negative. Even the chest X-ray may appear normal. Therefore, the diagnosis of TB can be difficult in children with HIV infection.

4. Is tuberculosis common in children with HIV infection?

Yes. It is one of the commonest HIV-associated infections. Children with pulmonary TB are classified as stage 3 while extra-pulmonary TB is classified as stage 4.

5. What are the typical presenting symptoms and signs of pulmonary TB?

A persistent cough for more than three weeks in a child who is generally unwell. Poor appetite, weight loss and fever are common.

6. When should prophylactic INH be used?

When HIV-infected children, who have no signs of TB, are exposed to an adult with TB in their home. It is also given to children under five years who are clinically well but have a positive Mantoux skin test. It is important to exclude TB before starting prophylaxis.

**CASE STUDY 4**

A seven-year-old boy has been on antiretroviral treatment for two months. He develops a cough and a chest X-ray suggests pulmonary TB. A grandfather at home has recently been diagnosed with TB. The medical officer is not sure whether she should stop antiretroviral treatment and start TB treatment.

1. How should this child be treated?

It is important not to stop antiretroviral treatment. Anti-TB treatment should be started. The child must be carefully monitored for signs of adverse effects (side effects) such as hepatitis. It would be best if this child was under the care of a doctor experienced in managing patients with HIV/TB co-infection.

2. What is the TB treatment regimen in children with HIV Infection?

Rifampicin, INH and pyrazinamide are given for two months followed by rifampicin and INH only for a further four months. This treatment course is longer than that used in children without HIV infection.

3. What adverse drug interactions may occur?

Rifampicin is the usual cause of adverse drug interactions when HIV and TB are treated at the same time. Rifampicin lowers the blood level of many drugs, especially nevirapine and lopinavir/ritonavir. Therefore, nevirapine is usually swapped for efavirenz and extra ritonavir is added to the lopinavir/ritonavir treatment. Not making these changes may lead to drug resistance and failure of antiretroviral treatment.
4. What shared side effects occur with combined anti-TB treatment and HAART?

Side effects are more common and severe when both treatment regimens are used together. Nausea, rash, hepatitis and peripheral neuropathy may be caused by both anti-TB treatment and antiretroviral treatment. It is important to monitor children for these side effects.

5. Can taking so many different medications cause a problem?

Yes. It increases the chance of poor adherence and making mistakes with taking the medication correctly.

6. Can TB cause neurological complications?

TB is an important cause of meningitis in children with HIV infection.
Tests

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