9
HIV infection

Objectives

When you have completed this unit you should be able to:
- Define HIV infection and AIDS.
- Describe how children may become infected with HIV.
- Reduce the risk of mother-to-child transmission of HIV.
- Recognise the clinical signs and symptoms of HIV infection.
- Confirm the diagnosis of HIV infection.
- Manage a child with HIV infection.
- Counsel parents of a child with HIV infection.

Introduction

9-1 What is HIV?
HIV stands for the Human Immunodeficiency Virus. The virus is infectious and can be spread from one person to another and is found in most body fluids, e.g. blood, semen, vaginal secretions and breast milk.

HIV is the Human Immunodeficiency Virus.

Note: HIV was first identified in Paris in 1983. It was probably transmitted to humans from monkeys in central Africa in the 1950s. From here it rapidly spread to all parts of the world, especially the USA, Europe, Asia and other parts of Africa.

9-2 Are there different types of HIV?
Two types of HIV are recognized: HIV 1 and HIV 2. Most infections in Southern Africa are caused by HIV 1 which has many subtypes (clades). The important subtype in Africa is subtype C while subtype B is the most common subtype in the developed world.

9-3 What is HIV infection?
HIV infects the CD4 lymphocytes of the immune system. The CD4 lymphocytes are a special group of white cell which play an important role in protecting the body from infections. HIV introduces its own genes into the nucleus of the CD4 lymphocytes giving instructions to produce millions of new HIV. These HIV are then released into the blood stream where they infect and kill other CD4 lymphocytes. When HIV causes illness it is called symptomatic HIV infection or HIV disease.

HIV belongs to a group of viruses known as retroviruses. Retroviruses usually cause long periods of silent infection before symptoms and signs of disease appear.
Retroviruses contain a RNA genetic code. The viral enzyme reverse transcriptase allows HIV to make DNA copies of its RNA. The DNA copy is then inserted into the nuclear DNA of CD4 lymphocytes. The addition of this new information enables the virus to take over control of the CD4 lymphocytes and instruct them to produce huge numbers of new HIV. Only retroviruses have this ability to make a cellular DNA copy of their viral RNA code.

9-4 What is AIDS?

AIDS is the Acquired Immune Deficiency Syndrome. This is an advanced stage of HIV infection presenting with serious clinical illness. It presents in both adults and children in many different ways. The main feature of AIDS is severe damage to the immune system leading to many viral, bacterial and fungal infections, many of which do not usually occur in people with a healthy immune system. These are called HIV associated infections or opportunistic infections. They take the ‘opportunity’ of infecting people with poor immune function (immune deficiency). At present AIDS can be controlled but cannot be cured. If not treated with antiretroviral drugs, AIDS is a fatal condition.

AIDS is a serious illness caused by the Human Immunodeficiency Virus (HIV).

Note: AIDS was first recognized among homosexual males and intravenous drug abusers in the USA in 1981. The next year it was diagnosed in heterosexual men and women in Africa and also recognized in infants born to drug addicted mothers.

9-5 Can a person have HIV infection but remain well?

Yes. Adults are usually infected with HIV for years while remaining clinically well (asymptomatic HIV infection). Only after this long latent period do the clinical signs of HIV infection develop (symptomatic HIV infection). In children the latent period may be as short as a few months. HIV infection is only called AIDS when the patient becomes seriously ill due to HIV related infections. Therefore, AIDS is the most advanced and serious form of HIV infection.

AIDS is the most advanced and serious stage of HIV infection.

HIV is frequently transmitted by people who appear to be clinically well and do not know that they are infected with HIV.

9-6 How common is HIV infection?

Most cases of HIV infection occur in Africa where the spread of the HIV epidemic is greatest in Southern Africa. Over 40 million people worldwide have HIV infection. South Africa has one of the fastest growing HIV epidemics with 1000 to 2000 people infected every day. Between 12 and 15% of all South Africans are currently infected with HIV. Approximately 30% of pregnant women in South Africa are HIV-positive (i.e. infected with HIV) and over 100 000 infants are infected annually.

Symptomatic HIV infection is causing a widespread epidemic in Africa.

HIV infection is having a devastating effect on the health of children and many of the gains made in child survival during recent years are now being reversed. In many hospitals in Southern Africa, most paediatric beds are now filled with children suffering from HIV infection.

Transmission of HIV to children

9-7 How can a person become infected with HIV?

HIV may be transmitted from one person to another by:
Unprotected heterosexual or homosexual intercourse (horizontal transmission). This includes rape or sexual assault.

Crossing from a mother to her fetus or newborn infant (vertical transmission).

Using syringes, needles or blades which are soiled with HIV-infected blood. This includes syringes and needles shared by intravenous drug abusers.

Accidental injuries in health care workers (a needle, lancet or blade contaminated with HIV-infected blood). HIV may also be able to enter via a skin lesion (cut or open wound).

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 as all blood products are screened for HIV.

There is no evidence that HIV can be spread by mosquitoes, lice or bed bugs. HIV infection is not spread by kissing, holding hands or sharing cups or eating utensils. In Africa HIV is most commonly spread between adults by heterosexual intercourse.

9-8 How are children usually infected with HIV?

In children HIV is usually spread from a mother to her fetus or young infant. This is called mother-to-child transmission or MTCT. An HIV-infected mother may pass the virus to her child by the following routes:

1. HIV may cross the placenta from the mother to her fetus during pregnancy.
2. The infant may be infected with HIV by contact with vaginal secretions and blood during labour and delivery.
3. HIV may cross to the infant in breast milk.
4. Young children may also be infected with HIV during rape or sexual assault while adolescents may be infected during consenting intercourse.

