# Tutorial Letter 102/1/2017

## HIV/Aids care and counselling

# PYC2605

## Semesters 1

## Department of Psychology

**IMPORTANT INFORMATION:**

This tutorial letter contains the first six chapters of your prescribed book.

# CONTENTS

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## 1 INTRODUCTION

Dear Student

Your prescribed book (Van Dyk, A., Tlou, E., & Van Dyk, P. 2017. *HIV and Aids education, care and counselling: A multicultural approach* (6th ed.). Cape Town: Pearson Education) will unfortunately not be available in the bookshops at the time of registration.

To assist you to start with your studies as soon as possible, Pearson Education provided us with the first six chapters of your prescribed book. These chapters are also available on myUnisa (under additional resources).

Please use this tutorial letter (with the six chapters) to start with your studies as soon as possible. You will be able to answer most of your Assignment 01 questions if you work through this tutorial letter.

Please order your prescribed book as soon as possible from your bookseller. The examination questions **will be based on the whole syllabus** (and not only on the six chapters in this tutorial letter).

We apologise for the inconvenience, and we wish you well in your studies.

## 2 ADDENDUM A: CHAPTERS 1 TO 6

Addendum A contains the cover page, the contents and the first six chapters of your prescribed book.

# ADDENDUM A

## CHAPTERS 1 TO 6

**From:** Van Dyk, A., Tlou, E., & Van Dyk, P. 2017. *HIV and Aids education, care and counselling: A multicultural approach* (6th ed.). Cape Town: Pearson Education).

# HIV AND AIDS

## Education, Care and Counselling

*A multicultural approach*

A van Dyk, E Tlou and P van Dyk

Pearson

# Contents

# PART 1

## Knowing the virus

Aids healthcare workers and counsellors must be very well informed about all aspects of **HIV** infection and **Aids**. In addition, they must have the resources and the motivation to keep up with developments in treatment. This is because whatever their function, be it psychological, physical, spiritual or social, they will always be asked very basic questions about HIV and Aids. Another reason is that most of the care and counselling needs of HIV-infected clients involve the effect of the virus on their lives. Part 1 of this book is designed to answer most of the questions that healthcare workers or their clients might have about HIV and Aids.

Chapter 1 gives a brief historic overview of the 'birth' of a new epidemic and the origin of HIV – the virus that causes Aids. The chapter also looks at the global spread of HIV and the response of both the world and South Africa to the epidemic.

Chapter 2 explains how the immune system functions and describes the unique characteristics of HIV. The chapter also explains the effect of HIV on the immune system.

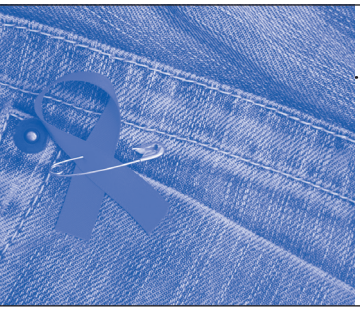
Chapter 3 examines how the virus is transmitted via sexual intercourse, by contaminated blood or by the mother to her baby. The chapter also explores important related issues, such as why it is difficult for disempowered women to avoid HIV infection and how poverty and other social problems contribute to the spread of HIV. It also looks at behavioural, biomedical and structural interventions to prevent HIV infection and includes the latest research on male circumcision, microbicides and antiretroviral therapy as prevention and vaccines.

Chapter 4 describes and discusses the symptoms of HIV infection, Aids and Aids-related illnesses in adults and children. Since tuberculosis (TB) is currently the most commonly occurring and serious opportunistic infection in HIV-infected individuals in Africa, this chapter devotes special attention to the prevention, diagnosis and treatment of TB. Chapter 4 also emphasises how important it is for healthcare professionals who work in Africa to recognise and treat the symptoms of other sexually transmitted infections (**STIs**).

You will learn what the terms and abbreviations on this page mean in the chapters where we discuss them.

Chapter 5 discusses the diagnosis of HIV infection. It looks at the various diagnostic tests we use, for example tests based on HIV antibodies (the **ELISA** and rapid antibody tests), as well as tests based on virus particles (such as the p24 antigen test, the DNA PCR and the RNA PCR). The chapter also provides the testing algorithms (or protocols) used in South Africa for testing adolescents and adults (including pregnant and breastfeeding women), children younger than 18 months and children older than 18 months who have been exposed to HIV.

Chapter 6 explains the role of antiretroviral (ARV) therapy (ART) in the management of HIV and provides guidelines for their use. The chapter also explains how drug-resistant viruses develop and how ARV adherence can be encouraged. The use of antiretroviral drugs for the prophylactic treatment of rape survivors, to prevent mother-to-child transmission of HIV and to manage hazardous occupational exposure to HIV (for example, by needlestick injuries) are also addressed in this chapter.



# Chapter 1

# HIV and Aids: A brief history

Alta van Dyk

### The coming of Raka

*He came out on the far side of the water,*
*out of the broken reeds,*
*and like a child laughing toothlessly …*
*grimaced, squatted, waited.*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- tell a friend the story about the history of Aids;
- participate intelligently in the debate about the possible origins of HIV;
- browse the Internet to get the latest statistics on the prevalence of HIV; and
- critically evaluate South Africa's response to the Aids epidemic.

## Chapter outline

- The birth of a new epidemic
- The origin of HIV
- The global Aids epidemic
- The world's response to the Aids epidemic

HIV has changed our world forever. Not only does it have serious effects on the human immune system; it also impacts profoundly on our belief systems, as well as on our social, sexual, economic and political lives. HIV has united scientists from various fields all over the world to pool their knowledge in an effort to stop both the effects of HIV on humanity and HIV itself. This chapter will take you to the very beginning of the HIV epidemic to see where it all started and what our response to it was.

**Glossary**

**Baffled** Mystified, perplexed or bewildered; having no logical idea for why something was caused.
**Haemophilia** A medical condition, usually hereditary, in which the ability of a person's blood to clot is greatly reduced, causing the person to bleed severely from even a slight injury.
**Isolate** Identify something and investigate it separately from everything else.

## 1.1 The birth of a new epidemic

The world first became aware of a new disease in June 1981 when the Centres for Disease Control and Prevention (CDC) in Atlanta in the USA pronounced the occurrence of not only an exceedingly rare form of pneumonia (***Pneumocystis* pneumonia** or PCP, then called *Pneumocystis carinii* pneumonia) but also of a very uncommon type of cancer (**Kaposi's sarcoma**) in five young homosexual men in Los Angeles. Scientists were **baffled** by this new disease because the causes and the modes of transmission were unknown. Initially, it was thought that this disease only affected homosexual men, but, by the end of 1981, PCP was also diagnosed in **haemophiliacs**, people who inject drugs and Haitian immigrants in the USA. Soon afterwards, this disease which compromised or damaged the immune system, was also identified in central Africa in heterosexual people. As a result of some of its symptoms, such as severe diarrhoea and weight loss, the disease was referred to as 'slim disease' in Africa.

### Enrichment: The history of *Pneumocystis jiroveci* pneumonia

*Pneumocystis jiroveci* pneumonia was previously called *Pneumocystis carinnii* pneumonia (PCP). It was believed that PCP was a parasitic infection caused by a protozoan, but it was discovered that the disease is actually caused by a fungus. The name of the disease was changed to *Pneumocystis jiroveci* pneumonia (in honour of the Czech parasitologist, Otto Jirovec, who described this microbe in humans). However, because the disease is widely known as PCP, and to prevent problems in the medical literature, it was decided to continue using the acronym PCP or *Pneumocystis* pneumonia.

In 1982 this new disease was named 'Aids' or acquired 'immunodeficiency syndrome' (see the Terminology box on page 5 for a detailed definition). The rivalry to find the cause of this new disease was intense, and, in 1983, Dr Luc Montagnier and other scientists in the Pasteur Institute in Paris, France, **isolated** a virus in a patient who had lymphadenopathy (swollen lymph nodes). Initially, the virus was labelled lymphadenopathy-associated virus or LAV, but the name was later changed to human immunodeficiency virus (or HIV). Final scientific proof that HIV was the cause of Aids was published in two journals, *Science* and *The Lancet* in 1984.

Aids was first reported in South Africa in 1983 when it was diagnosed in two homosexual men. As elsewhere in the world, Aids in South Africa was initially also associated only with homosexual men, haemophiliacs and blood transfusions. By the end of 1989, however, entry into the heterosexual population was confirmed and HIV spread rapidly in the 1990s. It was especially young women and older men who were infected, with a disproportionate number of people aged between 15 and 40 years old.

### Terminology: Aids

Aids is an acronym for 'acquired immunodeficiency syndrome'. The disease is acquired, which means that it is not inherited. Instead, it is caused by a virus that is outside the body (the human immunodeficiency virus or HIV) that finds its way into the body. HIV, once inside the body, destroys its ability to fight off infections and disease. Immunodeficiency thus refers to the inability (or deficiency) of the immune system to defend itself against infections. **Syndrome** is a medical term that describes a grouping of particular signs and symptoms that occur simultaneously and which characterise a particular condition.

The UNAIDS (2011: 2) defines Aids as follows: Aids is caused by HIV, the human immunodeficiency virus. HIV destroys the body's ability to fight off infection and disease, which can ultimately lead to death. Antiretroviral therapy slows down replication of the virus and can greatly enhance quality of life, but antiretroviral therapy does not eliminate HIV infection.

## 1.1.1 A controversial discovery

The history of the discovery of HIV is both interesting and controversial. As mentioned before, in 1983 Dr Luc Montagnier of the Pasteur Institute discovered the virus that causes Aids. However, a year later, Dr Robert Gallo of the USA claimed that he had been the first to discover the virus. A protracted court case about Gallo's alleged 'theft' of Montagnier's virus ensued. The emotions that this court case evoked were so intense that they threatened to derail the 1987 bilateral talks between Jacques Chirac (the French prime minister) and Ronald Reagan (the American president). The issue was, however, provisionally (and only temporarily, as it turned out) resolved by an 11th-hour compromise that officially acknowledged both Montagnier and Gallo as co-discoverers of the virus.

The source of the controversy was the fact that in 1983 Montagnier sent the virus that he had isolated from lymph nodes to Gallo in good faith for further investigation. Gallo's subsequent claim that he had discovered and described HIV was based on the genetic differences between his virus and the original virus he had received from Montagnier. The bitter dispute was renewed in 1990 when scientists at the Pasteur Institute decided to analyse the genetic structure of Gallo's virus and compare it with Montagnier's initial isolate of the virus (Schoub, 1999: 10). They concluded that the two viruses were so similar that it was very unlikely that they were not one and the same (taking into account natural changes and **mutations** in genetic structure that could be expected from different virus isolates). However, the scandal was somewhat dampened by the later admission by Montagnier's laboratory that some inadvertent contamination of Gallo's strain had taken place. It was then reaffirmed that the credit for the discovery of the virus should be shared between the two: Montagnier for the original isolation of HIV, and Gallo for being able to propagate the virus in cell culture. It was also acknowledged that Gallo's laboratory had played a massive part in the subsequent development of the first **HIV antibody tests** which became available in 1985.

But this reaffirmation of dual credit was still not the end of the story and the original controversy was once again revived in 2008 when Luc Montagnier and Francoise Barré-Sinoussi, both of the Pasteur Institute, were publically acknowledged for their discovery of HIV when they were joint winners (with

### Glossary

**Mutation** The changing of the structure of a gene, creating a variant form that can be transmitted to future generations.

**HIV antibody test** A test to determine if an individual has antibodies to HIV. The presence of HIV antibodies indicates that the person has been exposed to the HI virus and has raised an immune response. The most common HIV antibody test is the ELISA test (see Chapter 5).

a third scientist; see below) of the Nobel Prize for physiology and medicine. The three winners are shown in Figure 1.1. The Nobel committee motivated its decision by saying that it was now established without any doubt that the initial discovery of the virus had been at the Pasteur Institute. This was a bitter pill to swallow for the American researcher, Robert Gallo, who was not even mentioned.

An interesting fact about the 2008 Nobel Prize was that the two French scientists shared the prize with a third scientist, Harald zur Hausen, who was awarded the prize for his discovery of **human papilloma virus** (**HPV**) which causes cervical cancer. This discovery led to the development of a **vaccine** to prevent HPV infections, and, ultimately, cervical cancer.

The new disease and the dispute between the two countries' scientists (Montagnier and Gallo) grabbed the public's attention. A journalist, Randy Shilts (who later died of Aids), wrote a book called *And the Band Played On* about the politics and the people in the Aids epidemic in 1987. It was made into a major film in 1993.

**Glossary**

**Vaccine** A substance given to stimulate the immune system to protect the person from infection by a specific micro-organism. Vaccines are made from live attenuated pathogens, from killed whole organisms or from purified **proteins**. The search for an HIV vaccine is based on genetic engineering and protein-based technology.

**Figure 1.1** Luc Montagnier and Françoise Barré-Sinoussi (for discovery of HIV) and Harald zur Hausen (for development of the HP virus vaccine), won the Nobel Prize for physiology and medicine in 2008

## 1.2 The origin of HIV

No disease has ever captured the imagination of the world quite as much as Aids has, and the following questions are often asked about the disease: Where did Aids come from? Is it a new or an old disease? Where did the virus originate?

In the 1990s it was believed that we would probably never really know what the origin of the disease or the ancestry of the virus was. Schoub (1999: 13) summed up this view, saying 'little is known about the origins of any human virus, let alone HIV'. However, in those early days, there was much **speculation** about the origin of the Aids epidemic, as well as many theories. Some of these theories stated that Aids had been present in central Africa for centuries, but that it had remained unidentified as a result of the lack of sophisticated medical facilities able to diagnose the disease. Other theories blamed the polio vaccine of the 1950s,

**Glossary**

**Speculation** When people form theories about something, but without firm evidence to support their theories.

saying that it caused Aids because it was produced from cell cultures from the kidneys of the African green monkey. There were also theorists who blamed anti-malaria medication as the cause of Aids.

In time it was shown that none of these theories about the origin of the Aids epidemic was correct. However, the theory that the virus crosses the species barrier from primates (more specifically, simians) to people was correct.

## 1.2.1 Crossing the species barrier

After it was discovered that HIV (the human virus) was related to SIV (simian immunodeficiency virus) found in primates, the next step was to clarify the exact relationship between the two. The possibility that different strains of SIV (associated with different species of monkeys and apes) had crossed the species barrier to humans at different times, causing different strains of HIV, was then investigated. The results of these investigations are summarised in Figure 1.2 below.

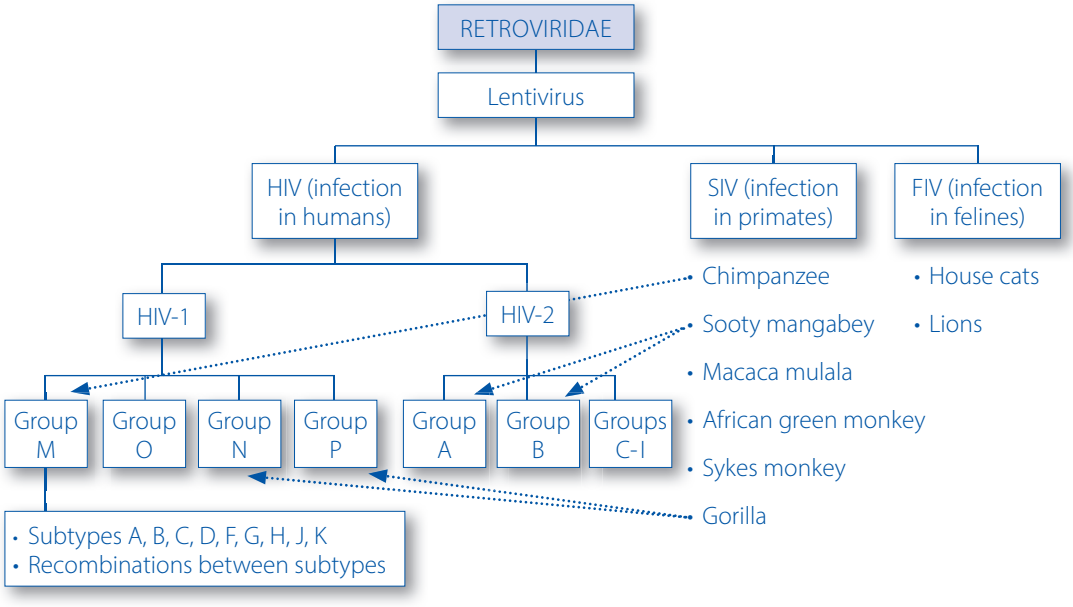



**Figure 1.2** HIV diversity and possible origin

As is illustrated in Figure 1.2, HIV (the human virus) and SIV (the virus found in simian primates) both belong to the family Retroviridae (because they are both retroviruses. They also belong to the genus Lentivirus (meaning slow virus, because it takes such a long time after infection for the disease to develop).

HIV can be further divided into HIV Type 1 (or HIV-1) and HIV Type 2 (or HIV-2). HIV-1 has been classified into four groups: M (major), O (outlier), N (non-M and non-O) and P. The global Aids epidemic is currently dominated by the group M HIV-1 viruses. This group (M) can be divided further, into subtypes or **clades**, of which nine have been described, namely HIV-1 subtypes A, B, C, D, F, G, H, J and K (with E and I missing, after it was discovered that they were not real subtypes but recombinants. You will learn more about recombinant viruses in Chapter 2). The virus that dominates in southern Africa (e.g. South Africa, Zimbabwe, Malawi and Botswana) is HIV-1 subtype C.

See Chapter 2, page 38 for an explanation of retroviruses.

**Glossary**

**Clades** Various subgroups of HIV predominating in different parts of the world. They are named using the letters A through K. In South Africa, the predominant clade of HIV-1 is clade or subtype C.

HIV Type 2 (or HIV-2) is restricted mainly to West Africa. Although HIV-2 is structurally similar to HIV-1, it is less pathogenic than HIV-1 and its progression to disease is slower. HIV-2 has been classified into nine groups (A to I) but only Groups A and B are epidemic. HIV-2 Groups C to I are crossovers, known in single individuals only.

Let's now look at the simian immunodeficiency virus (SIV) before we discuss the crossing of the species barrier from primates to humans. The simian immunodeficiency virus (occurring in primates) consists of various SIV strains. Each strain is peculiar to the primate species it infects. For instance, the mandrill ape is infected by SIVmnd, the African green monkey by SIVagm, the sooty mangabey monkey by SIVsm and the chimpanzee by by SIVcpz.

In an attempt to discover the origin of HIV, researchers took samples from a number of primate species and – in a process called 'sequence comparisons' – compared them with HIV. The final conclusion was that an ancestor of HIV-1 group M virus had been transmitted from a chimpanzee (*pan troglodytes troglodytes*). It was estimated that this interspecies transmission had occurred sometime around the 1930s in equatorial West Africa where primates were often hunted for bush meat (Williamson & Martin, 2010). The virus was probably transmitted from the chimpanzee to the hunter when he was bitten or cut while hunting or butchering the animal. Exactly how SIV transformed into HIV after infection of the hunter is unknown, but it probably occurred through natural selection which would favour a virus capable of adjusting so that it can infect, live and reproduce in a new host, namely in the T cells of a human being.

It was further established that HIV-1 groups N and P viruses probably originated from wild gorillas, while HIV-2 groups A and B originated from the sooty mangabey monkeys.

**Figure 1.3** It is now commonly accepted that an ancestor of the HIV-1 group M virus was transmitted from a chimpanzee (*pan troglodytes troglodytes*)

If you look at Figure 1.2 again, you will see that there is a third category of the Lentivirus, namely FIV or the feline immunodeficiency virus. This virus affects domestic (or house) cats worldwide, as well as wild cats like the African lion. The primary modes of transmission of FIV are bite wounds or scratches where the saliva of the infected cat enters the bloodstream of an uninfected cat. Although cats are carriers and transmitters of FIV, it is usually not fatal for them. FIV can however deplete the immune systems of the animals and they should be checked regularly for infections and treated as needed. There are no known cases of FIV infecting a human being, or of HIV infecting cats.

### 1.2.2 Urban legends

The origin of HIV not only captured the imagination of scientists but also that of the general population. **Urban legends** are rife and often consist of **conspiracy theories** or stories that blame somebody, some groups, some organisation or some government agency. Some examples of conspiracy theories are that the FBI developed the virus to destroy third world countries, that it was developed by the apartheid government in South Africa or that a New Age movement that wanted to destroy a specific portion of the population developed it.

Urban legends and conspiracy theories are often born out of fear and they have the function of making people feel that they have power over their situation. They are also used by people to make themselves feel blameless and instead blame someone or something else for their misfortune. It is important for educators and **counsellors** to arm themselves with scientific theories (in contrast to popular conspiracy theories) to correct some **misconceptions** about the origin of HIV in their communities. It is further necessary to develop a critical attitude (the basic principle of scientific thinking) and to question the urban legends and conspiracy theories that come to one's attention.

**Glossary**

**Urban legend** A popular story that is common in an area, but is completely unsubstantiated (has no evidence to support it).
**Conspiracy theory** The belief that some hidden organisations are responsible for serious events happening in a country.
**Counsellor** Someone who provides **counselling**. Counselling is a facilitative process in which the counsellor, working within the framework of a special helping relationship, uses specific skills to assist clients to develop self-knowledge, emotional acceptance, emotional growth and personal resources.
**Misconception** A false impression (idea, view or opinion) based on a wrong understanding or faulty thinking.

## 1.3 The global Aids epidemic

Although Aids is currently still one of humanity's most serious health challenges, many successes have been achieved by the solidarity across the globe in our response to Aids (UNAIDS, 2012: 8). The effect of the global Aids response is clearly written in the statistics. In 1996 the spread of HIV peaked with an estimated 3.5 million new infections worldwide occurring in that year alone. Two decades later, the number of new infections is estimated at about two million per year – a decrease of approximately 43%. Aids deaths have decreased significantly and dramatically since the scale-up and wider accessibility of **antiretroviral therapy**. However, the burden of the epidemic continues to vary considerably from country to country and among regions, with sub-Saharan Africa the worst-hit region in the world, where nearly 70% of the world's HIV infections occur, with women and children bearing the brunt of the disease.

### Enrichment: Statistics on HIV and Aids

For the most current statistics on HIV and Aids, visit the UNAIDS website at: http://www.unaids.org

## 1.3.1 Incidence and prevalence of HIV infection

How do we know how many people are infected by HIV? Before we answer this question, it is first necessary to understand the difference between these two concepts: HIV incidence and HIV prevalence.

**Glossary**

**HIV incidence** The annual number of new HIV infections as a proportion of previously uninfected people.

### 1.3.1.1 HIV incidence

**HIV incidence** is the number of new cases of HIV infection that occur in a specific time period (usually in one year), presented as a percentage. We calculate this percentage by dividing how many people are infected in a given time period (i.e. new infections) by how many people were previously uninfected. For example, if a million people are infected with HIV in a given year in a country with 27.8 million uninfected people, the HIV incidence for the country in that year would be 3.6% (see the Enrichment box below).

Although HIV incidence provides a good measure of the dynamics of the epidemic, it is unfortunately very difficult to measure. To calculate incidence, it is necessary to conduct a longitudinal study in order to observe a group of HIV-uninfected people over a specific time period to determine how many of them become infected with HIV during that time period. Although some studies have been done to estimate the HIV incidence in certain groups, such as female sex workers in KwaZulu-Natal and young uncircumcised men in Orange Farm (Gouws, 2010), it remains difficult and expensive to follow a cohort of people over time. Most incidence estimates are therefore instead obtained through mathematical and statistical modelling.