5. Children may be infected when sharp instruments are used in ritual scratching or scarification or circumcision if the instrument is contaminated with blood containing HIV from another person.

9-9 What is the risk of a child becoming infected with HIV by mother-to-child transmission?

If a mother is infected with HIV and is not being given antiretroviral prophylaxis:

1. There is a 5% risk that HIV will cross the placenta from a mother to her fetus during pregnancy. The risk is increased further if the woman has an amniocentesis, external cephalic version, becomes infected with HIV during the pregnancy or has AIDS.
2. There is a 15% risk of the infant becoming infected with HIV during labour and a vaginal delivery. The risk is increased if the mother has pre-term labour, chorioamnionitis, rupture of membranes for more than 4 hours, an episiotomy or assisted delivery (vacuum or forceps delivery), a scalp clip for foetal heart rate monitoring or foetal scalp blood sampling for pH. Elective caesarean section removes the risk of HIV transmission during labour and vaginal delivery.
3. There is an additional 15% risk of HIV transmission after delivery if the mother practices mixed breastfeeding (breast milk plus other fluids and foods) for up to 18 months.

Therefore, without antiretroviral prophylaxis, the risk of HIV transmission with vaginal delivery and no breastfeeding is 20% (i.e. 5% plus 15%). With mixed breastfeeding the risk increases to 35% (i.e. 5% plus 15% plus 15%). It is important to know that at least 65% or more of infants born to HIV-infected mothers are not infected with HIV.

Most infants born to HIV-infected mothers are not infected with HIV.
9-10 How can the risk of mother-to-child transmission be reduced?

1. If possible, all women should be screened for HIV infection early in pregnancy so that HIV-exposed infants can be identified before delivery. Antiretroviral prophylaxis should be offered to all HIV-infected mothers during pregnancy and delivery, and to the newborn infant to reduce the risk of mother-to-child transmission of HIV.
2. The management of pregnancy, labour and delivery should be altered to reduce the risk of exposing the fetus and infant to HIV. Avoid early rupture of the membranes, instrument delivery and episiotomy if possible. An elective caesarean section is an option, especially in communities that can afford it.
3. Women should avoid becoming infected with HIV during pregnancy and breastfeeding by practising safe sex.
4. The choice of infant feeding should be discussed with the mother.

9-11 What factors influence the risk of HIV transmission in breast milk?

HIV is present in breast milk and HIV can be transmitted in the mother’s milk to the breastfeeding infant. The risk is greatest if the mother both breastfeeds and gives other foods, such as water, fruit juice, formula feeds and solids (i.e. mixed breastfeeding). With mixed breastfeeding the risk of passing HIV to the infant is:

1. 5% in the first 6 months
2. 5% from 6 to 12 months
3. 5% from 12 to 18 months

The risk of HIV transmission with breastfeeding is further increased if:

- The mother becomes infected with HIV during the time that she is breastfeeding.
- The mother has AIDS.
- The mother has cracked nipples, mastitis or a breast abscess.
- The infant has oral thrush.

NOTE The risk of transmission is determined by the amount of HIV in the breast milk. This is very high soon after infection with HIV and again with symptomatic HIV infection.

9-12 How can the risk of HIV transmission in breast milk be reduced?

- By giving formula feeds only and no breast milk (exclusive formula feeding)
- By giving breast milk only and no other liquids or solids (exclusive breastfeeding)
- By preventing HIV infection of the mother (safe sex) during the breastfeeding period
- By good breastfeeding management to avoid mastitis or breast abscess
- By treating oral thrush correctly in the infant
- By pasteurising breast milk. This is very helpful with pre-term infants in hospital
- By giving antiretroviral treatment to HIV-positive mothers who elect to breastfeed

With exclusive breastfeeding, for the first 6 months, the risk of HIV transmission appears to be small. Further research is still needed to document the risk of HIV transmission with exclusive breastfeeding.

NOTE In the Durban study, which compared exclusive-breast- and exclusive-formula-feeding in HIV-positive women, the risk of HIV infection in the infant at birth and 3 months was 6% and 15% respectively in both groups. In the Harare study the risk of HIV transmission with exclusive breastfeeding between 6 weeks and 6 months after delivery was about 1%.

9-13 When is it best not to breastfeed?

The best feeding choice must be made by the mother herself after counselling to enable her to understand the risks and advantages of both forms of feeding. Formula feeding is usually only advised if all the following conditions can be met:

1. Formula is available and affordable.
2. Clean water is available and feeding cups or bottles can be sterilised.
3. The mother can mix the feeds correctly.
4. It is acceptable to her family and society to formula feed.
5. Primary health facilities are available to monitor the child's growth.

If any of these conditions cannot be met, which is common when mothers are living in or returning to rural areas, then exclusive breastfeeding for 4 to 6 months followed by rapid weaning off the breast is probably safest. In these infants, the risk of death due to gastroenteritis and malnutrition if formula fed is often higher than the risk of HIV infection via breastfeeding.

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

### DIAGNOSING HIV INFECTION IN A CHILD

#### 9-14 How is HIV infection diagnosed?

In older children (and adults) the ELISA or rapid screening tests are used to confirm the diagnosis of HIV infection. These tests detect antibodies against HIV in the blood and usually become positive between 2 to 6 weeks after the infection (i.e. after the window period for the screening tests). As maternal HIV antibodies cross the placenta to the infant, and can remain in the infant's blood for up to 18 months after delivery, the screening tests can only diagnose HIV infection in an infant if the test remains positive after 18 months of age. A positive screening test in the infant before 18 months may simply indicate that there are still maternal antibodies to HIV in an infant who is not infected (i.e. HIV-exposed but not infected).

A positive ELISA or rapid test in a child younger than 18 months does not necessarily mean the child has HIV infection.

A PCR test (polymerase chain reaction) detects HIV DNA (part of the genetic code of HIV). If the PCR blood test is positive the infant is infected with HIV. As the PCR test may take up to 6 weeks after the time of infection to become positive (the window period for the PCR test), an HIV-infected infant may have a negative test during this time (a false negative test).

If the mother is HIV-positive and does not breastfeed, the PCR test should be done on the infant 6 weeks after delivery (at the time of the first immunisation). If the mother breastfeeds, the test should only be done 6 weeks after the last breastfeed. It is a great advantage to establish whether an HIV-exposed child is infected with HIV or not.

**NOTE** The vast majority of infants (more than 98%) infected with HIV before or during delivery will have a positive PCR test by 6 weeks. The remainder will be positive by 3 months.

A positive PCR test indicates that the child has HIV infection.

**NOTE** The ultrasensitive p24 antigen test is as reliable as the PCR at 6 weeks but is not widely available yet. The PCR HIV RNA test is also probably an accurate method of identifying HIV infection in children under 18 months.

#### 9-15 What are the advantages of diagnosing HIV infection early?

There are many advantages of diagnosing HIV infection early in infants. If the infant has not been breastfed, PCR testing can screen the infant for HIV infection at 6 weeks after delivery. Most infants will be negative and their parents can be reassured. These infants do not need the routine care offered to HIV-exposed infants from 6 weeks and can be followed at a well baby clinic. Infants with a positive PCR test should be closely followed up as they need additional care and monitoring. Breastfed infants should only be rescreened later after they have received no breast milk for 6 weeks. As HIV can cause severe illness and even death in the first few months of life, it is important to make the diagnosis as early as possible so that treatment can be started.

HIV-exposed infants should be screened for HIV infection at 6 weeks of age.
9-16 How does HIV infection present clinically in children?

HIV infection can present in many different ways in children and, as a result, may present with a wide range of signs and symptoms. This makes the clinical diagnosis of HIV infection difficult at times. Clinical signs usually slowly develop over a number of months but can present earlier in some infants. The clinical presentation of HIV infection depends on which stage has been reached.

9-17 What are the clinical stages of HIV infection?

HIV infection in children is divided into 4 stages:

1. During stage 1 the child is generally well (asymptomatic).
2. During stage 2 the child has skin rashes and minor infections.
3. During stage 3 the child becomes ill with more serious infections.
4. During stage 4 the child becomes infected with unusual organisms which are very uncommon in healthy children. Stage 4 is also known as AIDS.

Some previously-well infants can present with stage 4 disease without first progressing through the other stages.

**Note:** This is the WHO classification. It has replaced the CDC classification which only used 3 stages and did not adequately address many common conditions in Africa such as pulmonary tuberculosis, malnutrition and chronic lung disease.

9-18 How is symptomatic HIV infection diagnosed?

A definite diagnosis of symptomatic HIV infection (i.e. HIV infection causing disease) can be made if both of the following are present:

1. Confirmation of HIV infection by ELISA or PCR testing
2. Clinical signs and symptoms common in HIV infection (Remember that young infants do not have symptoms as they cannot give a history.)

Additional blood tests showing a weakened or damaged immune system help to confirm the diagnosis of symptomatic HIV infection but are not essential. Therefore, when laboratory tests of immune function are not available, a diagnosis of illness due to HIV infection can still be made on clinical signs and symptoms together with blood tests confirming HIV infection.

9-19 What are the signs of stage 1 HIV infection?

These children are generally well (asymptomatic) but may have persistent generalised lymphadenopathy.

9-20 What are the clinical signs of stage 2 HIV infection?

Stage 2 HIV infection presents with any of the following:

- An enlarged liver (hepatomegaly) and spleen (splenomegaly), i.e. hepatosplenomegaly
- Bilateral enlargement of the parotid glands
- Mild skin rashes, especially itchy papules, warts or molluscum
- Recurrent mouth ulcers
- Chronic or recurrent upper respiratory infections especially otitis media

9-21 What are the signs of stage 3 HIV infection?

Stage 3 HIV infection is recognised by:

- Moderate unexplained weight loss or failure to thrive. These children are usually chronically unwell with a poor appetite. Their weight is 60 to 80% of that expected for their age.
- Unexplained fever
• Unexplained persistent diarrhoea for more than 14 days
• Oral candidiasis (thrush) after the newborn period. The candidiasis is often severe, recurrent and responds poorly to topical treatment.
• Pulmonary tuberculosis
• Severe recurrent presumed bacterial pneumonia
• Herpes zoster or severe herpes simplex infection
• Symptomatic lymphoid interstitial pneumonia (LIP)
• Unexplained anaemia, neutropaenia (low white blood cell count) or thrombocytopaenia (low platelet count)
• Gingivitis (gum infections and bleeding)

9-22 What are the signs of stage 4 HIV infection?
Stage 4 HIV infection is recognised by:
• Severe failure to thrive or weight loss with a weight less than 60% of that expected for age
• Oesophageal candidiasis
• Pneumocystis pneumonia
• Disseminated tuberculosis or extrapulmonary tuberculosis
• HIV encephalopathy
• Many other severe opportunistic infections
• Malignancy

The main feature of stage 4 HIV infection is severe opportunistic infection such as Pneumocystis pneumonia. Unlike adults, children with HIV infection rarely present with malignancies.

A detailed description of the 4 stages of HIV infection are given at the end of this unit.