### Enrichment: The difference between HIV incidence and HIV prevalence

$$\text{HIV incidence} = \frac{\text{Number of new infections in a specific year}}{\text{Number of previously uninfected people}} \rightarrow \frac{\text{1 million}}{\text{27.8 million}} = 3.6\%$$

$$\text{HIV prevalence} = \frac{\text{Number of people infected with HIV at a specific time}}{\text{Total population}} \rightarrow \frac{\text{5.51 million}}{\text{54 million}} = 10.2\%$$

**Glossary**

**HIV prevalence** The proportion of people living with HIV at a specific time, expressed as a percentage.

### 1.3.1.2 HIV prevalence

**HIV prevalence** is the number of people living with HIV (as a proportion of the total population) at a specific time, expressed as a percentage. Gouws and Abdool Karim (2010: 57) describe prevalence as 'a snapshot view' of the current number of people infected with HIV. For example, if South Africa had 5.51 million HIV-infected people at a specific time, and the South African population was 54 million at that stage, HIV prevalence would be 10.2% (see Enrichment for the formula).

## 1.3.2 How is HIV prevalence measured?

In countries with HIV epidemics, national estimates of HIV prevalence are usually based on data from a combination of the following surveys: antenatal (pre-birth) prevalence surveys, population and community-based surveys, studies among key populations at higher risk (see the Terminology box on page 15 for a definition of key populations) and reports of Aids-related deaths.

The antenatal **surveillance** programme involves the annual testing of the blood of pregnant women in the public health sector who visit antenatal clinics for the first time during a specific pregnancy. In South Africa, the first national antenatal survey amongst pregnant women was conducted in 1990. The surveillance is anonymous and unlinked, which means that there are no names attached to the tests and that the results cannot be linked to specific individuals. Blood samples are tested for HIV and, since 2012, for herpes simplex type-2.

The second source of information to establish the prevalence of HIV infection in South Africa are the National HIV Prevalence, Incidence and Behavioural surveys. The Human Sciences Research Council (HSRC) and colleagues at the Medical Research Council (MRC) conducted the first survey in 2002. It has been repeated every three years since then. These studies involve the testing (with **informed consent**) of the blood of large samples of individuals in households in South Africa. Questionnaires on various behavioural aspects, such as condom use, circumcision, sexual debut and awareness of HIV status are also completed.

### Enrichment: SA National HIV Prevalence and Incidence report

The results of the latest South African National HIV Prevalence, Incidence and Behavioural Survey can be found at: http://www.hsrc.ac.za

Type the words 'HIV Prevalence, Incidence and Behavioural Survey' into the search box.

Where data gained from antenatal surveys are especially useful for assessing general HIV trends in a country, the national household surveys help to fill out the picture by also providing the prevalence of HIV in terms of sex, age, race and geographical areas. Valuable information for both incidence and prevalence statistics is also gained from surveys conducted with specific groups, such as sex workers and truck drivers, or from reports of Aids-related deaths.

It is impossible to say exactly how many people are infected with HIV at any given time, and only estimates can be given based on the best available information. HIV infection estimates are therefore always reported in the literature using the following format: 'An estimated 36.9 million (34.3 million to 41.4 million) people worldwide were living with HIV in 2014'. Because the estimate number (36.9 million in this case) cannot be absolutely accurate, the number is always followed by a minimum and maximum figure between which the prevalence could actually range.

## 1.4 The world's response to the Aids epidemic

The world's initial response to the Aids epidemic was characterised by denial, blaming and moralising. It was believed that Aids was a 'gay disease' and that it would only affect homosexual people 'who brought it on themselves' and that it would taper off in time and disappear. When haemophiliacs became infected through infected blood products, the world of Aids became divided between the 'innocent victims' and the 'promiscuous guilty' who spread the disease.

### Glossary

**Surveillance** Carefully observing someone or something in order to obtain useful information.

**Informed consent** The kind of consent to medical testing or treatment that is accompanied by information and permission. Before an HIV test can be done, the client must understand the nature of the test and he/she must also give verbal or written permission to be tested. A client may never be misled or deceived into consenting to an HIV test.

Today we are paying a dear price for our early complacent moralism and the initial indifference to the Aids epidemic. HIV has established itself firmly in our communities and the effects of Aids have devastated many families, communities and economies – especially in developing countries.

## 1.4.1 South Africa's response to the Aids epidemic

In South Africa, the initial response to HIV and Aids was very similar to the worldwide one, except that it reached new depths of denial and inaction for various ideological reasons.

### 1.4.1.1 Inaction and denialism

**Glossary**

**Denialism** The refusal to admit the truth about something that is proved by scientific or historical evidence.

The response to the Aids epidemic in South Africa was tainted by government inaction, pseudoscience, **denialism**, dissident beliefs, conflict and harmful practices. In the 1980s, Aids was seen by the apartheid government as a 'gay' disease that 'would sort itself out' and a general atmosphere of distrust, disinterest and blaming prevailed. Although the first Aids Advisory Group was established by the government in 1985, and Aids Training and Information Centres (ATICs) saw the light in 1991, they could not really make any progress without proper leadership and support from the government. According to Abdool Karim and Baxter (2010: 41) the first major step forward was the creation of the National Aids Convention of South Africa (NACOSA) in 1993 – a coordinating body involving representatives of the apartheid government and representatives of anti-apartheid Aids activists. When the ANC with Nelson Mandela as president took office in 1994, there was great hope for a dedicated and concerted response to the Aids epidemic, especially since the first credible Aids strategy or plan (the NACOSA Strategic Plan) had been adopted. Unfortunately, Mandela's government was faced with so many challenges in the fledgling democracy that Aids and its co-infectant, TB, did not get the attention that they deserved. For example, instead of coordinating efforts to manage the epidemic, the country was racked by controversies caused by scandals, such as the *Sarafina II* play in 1996 (major mismanagement of funds) and the Virodene scandal in 1997 (when government supported a so-called cure for Aids consisting of toxic industrial solvent).

The most tragic oversight of the Mandela government was its refusal in 1998, four years after the drug had been proven successful in the USA, to provide **AZT** to pregnant women in South Africa to prevent mother-to-child transmission of HIV. That AZT should have been made available to these women is vividly illustrated by the fact that the number of pregnant women with HIV infection in South Africa increased from 4.3% in 1994 to an estimated 17% in 1998. The Treatment Action Campaign (TAC), led by Zackie Achmat, was established in 1998 to **advocate** for the right to treatment for people living with HIV. Zackie Achmat was nominated along with the TAC for the Nobel Peace Prize in 2004 for their dedicated work.

**Glossary**

**Advocate** Using activities, such as media campaigns, research, protest marches, public speaking and court cases to publicly support an issue and to get policies and laws around that issue changed.

### 1.4.1.2 Our darkest days

The Mbeki era (following the second democratic elections in 1999 and lasting until 2008) surely marked South Africa's darkest days in its response to the Aids epidemic. This era was characterised by a president who linked up with Aids dissidents who believed that Aids was not caused by HIV, and by a minister of health (Manto

Tshabalala-Msimang) who absolutely refused to approve antiretroviral treatment for pregnant women. After many actions taken by the TAC, the South African High Court finally, in 2002, ordered the government to provide pregnant women with **nevirapine** to prevent mother-to-child transmission of HIV. At that stage, HIV prevalence in pregnant women in South Africa had already risen to 24.5%.

One of the positive decisions of the Mbeki government was the decision in 2003 to provide antiretroviral therapy free to all South Africans who visited public health services. Although there was general excitement about this decision, many believed that it was 'too little too late'. According to Abdool Karim and Baxter (2010: 42), 'this decision should have been made three years earlier, which could have saved an estimated 330 000 lives.' Although Thabo Mbeki kept out of the HIV and Aids limelight during his second term, Manto Tshabalala-Msimang continued to cause much embarrassment with her support of untested and unlicensed 'vitamin' supplements as a cure for Aids (e.g. the Matthias Rath case).

## Enrichment: TAC court case against Rath and the South African Government

To read more about the TAC court case against Rath and the South African Government, go to the following website: http://www.tac.org.za/community/node/2024

Tshabalala-Msimang also embarrassed South Africa at the International Aids Conference in Toronto in 2006 with her promotion of vegetables (beetroot, garlic and lemon) as an alternative for antiretroviral treatment. After the Toronto debacle, certain positive changes were made in government with the deputy minister of health, Nozizwe Madlala-Routledge, taking over South Africa's response to the Aids epidemic. Her outspokenness cost her her job when she was dismissed by President Thabo Mbeki in 2007. Thabo Mbeki himself was asked to resign in 2008, and Jacob Zuma took over the presidency in 2009.


**Figure 1.4** The South African government was ordered to provide nevirapine to HIV-infected pregnant women

### 1.4.1.3 A new beginning?

Because of certain controversial HIV-related remarks Jacob Zuma had made prior to being elected the President of South Africa, once elected, the scientific Aids community was apprehensive about his role in addressing the Aids epidemic. However, a new breath of hope spread throughout the country when Zuma and his new government (with Dr Aaron Motsoaledi as minister of health) committed themselves to implementing the five-year National Strategic Plan for both Aids and TB. On World Aids Day in December 2009, Jacob Zuma announced a number of critical **interventions** to improve the access of special groups (such as pregnant women and patients with HIV/TB **co-infection**) to antiretroviral therapy. The aim of these interventions was not only to decrease the disease burden, but also to improve life expectancy and, at the same time, address child and maternal mortality. Consequently, new clinical guidelines that described how HIV and Aids in adults, adolescents and children should be managed, as well as guidelines for the prevention of mother-to-child transmission of HIV, were implemented on 1 April 2010. In a concerted effort to increase the **uptake** of testing and to provide an integrated service to all the people of South Africa, the health department also launched a major HIV counselling and testing (HCT) campaign in 2010. The testing campaign was deemed very successful with a reported 18 million people tested for HIV during the campaign. Although there were still gaps in South Africa's strategies to deal with the Aids epidemic, 2010 will probably be remembered not only for hosting the Football World Cup, but also for the new direction the country took in its response to the Aids epidemic.

As from January 2015, South Africa started treating HIV-infected people much earlier than previously. In line with the World Health Organization (WHO) guidelines adopted in 2013, South Africa started ARV treatment at **CD4+T cell** counts of less than 500 (as compared with a **CD4+T cell count** of less than 350 that was used before 2015). It was also decided that South Africa would no longer terminate the treatment of HIV-infected women when they stopped breastfeeding their infants, but that every pregnant HIV-infected woman would go on lifelong treatment, regardless of their CD4+T cell status. On 10 May 2016, the Minister of Health, Dr Aaron Motsoaledi, announced the South African Government's decision to remove CD4+T cell count as an eligibility criterion for ARV treatment. This means that all HIV-infected people should be started on treatment as soon as possible after diagnosis. The Government also announced it would provide PrEP (pre-exposure **prophylaxis**) to sex workers who participate in sex worker programmes (South African Government, 2016). South Africa's antiretroviral programme is currently the largest in the world.

**Glossary**

**Intervention** An action (can be political, economic, social, medical or behavioural) taken to improve a medical situation.
**Co-infection** When more than one pathogen infects a person at the same time.
**Uptake** Making use of something that is available.

**Glossary**

**Prophylaxis** The term prophylaxis refers to medical measures taken in order to prevent disease or health problems, rather than to treat or cure an existing condition. Prophylaxis is also a way to stem an outbreak of disease, or minimise the symptoms of someone who has been exposed to a disease or virus.

## Enrichment: Announcement by the South African Minister of Health, Dr Aaron Motsoaledi, 10 May 2016

The Minister of Health's speech (to remove CD4+T cell count as an eligibility criterion for ARVs) is very interesting. Access it at the following website: http://www.gov.za/speeches/debate-health-budget-vote-national-assembly-10-may-2016-dr-aaron-motsoaledi-minister-health%20

In December 2015, the Medicines Control Council (MCC) officially registered the use of the antiretroviral drug Truvada® to be used as PrEP (or pre-exposure prophylaxis). Truvada® (one tablet taken once a day) will greatly decrease the chances of **HIV-negative** people contracting HIV. Truvada® as PrEP will be especially useful in preventing HIV in key populations, such as sex workers, men who have sex with men (MSM), sexually active young women and people who inject drugs.

**Glossary**

**HIV negative** If a person is HIV negative there is no evidence of infection with HIV (e.g. an absence of antibodies against HIV) in a blood or oral fluid test. A person who is in the window period (the time between HIV exposure and detection of antibodies or viral particles) can be infectious to others.

### Terminology: The difference between key populations and vulnerable populations

The UNAIDS recommends that the term 'key populations at higher risk' should be used and not 'high risk groups'. 'Key populations' differ across countries. In South Africa, key populations refer mainly to sex workers, men who have sex with men (MSM) and young women. Key populations are crucial to both the epidemic's dynamics and the response to it. (For example, sex workers are vulnerable to HIV and are thus likely to infect their sex partners (key to *epidemic dynamics*). A key *response* to this situation is approval of the antiretroviral drug Truvada® to protect sex workers form HIV.) HIV key populations and vulnerable populations are not the same thing. Vulnerable populations are subject to societal pressures or social circumstances that may make them more vulnerable to exposure to infections, including HIV (UNAIDS, 2011: 2).

## 1.4.2 Positive worldwide responses

On a more positive note, it can be said that no other virus in history has led to so much research and so many new developments than HIV. Scientists have been motivated to learn more about the virus and the human immune system, as well as about ways to prevent and treat HIV infection. In 1994 (13 years after the first cases of HIV infection were described by the CDC), AZT was recommended to pregnant women in the USA, who were infected with HIV, to lower the risk of HIV being transmitted from mother to child. In that same year, infant HIV infections began to fall in developed countries where AZT was used. In 1995, the use of combination antiretroviral treatment (also known as **HAART**, or **highly active antiretroviral therapy**, or multidrug-therapy) was introduced, and in 1997 deaths as a result of Aids began to decline in developed countries because of the new antiretroviral treatment. In 2001, the '3 by 5' initiative was launched by the WHO and UNAIDS. Its aim was to place three million people, in low- and middle-income countries who were living with HIV, on antiretroviral treatment by the end of 2005. Although this goal was not reached by 2005, it initiated concerted efforts to improve access to treatment. For example, it saw antiretroviral therapy coverage rise from 7% in 2003 to 42% in 2008, with particularly high coverage of 48% achieved in eastern and southern Africa. Close on 11.7 million HIV-infected people in low- and middle-income countries had access to ARVs in 2013 (WHO, 2015).

Apart from the global response in terms of treatment, great efforts were also made to develop ways to prevent HIV infection. These included vaccine research, the development of an effective **microbicide** (vaginal cream, gel or ring) and male circumcision research. Although at the time of writing (2016) a successful

vaccine candidate still eludes the scientific world, a major study of an experimental HIV vaccine commenced in South Africa at the end of 2016, involving 5 400 adult volunteers. Results of the vaccine study are expected in 2020. The scientific world agrees that a vaccine will probably be the most effective way to stop the epidemic. South Africa is currently at the forefront of the development of a vaginal microbicide (1% tenofovir gel and the Dapivirine® vaginal ring) to prevent HIV infection in women, and circumcision research has shown that the risk of HIV infection among men who have been circumcised can be reduced by approximately 60%.

Table 1.1 on pages 17 to 23 summarises the history of HIV and Aids. It highlights some of the victories and disappointments South Africa and the rest of the world have faced in the struggle against Aids (Avert, 2015; Shisana, Rehle, Simbayi, Zuma, Jooste, Zungu, Labadarios, Onoya, et al., 2014).

## Activity

Study the historical timetable of HIV and Aids in Table 1.1 and then complete the tasks below.

- Look at each major incident on the timetable. What were you doing in your life at that time?
- Draw a circle in pencil around the year on the timetable when you first became aware of HIV and Aids.
- What made you aware of HIV and Aids at that stage of your life?
- Draw a circle around the date when you first became actively involved in HIV work.
- Why did you get involved in HIV work at that time? How did you feel about 'the Aids problem' then and how do you feel about it now?
- Think of all the things that have happened in the HIV field since 1981. Make two lists, one of our achievements and the other of our failures.
- HIV prevalence in South Africa increased rapidly between 1993 and 2000. Think of the political changes that took place during that time. Write an essay on the possible influences the political turmoil had on the spread of HIV at the time. Do you think that prompt action at the time would have lessened the severity of the epidemic?
- Using the information in Table 1.1 the table on the prevalence of HIV, draw a graph showing the spread of HIV infection in pregnant women in South Africa.

**Table 1.1** A summary of the outbreak and spread of HIV, and the world's response to it

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 1959 | First known case of Aids was discovered. A man died in Kinshasa (Belgian Congo). Years later, his stored blood sample showed that he had died of Aids. | | | |
| 1981 | First documented cases of Aids occurred. Homosexual men in New York and California with Kaposi's sarcoma and a rare form of pneumonia were diagnosed. | | | |
| 1982 | Aids was defined for the first time as acquired immunodeficiency syndrome. | | | |
| 1983 | Luc Montagnier and other scientists in the Pasteur Institute in France isolated the retrovirus responsible for Aids (then called LAV or HTLV-III). | A heterosexual Aids epidemic was exposed in Africa.<br>3 000 Aids cases reported in the USA; 1 000 have died. | The first documented case of Aids was recorded in South Africa. | |
| 1984 | Final scientific proof that HIV was the cause of Aids was published in Science and The Lancet.<br>Scientists become aware that Aids is widespread in parts of Africa.<br>World's first needle exchange programme – Amsterdam. | | | |
| 1985 | The first kits for HIV antibody testing became available to diagnose the HIV infection. | Aids diagnosed in China. | The South African government set up the first Aids Advisory Group. | |
| 1986 | The virus causing Aids was given a new name: human immunodeficiency virus (HIV). | HIV-2 was discovered in West Africa.<br>More than 38 000 cases from 85 countries reported.<br>Uganda begins sexual behavioural change programmes. | | |
| 1987 | AZT (also known as zidovudine) became the first antiretroviral drug to be used to treat HIV infection in the USA. | | | |
| 1988 | Condom use was shown to be effective in preventing the sexual transmission of HIV. | World Aids Day established. | | |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 1990 | | 8 million people with HIV worldwide. | | The first national antenatal survey in SA indicated that 0.8% of pregnant women tested were found to be HIV infected.<br>Total number of South Africans living with HIV was estimated to be between 74 000 and 120 000 people. |
| 1991 | | The total number of people worldwide living with HIV was estimated to be between 10 and 15 million. | A turning point for heterosexual transmission of HIV in SA was reached. The number of heterosexual transmissions overtook the number of homosexual transmissions.<br>The first Aids training, information and counselling centres (ATICs) were established in SA. | |
| 1992 | | The total number of people living in sub-Saharan Africa with HIV was estimated to be 10 million. | | |
| 1993 | | | Creation of the National Aids Convention of South Africa (NACOSA). Its mandate was to develop a national strategy to cope with Aids. | 4.3% of pregnant women tested were found to be HIV infected. |
| 1994 | AZT was recommended to pregnant women infected with HIV to reduce mother-to-child transmission (MTCT) of HIV in the USA. | | The South African Minister of Health accepted NACOSA's strategy as the foundation of the government Aids plan.<br>The Soul City multi-media project was created with the aim of developing media productions to educate people about health issues, including HIV and Aids. | |
| 1995 | The use of highly active antiretroviral therapy (HAART) was introduced.<br>The Joint United Nations Programme on Aids (UNAIDS) is established. | The total number of people worldwide living with HIV was estimated to be 19.5 million. | Deputy President Mbeki acknowledges seriousness of Aids in South Africa. | The total number of people in South Africa living with HIV was estimated to be 850 000 (2.1% of the population). |
| 1996 | | | *Sarafina* money scandal. | 12.2% of pregnant women tested were found to be HIV positive. |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 1997 | Aids deaths begin to decline in developed countries due to HAART | The total number of people worldwide living with HIV was estimated to be 22 million.<br>The total number of people living in sub-Saharan Africa with HIV was estimated to be 20.8 million. | A national survey of South Africa's response to Aids revealed a lack of political leadership.<br>Virodene scandal shook South Africa. | 17% of pregnant women tested were found to be HIV positive.<br>The total number of people in South Africa living with HIV was estimated to be 2.4 million. |
| 1998 | | | Refusal by the SA government to provide AZT to pregnant women to prevent MTCT of HIV.<br>The Treatment Action Campaign (TAC) was founded with the aim of being an advocate for rights of people living with HIV and Aids and to campaign for a national treatment plan.<br>Deputy President Mbeki launched the Partnership Against Aids and declared that there were an estimated 1 500 new infections every day in South Africa.<br>Gugu Dlamini, an Aids activist, was beaten to death by neighbours after disclosing her positive HIV status on World Aids Day. | |
| 1999 | | The total number of people worldwide living with HIV was estimated to be 34.3 million.<br>The total number of people living in sub-Saharan Africa with HIV was estimated to be 24.5 million. | LoveLife, an HIV and Aids youth education organisation, was launched. Its aim was to reduce teenage pregnancy, HIV and sexually transmitted infections (STIs). | The total number of people in South Africa living with HIV was estimated to be 4.2 million.<br>22.4% of pregnant women tested were found to be HIV infected.<br>The total number of children orphaned by Aids in South Africa was estimated to be 420 000. |
| 2000 | | The International Aids Conference is held in Africa (Durban) for the first time. | The South African Department of Health outlined its five-year plan to combat HIV and Aids and STIs and it set up a National Aids Council.<br>President Mbeki attracted criticism from the world for consulting dissident scientists. | |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 2001 | | The total number of children orphaned by Aids in sub-Saharan Africa was estimated to be 12.1 million. | The South African government launched Khomanani, a two-year media campaign. Its aim was to educate people about the dangers of HIV.<br>SA child activist, Nkosi Johnson, died of Aids at age 12. | An estimated 4.7 million South Africans are HIV positive. |
| 2002 | Botswana begins Africa's first national Aids treatment programme.<br>Global fund established to boost response to Aids, TB and malaria in developing countries. | | The South African High Court ordered the government to make nevirapine available to pregnant women to prevent MTCT of HIV. | 24.5% of pregnant women tested were found to be HIV infected. |
| 2003 | WHO and UNAIDS launched the 3 by 5 Initiative with the aim of reaching 3 million people in the developing world with ART by 2005.<br>ARVs become more affordable for developing countries.<br>First HIV vaccine candidates found to be ineffective. | The total number of people worldwide living with HIV was estimated to be 37.8 million.<br>The total number of people living in sub-Saharan Africa with HIV was estimated to be 23.5 million.<br>Of the 4.1 million people needing ARVs, only about 1% has access to ARVs. | The South African government finally approved the plan to make ART freely available in the public health sector. | 27.9% of pregnant women tested were found to be HIV infected.<br>The total number of children orphaned by Aids in South Africa was estimated to be 780 000. |
| 2004 | PEPFAR launched to combat Aids worldwide. | Uganda has reduced its HIV prevalence by 70% since the early 1990s. | The rollout of free antiretroviral drugs in SA began. | The total number of people living in South Africa with HIV was estimated to be 5.3 million. |
| 2005 | Feedback from the 3 by 5 Initiative indicated that 1.3 million people were on ART in developing countries.<br>The leaders of the G8 nations announced that their HIV and Aids goal was universal access to HIV treatment and prevention by 2010. | | Nelson Mandela announces that his eldest son has died of Aids.<br>At least one service point for Aids related care and treatment was established in all the health districts in South Africa.<br>The total number of people in the public sector on ART was estimated to be 85 000. (It was estimated that about 79% of South Africans who needed ART were not receiving it.) | 30.2% of pregnant women tested were found to be HIV infected.<br>The total number of children orphaned by Aids in South Africa was estimated to be 1.2 million. |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 2006 | It was estimated that more HIV-infected people in developing countries were on ART than in developed countries. Circumcision is shown to reduce HIV infection in heterosexual men. | The total number of people worldwide living with HIV was estimated to be 40 million.<br>The total number of people living in sub-Saharan Africa with HIV was estimated to be 24.5 million.<br>28% of people in sub-Saharan Africa who need treatment for HIV are receiving it. | Inmates at Durban's Westville prison won a court case against the government to provide ART through the prison system. (An estimated 41% of prisoners were thought to be HIV infected in 2004.)<br>The South African Minister of Health attracted criticism from the world when she presented her Aids diet at the Toronto International Aids conference.<br>On World Aids Day, South Africa's Deputy President, Phumzile Mlambo-Ngcuka, announced (and) headed the new National Aids Council. Its aim was to halve the rate of new HIV infections in the country by 2011 and to provide treatment, care and support to at least 80% of the people and the families living with HIV and Aids. | The total number of people living in South Africa with HIV was estimated to be 5.5 million. (This was estimated to be 18.8% of the adult population.) |
| 2007 | Another major HIV vaccine trial halted. | Botswana cuts it MTCT rate to under 4%.<br>Around 33 million people worldwide are infected with HIV according to revised statistics. | Halting of HIV vaccine trial major disappointment for South Africa. | |
| 2008 | Luc Montagnier and Francoise Barré-Sinoussi share Nobel Prize for Medicine for their discovery of HIV. | UNAIDS report stabilisation of most epidemics in sub-Saharan Africa.<br>± 2.93 million people on ART in sub-Saharan Africa. | President Mbeki resigns. | HIV prevalence in South Africa = 10.6% (9.8%–11.6%) |
| 2009 | President Obama announces the removal of the travel ban that prevents HIV-infected people from entering the USA. | Total number of people worldwide with HIV infection estimated to be 33.4 million.<br>Total number of people in sub-Saharan Africa with HIV infection estimated to be 22.5 million. | New president Jacob Zuma commits himself to implementation of new National Strategic HIV Plan. | Total number of people with HIV infection in South Africa is estimated to be 5.7 million.<br>29.4% of pregnant women tested were HIV infected. |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 2010 | The G8 nations have not reached their goal of universal access to HIV treatment and prevention by all.<br>24. 4 million people in developing and transitional countries are receiving ARVs; 9.5 million still in immediate need of treatment. | 3.9 million of the 10.6 million people in need for ARVs are receiving it in Africa. | New antiretroviral treatment guidelines accepted.<br>Positive results for South Africa's research on a vaginal microbicide gel (1% tenofovir gel); reducing HIV by 39%.<br>The Department of Health launches a massive HIV counselling and testing programme.<br>18 million people reported having been tested for HIV during the HCT campaign.<br>SA Government introduces the Voluntary Medical Male Circumcision (VMMC) campaign with target to complete 4.3 million male circumcisions by 2015. | |
| 2011 | Results show early initiation of ART reduces HIV transmission in discordant couples | 59% of pregnant women received treatment to prevent MTCT of HIV.<br>Roll-out of VMCC across 14 countries in Africa. | | |
| 2012 | UNAIDS release guidelines for ARV treatment as prevention for serodiscordant couples.<br>FDA (USA) approved PrEP for HIV negative people to prevent sexual transmission of HIV.<br>A majority of people eligible for ART (54%) receive it. | Over 7.5 million people on ART in Africa. | More than 2 million people in SA (31.2%) on ART.<br>46.6% of male respondents to the 2012 HSRC Prevalence Survey indicated that they were circumcised.<br>65.5% respondents have been tested for HIV before. | 12.2% (6.4 million) people are HIV positive in SA. (The increase is largely due to combined effects of new infections and a successful ART programme, which has increased survival among HIV-positive people.) |
| 2013 | Aids-related deaths down with 30% since peak in 2005 (UNAIDS). | Uganda passes Anti-homosexual Bill. | An estimated total of 1.23 million VMMCs were done between 2010 and August 2013. | |
| 2014 | Global leaders commit to ending HIV epidemic by 2013.<br>On 17 July delegates to the 2014 International Aids Conference in Melbourne died on Flight MH17.<br>'Fast-Track' target involving dramatic scale-up of HIV prevention and treatment programme aimed to avert 28 million new infections and to end the epidemic by 2030. | UNAIDS and partners initiate the 90-90-90 treatment target to help end the Aids epidemic. (By 2020: 90% of all people living with HIV will know their status; 90% people with diagnosed HIV will receive ART; 90% of all people on ART will have viral suppression). | | Aids deaths declined from 320,000 in 2010 to 140,000 in 2014 mainly due to ARVs. |