9-23 How is damage to the immune system documented in children?
HIV infects and damages the CD4 lymphocytes. These are important cells that control the whole immune system. HIV results in a fall in the number of CD4 cells in the blood (immunosuppression) which weakens or damages the function of the immune system (immunodeficiency).

The concentration or percentage of CD4 lymphocytes is used to measure the degree of immune damage. In children the number of CD4 cells is higher than in adults and normally reduces with age. Therefore, in young children (under 5 years) the number of CD4 cells is best expressed as a percentage:

1. The normal range of CD4 lymphocytes in children is 25% or above.
2. With mild immunosuppression the CD4 percentage may still be normal.
3. With moderate immunosuppression the range of CD4 lymphocytes is 15 to 24%.
4. With severe immunosuppression the range of CD4 lymphocytes falls below 15%.

The lower the CD4 percentage the greater is the damage to the immune system and, therefore, the higher the risk of serious HIV-related infections.

A CD4 percentage below 25% in young children indicates immunosuppression.

The absolute CD4 count is used in children aged 5 years and more. Healthy HIV-negative children of 5 years or above have a CD4 count above 500 cells/μL. A CD4 count below 200 cells/μL indicates severe immune suppression.

NOTE A low total lymphocyte count suggests a low CD4 percentage or count.

9-24 How is the clinical severity of HIV infection classified in children?
This depends on both:

1. The severity of the clinical signs of HIV infection (i.e. the clinical stage)
2. The severity of the immunosuppression
MANAGEMENT OF HIV-EXPOSED INFANTS

9-25 How should an infant born to an HIV-infected woman be managed after delivery?

1. All the routine care should be given. It is safe to give intramuscular vitamin K.
2. Infants should be dried well immediately after delivery to remove blood and amniotic fluid.
3. Whenever possible the decision to breastfeed or not should be made well before delivery.
4. HIV prophylaxis should be given to the mother and newborn infant to reduce the risk of mother-to-child transmission.

9-26 How should HIV prophylaxis be given to the newborn infant to reduce the risk of HIV infection during labour and delivery?

All pregnant women should be screened for HIV infection when they book for antenatal care. HIV-positive women must have their CD4 count measured and be offered HIV prophylaxis before delivery. Usually AZT 300 mg orally twice daily is given from 28 weeks gestation followed by a 300 mg oral dose 3-hourly during labour. In addition, oral Nevirapine 200 mg should be given to the mother at the onset of labour. After delivery the infant should be given both:

- AZT syrup 12 mg (1.2 ml) twice daily for 7 days, or 4 mg/kg (0.4 ml/kg) if the birth weight is less than 2 kg
- Nevirapine syrup within 72 hours of delivery as a single dose of 6 mg (0.6 ml), or 2 mg/kg (0.2 ml/kg) if birth weight is less than 2 kg

HAART (Highly Active Antiretroviral Treatment) with 3 antiretroviral drugs should be given to HIV-infected pregnant women with a CD4 count below 200 cells/μL. This will reduce the risk of HIV transmission to the fetus if it is started before 28 weeks.

NOTE The gestational age when AZT is started is controversial and differs between services from 28 to 34 weeks. Soon 3TC may be added to the AZT courses to reduce the risk of drug resistance with mono or dual therapy.

9-27 What is the management of HIV-exposed infants during the first year of life?

All HIV-exposed infants should be managed as follows unless appropriate PCR testing excludes HIV infection:

1. All the routine immunisations should be given.
2. Growth should be assessed by regularly plotting the infant’s weight on a Road-to-Health Card. The early detection of poor weight gain is especially important.
3. Ensure that the infant is receiving an adequate diet. Provide vitamins, especially vitamin A. This is best given as a multivitamin syrup.
4. Co-trimoxazole should be started at 6 weeks.
5. Signs of HIV infection should be looked for at each clinic visit. The early diagnosis and effective treatment of opportunistic infections can give these children longer and better lives.
6. The correct use of antiretroviral therapy is most important in children with AIDS.
7. It is very important to also provide the correct HIV management to the mother and other infected members of the family.

There are great advantages in identifying HIV-infected infants as soon as possible with PCR testing. Infants who are not infected with HIV can be followed at a well baby clinic.

9-28 Is it safe to give immunisations to infants who may be infected with HIV?

It is safe to give all routine immunisations to infants in the first months of life, provided they do not have signs of symptomatic HIV infection. Infants with HIV infection should not be given BCG.
What is the role of good nutrition in children with HIV infection?

Good nutrition plays an important role in helping to maintain the normal functioning of the immune system. Malnutrition (undernutrition) weakens the immune system, especially in HIV-infected children. Good weight gain on the Road-to-Health Card is the best indicator that the child is well nourished. A careful nutritional history must be taken in children who fail to thrive or lose weight. If necessary, supplementary feeds should be given. It is also important to regularly deworm children.

Vitamin A is important in maintaining a healthy immune system. To prevent vitamin A deficiency, children at risk of HIV infection should be given a multivitamin supplement 0.6 ml daily. This can be stopped if the child is found to be not infected with HIV. If multivitamin supplements are not available, give 50 000 iu of vitamin A orally once if under 6 months (best at 6 weeks). Then give 100 000 iu once at 6 months and 200 000 at 12 months and every 6 months thereafter to HIV-infected children.

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

How and when should prophylactic co-trimoxazole be given?