*continued*

| Year | Scientific developments, discoveries and other events | World epidemic/ sub-Saharan Africa | South African events and politics | South African epidemic |
|---|---|---|---|---|
| 2015 | Research shows that the optimum time to start ART is as soon as possible after diagnosis.<br>In December 2015 the WHO removed CD4+T cell counts as criterion for ART initiation. | 15.8 million people accessing ART.<br>36.9 million people living with HIV.<br>HIV-related deaths decreased by 42% since 2004. | SA follows WHO guidelines to start ART at CD4+T cell count <500.<br>Truvada® registered by MCC for use as PrEP in SA. | MTCT of HIV declined from 70 000 infected babies in 2004 to <7 000 in 2015. |
| 2016 | | | Minister Aaron Motsoaledi announces that the CD4 count will be removed as an eligibility criterion for ARV treatment in September 2016.<br>PrEP to be provided to sex workers in 10 sex worker programmes from June 2016. | |

## 1.5 Conclusion

This chapter has explored the history of HIV as well as our response to it. Blame, denial and indecision have cost us valuable time. So has political power games. But we have also learned a lot about this new threat to humanity. In Chapter 2 you will learn more about HIV and its effect on the immune system.

## Test your understanding

1. What do the acronyms HIV and Aids stand for?
2. Why is Aids called an acquired deficiency of the immune system?
3. Who received the Nobel Prize for physiology and medicine for discovering HIV?
4. What is the most convincing theory about the origin of HIV?
5. What are some of the functions of conspiracy theories?
6. Where do you think Aids comes from?
7. What is the difference between key populations and vulnerable populations?

## Reference list

Abdool Karim, S. S. & Baxter, C. 2010. Introduction. In S. S. Abdool Karim & Q. Abdool Karim (Eds.), *HIV/AIDS in South Africa* (2nd edn.) (pp. 37–44.). Cape Town: Cambridge University Press.

Avert. 2015. Aids Timeline. Retrieved on 9 September 2015, from: http://www.avert.org/timeline-aids-africa.htm

Gouws, E. 2010. HIV incidence rates in South Africa. In S. S. Abdool Karim & Q. Abdool Karim (Eds.), *HIV/AIDS in South Africa* (2nd edn.) (pp. 74–86). Cape Town: Cambridge University Press.

Gouws, E. & Abdool Karim, Q. 2010. HIV infection in South Africa: the evolving epidemic. In S. S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 55–73). Cape Town: Cambridge University Press.

Schoub, B.D. 1999. *AIDS and HIV in perspective. A guide to understanding the virus and its consequences* (2nd edn.). Cambridge: Cambridge University Press.

Shisana, O., Rehle, T., Simbayi, L.C., Zuma, K., Jooste, S., Zungu, N., Labadarios, D., Onoya, D., et al. 2014. *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012*. Cape Town: HSRC Press.

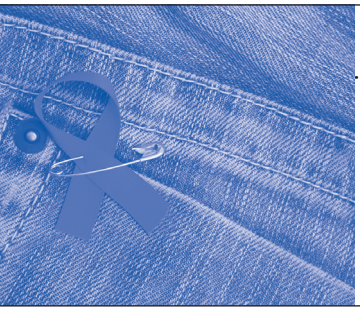
United Nations Programme on HIV/AIDS (UNAIDS). 2011. *UNAIDS terminology guidelines*. Geneva: UNAID.

United Nations Programme on HIV/AIDS (UNAIDS). 2012. *Global Report*. Geneva: WHO Library Cataloguing.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (p. 4). Cape Town: Nasionale Boekhandel Bpk.

Williamson, C. & Martin, D. P. 2010. HIV-1 genetic diversity. In S. S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 117–126). Cape Town: Cambridge University Press.

World Health Organization (WHO). 2015. Antiretroviral therapy (ART) coverage among all people. Retrieved on 07 September 2015 from: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/



# Chapter 2

# HIV and the immune system

Alta van Dyk and Peet van Dyk

### A barrier

*... And eventually Koki knew in his heart*
*That he'd come to a barrier, restrained*
*by something dark, dull and strong ...*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- describe how a healthy immune system works by drawing pictures on a white board;
- explain what a virus is;
- draw a picture of the structure of HIV and label all the important parts;
- draw a picture to explain how HIV invades a CD4+T cell; and
- explain why HIV mutates so quickly.

## Chapter outline

- The immune system
  - The first line of defence
  - The second line of defence
  - The third line of defence
  - Summary of the functions of the immune system
  - When the immune system fails
- The human immunodeficiency virus (HIV)
  - Viruses in general
  - The specificity of viruses
  - The uniqueness of HIV
  - HIV infection and replication
  - Variability and subtypes of HIV
  - Different responses to HIV infection

Thousands of **pathogens** confront the human body every day, and yet, we do not necessarily get sick every time we come into contact with **viruses**, bacteria, fungi and **protozoa**. How is this possible? The answer is that the human body has developed a truly amazing defence system, called the immune system. This system not only defends the body against new pathogens that attack it, but is also able to protect the body against future attacks by the same pathogens. What makes the immune system so effective is that it can both kill most pathogens immediately and adapt when new pathogens confront it. This is crucial for our survival because the human body is constantly being attacked by pathogens that are real enemies, trying to kill their hosts. Without a good, elaborate defence system, no human being (or any living creature, for that matter) would be able to survive for any period of time.

### Terminology: Avoid combatant words when you talk about HIV and Aids

The UNAIDS (2011) Terminology Guidelines recommend avoiding the use of combative language (such as fight, struggle, battle, campaign or war) when we talk about Aids. It suggests using alternative terms, such as 'response', 'management of', 'measures against', 'initiative', 'action', 'efforts' and 'programme'. The reason for avoiding the use of combative language is to prevent transference from the fight against HIV to a fight against people living with HIV. However, although combative language will be avoided as far as possible in this book, we feel that a military metaphor is the best way to explain the constant battle between the immune system and invading organisms.

## 2.1 The immune system

Like any good defence system, the body's immune system has several lines of defence. The reason for this is that if the first line of defence proves to be ineffective in killing pathogens that are attacking the body, then other lines of defence can come into play. Figure 2.1 on the next page summarises the most important role players in the immune system. Use this summary to work through the discussion of the immune system that follows.

### Enrichment: The immune system in pictures

Before you start reading about the immune system, go to the following website to watch a YouTube video that explains the immune system in terms of recognition, attack and memory: http://goo.gl/j5fYex

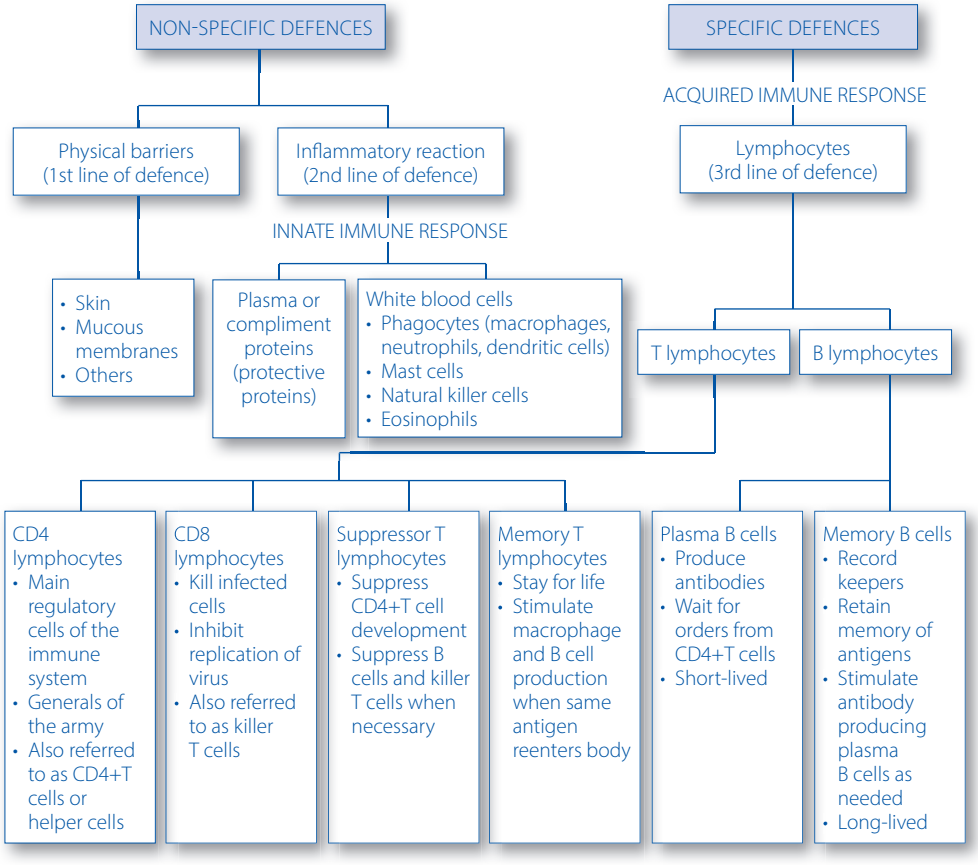



**Figure 2.1** The key role players in the immune system

## 2.1.1 The first line of defence

By far the most effective defence is of course to ensure that pathogens do not enter the body in the first place. Like any defensive building (such as a castle), the body has a defensive 'wall' around it (i.e., our skin) that is difficult for an enemy (i.e., pathogens) to breach. This can be called the first line of defence of the body.

However, just like the wall of a castle that has been breached, allowing the enemy access, so once the integrity of the skin has been compromised by a wound or lesion, it is possible for pathogens to enter the previously safe interior of the body and cause disease. The physical barriers (or first line of defence) are non-specific defences, meaning that they will try to keep out any pathogens that attempt to gain access to the inside of the body.

## 2.1.2 The second line of defence

Fortunately, no castle depends only on its walls for protection. They always have lookout guards posted to form a second line of defence. Not only are these lookout guards there to detect any breach of the perimeter, they are also armed so that they can immediately kill an enemy that tries to enter through the gaps in the breached walls. Like the lookout guards of a castle, the body's lookout guards are not specialists in warfare, but are 'crudely' armed generalists. They are, nonetheless,

**Glossary**

**Innate immune system** The body's second line of defence against invading organisms. It is made up of cells that attack and engulf all invading organisms. It is thus a nonspecific system and is innate because we inherit it.

effective in removing most pathogens and pollutants from the body. These so-called lookout guards of the immune system make up the **innate immune system**. This system is called 'innate' because we inherit it from our parents and it is not able to adapt to special circumstances.

When the skin is broken and pathogens enter the body (a breach of the first line of defence), this is usually followed by an inflammatory reaction at the area of entry. This is characterised by redness, pain, swelling and heat. This inflammatory reaction is the wake-up call for the innate immune system to take over and to deal with the infectious agents or pathogens that have entered the body (see Figure 2.1). The innate immune response is evolutionarily a very old immune system, and nearly all living organisms (plants and animals) have an innate immune system to defend themselves against pathogens.

This innate part of the body's immune system is also non-specific. We could say that the lookout guards use 'brute force' to overcome a pathogen or get rid of a pollutant (e.g. dust particles). This often involves engulfing or swallowing the enemy. These lookout guards are therefore known as **phagocytes** (which means 'eating cells').

For these immune system lookout guards to be effective, they first need to be able to identify any pathogen as a potentially damaging agent (just as soldiers need to distinguish between friend and enemy by looking at their distinctive uniforms or insignia). This is important because if the phagocytes were unable to distinguish the 'enemy' (pathogens) from the body's own cells, they would start killing their own 'friends'; that is, the body's own cells. It is therefore critical that the phagocytes are able to distinguish between 'us' (the body it is defending) and 'them' (the pathogens attacking the body). Phagocytes do not need specialist knowledge to be able to identify every kind of pathogen. All they need is to know: 'It is not one of us – kill it!'

The innate immune system consists of two groups of soldiers: plasma proteins and white blood cells (or leucocytes):

- *Plasma (complement) proteins:* The main functions of this group of lookout guards are to identify invaders, to assist (or complement) **antibodies** (part of the special forces of the immune system) to kill the pathogen, to call phagocytes to the site of infection so that they can eat or engulf the invader, or to directly attack the enemy and kill it by making holes in its protective membrane. One of the best-known **plasma proteins** is interferon, which is usually produced when the body is infected by a virus.
- *White blood cells (leucocytes):* The second group making up the innate immune system consists of different types of soldiers, including the mast cells, eosinophils, basophils and natural killer cells (note that natural killer cells are not the same as **killer T cells**). However, for our purposes, the group called the phagocytes is the most important. The phagocytes or 'eating cells' include the **macrophages**, neutrophils and dendritic cells. The main function of the phagocytes is to rush to an infection site (when called by the plasma proteins) and devour the invading organisms. Macrophages ('big eaters') and neutrophils also have the function of patrolling the body to look for invading pathogens, while macrophages also act as general scavengers or 'hyenas' by getting rid of all dead cells, for example old blood cells, bits of dead tissue and other debris. The other important function of dendritic cells (and to a lesser extent macrophages) is to go and warn the 'control room' of the body's immune system by carrying an ID of the invader to them.

In many cases of infection, the innate immune system (plasma proteins and various white blood cells) is entirely capable of killing off the invaders and no further immune response is therefore required. However, as we have seen, these lookout guards are not specialists. Consequently, in the case of more sophisticated or nasty enemies, they may not be able to kill all the invaders. It is then that they rush to the 'control room' of the body's immune system to seek help from the specialist forces.

## 2.1.3 The third line of defence

Like the Special Forces in an army, the third line of defence of the immune system comprises 'highly trained soldiers' with 'specialised weapons' to deal with specific invaders. In contrast to the general training and 'crude' weapons of the lookout guards, the specialist forces of the immune system are geared towards attacking and killing one specific kind of enemy only. In contrast to the primitive innate immune forces, the special forces have to be specifically designed or manufactured for their task. That is, they have to be adapted or acquire defences specific to their task. For this reason, this third line of defence is called the adaptive or acquired immune system – implying that its special forces did not merely inherit their attributes, but had to be adapted to a specific enemy by acquiring specific skills. Specialisation has the advantage that the forces are very effective in reacting to or killing the specific pathogen for which they were designed, but the negative side of it is that each group of 'special soldiers' can only react to the pathogen for which they were designed and nothing else.

The immune response of these Special Forces can be divided into four phases. These are: (a) recognition and warning; (b) mobilisation and battle; (c) demobilisation; and (d) active immunity and passive immunity.

### 2.1.3.1 Phase 1: Recognition and warning

Before the acquired immune system can react by attacking a pathogen, it first needs to be able to distinguish between enemies (pathogens) and friends (cells of the body). (This is the reason why soldiers in a conventional war also wear specific clothing or insignias.) To understand how the immune system is able to recognise a pathogen for what it is, we first need to explain some basic biology.

#### Cells and proteins

All living matter (plants, animals and pathogens) is made up of small units called cells. Cytology is the science that studies cells, so whenever you see a word containing 'cyto' or 'cytes' (such as cytoplasm, lymphocytes and phagocytes) it refers to such biological cells. For example, lymphocytes are cells that occur in the **lymphatic system** of the body.

Most living organisms consist of thousands or even millions of different cells, specialised to do different functions. For example, some cells are combined to form an almost impenetrable barrier, such as the skin, while others are specially designed to be able to absorb nutrients, like the cells lining the stomach wall. Other cells in the body are free floating in the blood, such as white blood cells (leucocytes). Some very small organisms consist of one cell only, for example one-cell protozoa and viruses. In such cases, all the biological functions of the organism are fulfilled by a single cell.

Cells are always surrounded by an outer membrane or barrier which controls the amount and type of fluids and nutrients that enter and leave the cell. Inside the cells are also various other components called organelles. Figure 2.2 is a diagram of the most important elements of a biological cell.

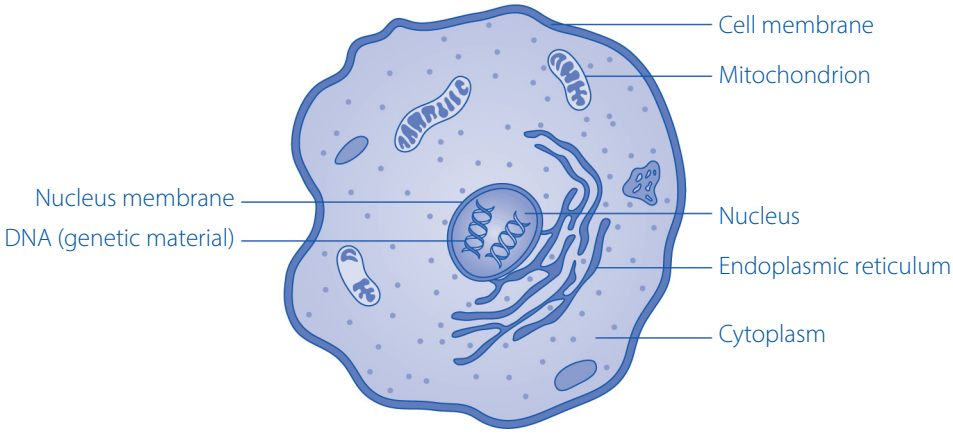



**Figure 2.2** Diagram of a cell

**Glossary**

**Genome** All the genetic material that an organism possesses.

In the diagram you will notice that, in addition to the outer cell wall, each cell also has an inner core surrounded by a second membrane called the core or nucleus membrane. Inside the core or nucleus of the cell is the **genome** or genetic material of the cell, consisting in most cases (but not all) of double stranded DNA. This DNA is the heart of all living matter, because it contains the detailed building plan of not only that specific cell but of the whole organism. That is, each cell in our body has a building plan for our whole body. These building plans are in a genetic code, which programmes the cell to replace (or clone itself) when it becomes old. During our lifetime, each cell in our body is replaced several times.

Now that you have a better understanding of cell biology, it will be easier for you to understand how the immune system is able to recognise a specific organism or pathogen. Such recognition is made possible by the unique genetic code of each organism. Although every individual life form has its own unique genetic code, the same species of animal, plant or pathogen nonetheless shares many similar genes, making them look more or less the same. For this reason, a human looks different from a chimpanzee and even more different from a fish. Species that are more closely related are therefore more similar genetically than distantly related species.

**Glossary**

**Antigen** Any foreign (or invading) substance which, when introduced into the body, elicits an immune response such as the production of antibodies that react specifically with these antigens. Antigens are almost always composed of proteins and they are usually present on the surface of viruses or bacteria.

One can therefore distinguish between different species by looking at the differences between their genetic codes. But to look for these differences between complete genetic codes would be a huge and difficult task. The immune system, however, has a way to simplify this task. Instead of looking at the complete and complex genetic code of each invading pathogen, it looks only at the proteins of the pathogen. This is possible because the genetic code of each species manufactures unique proteins, which can be identified as belonging to that species only. In the context of the immune system, these unique proteins are called **antigens** (short for antibody-generating proteins).

The antigens of a pathogen can therefore be regarded as the 'unique insignia' that can be used by the body's immune system to recognise foreign pathogens from outside the body. Even more importantly, the immune system also uses these

antigens to manufacture or mobilise appropriate 'soldiers' or immune cells that can effectively combat the pathogens and destroy them.

### Known versus unknown pathogens

In the case of a pathogen or disease that has previously attacked a person, such a pathogen is already 'known' to the body's immune system and the reaction of the immune system is so quick and effective that the person does not even get sick. This is because the person has become immune to the disease. This quick response is possible because the immune system has a memory or databank of all previously known antigens (associated with specific pathogens) stored in the so-called 'memory cells' of the immune system (see Figure 2.1). These are known as **memory T cells** and **memory B cells** (see active and passive immunity on pages 34 and 35). The memory of the immune system enables it to activate the immune response much more quickly than would be the case if attacked by an unknown pathogen. For example, if you had measles as a child, you would have developed symptoms and got very sick at the time. If you are exposed to the measles virus again later in life, you will not get sick again because your immune system will 'remember' the antigen and will immediately mobilise the special forces of the immune system to take care of the virus.

> **Note**
>
> All immune cells that are manufactured by the thymus gland are called T cells and all immune cells manufactured by the bone marrow are called B cells.

In the case of a new pathogen, which the 'primitive' innate immune system cannot deal with and where no previously designed special forces exist which can be immediately mobilised, the acquired immune system has to start from the beginning. In this immune response, a number of different immune cells have to be warned so that they can manufacture new special forces to be able to combat the new brand of invaders. As can be appreciated, this process takes time (usually at least a couple of weeks) and the infected individual will get sick. To use our example of the measles virus again – if you are exposed to the virus for the very first time, your immune system will not have any knowledge or memory of this specific virus and it will need about 12 days to get a proper immune response ready to fight the virus. You will therefore get sick and show the symptoms of measles until the immune system starts fighting back, before you start to get better.

### Warning of the 'special forces' or T cells

If we go back to our castle comparison, we can say that when the lookout guards detect foreign invaders and they cannot kill them, they have to go to the 'control room' and warn the generals about the situation. However, a mere warning is not enough. They also have to give the generals a fool-proof way of identifying the invaders, which would enable them to 'train' and equip a new brand of special forces to combat the new enemy. For this reason, some cells of the innate immune system function as **antigen-presenting cells** (APCs). These APCs grab part of an antigen (called an epitope) from one of the invaders and display this on their own surface. They then continue by 'presenting' this antigen or epitope to the T cells. T cells (in contrast to B cells) cannot recognise pathogens if their antigens have not first been processed by the APCs by cutting up the pathogen into smaller pieces and then presenting the antigen. APCs therefore have a vital function in the warning of the special forces of the immune system.

Special cells from the innate immune system, namely **dendritic cells** and macrophages, fulfil this antigen-presenting role by engulfing and processing pathogens. Dendritic cells are the most important antigen-presenting cells (or

APCs), and they have the ability to present antigens to both CD4+T cells and CD8+T cells.

Dendritic cells occur both inside the lymphatic system of the body (e.g. lymph nodes) and in non-lymphoid tissue, for example the skin, stomach, intestines, lungs and brain. They also occur in the mucous membranes of the vaginal tract where they are known as **Langerhans cells**. (These Langerhans cells play an important part in transporting HIV into the body). Macrophages are less powerful than the **dendrites** as antigen-presenting cells.

### 2.1.3.2 Phase 2: Mobilisation and battle

The main role players of the acquired immune system are specialised white blood cells called lymphocytes, that is, cells that are mainly stored in the lymphatic system. Lymphocytes are subdivided into two main groups, namely **T lymphocytes** (T cells) and **B lymphocytes** (B cells), and – as noted earlier – are produced in either the thymus gland or in the bone marrow, respectively (see Figure 2.1).

#### T lymphocytes

CD4+T cells (also known as **T helper cells**) and CD8+T cells (also known as Killer T cells) are the main T cells involved in the mobilisation of the immune system and the killing of pathogens, respectively. T cells are pre-programmed in the thymus to recognise antigens of foreign pathogens by their shapes. For this purpose, T cells have specific receptors (**T cell receptors** or TCRs) and co-receptors on their surfaces which can connect or bind with their associated antigens. We can depict this as a lock-and-key system where the antigen of the pathogen fits perfectly into the receptors of the T cells (see Figure 2.3). For example, CD4+T cells have CD4 receptors and co-receptors on their surfaces which recognise antigens, while killer or CD8+T cells have receptors called CD8+ receptors on their surfaces. In this way, one type of T cell may be designed to recognise (or fit) the antigen of the hepatitis virus, while another type may recognise a particular type of flu antigen.

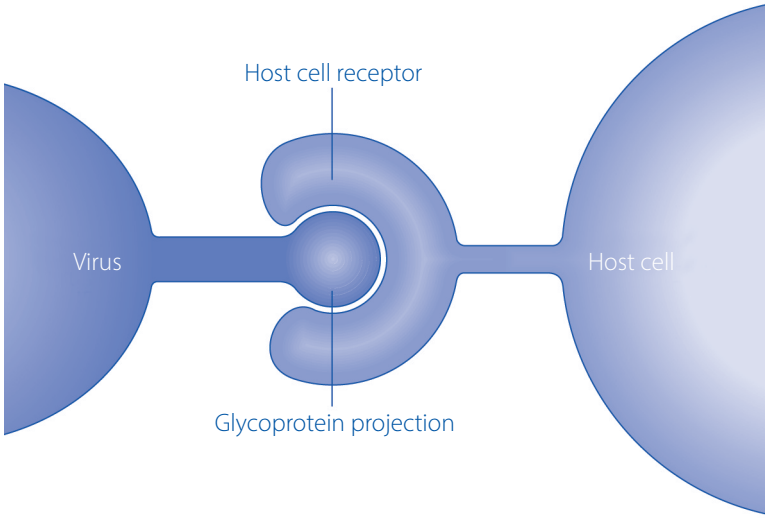



**Figure 2.3** The lock-and-key system of attachment

The CD4+T cells are the main regulatory or controlling cells of the immune system. Consequently, they can be described as the generals, manning the control room of the immune system. CD4+T cells regulate the innate as well as the acquired immune responses and assist in determining the type of immune response the body must muster to combat a specific pathogen. After the APCs have presented foreign antigens to the CD4+T cells, these T cells stimulate an immune response from the macrophages and other lymphocytes, such as the CD8+T (killer) cells, as well as from the B lymphocytes. Although CD4+T cells do not attack or kill pathogens themselves, they have the important function of organising the body's army to fight the invading pathogens. They are therefore indispensable in any effective immune response.

When activated as part of the immune response, the killer T cells (CD8+T cells) directly bind with infected cells, which carry foreign antigens on their surfaces. The killer T cells then release cytotoxins, such as perforin, which form holes in the infected cell's membrane. This enables ions, water and toxins to enter the cell, resulting in its collapse and ultimate death. The killing of the infected cell is important to prevent pathogens (like viruses) from replicating. Killer T cells also attack infected cells by producing soluble proteins that inhibit the replication of viruses inside infected cells.

### B lymphocytes and antibodies

B lymphocytes (or B cells) are located in the lymph nodes. They can be regarded as the munitions factories of the immune system because they provide the immune system with ammunition to fight off invaders (viruses, bacteria and other pathogens).

What makes B cells different from T cells is that they can recognise whole pathogens without the need for pathogens to be processed first before the antigen can be recognised. When B lymphocytes are activated by the generals (CD4+T cells), and when they encounter a pathogen carrying an antigen which fits their receptors, this stimulates the B cell to divide many times and produce huge numbers of **plasma B cells**. For their part, these plasma B cells start mass producing antibodies against that specific antigen. Antibodies and antigens (antibody generators) are always linked, in the sense that the one (antigen) generates the other (antibody), and both are specific to a particular pathogen. For example, antibodies formed as a response to HIV infection would be different from antibodies formed as a response to infection by the flu virus. This means that during our lifetime our immune systems produce billions of different antibody types to combat all the pathogens we have encountered. Antibodies, with their specifically designed receptors, swarm around a pathogen and then attach themselves to the outermost proteins (or antigens) of the pathogen for which they were designed. In this way, they completely cover the outer surface of, for example, a virus and act as a shield between the virus and its potential host cell, thus preventing the infection. Antibodies also attract phagocytes and macrophages to the scene of infection and further slow the pathogens down, which makes them vulnerable prey for the phagocytes and macrophages to ingest or eat.

**Note**

Antibodies and antigens are always linked. Antigens always generate antibodies.

See Section 2.2.1 for details about viral infection of cells.

### 2.1.3.3 Phase 3: Demobilisation

After the war is won, all that remains to be done is demobilisation of the army. The **suppressor T cells** (or peacemakers) then take charge by 'ordering' the CD4+T cells to stop mobilising the army's soldiers, and the CD8+T cells to cease their attacks. They also release a substance to stop B cells from making more antibodies.

### 2.1.3.4 Phase 4: Active and passive immunity

As mentioned earlier, the body's immune system retains a memory or databank of previous pathogens. This enables the body to react quickly and efficiently if it is attacked by the same pathogen again, preventing the person from becoming sick a second time. In other words, the body has become immune against that specific pathogen. There are two forms of immunological memory: active long-term memory and passive short-term memory. Use Figure 2.4 to help you to distinguish between the two forms of immunity.

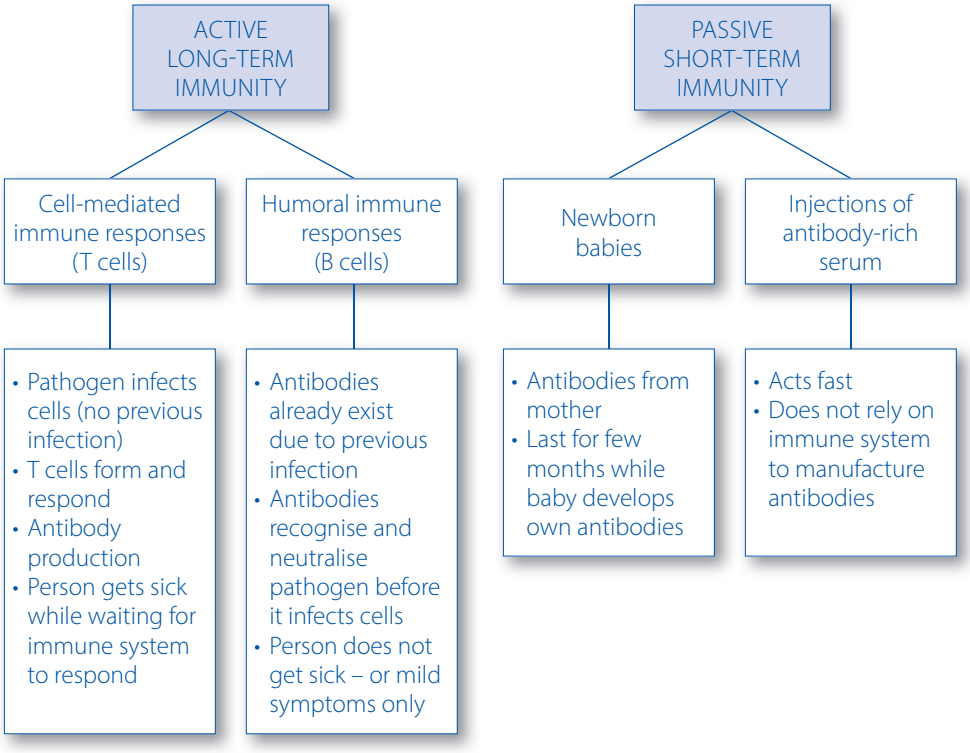



**Figure 2.4** Active and passive immunity

**Glossary**

**Active immunity** When a person has been infected by a pathogen, the immune system (through memory T and memory B cells) 'remembers' the specific invader or antigen. If the body is attacked by the same pathogen again in the future, the immune system can react quickly and efficiently against the pathogen without the person becoming sick a second time. We can say that the body has become immune against that specific pathogen. Active immunity can also be generated by immunisation (or vaccination).

#### Active immunity

*Active long-term memory* or **active immunity** follows infection by a pathogen. Some of the surviving T cells and B cells, following an infection, become memory T and memory B cells and they will forever remember the specific invader (antigen). For example, about 10% of the plasma B cells remain in the bloodstream as long-lived antigen-specific memory B cells. If the same antigen again enters the system in the future, memory B cells will rapidly divide and make new antibody-producing plasma cells. Memory B and memory T cells are what make active, long-term immunity possible.

Two kinds of long-term immunity can develop within the body: cell-mediated and humoral immune responses. T cells are involved in a cell-mediated immune response. This means that T cells are only formed after the pathogen has already infected some of the body's cells. In contrast, B cells are part of the humoral immune response where antibodies are produced by the immune system to recognise and neutralise the pathogen before it can infect the body's cells.

Active immunity can also be generated by immunisation (or vaccination). A vaccine is a substance that simulates an infection by a specific pathogen. This is done by introducing a protein component (antigen) of the relevant organism to the immune system which then stimulates it to produce memory B and memory T cells, similar to a true infection. Vaccines thus mimic the process in which the immune system interacts with an infection. If a person is immunised or vaccinated against a specific pathogen and is infected with this specific pathogen at a later stage, the secondary immune response takes effect, giving the person full or partial protection.

### Passive immunity

*Passive short-term memory* (**passive immunity**) is the short-term immunity that a newborn baby gets from its mother. Newborn babies do not have their own antibodies to fight off infections. To protect them, a special type of antibody (called IgG) is transported across the placenta from the mother to the baby. Consequently, babies have high levels of IgG antibodies after birth. Colostrum (first breast milk) also has antibodies (IgA) in it, which are transferred from the mother, during breastfeeding, to the baby's gut to protect it against pathogens. Passive immunity or 'borrowed' immunity is usually short term and only lasts from a few days to several months after birth. After that, the baby's body has already started to produce its own antibodies and active memory.

**Protective passive immunity** can also be given to adults by injecting them with antibody-rich serum, or immunoglobulin preparations to provide short-term protection. Immunoglobulin contains antibodies that are prepared from the serum of individuals who have recovered from serious illnesses such as lassa fever, **hepatitis B** or tetanus. The preparation is usually given to a patient who has unexpectedly been exposed to an infectious disease (such as hepatitis B) to create passive immunity and thereby prevent the illness. This passive immunity acts more quickly than the person's own immune system because it does not depend on the person's immune system to first make its own antibodies. Immunoglobulin preparations are safe and do not carry a major risk because the immunoglobulin proteins are freed from any contaminating viruses in the blood during the preparation process.

**Glossary**

**Passive immunity** Passive immunity is the short-term immunity that a newborn baby gets from its mother. To protect newborn babies, a special type of antibody (called IgG) is transported across the placenta from the mother to the baby. Colostrum (first breast milk) also contains antibodies that are transferred from the mother to the baby's gut during breastfeeding to protect it against pathogens.

## 2.1.4 Summary of the function of the immune system

Figure 2.5 on the next page summarises the functioning of the immune system according to the four phases discussed above. This figure will assist you to put all the information together and to understand what the role is of each of the white blood cells discussed so far.

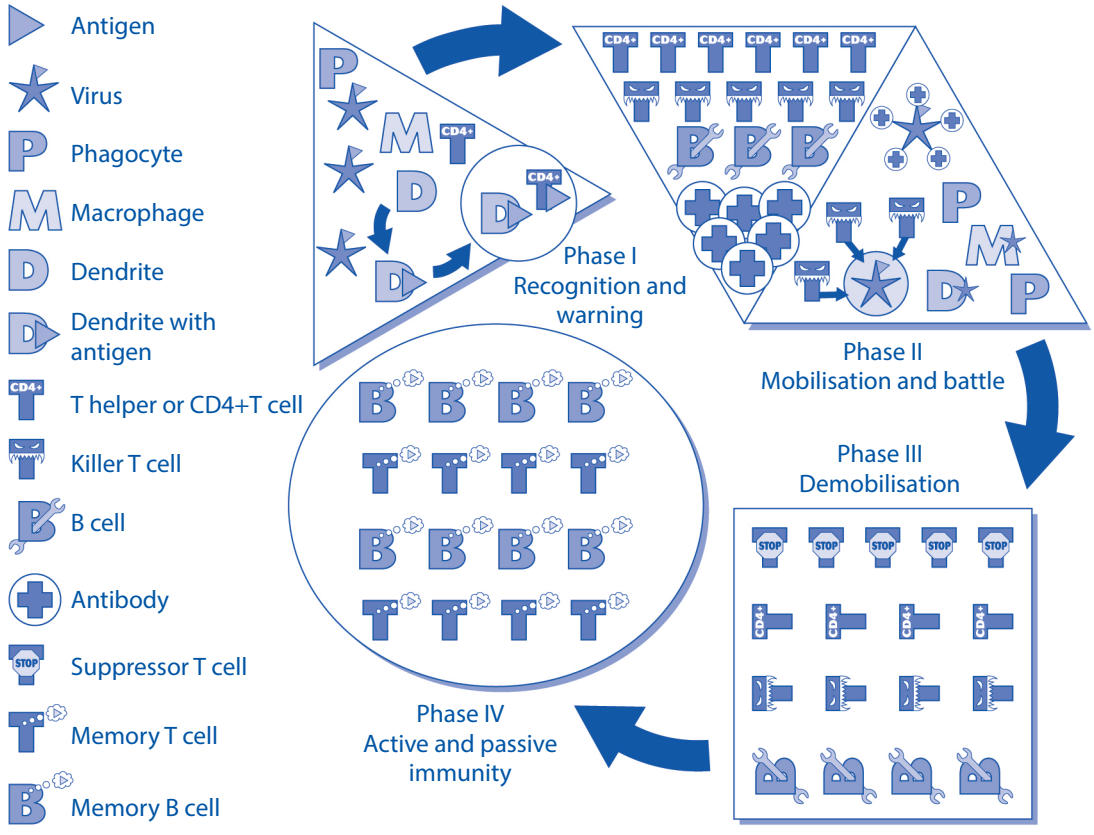



**Figure 2.5** How the immune system functions

**Phase I – Recognition and warning:** Phagocytes patrol the whole body to identify foreign objects. They detect a virus and send for macrophages and dendrites to help them. The dendrites engulf the virus, break it into pieces and display one of the pieces (an antigen) on its surface which it presents to the CD4+T cell – or the general of the army – to warn them (see circled section).

**Phase II – Mobilisation and battle:** After the CD4+T cells have combined with the dendrites, they activate the rest of the soldiers of the immune system to mobilise its full power. They activate more phagocytes, and they send chemical messages to the CD8+T cells (the killer T cells) and the B cells to multiply. The plasma B cells start manufacturing antibodies to assist in the battle. The CD8+T cells kill pathogens and destroy infected cells. The antibodies neutralise pathogens by clinging to the pathogen surfaces to prevent them from infecting other cells. This also slows them down and makes them vulnerable prey for the phagocytes and macrophages to eat or digest.

**Phase III – Demobilisation:** After the war is won, all that remains to be done is demobilisation of the army. The suppressor T cells (or the peacemakers) take charge by 'ordering' the CD4+T cells to stop mobilising the army's soldiers and the CD8+T cells to cease their attacks. They also release a substance to stop B cells from making antibodies.

**Phase IV – Active and passive immunity:** Some of the surviving T cells and B cells become memory T and memory B cells and they will forever remember the specific invader (antigen), thus providing active immunity against the disease. Passive immunity (IgG antibodies) is transferred from a mother to her baby, but has a limited lifespan.

### 2.1.5 When the immune system fails

In the majority of infections, the body's immune system is quite capable of eventually fighting off the invading pathogens, even if the person becomes very sick in the process. Only in exceptional cases is an attacking pathogen so deadly (e.g. the rabies virus) that it may kill a person before the immune system can raise a proper defence.

Another way in which the immune system can fail is when it becomes so weakened that it can no longer protect the body, even against pathogens that are not very deadly. In such a case, a person may die as a result of an otherwise non-deadly infection. A damaged or weakened immune system may be the result of old age, stress or unhealthy eating habits, or because the immune system is impaired by an inherited (not acquired) condition. In the case of a weakened immune system, medicines can often assist the immune system in fighting off any infection by starting to kill some of the pathogens, while the immune system is still in the process of being mobilised. This would also help the patient to recover more quickly.

In contrast to inherited **immune deficiencies** (where a baby is born with an impaired system), HIV is an a**cquired disease or condition** in the sense that a person is infected by (or acquires) a virus, which causes an immune deficiency. The virus attacks the previously healthy immune cells of the body and weakens them. There is no medicine available that can actually kill HIV (ARVs only delay the replication of HIV). Exactly how HIV attacks the immune system is explained next.

**Glossary**

**Immune deficiency** A weakening of, or failing in, the immune system.

## 2.2 The human immunodeficiency virus (HIV)

In the case of HIV, the infecting agent is a virus that invades the body, and, like any other pathogen, it causes a reaction from the body's immune system. But this reaction of the body's immune system eventually becomes ineffective as HIV continues its onslaught on the body. We can compare the immune system with a bucket that is constantly being filled with water (just as new immune cells are constantly being produced by the immune system). However, if the immune system is increasingly being damaged, it is like punching holes in the bucket, causing it to leak more and more. Eventually this would reach a stage where there are so many 'holes in the bucket' that it is impossible for the immune system to create enough new immune cells to replace the ones that have been killed. In the case of HIV, the immune cells most affected by this damage are the CD4+T cells because HIV causes their number to decline gradually as they are 'drained' from the system.

To appreciate how HIV infection progresses in the human body, we first need to look at viruses in general and how they infect a person.

### 2.2.1 Viruses in general

Pathogens that may cause disease include organisms of various kinds such as bacteria, viruses, protozoa and fungi. The virus is the smallest member of the pathogens. They are so small that they can only be seen through the strongest electron microscopes. Unlike other life forms, such as bacteria or human cells, viruses cannot reproduce or replicate themselves without the help of other cells. Whereas most bacteria and fungi live in the spaces outside cells and only use them

as food, viruses actually need to insert themselves into a cell (infect them) where they can 'hijack' the normal mechanisms of the cell to divide and form new copies of themselves. After these cells have been hijacked, the cells then stop making copies of themselves (more cells) and, instead, start producing more viruses. Viruses do this by inserting their own genetic code into the genetic code of the host cell through a process known as integration of the genetic material. Viruses are therefore intracellular parasites because they need to use the biochemical facilities of living cells (such as human cells) to multiply. Outside of a living cell, viruses are nothing more than chemicals that are inactive, lifeless and harmless.

Like all living cells, viruses consist basically of an outer cell membrane (protecting the virus as a whole) and an inner membrane surrounding the genetic material (usually DNA) in the core or nucleus. In the case of a virus, the outer membrane is called the **capsule** or shell. Some viruses (such as HIV) also have a third component called a **lipid envelope**, which is a loose, fragile membrane on the outside of the capsule. In the case where an envelope is present, various forms of glycoproteins (or 'spikes') from the underlying capsule protrude through the envelope so that they are visible on the surface of the virus. These glycoprotein projections have an important function in enabling the virus to attach to a potential host cell so that it can inject its genetic code into the host cell and thus infect it.

However, these glycoprotein projections on the virus can only attach to a potential host cell if the host cell has the correct receptors on its surface. We can again compare the system of glycoproteins and receptors with a lock-and-key system: The key on the virus (glycoprotein projection containing a unique antigen) can only fit into a specific lock (i.e., the receptor or binding site on the capsule of the host cell). Look at Figure 2.3 on page 32 again, which illustrates this lock-and-key principle.

## 2.2.2 The specificity of viruses

Due to the unique lock-and-key system of attachment to potential host cells, a specific virus can only infect cells that have the correct receptor cells on their surfaces. This makes viruses highly specific. The antigens on the glycoprotein projections of HIV can, for example, only attach to host cells with CD4 receptors on their surfaces. They cannot attach to any other cells that do not have these specific receptors on their surfaces.

As explained earlier, the immune system also uses this specificity of viruses (their unique antigens) to produce antibodies that attach themselves to the outermost proteins (or antigens) of the virus, either to prevent them from infecting a host cell or to facilitate their killing.

An important question that needs to be answered at this stage is why the immune system may fail to recognise a virus which has previously infected the body. For example, why do we need to be vaccinated anew every year against the flu virus? The answer to this question can also shed light on the reasons producing an HIV vaccine is so complex and why the body's immune system is so ineffective in killing HIV. The answer is that viruses (especially certain kinds of virus, called **retroviruses**) change or mutate so quickly (and with that the antigens on their surfaces) that the previously produced antibodies no longer fit onto the antigens of the virus. In effect, we can say that the virus has changed its unique and identifying

**Glossary**

**Retrovirus** A type of virus (of which HIV is one) that replicates by changing its genetic RNA into DNA by using the host's cells.

insignia. If the structure of the antigen changes, the antibody cannot attach to it, and then the host's immune protection system cannot function.

This is why new flu vaccines, appropriate to the changed antigens of the flu virus, need to be manufactured each year as new strains of the virus emerge. Because the flu virus mutates relatively slowly, it is possible to make a vaccine that is effective for at least one season. The same is not true of HIV. In the case of HIV, it changes so quickly that almost as soon as a vaccine has been produced it has already become ineffective against the new strains of viruses which have emerged.

Now that we have discussed viruses in general, let us look more specifically at HIV.

### 2.2.3 The uniqueness of HIV

HIV is a retrovirus and it is roughly circular in shape (see Figure 2.6 on page 40). Like other viruses, HIV is a very small organism and each HI virus particle (or virion) measures only 0.0001 mm in diameter and can only be seen under an electron microscope.