All infants born to HIV-positive women should be given prophylactic co-trimoxazole from 6 weeks until one year or until HIV infection in the child has been excluded by PCR testing. Prophylaxis should be continued beyond one year in any child with clinical signs of HIV infection. Prophylactic co-trimoxazole syrup is usually given daily for 5 days a week (Monday to Friday). The dose depends on the child’s weight:

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<thead>
<tr>
<th>Weight</th>
<th>Daily dose</th>
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<tr>
<td>&lt; 5 kg</td>
<td>2.5 ml paediatric suspension</td>
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<tr>
<td>5–9 kg</td>
<td>5 ml paediatric suspension</td>
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<tr>
<td>10–14 kg</td>
<td>7.5 ml paediatric suspension</td>
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<tr>
<td>15–22 kg</td>
<td>10 ml (or 1 regular strength tablet)</td>
</tr>
<tr>
<td>&gt; 22 kg</td>
<td>15 ml (or 1.5 regular strength tablets)</td>
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NOTE Co-trimoxazole can also be given 3 times a week (e.g. Monday, Wednesday and Friday)

Prophylactic co-trimoxazole decreases the risk of pneumonia caused by Pneumocystis. It also reduces the risk of other bacterial infections and diarrhoea due to some opportunistic infections.

Side effects to co-trimoxazole are uncommon in children. However, co-trimoxazole must be stopped immediately and the child referred if a maculopapular rash (red and easily palpable) develops as this may be the first sign of severe allergy to the drug.

Prophylactic co-trimoxazole reduces the risk of pneumocystis pneumonia.

What is the value of antiretroviral therapy in children?

- When started early it can prevent severe damage to the immune system and thereby prevent severe, recurrent opportunistic infections.
- If the immune system is already damaged, it allows partial recovery and lessens the risk of opportunistic infections.
- With an improvement in the functioning of the immune system, the child will start to thrive and feel much better.
- In the future, it is hoped that new developments in antiretroviral therapy may be able to cure HIV infection.
- With antiretroviral therapy AIDS is a chronic, manageable disease.

Early, correct treatment of HIV infection can enable children to enjoy a good quality of life for many years.
9-32 What is the expected outcome for children with HIV infection?

Although HIV infection is believed to eventually have a fatal outcome, much can still be done to improve the quality and length of these children's lives.

Because young children, especially those born pre-term, have an immature immune system, the course of the disease is more rapid than in adults.

The earlier the onset of symptomatic HIV infection, the poorer the expected outcome. Infants who are infected before delivery probably present early while infants infected via breast milk probably present late.

The clinical categories and immunological status (CD4 percentage) can be used to give an idea of the expected outcome. Children with asymptomatic HIV infection and an intact immune system (normal CD4 percentage) do best while the children with stage 3 or 4 HIV infection and a damaged immune system have the worst outlook.

Children with AIDS who do not receive antiretroviral therapy die much sooner than those who receive full treatment.

The progress in HIV-infected children can be roughly divided into 3 groups:

1. About a third of children present with clinical signs of HIV infection within the first year of life. Without antiretroviral therapy they have a rapid progression of their disease and usually die before 2 years of age (‘fast progressors’).
2. Another third of children present later, between the ages of 1 and 5 years. Their disease runs a slower course.
3. The remaining third present after the age of 5 (‘slow progressors’). They have the best outlook and may live for 10 years or more (similar to adults) even without antiretroviral therapy.

9-33 What factors other than age determine how fast HIV infection will progress?

- The amount of virus present (the viral load). A lot of virus leads to rapid progression of the disease.
- The amount of damage to the immune system (the degree of immunosuppression). The greater the damage (the lower the CD4 percentage), the faster the disease progresses.
- The nutritional status of the child. Poor nutrition results in a worse outcome as it lowers the number of CD4 cells.
- The number of HIV related infections. These co-infections (e.g. TB) may further depress the immune system and accelerate the course of HIV infection.
- Access to health care. Children die sooner if they do not have access to good health care as early diagnosis and treatment of infections is essential.
- The amount of organ damage done before antiretroviral treatment is started.

**NOTE** The genetic make up of the child and the type of the virus are probably also important. The viral load during the asymptomatic phase of HIV infection (viral set point) determines how fast the HIV infection will progress.

9-34 What are important respiratory problems in children with HIV infection?

- 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 influenzae* B
- Pneumocystis pneumonia
- Viral pneumonia and bronchiolitis
- Tuberculosis
- Bacterial ear infections (otitis media), bronchitis and sinusitis
- Lymphoid interstitial pneumonitis (LIP)
- Chronic lung disease especially bronchiectasis

**Children with an early onset of symptomatic HIV infection have the worst outcome.**
Pneumocystis pneumonia and lymphoid interstitial pneumonitis are seen very rarely in HIV-negative children.

9-35 What is pneumocystis pneumonia?

Pneumocystis pneumonia is a severe opportunistic infection caused a fungus called *Pneumocystis jiroveci*. This fungus does not cause pneumonia in healthy children. 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.

The risk of Pneumocystis pneumonia can be greatly reduced with co-trimoxazole prophylaxis from 6 weeks in all HIV-exposed infants (i.e. infants born to HIV-positive women).

Infants with suspected Pneumocystis pneumonia must be urgently referred to hospital for treatment with intravenous co-trimoxazole.

**Note** The diagnosis can be confirmed by finding cysts of Pneumocystis in the sputum using a special stain. Pneumocystis pneumonia is one of the AIDS defining illnesses (i.e. stage 4 HIV infection).

9-36 Is tuberculosis common in children with HIV infection?

Yes. Tuberculosis is one of the commonest serious bacterial infections seen in children with HIV infection.

**Tuberculosis is common in children with HIV infection.**

**Note** Lymphoid interstitial pneumonitis or LIP may be confused with tuberculosis, both clinically and on X-ray. The cause of LIP is uncertain. It usually occurs in older children. LIP presents with mild to severe respiratory signs, a persistent cough, and responds symptomatically to oral steroids. Parotid enlargement and finger clubbing are common.