The core or nucleus of HIV is cone shaped, and this is the chief feature by which HIV is recognised through an electron microscope. The genetic material of the virus (single-stranded RNA), as well as several proteins called enzymes, is housed in the core of the virus (see Figure 2.6). These viral enzymes (namely the **reverse transcriptase enzyme**, the **protease enzyme** and the **integrase enzyme**) help in the copying of the virus inside the host cell and are injected, with the viral genetic material, into the host cell during infection. The viral enzymes are the main targets for antiretroviral treatment – but more about this later. Like the outer membrane of the virus, the inner core membrane contains various unique proteins or antigens that are specific to HIV. One of these core proteins is called **p24**, and it plays an important role in diagnosing HIV infection.

As mentioned earlier, the core of HIV is surrounded by an envelope through which glycoproteins protrude from the underlying capsule. For our purposes, the two most important of these proteins are a knob-like protein called **gp120**, and a smaller spike-like protein called **gp41** (gp stands for glycoprotein). These glycoproteins play a critical role in the initial steps of infection by the virus, this being attachment and penetration into the host cell. The same glycoproteins are also used by the body's immune system as antigens to produce antibodies that may neutralise the virus.

What makes the process of infection by HIV unique is the kind of host cell it attacks. Different from other viruses, HIV is able to directly attack and infect the human immune system's most vital defensive cells: the 'generals' or CD4+T cells. By doing this, HIV slowly reduces the total number of healthy CD4+T cells in the body, thus progressively weakening the immune system's ability to defend itself. Not only is the immune system then unable to fight against HIV; it is also unable to defend itself against the attack of other pathogens it would normally have been able to kill. These co-infections with other pathogens play an important role in the Aids context and are called **opportunistic infections**.

**Glossary**

**Opportunistic infections**
Infections that would not normally cause disease in a healthy body but which exploit the opportunity presented by an infected person's weakened immune system to attack the body.

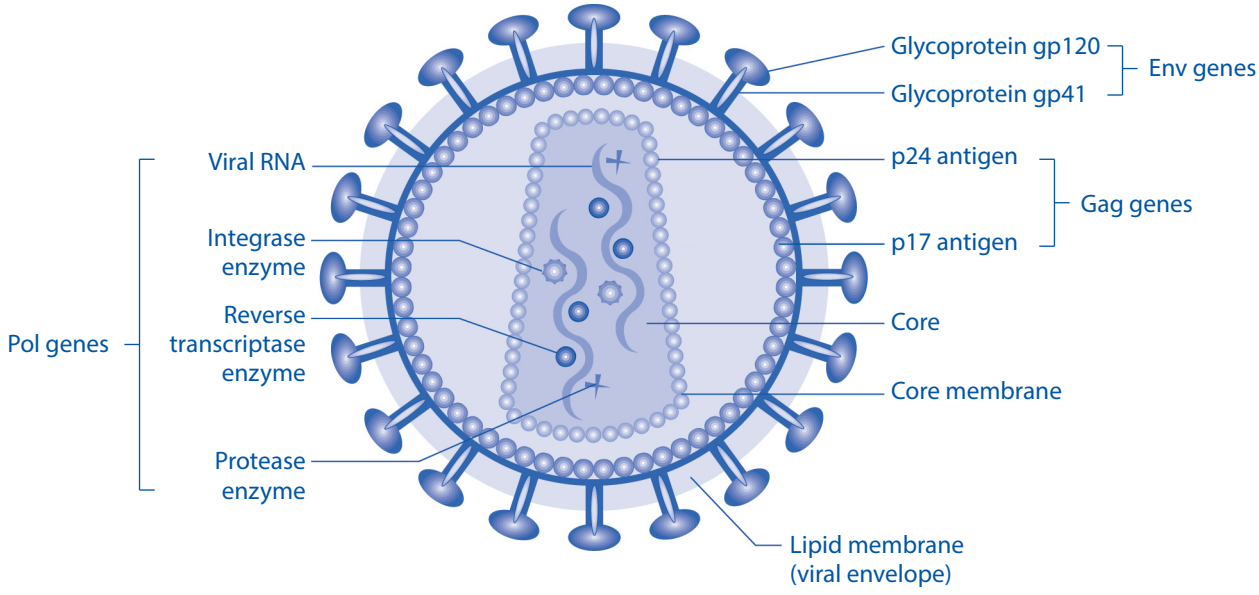



**Figure 2.6** A model of the structure of HIV

## Enrichment: The genes of HIV

When you read scientific sources about the development of antiretroviral drugs or about the search for a vaccine, you will probably read about the different genes of HIV. The following explanation may make the information a bit more comprehensible.

All retroviruses (including HIV) have three genes that code for (meaning that they direct the synthesis of) the inner core proteins, the envelope proteins and the virus enzymes. These genes are named the gag gene, the env gene and the pol gene.

- The gag gene directs the synthesis of the inner core proteins of the virus. The three gag proteins for HIV are p17, p24 and p10.
- The env gene directs the synthesis of the envelope proteins of the virus. A protein coded by the env gene is responsible for binding the virus to the host cell receptor. HIV has two env proteins, namely gp120 and gp41.
- The pol gene directs the synthesis of the virus enzymes used in the reproduction of the virus, namely the reverse transcriptase, protease and integrase enzymes. (See Figure 2.6 for the positions of some of these proteins and enzymes in HIV.)

HIV also has regulatory genes, which can be divided into the following three groups:

- Positive regulatory genes, namely the tat, rev, vif and vpu genes, positively regulate the formation of viral particles. These genes do this by promoting the production of proteins as well as the assembly of the components of the virus (thus they help to form new viruses).

- The negative regulatory gene, namely the nef gene, inhibits the production of structural proteins. This inhibition is needed by the virus for efficient replication. Researchers are studying this gene, and its products, to see if they can use it in therapy to slow down virus replication.
- The third group comprises the vpr and vpt genes. Their functions as regulator genes are not yet clear.

## 2.2.4 HIV infection and replication

We will now look at the ways in which HIV enters the body and how it replicates.

### 2.2.4.1 How HIV enters the body

Initially it was thought that HIV can only enter the body when there is an opening or lesion in the skin (e.g. in the vaginal tract or mouth). Research has shown, however, that HIV can be transferred through an intact mucous membrane in the vagina and elsewhere, because of the dendritic cells called the Langerhans cells present in the mucous membranes. While these cells usually offer protection to the body by acting as antigen-presenting cells (APCs) and thus warning the CD4+T cells, in the case of HIV they act as 'traitors'. For example, when HIV-infected semen is present in the vaginal tract, the Langerhans dendritic cells attempt to do their usual job by capturing a particle (an antigen) from HIV, but in the process they actively transport the virus into the body and then carry HIV to the CD4+T cells in an attempt to warn them.

Transporting the virus and presenting it to the CD4+T cell directly plays into the hand of HIV, because CD4+T cells are exactly those cells HIV prefers to infect. This 'treacherous' function of the Langerhans cells and the vulnerability of CD4+T cells to HIV infection is unique to HIV infection and explains why it is so dangerous (and ultimately fatal) to human beings.

### 2.2.4.2 Steps of infection and replication

We will now explain how HIV invades CD4+T cells. Use Figure 2.7 (page 43) to follow each step in the process.

#### Step 1 – Attachment

The infection of a host cell by HIV generally follows the same pattern as infection by any other virus (as described earlier). In the case of HIV, the gp120 glycoprotein makes contact with the potential host cell (mostly a CD4+T cell) and then attaches itself to the CD4 receptors which are present on the surface of the host cell. (See Step 1 in Figure 2.7.)

Binding to the CD4 receptor alone is, however, not enough to allow the virus entry into the cell. The gp120 protein also has to attach to a co-receptor on the cell surface to bring the gp41 protein of HIV into closer contact with the cell membrane. These **co-receptors** are called CCR5 and CXCR4. The CCR5 co-receptor is expressed on activated lymphocytes, macrophages, dendritic cells and brain cells, while CXCR4 is expressed on resting T cells and monocytes. (There are also other co-receptors in the CCR family utilised by some HIV strains to cause infection.)

**HIV infected**

The term 'HIV infected' is used to indicate that evidence of HIV has been found via a blood test (either HIV antibodies or viral particles, depending on the test used). An HIV infected person is able to transmit the HI virus during sex, through his or her blood, or during pregnancy, childbirth and breastfeeding.

**Note**

HIV antigens do not only attach to the Langerhans dendritic cells or the CD4+T cells. All cells with CD4 receptors and co-receptors on their surfaces, like monocytes, macrophages, other dendritic cells and certain brain cells can be infected by HIV.

**Co-receptors for HIV**

For HIV to bind to and infect a cell, it needs to bind to surface CD4 receptors (or cell proteins), as well as to co-receptors or cell surface molecules. The two predominant HIV co-receptors are CCR-5 and CXCR-4. CCR-5 is the co-receptor found on macrophages and CXCR-4 is the co-receptor found on lymphocytes, such as on CD4+T cells.

### Step 2 – Fusion

After attachment of the gp120 protein to the CD4 receptor, the gp120 protein splits open and thereby exposes the gp41 protein, which is otherwise covered by the gp120. The gp41 now causes fusion to take place between the outer envelope of the virus and the outside membrane of the host CD4+T cell. This fusion of membranes effectively combines the virus and host cell into one unit. (See Step 2 in Figure 2.7.)

### Step 3 – Injection

The virus then sheds its outer layer and injects its genetic material (two copies of single stranded RNA) and enzymes (reverse transcriptase, integrase and protease) into the CD4+T cell. (See Step 3 in Figure 2.7.)

### Step 4 – Reverse transcription

In order for the HIV's viral RNA to use the CD4+T cell to manufacture new viruses, the HIV viral RNA must be changed into proviral DNA, through a process called **reverse transcription**. To transcribe its single-stranded viral RNA into double-stranded DNA, HIV needs the enzyme reverse transcriptase (which it brought with it). (See Step 4 in Figure 2.7.)

**Note**

Proviral DNA can in some cases remain dormant for long periods in the host cell, thus forming long-lived cellular reservoirs, where ARVs cannot target them.

### Step 5 – Integration of genetic material

In this step, the proviral DNA is transported to the nucleus. Once at the nucleus, it fuses with the host cell's own DNA. This process of integration is facilitated by another viral enzyme known as integrase. (See Step 5 in Figure 2.7.)

### Step 6 – Replication of genetic material

After the viral genetic material has hijacked the genome of the host cell by integrating with it, it employs the machinery of the host cell to replicate the genetic material (RNA) necessary for new viruses to be manufactured. (See Step 6 in Figure 2.7.)

### Step 7 – Production of new viruses

Another viral enzyme, **protease**, enables the newly produced viral RNA (previous step) and viral proteins to be assembled into new copies of the former virus. These new viruses are then released from the cell as fully functional HI viruses, which eventually also cause the death of the original host cell. These new viruses subsequently travel into the bloodstream or surrounding tissue where they infect additional cells. They then repeat the whole process of infection and replication all over again. (See Step 7 in Figure 2.7.)

The infection by HIV and ultimate death of CD4+T cells causes two unwanted results. In the first place, it produces more and more viruses and, secondly, it depletes the number of CD4+T cells more quickly than it takes the thymus gland to manufacture new ones. This severely impairs the function of the whole immune system because without its 'generals' it becomes helpless. Even though the immune system succeeds in manufacturing some antibodies against HIV, they are insufficient to protect the body against the long-term destructive effects of HIV and, consequently, the body is left defenceless.

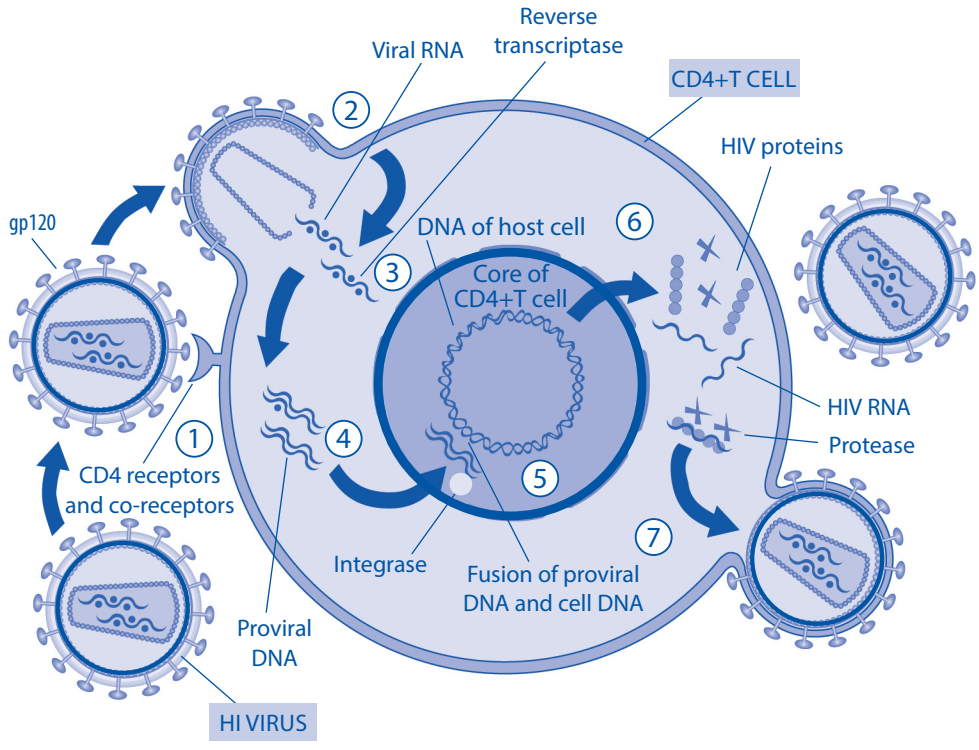



**Figure 2.7** Steps of infection of a CD4+T cell by an HI virus

**Step 1 – Attachment:** HIV (gp120) attaches to the CD4+T cell's receptors (CD4 receptors) and co-receptors.
**Step 2 – Fusion:** The CD4+T cell and HI virus join membranes.
**Step 3 – Injection:** HIV injects its RNA (as well as the enzymes reverse transcriptase, integrase and protease) into the CD4+T cell.
**Step 4 – Reverse transcription:** Viral RNA is changed into proviral DNA through a process called reverse transcription.
**Step 5 – Integration of genetic material:** The proviral DNA joins with the cell's DNA in the core of the cell, with the help of the integrase enzyme.
**Step 6 – Replication of genetic material:** The virus uses the machinery of the host cell to replicate the genetic material (RNA) to manufacture new viruses.
**Step 7 – Production of new viruses:** The viral RNA and viral proteins assemble into more HI viruses with the help of the protease enzymes. The new viruses break free from the cell, killing it and infecting more cells.

## Enrichment: HIV infection in pictures

Watch the following two videos on YouTube to see how HIV infects a CD4+T cell and how it replicates to produce more viruses:
http://goo.gl/IsCPQq
http://goo.gl/8u1494

## Frequently Asked Questions

### Why is HIV called a retrovirus?

HIV is called a retrovirus because, like other retroviruses, it has RNA instead of the usual DNA in its nucleus. However, the host cell cannot use this RNA to produce new viruses. Instead, the RNA must first be transcribed into DNA. This is the reverse order of the ordinary meiotic division of cells which is from DNA to Messenger RNA. In the case of retroviruses, transcription is from RNA to DNA to Messenger RNA. For this reason, such groups of viruses are called retroviruses.

### Why is it important to understand the replication process of HIV?

An understanding of the replication process of HIV helps us to understand why and how HIV eludes the immune system. Each stage in the replication cycle also provides an opportunity for the design of effective antiretroviral drugs. For example, if we did not realise the importance of viral enzymes (reverse transcriptase, protease and integrase) in the reproduction of HIV, we would never have been able to interfere with the working of these enzymes (by using ARVs) to inhibit the production of new viruses. **Reverse transcriptase inhibitors** inhibit the activity of reverse transcriptase and prevent them from transcribing RNA to viral DNA. **Protease inhibitors** inhibit the late stages of HIV replication by preventing cleavage of viral proteins, which then results in the production of immature viruses. **Integrase inhibitors** interfere with the integrase enzyme and prevent HIV from integrating with the host cell's genome. **Entry inhibitors** function by blocking the fusion of the viral and host cell membranes. (The inhibitors discussed above refer to the different ARV classes – they are called 'inhibitors' because they inhibit the viral enzymes from doing their jobs).

### Can HIV infect only CD4+T cells?

HIV does not infect only CD4+T cells. CD4 receptors and co-receptors are present on various types of cells, such as monocytes (a large phagocytic white blood cell), macrophages, dendritic cells (like the Langerhans cells) found in the skin and in the mucous membranes of the body, and in certain brain cells. The glycoprotein projections (gp120) on the outer layer of the virus attach themselves to these CD4 receptors and co-receptors. At first, scientists were very surprised to find the virus in the brain because the blood–brain barrier usually does not allow any foreign substances, such as viruses, to enter the brain. However, since monocytes are one of the few types of cells that can transfer across the blood–brain barrier, researchers then realised that HIV gets into the brain by hiding in these cells in a Trojan-horse fashion.

### Is it true that some people are 'immune' to HIV?

Various researchers found sex workers in certain areas of Africa who remained HIV-uninfected even after years of high exposure to HIV. Moore et al. (2012) identified two women who naturally developed rare broadly neutralising antibodies, which were able to kill most HIV types found across the world. Poudrier et al. (2012: 6) concluded that resistance in the context of HIV may be associated with 'the host's capacity to induce a strong innate and HIV-specific

immune response and, at the same time, control or maintain low inflammatory conditions and fewer HIV target cells at the initial exposure site'. Research on highly exposed HIV-negative individuals is ongoing since it has major implications for vaccine development.

**Why can HIV not be eradicated by drugs?**

HI viruses have the ability to 'hide' in cells like inactive memory T cells where they build up a supply of viruses that lie quietly in waiting until they become active at a later stage. This inactive supply of HI viruses in inactive memory T cells is called a 'latent reservoir' of viruses, and it is one of the reasons why HIV cannot be eradicated completely by drugs. HIV genetic material exists both as RNA inside viral particles and as proviral DNA in the nucleus of infected cells. Both forms are infectious, and proviral DNA allows HIV to persist in long-lived reservoirs, which makes it difficult to clear HIV completely from the body (Morris & Cilliers, 2010). It is believed that latent cells can live for more than 44 months and are probably activated by infections.

## Activity

Explain the effect of HIV on the immune system of children. Note the following in your explanation:

- Outline what happens to the body when it is attacked by an HI virus instead of a flu virus.
- Keep the explanation simple.
- Make use of a story or metaphor rather than using 'big' words.

## 2.2.5 Variability and subtypes of HIV

One of the most important properties of HIV is its extreme genetic diversity. HIV has the ability to mutate or change very rapidly, and this ability makes it very hard for the immune system and for antiretroviral drugs to kill the virus. The immune system is very dependent on its ability to use the outer protein layer of pathogens to recognise them. Because HIV changes its outer layer so rapidly, it is extremely difficult for the immune system to detect and identify the virus. The body cannot defend itself against an enemy that is constantly changing its identity. The genetic diversity of HIV is also one of the reasons developing an HIV vaccine is so difficult.

### 2.2.5.1 Why does HIV change so rapidly?

There are basically two reasons why HIV changes so rapidly: (i) the introduction of mutations into the viral genome during reproduction, and (ii) recombinations between viral genomes that shuffle these mutations.

**Introduction of mutations into the viral genome during reproduction**

The **variability** of HIV is due mainly to the inaccuracy of its genetic copying mechanism and the tendency of this mechanism to make errors. To reproduce, HIV relies on the reverse transcriptase enzyme to make DNA copies from the

**Glossary**

**Variability** The ability of something to change constantly; consistent without any fixed pattern.

viral RNA. The problem is that the reverse transcriptase enzyme is error prone in nature and every time the reverse transcriptase makes a copy of the RNA viral template and replicates the HI virus, it makes approximately five errors. The RNA replication mechanism does not have a facility to 'proofread' for mistakes and to repair mistakes (as is the case with DNA viruses or human cells that have the ability to repair their mistakes). These errors – also called mutations – are then reproduced. This is the reason why different strains of HIV can be found in one HIV-infected person. These strains may vary significantly in terms of their rate of growth, their virulence in killing cells, their sensitivity to antibodies produced by the host and their ability to evade the host's immune response.

#### Recombinations between viral genomes that shuffle mutations

The second mechanism used by HIV to generate diversity is recombining viral genomes to form new recombinant viruses. Recombinant viruses are generated when two viruses enter the same cell. The RNA of both viruses will then be combined and the reverse transcriptase will then produce a new virus containing RNA from both original viruses. The recombination of viral genomes also has the advantage that it can shuffle the mutations to get a stronger virus.

### 2.2.5.2 HIV groups and subtypes

When we discussed the origin of HIV in Chapter 1, we explained that HIV strains are classified into one of four groups, namely:

- group M (major group);
- group O (outlier groups);
- group N (non-M non-O group); and
- group P.

We now need to repeat some of this information to explain the variability of HIV. We will concentrate only on Group M, which is the main group behind the global HIV and Aids epidemic. The classification of HIV was illustrated in Figure 1.2 on page 7.

Group M is divided into subtypes (or clades), namely A, B, C, D, F, G, H, J and K. Some of the HIV subtypes also recombine to form circulating recombinant forms (CRFs). This means, for example, that HIV-1 subtype A may combine with subtype C to form a new recombinant subtype of the virus. Subtypes are often divided into sub-subtypes such as A1 and A2 or F1 and F2. According to Williamson and Martin (2010: 118) the current classification of HIV subtypes and CRFs does not give a complete picture of HIV diversity. There are many group M viruses that cannot be placed within the existing subtypes or CRF groupings. They are generally referred to as unique variants or unclassified recombinants.

Each of these subtypes predominates in different parts of the world. For example, the epidemic in southern Africa is essentially driven by HIV-1 subtype C viruses, which are also predominant in Eastern Africa, Nepal, India and parts of China. Subtype A is common in West Africa, while subtype D is dominant in certain parts of Eastern and Central Africa. The AG recombinant is dominant in many countries in West and Central Africa. HIV-1 subtype B is the predominant strain in Europe, North America, Australia, Thailand and Japan, while researchers have found subtype F in Eastern Europe, Central Africa and South America. The most extreme examples are found in equatorial West/Central Africa where

just about every known subtype, with circulating recombinant forms and unique recombinant forms, is seen (Kahn, 2005). This is also the region where it is believed that HIV originated. It is therefore not surprising that all these forms of HIV occur there since the virus circulated and **evolved** within the human population there for much longer than it did anywhere else in the world (Williamson & Martin, 2010). Migration in Africa will probably lead to a situation in future where the association between certain subtypes and specific regions will no longer be clearly defined.

HIV-2 is classified into nine groups (A to I), but only groups A and B are epidemic. The other groups are crossovers known in single individuals only. HIV-2 infections are not as **pathogenic** as HIV-1 infections and are mainly found only in West Africa.

For vaccine development, it is vital to know what the main subtype of HIV is in a specific part of the world. For example, a vaccine developed against HIV-subtype B will probably have no effect in southern Africa, where HIV-1 subtype C is the predominant subtype. The extreme diversity of HIV is one of the major reasons making a vaccine is so complex, and researchers are looking for a vaccine that will target greater diversity.

**Glossary**

**Evolve** Develop and change over successive generations as a result of adapting to their environment.

**Pathogenic** The ability of a pathogen (virus, bacteria, etc.) to cause disease. If we say that HIV-2 is less pathogenic than HIV-1, it means that HIV-2 is less prone to causing Aids than HIV-1.

### 2.2.6 Different responses to HIV infection

In the absence of antiretroviral therapy, the median time from HIV infection to death is 10.5 years for females and 11.5 years for males. The median time in Africa is one to two years shorter than in the developed world. While we are not absolutely sure why this is the case, it might be related to differences in viral subtypes, to socioeconomic factors such as poverty and malnutrition, poor access to healthcare, or to the higher burden of infectious and other diseases in Africa, such as TB and malaria, that compromise the immune system (Morris & Cilliers, 2010: 94). If a person is not treated with antiretroviral drugs, they usually die within 18 months to two years after the diagnosis of the severe symptomatic stage (or Aids).

Although the majority of HIV-infected individuals have good viral control and progress at a 'normal' pace (without antiretroviral therapy), some individuals progress from HIV infection to Aids within two to three years (rapid progressors), whereas others remain disease free for many years. The reasons why some individuals progress exceptionally quickly or slowly are not known yet. Research, especially on slow progressors, is very important since it will tell us something about an immune system that can control HIV.

## 2.3 Conclusion

Scientists now have a clear and precise understanding of how HIV destroys the body's immune system, but so far all attempts to eliminate the virus completely from the body, or to make the human body immune to the virus, have failed. At this stage the only way to stop Aids is to prevent transmission of the virus. This is only possible when one has a proper understanding of exactly how the virus is transmitted from one person to another. The transmission of HIV from one person to another is the theme of the next chapter. We will also discuss our responses in trying to curb the epidemic.

## Test your understanding

1. What makes HIV different from ordinary viruses?
2. Why can we call CD4+T cells the 'generals' of the immune system?
3. What is the difference between active and passive immunity?
4. Why are antibodies ineffective against HIV?
5. What is the role of antigen-presenting cells or APCs? Can you name a few APCs?
6. What is an antigen?
7. What is the function of the CD4+T cells in the immune system?
8. Why does HIV change or mutate so rapidly?

## Reference list

Kahn, P. (Ed.). 2005. *AIDS vaccine handbook: global perspectives* (2nd edn.). New York: AIDS Vaccine Advocacy Coalition (AVAC).

Moore, P. L., Gray, E. S., Wibmer, C. K., Bhiman, J. N., Nonyane, M., Sheward, D. J., Hermanus, T., Bajimaya, S., Tumba, N. L., Abrahams, M., Lambson, B. E., Ranchobe, N., Ping, L., Ngandu, N., Abdool Karim, Q., Abdool Karim, S. S., Swanstrom, R. I., Seaman, M. S., Williamson, C., & Morris, L. 2012. Evolution of an HIV glycan-dependent broadly 1 neutralizing antibody 2 epitope through immune escape. *Nature Medicine* 18(11): 1688–1692.

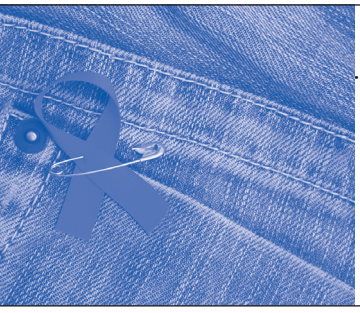
Morris, L. & Cilliers, T. 2010. Viral structure, replication, tropism, pathogenesis and natural history. In S. S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 87–96). Cape Town: Cambridge University Press.

Poudrier, J., Thibodeau, V., & Roger, M. 2012. Natural Immunity to HIV: A Delicate Balance between Strength and Control. *Clinical and Developmental Immunology* 2012: 1–10. doi:10.1155/2012/875821

United Nations Programme on HIV/AIDS (UN AIDS). 2011. *UNAIDS terminology guidelines*. Geneva.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (pp. 12–13). Cape Town: Nasionale Boekhandel Bpk.

Williamson, C. & Martin, D. P. 2010. HIV-1 genetic diversity. In S. S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 117–126). Cape Town: Cambridge University Press.



# Chapter 3

# Transmission and prevention

Alta van Dyk

### Raka wants to enter

*But now Raka, doglike, hung round the kraal:*
*in the dark, he'd roam round the kraal*
*like the rustling of small night-creatures;*

*A woman would fitfully stir on her mats,*
*heavy with dream, and suddenly cry*
*in the still of the hut*
*from terror and ecstasy, then half-awake*
*sense the huge animal, naked*
*and restless out in the dark.*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- counsel your peers about the ways in which HIV is transmitted;
- explain to an HIV-infected pregnant woman how HIV can be transmitted through breastmilk and counsel her on the choices available to her for feeding her baby;
- write an article to your local newspaper discussing the role of depressed socioeconomic conditions, poverty and disempowerment of women as contributory factors in the spread of HIV infection;
- dispel myths about the transmission of HIV in your community;
- critically discuss behavioural, biomedical and structural interventions to prevent HIV transmission;
- talk to a group of young men about the HIV preventive value of medical male circumcision; and
- understand how antiretroviral therapy can be used to prevent HIV infection.

## Chapter outline

- Sexual transmission of HIV infection
- Transmitting HIV through contaminated blood
- Mother-to-child transmission of HIV
- Myths about the transmission of HIV
- Prevention of HIV
  - Behavioural intervention
  - Biomedical intervention
  - Structural intervention

HIV infection is transmitted primarily by the following ways: sexual intercourse; HIV-infected blood that passes directly from an infected person into the body of another person; and from a mother to her baby, either during pregnancy or childbirth, or as a result of breastfeeding.

Researchers have identified HIV in various body fluids, such as saliva, tears, sweat and urine. However, the **concentration** of the virus in these body fluids is too low for successful transmission. There are also no CD4+T cells or CD4 receptors in these body fluids, so there is no way for HIV to replicate in these body fluids.

Two things need to occur for a person to become infected with HIV: the virus must find a way to enter the person's the bloodstream; and, when the virus has entered the bloodstream, it must be able to **embed** itself. It is likely that these two things will happen if:

- there are sufficient quantities of the virus in the person (in the semen, vaginal fluid, blood or breastmilk);
- the virus is able to enter into the bloodstream; and
- the virus is in the bloodstream for long enough to 'take hold' in the person. This is because the longer a person is exposed to the virus, the greater the risk is of becoming infected.

**Glossary**

**Concentration** The amount of a specific substance that is contained within a solution.
**Embed** insert and fix something deeply and firmly into surrounding material.

Consequently, because blood, semen and vaginal fluids meet the three conditions for HIV transmission described above, HIV is particularly highly concentrated in these body fluids. This chapter concentrates on the transmission and prevention of HIV.

## 3.1 Sexual transmission of HIV infection

The primary way that HIV infection is transmitted sexually is through unprotected (i.e., without a condom) penetrative vaginal or anal intercourse, and through oral sexual contact under certain conditions. In sub-Saharan Africa, the primary mode of HIV transmission remains heterosexual intercourse.

HIV is transmitted when the body fluids of an HIV-infected person enters another person's bloodstream. As explained in Chapter 2, to gain entry into the body, HIV must connect to CD4 receptors and co-receptors, which are found on various types of cells, such as macrophages, dendritic cells and CD4+T cells. Many of the cells in the linings of the genital and anal tract have these types of receptors. Consequently, HIV can easily enter the cells in the genital and anal tract linings. In addition, the mucous membranes of the genital tract have an abundance

of antigen-presenting cells (APCs), such as Langerhans cells (a type of dendritic cell) that are poised to transport the HIV antigens to the CD4+T cells. The Langerhans cells circulate continually between the peripheral mucous membranes and the CD4+T cell lymphocytes found in the lymph nodes and other lymphoid tissue, like the spleen, tonsils and thymus.

In the beginning, researchers and scientists thought that there had to be a break in the mucous membranes of the genital tract before HIV could enter the bloodstream. This belief was shattered by observations of HIV transmission by artificial insemination where it was established that sexual transmission of HIV could occur across an intact mucous membrane. Langerhans cells provided the answer. As soon as HIV in the mucous membrane infects a Langerhans cell, the natural migration route of the Langerhans cell transports it to the CD4+T cells in the lymphoid tissue. In the lymphoid tissue, the Langerhans cell functions as an antigen-presenting cell, presenting the HIV antigen directly into the CD4 receptors and co-receptors of the CD4+T cell. Consequently, the Langerhans cells have become known as the 'taxi' cells of the immune system.

Apart from HIV transmission across intact genital mucous membranes, HIV can also move directly into the bloodstream during sex. This is a result of the delicate nature of the membrane linings of some body cavities, particularly in the anal-rectal area and in the vagina, although to a lesser extent. Consequently, it is easy for friction generated during sexual intercourse (particularly during rough sex, dry sex or rape) to tear these linings. The virus can then easily enter the uninfected person's bloodstream through these often microscopic tears.

## 3.1.1 Contributing factors influencing the spread of HIV

There are various biological, epidemiological and socioeconomic factors that influence the spread of HIV infection in a community. Some of these factors are discussed in the next section.

Do you remember the difference between HIV prevalence and HIV incidence? We will be using these concepts in the discussions that follow, so if you cannot remember the difference, revise them on pages 10 and 11.

### 3.1.1.1 Gender

It is more likely that women and girls than men or boys will become infected with HIV during unprotected vaginal intercourse. In 2012, the overall HIV prevalence in South Africa was 14.4% for women and 9.9% for men. Among youth in the 15 to 24 age group HIV prevalence of females was 11.4% while prevalence for males was 2.9%. The HIV incidence among young females aged 15 to 24 in 2012 was over four times higher than the incidence in males in the same age group (2.5% and 0.6% respectively). Teenage girls aged 15 to 19 years are especially vulnerable with an estimated HIV prevalence of eight times higher than that of their male counterparts (Shisana et al., 2014: 36, 42).

There are various biological, cultural and social reasons for greater **susceptibility to** HIV infection among women than men. Because a woman receives the male's semen, it remains in the woman's body for a few hours, whereas the male is exposed to woman's body fluids for only a short time. In addition, because the concentration of HIV may be higher in semen than in vaginal fluids, it is more likely that transmission will take place from male to female than the other way round. Furthermore, a woman also has a larger surface area of **mucosa** exposed to the partner's secretions during sexual intercourse. Another **exacerbating** factor is that some women may be unaware that they have cervical or vaginal conditions

**Glossary**

**Susceptibility to** Having the likelihood of being harmed by something, getting infected or becoming sick.
**Exacerbating** Making something, such as a bad situation, problem or negative feeling, even worse.

**Glossary**

**Conspicuous** Something that is clearly noticeable. Women with painless STIs are often not aware that they have an STI because it is hidden inside the vagina or cervix and they cannot see it (i.e. it is not outwardly conspicuous).

**Copious** Plentiful or abundant. In this sense it means that young women do not have a lot of vaginal secretions yet to protect the vaginal lining from laceration.

**Note**

The presence of HIV-infected blood in menstruating HIV-infected women makes them highly infectious during menstruation.

(such as STIs, erosions, open sores and infections) that make the transmission of HIV easier. Some of these conditions often go undetected because they are symptom free, painless and not outwardly **conspicuous**, being hidden inside the vagina or cervix. Apart from STIs or infection, damage to the vaginal walls is often caused by the use of herbal and other substances for the practice of 'dry sex' – a practice that many disempowered women in Africa perform to please their partners (see 'The dangerous practice of 'dry sex' on page 243). Women also often use preparations such as spermicidal (sperm-killing) creams that may cause allergies, irritation and inflammation of the vaginal walls.

The most likely time for transmission of HIV to occur is either very soon before menstruation, or during or immediately after it. This is because the large, raw area of the inner uterine lining is exposed during these times. Not all women appear to be equally vulnerable to HIV infection. In fact, evidence suggests that girls, young women and women after **menopause** are most vulnerable. There are three factors that make girls and young women vulnerable: their genital tracts are not yet fully mature; they do not have **copious** vaginal secretions; and their vaginal mucosa lacerates more easily. As far as women after menopause is concerned, the risk of HIV infection increases because of the thinning and increasing dryness of the mucosal walls. The risk of HIV transmission is also increased by any tearing or bleeding of the genital-anal area. Consequently, rape and rough sex, as well as previous female genital mutilation (female circumcision) and anal sex all increase the risk of HIV transmission.

The occurrence of anal sex (where the woman is the passive partner and recipient of semen) is underestimated in Africa and seldom included in educational programmes. Many women and girls practise anal sex to preserve their virginity, to prevent pregnancy, to experience new forms of sex, to please a partner, to trade anal sex for money or drugs, to avoid vaginal sex during menstruation and because they erroneously think that anal sex will protect them from HIV. Research on female sex workers at truck-stops in KwaZulu-Natal noted an increase in the practice of anal sex between 1992 when the practice of anal sex was rare to 42.8% in 1996 (Abdool Karim & Frohlich, 2000). The researchers further established (based on self-reported anal sex) an HIV prevalence of 61.3% among sex workers who practised anal sex compared with 42.7% in those who did not practise anal sex. It should however be emphasised that not only sex workers practise anal sex. It is becoming an increasing sexual activity of choice, especially in schools.

Apart from their biological vulnerability, women are also more vulnerable in societies in which they are regarded as having lower status than men. This makes women dangerously vulnerable in sexual relationships because they do not have the status or power to express their needs or ensure that they are met. Because of their low status, most women from poor (socioeconomically depressed) communities have little or no control over their sex lives. They are not in a position to negotiate safer sex practices because they fear violence and abandonment should they try to do so. A survey carried out in Lesotho in 2007 found that 40% of women and 47% of men believed that women had no right to refuse sex with their husbands or boyfriends (Andersson et al., 2007). The husbands of women from poor communities often have casual sex when they have to leave their families behind to find work in the cities. Sometimes dire material and financial need and poverty force women from such communities to sex work in order to earn some

sort of living. Their consequent low self-image coupled with their lack of personal authority make these women especially vulnerable to rape.

Although the disempowered position of many women in sub-Saharan Africa is a reality, we should be careful not to perpetuate the stereotype of African women as powerless, passive victims subordinated by men. De Coninck et al. (2014) found a significant increase in knowledge of HIV and ability to negotiate safer sex amongst married Ethiopian women between 2005 and 2011, reflecting a positive trend in gender empowerment. Skafte and Silberschmidt (2014) similarly found that while Rwandan women do comply with **prevalent social norms**, they also challenge these norms and sex becomes a domain in which they can exert power and insist on practising safer sex.

Although research on HIV-related risks among men who have sex with men (MSM) has increased, this is still a group that does not get enough attention in HIV education programmes. In a study undertaken in Cape Town, Durban and Pretoria, it was found that one third of the men who have sex with men (who also injected drugs) tested HIV positive (Parry et al., 2008). It is clear that a major prevention, care and treatment programme is necessary for men who have sex with men. Unfortunately, this is still a highly criminalised group in many sub-Saharan African countries, which makes it very difficult for these men to access health education, treatment and care. Same-sex activity between consenting adults is prohibited by law in more than 30 countries in sub-Saharan Africa, where it is regarded as a 'violation' that is often punished with the death penalty.

**Glossary**

**Prevalent social norms**
Expected social behaviour that is widespread in a particular area or during a specific time.

### Terminology: Men who have sex with men versus gay

The term 'Men who have sex with men' (or MSM) refers to men who have sex with men, regardless of whether they identify themselves as being gay (homosexual), straight (heterosexual) or bisexual (having sex with both women and men). If you ask a heterosexual (often married) man, who also has sex with men on the side, if they are gay, they will probably deny it and insist that they are straight. HIV prevention programmes that only focus on gay men fail all those men who have sex with men, but who do not see themselves as being gay. To rectify this situation, it was decided in the 1990s to refer rather to 'men who have sex with men' than to 'gay men' only. The term MSM thus focuses on the *behaviour* of the men (having sex with other men) rather than on their *social self-identification* (e.g. being gay).

According to the UNAIDS (2011) Terminology Guide (pp. 8, 15) the expression 'men who have sex with men' should be used unless individuals or groups self-identify as gay. Similarly, the term 'women who have sex with women' should be used, unless individuals or groups self-identify as lesbians.

### 3.1.1.2 Age

Younger people – primarily those in their reproductive years – are more vulnerable to HIV than older people. In 2012, HIV incidence in the 15 to 24 age group was 1.49% and 1.41% in people older than 25 years (Shisana et al., 2014). This means that 1.49% of young people in Shisana's sample (aged 15 to 25 years) were infected with HIV in 2012 alone.

Behavioural factors that increase the vulnerability of especially young girls or women to HIV infection are starting to have sex before the age of 15 years and having sex with older men (i.e. age-disparate sexual relationships where the

Did you note that most of the young girls involved in intergenerational or age-disparate sex are schoolgirls? In Chapter 10 you will learn about what we can do to keep adolescent girls healthy and in school.

age gap between sexual partners is five years or more). One tenth (10.7%) of the young people who participated in the South African National HIV Survey in 2012 reported having sex for the first time before the age of 15 years (Shisana et al., 2014). Significantly, three times as many males than females reported having their first sexual encounter before the age of 15 years. Young people engage in early sex for a number of reasons, such as low **self-esteem**, pessimism, peer pressure, sexual coercion and money or other favours (transactional sex).

**Glossary**

**Self-esteem** The personal assessment of value or worth that we attach to ourselves.
**Stigmatised** When a particular situation, such as having HIV, becomes a mark of social or cultural disgrace, we say it has become stigmatised.

**Terminology: Prostitution versus sex work**

The term 'prostitution' or 'prostitute' should no longer be used as it has become a **stigmatised** concept. Preferred terms are: sex work, sex worker, transactional sex, or the sale of sexual services. These terms are intended to be non-judgemental. 'Sex work' for example, focuses on the conditions under which sexual services are sold. When children are involved, refer to 'commercial sexual exploitation of children' (UNAIDS, 2011: 2).

HIV prevalence was higher in young people aged 15 to 24 years (male and female) who were involved in age-disparate sex than in those who had sexual partners within five years of their own age (Shisana et al., 2014). In the 2012 South African National Survey, 19.7% of respondents aged 15 to 19 years said they'd had sexual partners who were more than five years older than them. Interestingly, the adolescent female to male proportion in this age group was of 33.6% female to 4.1% male, respectively. Among the adolescent girls in this age group, 11% who'd had sex partners five years and older than them were HIV positive, while 9.3% who'd had sex partners less than five years older than them were HIV positive (Shisana et al., 2014). Poverty often drives age-disparate sex relationships, where sex is exchanged for financial or social benefits, or gifts.

**Activity**

Develop a government programme to educate female adolescents about the dangers of age-disparate relationships (where the sex partner is five or more years older than the adolescent).

- List the reasons women (and especially young girls) are especially vulnerable to HIV infection.
- Suggest how each reason (factor) can be neutralised.

### 3.1.1.3 Other sexually transmitted infections

The presence of other sexually transmitted infections (STIs) also influences sexual transmission of HIV. Individuals who have sexually transmitted infections that cause genital ulcers (such as **syphilis**, **chancroid** and herpes) or a discharge (such as **gonorrhoea**, **chlamydia** and **trichomoniasis**) are especially susceptible to HIV infection. STIs increase the risk of HIV transmission on average about fourfold.

Individuals with **genital herpes**, or genital ulcers or sores are particularly vulnerable to HIV infection because these STIs cause breaches in the epithelial barrier that HIV can move through. Discharges caused by STIs result in genital inflammation. This attracts various immune cells with CD4 receptors to the

site of infection, which creates ideal conditions for HIV to latch onto the CD4 receptors in and around the genital tract. The dendritic 'taxi' cells that transport the pathogens to the lymph nodes also play a role. Because of this relationship between genital infections and immune cells, it is so much easier for HIV to enter the body cells of people with STIs. The discharges produced by many STIs contain a very high concentration of HIV. This means that there is an increase of viral shedding and that an HIV-infected partner will be more infectious to sex partners if they are co-infected with an STI.

The effect of STIs on the probability of HIV transmission is generally greater when the STIs are symptomatic (i.e. when there is an open sore or a discharge) than when they are asymptomatic. It is therefore important to treat STIs as soon as they show symptoms.

#### 3.1.1.4 Socioeconomic and cultural conditions

The devastating plagues of history (e.g. the bubonic plague of the 14th century, also known as the Black Plague) usually emerged from specific social and economic environments that provided fertile grounds for the spread of infection. During the Industrial Revolution in Europe in 1844, community vulnerability to sexually transmitted and other infections was often ascribed to social disorder and chaos, migration, uncontrolled and rapid **urbanisation**, prostitution, child labour, syphilis, TB, infant deaths, homelessness, poverty, and social and cultural transition.

**Glossary**

**Urbanisation** The movement of large numbers of people from rural areas into towns and cities.

Similar socioeconomic conditions exist today in Africa and other developing countries. HIV and other sexually transmitted infections are often more common in communities living in depressed socioeconomic conditions. The following factors aggravate the situation:

- High unemployment levels force men (and women) to migrate to cities. This disrupts family and social lives and new sexual networks are established.
- Tradition often accords a low status to women, and they are denied the authority to negotiate safer sex practices.
- Extreme poverty forces women into selling sexual services.
- People often live in extremely grim conditions and have limited or no access to health services.
- Disempowered people often lack health-seeking behaviours.
- The prevalence of sexually transmitted infections is often very high in depressed socioeconomic conditions, and the use of contraceptives is low.
- There is widespread illiteracy and poor education.
- There is a lack of information and support services.
- Alcohol abuse is common. This lowers thresholds of inhibition and compromises sensible decision making.
- The community is subject to famine, wars, conflict, crime and high levels of corruption.
- Traditional social and sexual morality is disintegrating. Old traditions that created cohesion and mutual help in communities have either been undermined or have disappeared altogether.
- Fear of violence, especially in communities where women are disempowered and physical and sexual domination by males exist.

It will take much more than distributing condoms to prevent HIV and reclaim our world from Aids. Programmes to uplift poor communities, improvement of

working conditions, a decrease in unemployment, empowerment of women and a strong policy to protect women and children are all issues that society will have to address before an Aids-free society can become a reality.

### Frequently Asked Questions

**What is the risk of acquiring HIV infection after a single sexual exposure?**

The risk of acquiring HIV infection after a single sexual exposure is estimated to be less than 20 per 100 000 contacts (Morris & Cilliers, 2010: 93). This means that sexual transmission is not highly effective as means of transmission. Several factors may contribute to the chances of contracting HIV infection, such as frequency of sex, multiple sex partners, condom use, immunological status (including the viral concentration or **viral load** in the blood, semen or vaginal fluids of the infected partner), the presence of other sexually transmitted infections and trauma (or bleeding) during sex (e.g. violent rape) and male circumcision. A person's risk of contracting HIV is much higher if, for example, the sex partner has a high viral load in the blood. An HIV-infected person on antiretroviral therapy (who has strictly **adherence** to the medication regime) will have a much lower viral load and will therefore be less likely to transmit the virus to a sex partner.

**When is an HIV-infected person who is not on ART most infectious to other people?**

Although it is possible for HIV to be transmitted at any time during the course of the disease, HIV-infected people are considered most infectious soon after becoming infected with the virus (during **seroconversion**) and during the final phase of Aids when severe symptoms appear. HIV-infected people are more infectious during these phases because the viral load in their blood is very high at these times. A high plasma level of HIV (HIV in the blood) is also an indication of high viral loads in genital secretions. Some studies have found that the viral load in semen peaks three weeks after infection, and that during this stage HIV is 20 times more transmissible per sex act. (Note that the answer to this question will be different when an HIV-infected person is receiving antiretroviral therapy. ARVs reduce the viral load in the body and the person will thus be less likely to transmit HIV to the sex partner.)

### Glossary

**Viral load** The amount of viral RNA (or virus particles) detectable in the blood of an infected person. The quantitative PCR technique is used to 'count' the HI virus particles or viral load in the blood of an HIV-positive person.

**Adherence** To take every dose of medication strictly as prescribed. Strict adherence to antiretroviral therapy is important to achieve viral suppression and to avoid the risk of mutation, the development of resistant strains and drug failure.

## 3.2 Transmitting HIV through contaminated blood

HIV can be transmitted to someone if that person receives HIV-contaminated blood in a blood transfusion, uses needles that are contaminated with HIV-infected blood to inject drugs or is injured with blood-contaminated needles, syringes, razor blades or other sharp instruments. The re-use of instruments in traditional African healing or in cultural practices, such as circumcision and scarification, also pose the risk of HIV transmission.