9-37 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) 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 severe in children with HIV infection.

TB in HIV-infected children usually responds well to treatment. However, multiple drug resistant TB is becoming a problem with HIV-infected children. It is the result of inadequate or incomplete treatment.

**Note** Infection with *Mycobacterium avium* complex (MAC) is rare in children with AIDS.

See unit 8 for details on tuberculosis.

9-38 What gastrointestinal problems are common in children with HIV infection?

- **Oral candidiasis** (moniliasis or thrush): This may be severe, persistent or recurrent. Oral candidiasis after 2 months of age is uncommon in children who are not HIV-infected.
- **Oesophageal candidiasis**: Infants who have severe oral candidiasis and have difficulty swallowing and drool probably have oesophageal candidiasis as well. This serious complication rapidly results in dehydration.
- **Herpes stomatitis**: This is often severe in children with HIV infection, resulting in dehydration. Aphthous ulcers and gum infections are also common. Severe herpes stomatitis should be treated with acyclovir.
- **Acute diarrhoea**: This is usually due to bacteria and viruses which also cause diarrhoea in children who are not infected with HIV.
- **Chronic diarrhoea**: This may complicate acute diarrhoea or be due to opportunistic infections such as Cryptosporidium.
• **Lactose intolerance**: This may complicate chronic diarrhoea.

Except for children with mild, acute diarrhoea, all these children should be referred to hospital for further investigation and management. Oral candidiasis can usually be treated with local mycostatin or miconazole at a primary care clinic.

**9-39 What skin conditions are common in children with HIV infection?**

Many common skin conditions 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 conditions in children with HIV infection are:

- Pruritic papular urticaria (‘itchy bump disease’)
- Severe molluscum contagiosum
- Severe candidiasis nappy rash, which may ulcerate
- Widespread warts
- Severe chicken pox or shingles due to *Varicella zoster* virus
- Severe scabies, which may involve the whole body
- Severe tinea capitis (ringworm of the scalp)
- Severe impetigo
- Severe seborrhoeic dermatitis

Any of these severe skin conditions, especially shingles, suggests that the child is infected with HIV. 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.

_Skin conditions and their management are discussed in unit 12._

**9-40 What is the effect of HIV infection on neurodevelopment?**

The neurodevelopment of children with HIV infection is often retarded. They may even lose developmental milestones that have earlier been achieved. Slow development may be due to chronic illness, hospitalisation, lack of stimulation at home or depression. However, HIV may infect the brain causing an encephalopathy. Children with HIV infection are also at increased risk of bacterial and tuberculous meningitis.

*Note* Cryptococcal meningitis is an uncommon opportunistic infection in children.

**MANAGEMENT OF CHILDREN WITH SYMPTOMATIC HIV INFECTION**

**9-41 What are the major components of management?**

1. Nutritional support
2. Preventing and treating opportunistic infections
3. Antiretroviral therapy
4. Emotional and family support
5. Palliative and terminal care

**9-42 How important is nutrition support?**

Very important. Children with HIV infection should receive an adequate balanced diet and a multivitamin supplement. Many children feel much better and become hungry once antiretroviral therapy is started. Therefore they may need financial support or free food supplements.

**9-43 How should opportunistic infections be managed?**

It is very important that opportunistic infections (HIV-associated infections which occur because the immune system has been weakened) are treated early and aggressively. If possible, tuberculosis should be well controlled before antiretroviral therapy is started. The use of prophylaxis with co-trimoxazole in children with immune suppression is important. INH prevention (prophylaxis) must be given to young children.
who have household contact with adults suffering from pulmonary tuberculosis.

9-44 What are the goals of antiretroviral therapy?

1. To stop or reverse the progress of AIDS
2. To return growth and development to normal
3. To prolong and improve the quality of the child's life

With antiretroviral therapy, the aim should be to return the child to normal health, growth and development and maintain this for as long as possible. Antiretroviral therapy has changed AIDS from a rapidly fatal to a chronic, manageable illness.

9-45 When should antiretroviral treatment be started?

There remains a lot of debate as to when treatment should be started and guidelines are changing rapidly as more information becomes available. In South Africa, treatment is started when either:

1. The child is graded as having stage 3 or 4 HIV infection (i.e. moderate or severe clinical signs of HIV infection).
2. The CD4 percentage falls below 20% in asymptomatic children less than 18 months and below 15% if 18 months and older, or a CD4 count below 350 cells/μL in children of 5 years or more.

The mother or carer must also be ready to accept the diagnosis and make a commitment to treatment ('treatment-ready').

9-46 What are the guidelines for antiretroviral therapy?

1. Usually, 3 drugs are used together (multi-drug therapy).
2. The drugs must be given regularly and correctly, at the same time every day (good adherence or compliance).
3. Once or twice daily drugs that taste pleasant and can be given as a liquid are ideal.
4. The dose is calculated for body weight (or body surface area). The most common mistake is not to increase the dosage as the child grows.
5. Someone must take responsibility for the medication. There must be firm parental commitment to life-long treatment.
6. Educating the parents and child about correct medication is essential.
7. Treatment should be started and monitored for the first 6 months by an infectious disease clinic (AIDS clinic). Follow-up can then be done at a primary care clinic.

It is most important that antiretroviral therapy is given correctly every day.

9-47 What drugs are used for antiretroviral therapy?

The first line choice of antiretroviral treatment with highly-active antiretroviral therapy (HAART) in South Africa is a combination of:

1. Two nucleoside reverse transcriptase inhibitors ('nucs'), usually stavudine (d4T) and lamivudine (3TC)
2. One protease inhibitor in younger children, usually Kaletra (lopinavir with ritonavir), or one non-nucleoside reverse transcriptase inhibitor ('non-nuc') in older children, usually nevirapine or efavirenz

If there are serious side effects to one or more drugs, or if the patient fails to respond, a second line of treatment with a different combination of drugs will be necessary. These decisions will be made at an infectious disease clinic.
Highly-active antiretroviral therapy (HAART) is given with a combination of 3 drugs.

9-48 What side effects are seen with antiretroviral drugs?

All antiretroviral drugs have side effects. Most are mild, especially in children. However some can be severe and even fatal in rare cases. Nausea, vomiting, headache, fatigue and mild rashes are common. Rash, raised liver enzymes, peripheral neuropathy and anaemia must be looked for. Most serious side effects occur within one month of starting treatment.

Poor drug compliance (not taking the medication on time every day) may lead to drug resistance and treatment failure.

**Note**: Immune reconstitution inflammatory syndrome (IRIS) may present soon after antiretroviral therapy has started. An inflammatory response may develop as the immune system starts to recover. During this period severe bacterial, viral or opportunistic infections may present or become worse, especially TB.

9-49 What monitoring is need with antiretroviral therapy?

All children on antiretroviral therapy must be monitored:

1. Check compliance.
2. Growth should be monitored using the Road-to-Health Card.
3. The CD4 percentage and viral load should be measured every 6 months.
4. Full blood count, liver enzymes and/or fasting lipids according to the specific antiretroviral treatment regimen.

9-50 Is there a vaccine against HIV infection?

Unfortunately, there is not. However, an enormous amount of research is being done to develop an HIV vaccine. This holds the most promise of stopping the spread of the HIV epidemic.

9-51 How can emotional and family support be provided?

HIV affects the whole family. Counselling is needed when the diagnosis is made and for some time afterwards until the family comes to both accept and disclose the diagnosis. HIV counselling is usually provided by lay counselors. The support of the community is also very important.

Families with AIDS are often very poor with little or no income. The bread winners are often ill or have died. A child may be head of the family. Many children with AIDS, and children from families with AIDS, become orphans. Social services and community organizations need to be involved in the management of children with AIDS. Financial grants may also be needed.

Almost all children with AIDS have parents who are HIV-infected. It is important that the whole family receives good care. In poor communities, the death of a mother often results in the death of her children, even if they are not HIV-infected.

**The family of a child with AIDS usually needs emotional, medical and financial support.**

9-52 What is palliative and terminal care?

Palliative care is the care given to patients who cannot be cured of their illness. It addresses the physical, emotional and psychological needs of the child and family. Because HIV infection is incurable, palliative care starts when HIV infection is first diagnosed and continues for the duration of the illness. Emotional and spiritual support is also important. The aim of palliative care in children is to achieve the best quality of life for the child and family.

Terminal care is the care given to children in the last stages of AIDS. Pain management is an essential part of terminal care. Terminal care is best provided at home (home-based care) by a multi-disciplinary team of nurses, doctors, social workers and members of the community.
It should be compassionate and patient-centred (what is best for the patient). The Hospice movement has greatly improved the quality of terminal care both at home and in institutions. Palliative care includes terminal care. During the final stages of the disease the aim shifts to keeping the patient comfortable with love and dignity, relieving distress, limiting or reducing the duration of any hospital admissions, and providing the family with additional support. Therefore the total risk of mother-to-child transmission of HIV is 35% (5% + 15% + 15%).

CASE STUDY 1

A young woman is counselled and screened during pregnancy and found to be HIV-positive. She delivers at home and takes her infant to the clinic 3 days later. She breastfeeds for 24 months and introduces formula and solids from one month after delivery. The clinic refuses to give the routine immunisations because the child is positive for HIV on an ELISA screening test.

1. What is the risk of HIV transmission to this child before and during labour and delivery?
There is a 5% risk of HIV transmission during pregnancy plus a 15% risk during labour and vaginal delivery, giving a combined risk of 20%.

2. How could the risk of mother-to-child transmission of HIV at birth have been reduced in this child?
By giving both the mother and newborn infant prophylactic antiretroviral drugs.

3. What is the risk of HIV transmission to this child during the first years of life?
About 15% as mixed breastfeeds (breast milk plus other foods) were given for 2 years.

4. What would have been a better method of feeding this child during the first 6 months?
Either exclusive breastfeeding (breast milk only with no other fluids or solids) or exclusive formula-feeding (formula but no breastfeeds).

5. Do you agree with the clinic’s decision not to immunize this child?
No. HIV-exposed infants should receive their routine immunisations.

6. Is this child infected with HIV if the ELISA screening test is positive?
Not necessarily. Antibodies from an HIV-positive mother cross the placenta, giving the infant a positive screening test up to 18 months. A positive PCR test would indicate that this child was HIV-infected. However, a negative PCR test cannot exclude HIV infection until 6 weeks after the mother has stopped breastfeeding.

CASE STUDY 2

A 4-year-old child presents at a local clinic with loose stools for 6 weeks and a sore mouth. The Road-to-Health Card shows failure to thrive for the past 3 months. On examination the child is generally unwell and thin, has oral thrush, a rash and generalized lymphadenopathy. After counselling the mother, an HIV screening test (rapid test) is done. This is positive. The CD4 percentage is 20%.

1. Why would you suspect on the history alone that this child has HIV infection?
Because failure to thrive with chronic diarrhoea and a sore mouth are common presenting signs of HIV infection.
2. Are the findings on clinical examination suggestive of HIV infection?