### 3.2.1 Blood transfusions and blood products

Because of the large volume of blood received during a blood transfusion, there is a 98% to 100% chance that a person who receives blood from an HIV-infected

donor will be infected with HIV (Heyns & Swanevelder, 2010). Nobody will ever forget the devastating effect of HIV on haemophiliacs in the 1970s and 1980s before the virus was discovered and before donated blood was routinely screened for HIV antibodies. An estimated 6 000 to 10 000 haemophiliacs in the United States of America were infected with HIV during those years. Today, most countries have very strict policies about blood safety, and most follow the WHO (2015) recommendations on universal access to safe blood and blood products. These recommendations include:

- establishment of a national blood system with well-organised and coordinated blood transfusion services and policies;
- collection of blood, plasma and other blood components from low-risk, regular, voluntary unpaid donors and the phasing out of family/replacement donations;
- quality-assured screening of all donated blood for transfusion-transmissible infections (TTIs), including HIV, hepatitis B, hepatitis C and syphilis;
- rational use of blood and blood products to reduce unnecessary transfusions and minimise the risks associated with transfusion by using alternatives to transfusion;
- safe and good clinical transfusion practices, including patient blood management; and
- implementation of effective quality systems, including quality management, standards, good manufacturing practices, documentation, training of all staff and quality assessment.

Blood safety is still a problem in the developing world. In 2012, for example, 40% of middle-income countries and 56% of low-income countries in the world did not have legislation that specifically covers the safety and quality of blood transfusions. In addition, more than 50% of the blood supply in 72 countries still depends on family/replacement and paid blood donors – practices that are associated with a significantly higher prevalence of transfusion-transmissible infections, including HIV (WHO, 2015).

The greatest risk of HIV infection from blood transfusions occurs in the infectivity **window period**. This is the period between a person being infected with HIV and a laboratory test detecting and confirming the presence of antibodies or virus particles in the person's blood. The window period varies from test to test depending on the sensitivity of the test. Older generation tests took much longer before they could produce positive results (we say they had a much longer window period). For example, in the late 1990s, the South African National Blood Services (SANBS) used first-generation antibody tests (enzyme-immune-assays or EIA) which had a window period of 45 days. If a donor was newly infected with HIV and donated blood in this period (up to 45 days), the tests would not have been able to pick up the infection and the blood would be used for transfusions. Fortunately, tests have improved continuously, and since October 2005 the SANBS screens all blood donations in South Africa for viral nucleic acid (a part of the virus itself) with a PCR procedure. This is also called **nucleic acid testing** or **NAT**. The NAT test is very sensitive and it detects the presence of HIV, hepatitis B, hepatitis C and syphilis in blood. The window period for NAT is about 12 days. NAT is much more expensive than antibody testing and not all countries can afford to use NAT.

**Glossary**

**Window period** The time between infection with HIV and the development of detectable HIV antibodies or viral particles. Any HIV test done during this time will render false negative results, which means that the patient is infected with HIV but the test result is negative.

The key to a safe blood supply is a donor population that falls into a low-risk category for HIV infection. The South African National Blood Service (SANBS) attempts to achieve this through the following measures (SANBS, 2014):

- They recognise that the voluntary, non-remunerated (unpaid) donor, who donates regularly, is the safest donor.
- Blood donors fill in a Self-Exclusion Questionnaire with questions on a person's health and lifestyle based on activities and exposures in the preceding six months. Donors are educated not to donate blood when they were exposed to HIV, or to ask the service to destroy donated blood if necessary.
- The red blood cells of first-time donors are not used and plasma gets quarantined until the person's next donation. If all tests come back negative for sexually transmissible diseases after the second donation, the quarantined plasma from the first donation will be used. Once a person made three donations and the blood still tests negative for sexually transmissible diseases, all the components (red blood cells, platelets and plasma) are used.
- Blood is tested for HIV, hepatitis B, hepatitis C and syphilis.
- There is no random testing of blood samples. Every unit of blood collected goes through the same stringent testing.

The rate of HIV positivity in all blood donations in South Africa decreased from 0.26% before the risk management programme was instituted in 1998 to 0.14% in 2007 (Heyns & Swanevelder, 2010: 233). According to the SANBS annual report (2014) the HIV prevalence among donors was 0.18% in 2013 and 0.24% in 2014.

Healthcare professionals also have a role to play in blood safety. The necessity of a blood transfusion should be carefully evaluated and should be given to patients only when it is essential to save their lives. There are various other options that can be used instead of a blood transfusion. HIV is also present in the organs, tissue and semen of infected donors. All donor products are therefore tested for HIV before they are accepted for transplant use.

### 3.2.2 Injecting drug use

People who share syringes and needles to inject drugs run a very high risk of being infected with HIV. HIV is easily transmitted when needles are shared because drug users usually inject drugs directly into their bloodstream. To make sure that their needle has penetrated a vein, drug users usually first draw blood into the syringe prior to injecting the drug into their bloodstream. Consequently, a small amount of blood stays in the syringe. When the next user uses the syringe to inject drugs, this blood is injected directly into their bloodstream. Because the virus is highly concentrated in blood, these tiny 'blood transfusions' of HIV-infected blood between drug users using the same infected needle constitute an ideal method for passing on the virus.

People who inject drugs put both themselves and their sex partners at risk. The problem of HIV transmission is aggravated by the fact that many people who inject drugs resort to sex work to obtain the money they need to support their drug habit. Many sex workers admit that they cannot cope with the demands of sex work if they are not 'high' on drugs (personal communications with sex workers in Johannesburg, 2002). Sex workers often introduce substance use to their clients in the hope that the client will pay for mutual consumption.

Although Africa (relatively speaking) does not yet have a very large number of people who use syringes for the self-administration of drugs, the authorities should not wait until it is too late before educating people about how easy it is to transmit HIV by sharing infected needles. South Africa is becoming an increasingly popular transit route and destination for drug traffickers. It is thus very likely that intravenously injected drugs will become a very serious problem in this country. Although it is difficult to estimate how many people are using drugs in South Africa, reports on the escalating national demand for treatment for addiction gives a good indication. For example, the proportion of heroin admissions to treatment in Gauteng grew from 0% in 1998 to 14% in 2007 (Leggett, 2010: 241). The majority of patients seeking treatment in Gauteng used to be young and white, but black patients increased from 1% of heroin admissions in 2001 to 41% in 2007. According to Leggett, heroin use is not only a problem in the cities but has also emerged in more remote parts of the country, such as rural Mpumalanga which is situated along the drug trafficking routes between Mozambique and the major urban centres in South Africa.

If we do not act now by introducing harm-reduction programmes, we may lose our window of opportunity to curb a major driver of the HIV epidemic.

See section 9.4 (page 248) for additional information about harm-reduction programmes.

### 3.2.3 Blood-contaminated needles, syringes and other sharp instruments

HIV can be transmitted through contaminated needles and sharp instruments in hospitals or clinics, either as a result of poor medical hygiene or through accidental exposure to contaminated needles or other sharp instruments. It can also be transmitted through tattooing with needles, ear piercing and ritual circumcision or scarification. Those who carry out tattooing and ear piercing, and traditional healers, as well as their clients, should be educated about the importance of using clean instruments.

Many healthcare workers get worried about the danger of being infected with HIV. However, all known cases of HIV transmission in healthcare settings have occurred in the context of accidents; that is, occasions when a healthcare worker has been accidentally exposed to infected blood and/or other body fluids in a way that permits transmission of the virus. Examples of such accidents are:

- when a person is accidentally pierced with a needle containing blood from an infected patient (a **needlestick injury**);
- when a person is cut by a scalpel, glass or other sharp instrument that is contaminated with infected blood;
- when a person not wearing gloves makes prolonged contact with an infected person's blood;
- when a person whose skin is chapped, has abrasions or is affected by **dermatitis** is exposed to large amounts of HIV-infected blood; and
- when HIV-infected blood accidentally splashes into the eyes or mouth of a caregiver.

There is a small but significant risk of transmission of HIV as a result of occupational exposure. According to the Centres for Disease Control (CDC) the average risk of HIV transmission after a **percutaneous** exposure to HIV-infected blood (i.e. needlesticks or injuries with other sharp instruments) is approximately 0.3% (or

**Glossary**

**Needlestick injury** This is when a needle containing HIV-infected blood penetrates the skin of another person.

**Percutaneous** Made, done or produced through the skin. Percutaneous exposure thus means that the skin was breached (cut or pierced) and is exposed to potentially infectious body fluids.

one chance in 300). This means that 99.7% of needlestick or cut exposures to HIV-contaminated blood will not lead to HIV infection. Mucous membrane exposure (e.g. splashes of blood or body fluids contaminated with blood, semen or vaginal fluids into the eyes or mouth of the caregiver) carry a considerably lower risk of about 0.1% (or one chance in 1 000). The risk after exposure of the skin to HIV-infected blood is estimated to be less than 0.1%. A small amount of blood on intact skin probably poses no risk at all (CDC, 2013).

See 'Post-exposure prophylaxis after occupational exposure' on page 171.

The risk of HIV transmission may be higher if an injury involves large volumes of blood (e.g. in the case of a deep-penetrating wound); if the needle has been in the vein or artery of the HIV-infected person; or if the viral load in the blood is high (as is the case in terminal Aids patients or during acute **seroconversion illness**). **Post-exposure prophylaxis** (PEP) in the form of antiretroviral medication should be made available to all healthcare workers who have sustained needlestick injuries or other accidents with HIV-infected blood and who are HIV uninfected at the time of the injury.

Healthcare workers should note that amniotic (pregnancy) fluid, cerebrospinal fluid and pleural (chest) fluid, as well as fluid from the abdomen (peritoneal fluid), heart (pericardial fluid) and joints (synovial fluid) should be considered potentially infectious. The risk for transmission of HIV infection from these fluids is unknown.

## Enrichment: Hepatitis B or HIV: Which is more infectious?

While many healthcare workers are afraid of HIV infection, some may be unaware of the risks posed by hepatitis B. Hepatitis B is a blood-borne viral infection of the liver which is caused by the hepatitis B virus (**HBV**). HBV is transmitted in the same way as HIV, namely through sexual contact, needle-sharing, the infection of a baby by its mother, and contaminated blood or blood products. Like HIV, HBV is not transmitted by casual contact such as shaking hands, sharing eating utensils, and so on. In the case of both HIV and HBV the occupational risk of infection is directly proportional to the degree of contact that a healthcare worker has had with infected blood or blood products. However, given similar exposure to a similar volume of infected blood, the risk of transmission is much greater for hepatitis B than it is for HIV: the chance of becoming infected by a single exposure to HIV-infected blood after being pricked by an HIV-contaminated needle is 0.3%, whereas the danger of HBV transmission under similar circumstances ranges from 6% to 30% in unvaccinated people. Although most people recover from hepatitis B in about six months, others may continue to suffer from chronic infections or develop severe liver problems, or develop cirrhosis, cancer or even acute fatal liver failure. Healthcare workers should therefore be extremely cautious when they handle body fluids to avoid being infected by either HIV or HBV. One of the important differences between HIV infection and hepatitis B is that hepatitis B is preventable through vaccination. Healthcare workers who work in situations in which they are exposed to blood and body fluids should insist on being vaccinated against hepatitis B. (Three doses of Engerix-B give protection lasting three to five years. This vaccine is readily available at most pharmacies.)

### Frequently Asked Questions

**What quantity of infected blood needs to be present before HIV is transmitted?**

It is impossible to say exactly how much blood is required to transmit HIV. The risk of infection is directly proportionate to the concentration of HIV (the viral load) in the blood. Recently infected individuals with acute seroconversion illness and patients in the final stage of infection (Aids) usually have very high viral levels in their blood. The higher the concentration of HIV in the blood, the lower the quantity of blood required to transmit the virus. If a person is on antiretroviral treatment (and adhering to the treatment) the viral load in the body fluids should be low. Rather than asking how much blood is needed to transmit HIV, healthcare workers should instead be guided by the following golden rule: Always take proper precautions when handling blood and any other body fluids to which **universal precautions** apply.

**For how long can the virus survive outside the body?**

We must differentiate between the lifespan of HIV when it is outside the body and outside body fluids (e.g. blood or semen), as opposed to when it is outside the body but still inside body fluids. As soon as HIV is no longer inside a body fluid, or when it is exposed to oxygen, heat and dryness in the atmosphere, it becomes very fragile and dies. Although HIV cannot survive outside body fluids for very long, it can survive outside the body for many hours as long as it remains in some or other body fluid, such as blood. According to some sources, HIV can survive and be infectious for up to 24 hours in body fluids outside the body, for example in the case of blood spills. Body fluid spills should therefore always be dealt with extremely carefully. One should always take proper precautions when handling blood or body fluids that contain visible blood. Universal precautions should also be strictly adhered to when handling the body of a patient who has died of Aids. Cultural cleansing rituals on the bodies of their dead played a major role in the spread of the Ebola virus in Africa – including the most recent outbreak in 2014.

**Glossary**

**Universal precautions**
A variety of precautions that all people who come into contact with blood and certain other body fluids or products in a healthcare setting should apply so as to prevent themselves from becoming infected by HIV (or any other dangerous pathogen such as the highly infectious hepatitis B virus).

See page 563 for methods of cleaning up body fluid spills.

## 3.3 Mother-to-child transmission of HIV

Mother-to-child transmission (MTCT) or vertical transmission of HIV is one of the major causes of HIV infection in children. The majority of young children with HIV infection (90% to 95%) contracted the infection through mother-to-child transmission. The rest mainly contracted HIV through the use of unsterile equipment in poorly managed health facilities. Unless preventive measures are taken (such as antiretroviral therapy, elective or planned Caesarean section or safe delivery and safe infant feeding) between 25% and 45% of all children born to HIV-infected women in Africa are likely to be infected (Coovadia, 2010). It is believed that the provision of antiretroviral prophylaxis and safe feeding can reduce mother-to-child transmission to about 1% to 2% (instead of 25% to 45%). According to the South African Minister of Health (2016) mother-to-child-transmission of HIV reduced from 70 000 babies born to HIV-positive women in 2004 to less than 7 000 in 2015.

An infected mother can transmit HIV to her baby via the placenta during pregnancy, through blood contamination during labour and delivery or through breastfeeding. The likelihood of a mother transmitting HIV to her baby during pregnancy, childbirth or breastfeeding increases if:

- she is infected with HIV just before the pregnancy, or during the pregnancy or breastfeeding period (when the viral load in her blood or breastmilk is very high because of seroconversion); and if
- she has advanced, severe symptomatic HIV disease (Aids) with
  - a high viral load (>50 000 viral particles/ml);
  - a low CD4+T cell count (<200 cells/mm$^3$); and
  - symptoms of Aids.

However, there are cases where transmission occurs at low viral loads and high CD4+T cell counts – an indication that other risk factors are also involved. In breastfeeding especially, the relationship between viral load and transmission is not always clear. Generally speaking, however, if the mother has a low viral load during pregnancy, childbirth or breastfeeding (<1000 viral particles/ml), the chances of her transmitting the virus to her baby are also low. Antiretrovirals therefore play an extremely important role in decreasing the viral load in the mother's blood or breastmilk and keeping the baby safe.

See Prevention of MTCT on page 169.

### 3.3.1 Pregnancy

Most mother-to-child HIV transmission happens close to delivery or during the actual birth process. However, transmission of HIV can also occur in utero, especially if the mother has a high viral load. High viral loads can result from additional infections, such as tuberculosis or hepatitis, which worsen the risk of the mother transmitting the virus to her baby. Consequently, to reduce the risk of mother-to-child transmission of HIV during pregnancy, and to enhance the health of the mother and her baby, make sure of the following:

- Prevent new HIV infections. New infections during pregnancy may increase the viral load, which will increase the risk of mother-to-child transmission.
- Prevent and treat STIs and genital infections because they may result in infections of the placenta.
- Initiate lifelong ART with appropriate counselling immediately, regardless of the mother's CD4+T cell count or gestational age. (This option is known as option B+.)
- Provide iron, folate and calcium supplementation.
- Encourage frequent follow-up visits to the clinic so that the mother's health can be monitored regularly.
- Perform foetal monitoring with non-invasive procedures.
- Screen for tuberculosis (TB) and offer TB preventive therapy if the mother tests negative for TB. (Women who test positive for tuberculosis should receive a full regime of anti-TB medication.)
- Offer co-trimoxazole prophylaxis when needed (HIV/TB co-infection or WHO stage 2, 3 or 4) to provide protection against *Pneumocystis jirovecii* pneumonia (PCP), **toxoplasmosis**, malaria and many other bacterial infections. (Co-trimoxazole is an antibiotic.)
- CD4+T cell count should be monitored.

**Note**

Treatment with acyclovir for genital infection caused by the herpes virus has the potential for reducing MTCT of HIV (Coovadia, 2010).

- Offer counselling on safer sex practices, family planning, postnatal contraception and partner testing.
- Provide guidance on safe infant feeding practices.

## Enrichment: Re-infection with HIV should be avoided

HIV-infected individuals often think that they no longer have to protect themselves against infection by HIV. It is, however, very important for HIV-infected people to protect themselves against re-infection with HIV, even if they are receiving antiretroviral therapy. This is because, for example, if a person is infected by a new strain of the virus, the antiretroviral medication might not be effective against this new strain and the viral load in the blood will increase. HIV-infected pregnant women should always use condoms to prevent re-infection and to protect their babies from HIV.

### 3.3.2 Labour and delivery

The risk of MTCT during labour and vaginal delivery is high because the birth process involves direct contact with the mother's blood and mucus in the birth canal. Vaginal delivery also increases the newborn's ingestion of infected maternal blood, plasma and other secretions.

Mother-to-child transmission during labour can be reduced in the following ways (National Department of Health, 2015):

- HIV-positive women who started antiretroviral therapy during the pregnancy should continue to receive the medications throughout labour and delivery.
- Unbooked women in labour or newly diagnosed women in labour should be counselled and provided with antiretroviral drugs to prevent MTCT, and initiated on lifelong ART before being discharged.
- Avoid prolonged rupture of the membranes.
- Avoid **episiotomy** (cutting the vulva to avoid lacerations of the perineum during labour) unless it is absolutely necessary.
- Minimise trauma to the baby by avoiding procedures such as invasive monitoring procedures, **amniocentesis**, assisted instrument delivery and vacuum extraction.
- Avoid invasive suctioning of the neonate's nose and airway which may cause trauma to mucous membranes. Wipe away secretions from the baby's face.
- Perform an elective Caesarean section if possible and feasible. Elective Caesarean section decreases perinatal transmission of HIV by 80% (Coovadia, 2010). Elective Caesarean sections are, however, not recommended as a routine measure in resource-constrained settings, because they are costly and impractical in these settings and pose the risk of postoperative complications such as sepsis. The National Department of Health (2015) recommends in their Consolidated Guidelines that Caesarean sections should only be done for obstetric indications and not to reduce MTCT.
- It is recommended that all HIV-infected women who undergo Caesarean sections should receive prophylactic antibiotics.
- HIV-positive women not on ART must receive antiretroviral drugs before a Caesarean section.
- Initiate **HIV-exposed** newborn infants on ARV prophylaxis immediately after birth or very soon after.

**Glossary**

**HIV-exposed** This refers to a person who was exposed to HIV (e.g. a baby born to an HIV-infected mother), but it is not certain if they are HIV-infected themselves. A test has to be done to determine an HIV-exposed person's HIV status (positive or negative).

## 3.3.3 Breastfeeding

There are HIV-infected cells in the breastmilk of HIV-infected mothers for the whole breastfeeding period. However, research evidence shows that the risk of postnatal transmission of HIV through breastfeeding can be significantly reduced by antiretroviral drugs to either the HIV-infected mother or the HIV-exposed infant. Breastfeeding and ART intervention combined has the potential to improve significantly infants' likelihood of surviving and remaining free from HIV infection.

As discussed in the section on pregnancy, lifelong ART should be immediately initiated for all HIV-infected women who are pregnant or breastfeeding, or within one-year post-partum, whatever their CD4+T cell count. In addition, HIV-exposed infants should be started on ART prophylaxis immediately or very soon after birth, and should be continued for six weeks (or 12 weeks under certain circumstances).

There are many factors in breastfeeding that may contribute to the baby's risk of infection, such as duration of breastfeeding, pattern of breastfeeding, health of the mother's breasts and the baby's mouth, and the mother's sexual behaviour during the breastfeeding period.

### 3.3.3.1 Duration of breastfeeding

Some 80% to 90% of women in rural and remote areas in Africa breastfeed their babies for as long as two years. Some African studies have shown that breastfeeding increases the risk of HIV infection by 15% to 45%, depending on the duration of breastfeeding, especially for women who are not on ART. It has now been established that the optimum period to exclusively breastfeed a baby (HIV-infected and HIV-uninfected babies) is six months.

How did researchers decide on six months? Studies from sub-Saharan Africa show that the estimated rate of HIV transmission over 24 months of breastfeeding is about 16%, while it is about 15% after 18 months, 9% at 12 months, 5% at six months and 3% at two months (Coovadia, 2010: 204). Although these studies show a constant risk throughout breastfeeding, the optimum time with the most benefits for the baby is six months. If an HIV-infected mother is on ART, it is recommended that she exclusively breastfeeds her baby for the first six months of life, introducing appropriate complementary foods thereafter but continues breastfeeding until the baby is 12 months old (WHO, 2016). Breastfeeding should then only stop when the baby is on a safe and nutritious diet. If the mother decides to stop breastfeeding her baby, it should be stopped gradually over the period of one month.

When ARV drugs are not (immediately) available for an HIV-infected mother, the WHO (2016: 6) recommends that breastfeeding may still provide infants a greater chance of HIV-free survival. ARVs should then be introduced to the mother as soon as possible. Mothers who are HIV uninfected (or whose HIV status is unknown) should be advised to exclusively breastfeed their babies for six months and then to introduce complementary foods while continuing breastfeeding for 24 months or beyond (WHO, 2016: 7).

**What is exclusive breastfeeding?**

Exclusive breastfeeding is a feeding practice in which the infant receives only breastmilk and absolutely no other liquids or solids, including water. The baby may however receive syrups or drops that contain vitamins, mineral supplements, rehydration fluids or medicines that are medically necessary for its health. The same principles apply for babies who receive expressed breastmilk. Complementary foods and fluids should only be introduced after six months.

### 3.3.3.2 Pattern of breastfeeding

The pattern of breastfeeding (exclusive versus mixed feeding) may also influence MTCT. As noted, it has been established that exclusive breastfeeding for six months is the optimal feeding type for all babies, irrespective of their HIV status (Coovadia, 2010). The WHO recommends exclusive breastfeeding for all babies born in constrained settings in developing countries because the advantages of breastfeeding far outweigh those of commercial infant formula milk or replacement feeding. The number of babies who die from **gastroenteritis**, malnutrition and respiratory infections in Africa is so high that the benefits they get from breastmilk are much higher than the risk of getting infected with HIV, if they are exclusively breastfed for six months only.

All HIV-infected mothers should receive counselling, and they should be informed about the risks and benefits of various infant-feeding options in an unambiguous and unbiased way. The risks of not breastfeeding in their circumstances should be discussed and they should be guided in selecting the option that is most suitable for their situations. The benefits of ARVs (with full adherence) to protect the mother and her baby should be explained to the mother.

#### Conditions for safe replacement (formula) feeding

When HIV-infected mothers decide to stop breastfeeding, infants should be provided with safe and adequate replacement feed that enable their normal growth and development. Alternatives to breastfeeding for babies younger than six months include commercial infant formula milk or expressed, heat-treated breastmilk as an **interim** feeding strategy. Home-modified animal milk is not recommended as a replacement food for babies in the first six months of their lives. Children over six months of age can be given commercial infant formula milk or animal milk, which should be boiled for infants younger than 12 months of age (WHO, 2016: 8). (Some sources recommend animal milk only for babies older than a year. Local recommendations should be followed.) If a mother decides to use replacement feeding, this should be done exclusively and all breastfeeding should be avoided.

Healthcare workers should evaluate the feasibility of replacement feeding (commercial infant formula milk) by assessing (with the mother or caregiver and the family) if replacement feeding is acceptable, feasible, affordable, sustainable and safe for her and her infant (previously called the AFASS criteria).

HIV-infected mothers should only give commercial infant formula milk as a replacement feed to their babies when they can meet the following conditions:

- Safe water and sanitation are assured at the household level and in the community.
- The mother or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant.
- The mother or caregiver can prepare the formula feed cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition.
- The mother or the caregiver can, in the first six months, exclusively give infant formula milk.
- The family is supportive of the practice of giving the baby formula milk.
- The mother or caregiver can access health care that offers comprehensive child health services.