Yes. Wasting, oral thrush (candidiasis), a rash and generalized lymphadenopathy are typical of symptomatic HIV infection.

3. How would you grade the clinical severity?

Stage 3 as the child is generally unwell with chronic diarrhoea and oral candidiasis.

4. Does the positive screening test confirm the diagnosis of HIV infection?

Yes, as the child is older than 18 months.

5. What does the CD4 percentage indicate?

It shows that the child’s immune system has been weakened (normal above 25%).

6. How should this child be managed?

The child should be referred to an HIV clinic where he can be evaluated for antiretroviral therapy. His oral thrush must be treated. Co-trimoxazole prophylaxis should be started. He needs an adequate balanced diet and the parents must be counselled. They may also need emotional and financial support.

CASE STUDY 3

A 1-year-old child presents with severe pneumonia. The mother is known to be HIV-positive. On examination the child also has extensive scabies and chronic otitis media. The infant has not started to crawl yet.

1. Do you think this child has symptomatic HIV infection?

Yes. With extensive scabies, you should always think of HIV infection. The pneumonia and chronic ear infection also suggest that this child has a suppressed immune system. Knowing that the mother is HIV-positive makes the diagnosis very likely.

2. What are the probable causes of the pneumonia?

Probably bacterial pneumonia, pulmonary tuberculosis or Pneumocystis pneumonia. This child needs urgent referral for investigation and treatment. A chest X-ray may show the typical appearance of pneumocystis pneumonia.

3. How can Pneumocystis pneumonia be prevented in an HIV-infected infant?

Prophylactic co-trimoxazole from 6 weeks is very effective in preventing Pneumocystis pneumonia in HIV-infected infants. It will also reduce the risk of other bacterial infections such as otitis media. There is no history that this child received prophylaxis.

4. Do children with HIV infection often have retarded development?

Yes. Retarded development is common in children with symptomatic HIV infection. It may be one of the first clinical signs of HIV encephalopathy, indicating stage 4 disease.

5. What is this child’s prognosis?

He has stage 4 HIV infections (i.e. AIDS) with severe immunosuppression. Without correct treatment, including antiretroviral therapy, he will probably die within months.

CASE STUDY 4

A 5-year-old girl, who was infected with HIV following a sexual assault, has been followed for 2 years at an HIV clinic. She has remained well until now when she presents with tuberculosis. On examination it is noted that she has bilateral parotid enlargement and an itchy papular rash. Her CD4 percentage is less than 15%. She is started on TB treatment, followed 2 months later by antiretroviral therapy. Soon after beginning the antiretroviral therapy she feels nauseous and has headaches.
1. What is the importance of bilateral parotid enlargement?
This is a very common early sign of HIV infection, as is an itchy papular rash.

2. Is tuberculosis common in children with HIV infection?
Yes. HIV infection should be suspected in all children and adults with TB.

3. Should antiretroviral treatment not be started before the tuberculosis?
No. If possible the TB should be controlled first before the antiretroviral therapy is started.

4. How many drugs are used to treat AIDS?
Antiretroviral therapy (HAART) should always be started with 3 drugs (multi-drug therapy). This lessens the risk of drug resistance and treatment failure.

5. What drugs are usually started as first-line treatment of AIDS?
In South Africa the first-line treatment regime is d4T and 3TC (both nucleoside reverse transcriptase inhibitors) together with Kaletra (a protease inhibitor) in young children and nevirapene or efavirenz (a non-nucleoside reverse transcriptase inhibitor) in older children.

6. Do antiretroviral drugs have side effects?
Yes. These are usually mild, especially in children. Nausea, vomiting, headache, fatigue and mild rashes are common and improve with time. Severe side effects can occur, but they are rare.
REFERENCE: THE 4 STAGES OF HIV INFECTION

Stage 1
- Asymptomatic
- Generalised persistent lymphadenopathy

Stage 2
- Hepatosplenomegaly (enlarged liver and spleen)
- Chronically enlarged painless parotid glands
- Repeated or chronic upper respiratory tract infections (e.g. otitis media, pharyngitis and sinusitis)
- Skin rashes (‘itchy bump disease’, extensive warts or molluscum) and fungal nail infections
- Recurrent mouth ulcers (aphthous ulcers) and inflamed gums
- Angular chelitis (cracks on the lips at the angles of the mouth)
- Herpes zoster

Stage 3
- Unexplained moderate malnutrition with no response to feeding
- Unexplained persistent fever for longer than 1 month
- Unexplained persistent diarrhoea for 14 days or more
- Oral candidiasis (thrush) after 2 months of age
- Oral hairy leukoplakia (white lines on the edge of the tongue)
- Severe ulceration and bleeding of the gums
- Pulmonary tuberculosis (TB) or lymph node TB
- Severe, recurrent pneumonia
- Symptomatic lymphoid interstitial pneumonitis (LIP)
- Chronic lung disease including bronchiectasis
- Unexplained anaemia, neutropenia (low white cells) or thrombocytopenia (low platelets)

Stage 4
- Unexplained severe malnutrition with wasting that does not respond to feeding
- Recurrent severe bacterial infections other than pneumonia, e.g. meningitis or osteitis
- Pneumocystis pneumonia
- Oesophageal candidiasis
- Severe chronic herpes simplex infection
- Extrapulmonary or disseminated TB
- HIV associated malignancies (e.g. Kaposi sarcoma)
- HIV encephalopathy
- Severe HIV associated infections (i.e. CMV, Toxoplasmosis, Cryptococcosis, Cryptosporidiosis, Isosporidiasis)