**Glossary**

**Interim** A temporary time period between two events.

**Why are mixed feeds bad for the baby?**

It is hypothesised that babies who are mixed-fed are more vulnerable to HIV and other childhood infections. The reason for this is that any liquids other than breastmilk or any solid foods may disturb the lining of the gastrointestinal tract (or gut) of the baby, which facilitates the entry of HIV (or other pathogens) into the baby's system.

### Frequently Asked Questions

**What is the difference between replacement and complementary feeding?**

**Replacement feeding** is feeding a baby who is not receiving any breastmilk with a diet that provides all the nutrients children need until they can be fully fed on family foods. During the first six months, breastmilk can be replaced with a suitable breastmilk substitute, like commercial infant formula milk. Babies older than six months should receive a breastmilk substitute plus complementary foods.

**Complementary feeding** is providing a baby older than six months with nutritious and adequate foods to supplement their milk (either breastmilk or commercial infant formula milk). They usually eat appropriately prepared family foods given three to five times per day (WHO, 2016: vii).

## Heat-treated, expressed breastmilk

HIV-infected mothers may consider expressing and heat-treating breastmilk as an interim feeding strategy. According to the World Health Organization (WHO, 2016: 9) mothers may consider this feeding option under the following circumstances:

- in special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; or
- when the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as **mastitis**; or
- to assist mothers to stop breastfeeding; or
- if antiretroviral drugs are temporarily not available.

Pasteurisation usually occurs at temperatures of 62 °C for 30 minutes, up to 72 °C for 15 seconds. To pasteurise the milk in hospitals, it should be heated to 62.5 °C for 30 minutes. This temperature is sufficient to inactivate HIV because its protein structure will be broken down at this temperature. At home, expressed milk can be heated and then cooled immediately by putting it in a refrigerator or standing the container in cold water. Heat-treated breastmilk should be put in a sterilised or very clean container and kept in a refrigerator or in a cool place before and after heat treatment to minimise contamination.

One of the first methods used to heat-treat expressed breastmilk was developed by researchers at the Kalafong Hospital in South Africa (Gray et al., 2007). They proposed the following method:

- The mother boils 500 ml of water in an aluminium pot.
- After the water has reached boiling point, she takes the pot off the stove and places a glass container (for example a clean peanut butter jar) containing her expressed milk into the pot.
- As soon as the glass container is placed into the water, the temperature of the water begins to cool down while the temperature of the milk begins to rise to about 60 °C – the ideal temperature for pasteurisation.

The preferred method to heat-treat expressed breastmilk is flash-heating. The procedure is as follows:

- Put expressed milk (between 50 ml and 150 ml) in a clean, heat-resistant glass (not plastic) jar.

- Place the jar of milk in a small pan or pot with water in it. The water should be about two fingers above the level of the milk to make sure that all the milk will be heated well.
- Heat the water on a very hot fire or stove until it reaches boiling point (the water will form large bubbles).
- Remove the jar of milk from the boiling water immediately.
- Place the jar of milk in a container of cool water, or let the jar cool down on its own until it reaches room temperature.
- Cover the jar with a lid or clean cloth to protect it from contamination.
- Use the milk to feed the baby within six hours.

**Note**

Never let the water boil for too long, but take it from the stove as soon as bubbles appear. If left boiling for too long, it will damage some of the nutrients in the milk.

### Health of mother and baby

Factors that may also affect mother-to-child transmission during breastfeeding are breast diseases such as mastitis and cracked nipples in the mother, and diseases such as **thrush** and gastroenteritis in the infant. These conditions should be prevented or treated immediately. Vitamin A or multivitamin supplements may improve the general health of the baby, but there is no evidence that they reduce MTCT of HIV.

### 3.3.3.4 Sexual behaviour and birth control

Condoms are the best choice for contraception because they also prevent HIV transmission during sexual intercourse. Women who use other contraceptives (such as the pill) should be informed that these contraceptives do not prevent HIV infection and that they may infect their sexual partners (or get re-infected) if they do not use condoms as well.

Intrauterine contraceptive devices (IUCDs) are not recommended for HIV-infected women because they sometimes cause pelvic inflammation. The string of the **IUCD** may also cause minor abrasions to the partner's penis, which can increase the risk of HIV transmission to the partner. IUCDs may also increase menstrual blood flow and thus the chance of HIV transmission. Women on ARVs can use non-hormonal IUCDs (e.g. the 'coil') if they are well tolerated.

HIV-infected mothers who breastfeed should be encouraged to use condoms to prevent re-infection with new strains of the virus, and to prevent an increase in their viral loads.

**ARVs and birth control**

The only type of birth control allowed for women on ARVs is injectable progesterone (Depo Provera®). All other types of hormonal contraceptives (implants as well as oral) are affected by antiretroviral medication.

**Glossary**

**IUCD** An IUCD or intrauterine contraceptive device is a small, long-acting, contraceptive device that is inserted into the uterus.

## 3.4 Myths about the transmission of HIV

More than 30 years of practical experience with and research into the HIV epidemic have shown that HIV is NOT transmitted through the following:

- Airborne routes such as coughing and sneezing. However, in the case of TB a mask should be worn when the sputum contains blood.
- Casual skin contact such as handshaking, hugging and touching. The virus cannot penetrate normal intact skin and does not readily enter through a healthy mouth or eye.
- Sharing food, water, plates, cups, spoons, toilet seats, showers or baths with an HIV-infected individual. HIV is not stable and does not survive for long periods outside the human body.
- Sharing clothing, towels and bed linen with an infected individual, provided that the linen is not soiled with blood.

See the Enrichment box 'Mosquitoes and Aids' below and on the next page.

- Public swimming pools. Chlorine destroys and water dilutes the virus.
- Pets or insects such as mosquitoes, bedbugs and moths.
- Playing team sports, provided that there is no contact with blood.
- Restaurants and cafeterias. Exposure to heat, air and gastric juices destroys HIV.
- Sharing telephones, drinking fountains and public transport with HIV-infected people.
- Living with an HIV-infected person and sharing household equipment. Research shows that the people living with an HIV-infected person do not contract the disease if they take the necessary precautions, such as adhering to the rules of basic hygiene, not sharing razors and toothbrushes (a person may have bleeding gums), avoiding contact with body fluids and covering possible blood spills with a bleach solution.
- Social contact. Schoolchildren playing together and sharing school facilities, provided that practices such as the mingling of blood are avoided, cannot result in HIV transmission.
- Kissing. The virus occurs in very low concentrations in saliva and kissing appears to be safe. However, people should be warned to avoid French or deep kissing if there are sores or punctures in the oral cavity, for example in a person who has bleeding gums.
- Donating blood. Although HIV can be transmitted through blood transfusions or through receiving infected blood, there is no way that a person can become infected through the process of donating or giving blood – provided that the instruments used during the process are clean (e.g. sterile needles are used and destroyed after use).

**Glossary**

**Myth** A false idea that many people believe in.

There are some truly horrifying **myths** circulating in some communities about how to avoid HIV infection. These myths are extremely dangerous and should be counteracted by means of intensive public education. For example, some people mistakenly believe that they will not get Aids (or that Aids can actually be cured) if they have sex with virgins, or with girls younger than 12 years of age, or with very young boys. Beliefs such as these can cause criminal behaviour and result in the further spread of HIV infection.

See the Enrichment box, 'Virgin cleansing and history' on page 69.

It is unnecessarily stressful to live with countless unfounded fears about Aids. We must remember that the virus is transmitted ONLY when body fluids are exchanged in sexual intercourse, when a person is exposed to contact with HIV-contaminated blood, and from a pregnant or breastfeeding HIV-infected mother to her child, especially when the HIV-infected person is not on ART.

## Enrichment: Mosquitoes and Aids

The question: 'Why can mosquitoes not transmit HIV?' can be answered at various levels of complexity. The most straightforward answer is epidemiological (to do with the science of the transmission of disease). There is absolutely no epidemiological evidence that mosquitoes (or any other biting insects) play any role in HIV transmission (Schoub, 1999: 122). It has been found that children who are sexually inactive and who live in mosquito-infested areas are NOT infected with HIV, even though they may regularly be infected by mosquito-borne diseases such as malaria and yellow fever. There is therefore no evidence that mosquitoes can also transmit HIV.

Why can mosquitoes transmit other diseases such as malaria and yellow fever, and not HIV? This question can best be answered by comparing mosquito-borne diseases with HIV. Arboviruses (e.g. yellow fever and dengue) and the malaria parasite can be transmitted by mosquitoes because they are adapted to multiply in the body of the mosquito before the mosquito infects a human. However, HIV cannot even survive the hostile environment of the mosquito's stomach, let alone multiply there. It is also important to emphasise that, during feeding, mosquitoes do not inject blood into their victim but only their saliva (which is an anti-clogging agent).

But is it not possible for the HIV-infected blood to be mechanically transmitted by the proboscis (the needle-like feeding instrument) of mosquitoes? The following facts show that this way of transmitting HIV is highly unlikely (if not impossible). The proboscis of a mosquito is many times smaller than the needle of a syringe. Even in the case of much larger needles the rate of transmission of HIV through needlestick injuries is extremely low (0.3%). Less blood can stick to the much smaller proboscis of the mosquito, making the chance of transmitting HIV even lower. A virus would need to be far more infectious than HIV before it could be transmitted by such a small quantity of blood. The feeding behaviour of mosquitoes also makes it unlikely for HIV to be mechanically transmitted. Female mosquitoes usually take their blood meal from one person only. After drinking their fill, they sit for more than an hour, usually on a vertical surface like a wall, to get rid of all the excess fluids from the ingested blood, retaining only the high concentration of blood proteins which they need for the development of their eggs. After that they fly away, and it may be many days before they need another blood meal (Spielman & D'Antonio, 2002).

In conclusion, there is absolutely no scientific evidence that mosquitoes can transmit HIV. The fact that other diseases may be transmitted by mosquitoes is not evidence that they can also transmit HIV. Or to sum it up: Mosquitoes are not flying needles.

## Enrichment: Virgin cleansing and history

Virgin cleansing was once believed to be a way to cure venereal disease in Europe. English men in the 1800s believed that intercourse with a child virgin would cure syphilis. In the 1820s in Liverpool people pretending to be medical doctors kept special brothels to provide this 'cure'. The girls used were often mentally impaired. A court case was reported in 1884 about a man with 'bad syphilis ulcers' who had raped a 14-year-old girl. His defence was that he had not intended to harm her, but only to cure himself. Similar types of stories have made the newspapers in some African countries, including South Africa, in recent years.

## Activity

Organise a discussion group at work or in your community.

- Talk about the psychological function of myths and urban legends. Focus on these questions:
  - Why do we share myths and urban legends with one another?
  - How do these myths and urban legends make us feel?

- Share a few generally believed myths or urban legends with each other. These myths may concern Aids or any other burning issue in your community.
- Discuss each myth or urban legend objectively and provide reasons why the myth is not true.
- Discuss the following question: 'Are myths harmful?'

## 3.5 Prevention of HIV

Although there are many HIV-prevention success stories throughout the world, we are not yet close to turning the tide of the Aids epidemic – especially in sub-Saharan Africa. HIV-prevention programmes are often not well planned, co-ordinated, delivered or evaluated. The focus of these programmes is often on singular outcomes (e.g. condom use) and on short-term change. We can no longer afford prevention programmes that do not form part of a bigger national or global plan with an emphasis on a long-term solution. The time is ripe to combine all our prevention efforts into one approach to address all the aspects of the epidemic.

Figure 3.1 below illustrates the principle of combination HIV prevention, where the focus is on combining various interventions to prevent HIV infection. These interventions to prevent HIV infection can broadly be classified into three main categories:

- behavioural interventions;
- biomedical interventions; and
- structural interventions.

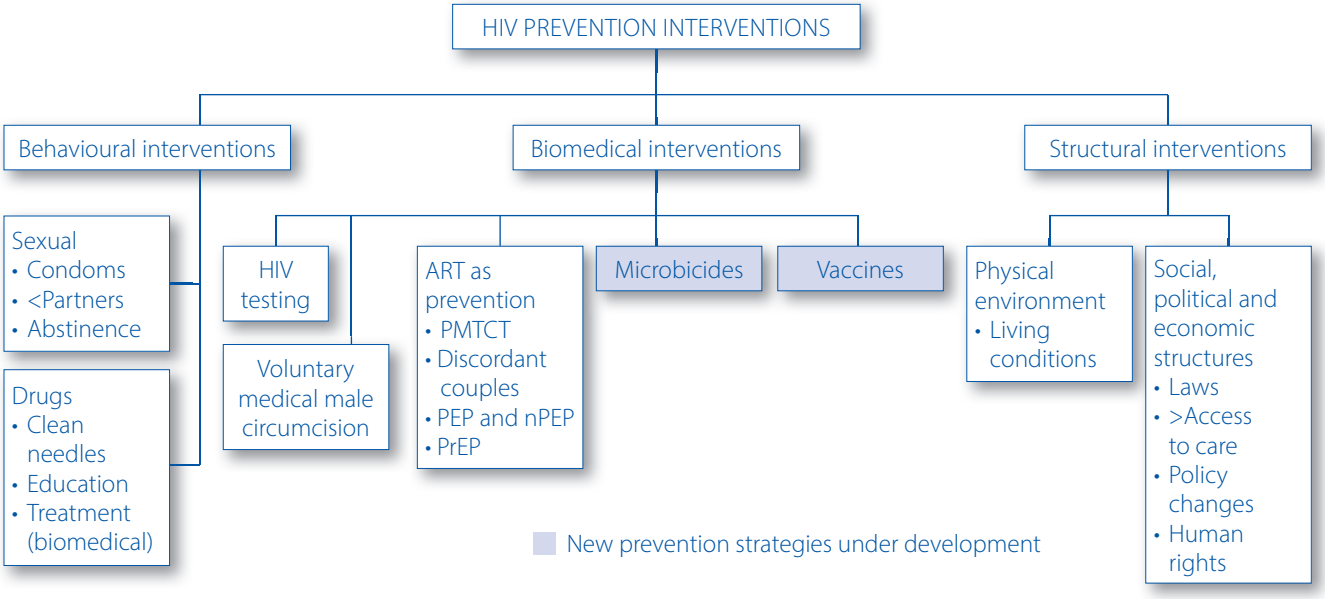



**Figure 3.1** Combination HIV-prevention interventions

Behavioural interventions usually include our efforts to change people's behaviour to make sex or drug-taking behaviour safer. Biomedical interventions involve the development of biological or medical tools to prevent HIV infection. Structural

interventions focus on the social, political, economic and physical environment of individuals that may impact on their vulnerability to HIV infection. HIV testing, circumcision and antiretroviral treatment (all biomedical interventions) can only work in combination with behavioural and structural interventions. Antiretroviral treatment can, for example, only succeed with simultaneous behaviour interventions (e.g. adherence counselling) and structural interventions (e.g. government commitment to provide ART for free in a sustainable manner). We now discuss each of these interventions and methods to prevent HIV.

## 3.5.1 Behavioural intervention

Behavioural interventions to prevent HIV infection focus mainly on safer sexual practices and harm reduction in injecting drug use. The prevention of HIV infection resulting from sexual transmission is based on the following strategies:

- total abstinence from sex;
- postponing or delaying first sexual intercourse;
- reducing the number of sexual partners;
- faithfulness to one partner; and
- correct and consistent use of condoms in relationships where partners are not mutually faithful.

It should, however, be kept in mind that these choices are often not under a person's control. Many disempowered women and girls, for example, have no say at all in sexual relationships.

Behavioural interventions to prevent HIV infection in people who inject drugs are based on harm-reduction strategies, such as the following:

- needle-exchange programmes;
- wider availability of clean needles;
- education of people using drugs on the prevention of HIV infection (e.g. how to clean equipment if sterile equipment is not available, safer sex practices, blood-borne diseases and other problems of needle use); and
- methadone treatment (which is a biomedical intervention).

The prevention of sexual transmission of HIV and harm reduction in people who inject drugs is discussed in more detail in Chapter 9

## 3.5.2 Biomedical intervention

Biomedical interventions play a huge role in the prevention of HIV infection. It is believed that our only hope of eradicating HIV in future relies on biomedical interventions, such as a successful vaccine. Four of the most effective biomedical interventions – male circumcision, microbicides, ARVs and vaccines – are discussed.

### 3.5.2.1 Male circumcision

Male circumcision is one of the oldest and most common surgical procedures worldwide. Male circumcision is shown on Egyptian wall paintings dated 2345 to 2182 BCE. Male circumcision is undertaken for mainly religious, ethnical, social and medical reasons. Male circumcision has also been practised for many thousands of years in many ethnic groups in sub-Saharan Africa. In the majority of cultures, circumcision is an integral part of a rite of passage to manhood.

Medical male circumcision (MMC) involves the full removal of the foreskin, fully exposing the head of the penis. Since the 1980s, over 30 observational studies

have suggested a protective effect of male circumcision on HIV acquisition in heterosexual men (Siegfried et al., 2009). Three large randomised controlled trials (with over 11 000 men) conducted in South Africa, Kenia and Uganda between 2002 and 2007, consistently demonstrated that medical male circumcision reduces the risk of heterosexually acquired HIV infection in men by about 60% (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007). Based on the results of these studies, male circumcision was adopted by global and national HIV policy-makers as an additional intervention for HIV prevention. Voluntary medical male circumcision (also known as VMMC) is now being implemented in 14 sub-Saharan African countries (Wamai et al., 2015). Mathematical modelling shows that widespread implementation of male circumcision may prevent millions of new HIV infections in sub-Saharan Africa.

Male circumcision is, however, not a magic cure, and it should never be seen as sufficient protection against HIV. It is important to emphasise that male circumcision reduces but does not eliminate the risk of HIV infection. Simulation models show that if newly circumcised men were to increase the number of sexual partners by an average of more than 25%, this would offset any beneficial effects of circumcision, even assuming a high efficacy of 60% (Gray et al., 2007).

Male circumcision should be used as part of a comprehensive HIV-prevention package that includes counselling on safer sex (e.g. the correct and consistent use of male and female condoms). It should also be used as an opportunity to educate young men about a range of sexual and reproductive health topics, such as hygiene, sexuality, gender relations and ways to further decrease the risk of HIV infection and transmission. There is no evidence that male circumcision has any direct impact on the risk of infection for women, on the risk among men who have sex with men or on the risk for heterosexual anal intercourse. This means that male circumcision only protects the male partner during vaginal intercourse.

As with any surgical procedure, there are risks involved in male circumcision, such as bleeding or infection. Inexperienced providers who undertake circumcision with inadequate instruments and poor after-care can cause serious complications. Proper education (including for traditional healers) and the supply of sterile equipment are important for the provision of safe male circumcisions. Those who have been circumcised must be counselled to abstain from sex and masturbation until the wound has completely healed, which takes a minimum of six weeks. A nurse or a doctor must confirm at the six-week follow up if the wound has healed sufficiently for the client to commence his sexual activities.

## Enrichment: Methods and devices used for VMMC (voluntary male medical circumcision)

Apart from surgical circumcision (requiring anaesthesia and trained doctors with surgical skills), non-surgical circumcision methods and devices for use on adolescents and adults in low resource countries are available. Examples of some of these methods and devices are the Forceps Guided Method, the Sleeve Resection Method, the Tara Klamp and the PrePex device. The PrePex device was approved by WHO in 2013. PrePex is an elastic ring device that requires no injected local anaesthetic and can be placed and removed by trained mid-level healthcare workers. It works by stopping the flow of blood to the foreskin due to

the compressive force of the elastic ring. The foreskin tissue will eventually die. The unwanted foreskin tissue is then safely removed after a week by a healthcare worker. PrePex male circumcision requires no needles, there is no loss of blood, discomfort is minimal, there is no bulging in clothing and the male is back to his daily routine immediately after the procedure (SAHIVSOC, 2014).

To learn more about the other methods and devices (and to see what they look like), download 'Male circumcision, HIV and Health: A guide' from the Aids Foundation at: http://www.aids.org.za/wp-content/uploads/2015/05/Male-Circumcision-HIV-Health.pdf

How does male circumcision decrease the chances of HIV and other reproductive tract infections? This can be explained in terms of several biological mechanisms. The area under the foreskin is a warm, moist environment that may enable some pathogens to persist and replicate, especially when penile hygiene is poor. The inner mucosal surface of the foreskin is also much thinner than the surface of the penile shaft or outer surface of the foreskin. This makes this thinner surface more susceptible to minor trauma and abrasions which facilitates the entry of pathogens. Tissue from the inner surface of the foreskin mucosa further contains cells with CD4 receptors (CD4+T cells, macrophages and Langerhans cells) which transfer the virus to the lymph nodes. Although these cells are also abundant on the glans penis and outer foreskin, those in the inner foreskin are much closer to the epithelial surface. The Langerhans cells are likely to be the first to be infected by HIV-1 (Patterson et al., 2002).

During intercourse, the cells in the inner foreskin and frenulum (attaching the foreskin to the glans) in an uncircumcised man are exposed directly to vaginal secretions. This superficial location of the cells (e.g. Langerhans cells) may thus increase risk of infection. In a circumcised man, the previously thin surface of, for example, the glans penis, is now covered with a thickly keratinised epithelium (thickened skin) which provides some protection from infection (Brinton et al., 1989).

Counsellors should be sensitive when they promote voluntary medical male circumcision (VMMC) and they should take cultural beliefs and practices into account. Stigma associated with circumcision status should be minimised and medical ethics and human rights principles should be adhered to. Informed consent, confidentiality and absence of coercion should be assured.

Male circumcision is very different from female genital mutilation (previously called female circumcision). Female genital mutilation has very adverse effects on the health, sexual pleasure and obstetric outcomes in women and has no medical benefits at all.

**Note**

In South Africa, the legal age of consent is 16 years for circumcision.

### 3.5.2.2 Microbicides

Many women are not able to insist that their partners use condoms because they fear that their partners will either reject them or react violently if they do so. Ideally, these women need a non-barrier method that they can apply and control without their partners' knowledge. A microbicide in the form of a vaginal cream, gel or foam might be the answer and may turn out to be a major factor in controlling the spread of HIV.

A microbicide could be produced in the form of a gel, cream, suppository, film or lubricant, or in the form of a sponge or vaginal ring that slowly releases the active

**What is a microbicide?**

A microbicide is a substance that kills microscopic organisms such as bacteria, viruses and parasites. Researchers are currently developing microbicides that can be inserted into the vagina (or into the rectum) with the aim of destroying infection-causing organisms, including HIV. In other words, microbicides could be used to prevent the sexual transmission of HIV and other STIs.

ingredient over time. As a female-controlled prevention method, microbicides would empower women to take control over their own sexual health. Women who cannot insist on condom use would now be able to protect themselves without the partner's knowledge.

Scientists are currently developing and testing many microbicides which they hope will prevent HIV and other STIs. Microbicides are being designed to work in one or more of the following ways (Abdool Karim & Baxter, 2010: 275):

- to support natural vaginal defences;
- to kill or immobilise surface pathogens by disrupting their membranes;
- to inhibit pathogen entry into mucosal cells by creating a barrier between the pathogen and the mucous membranes of the vagina;
- to prevent fusion between the membranes of the pathogen and mucosal cells; and
- to inhibit a virus from replicating once it has infected the cells than line the vaginal wall.

A successful microbicide will probably include a combination of the mechanisms mentioned above.

**Glossary**

**CAPRISA** Centre for the Aids Programme of Research in South Africa.

**Note**

Herpes simplex virus type 2 infection is the most common cause of genital ulcer disease.

Although microbicides research has suffered some setbacks in the past, a breakthrough has been made by the **CAPRISA** 004 tenofovir gel trial. The CAPRISA 004 trial used a microbicide gel containing the widely used antiretroviral drug **tenofovir** (**TDF**). The functioning of the tenofovir gel is to inhibit the virus from replicating once it has infected the cells that line the vaginal wall. The findings of the CAPRISA 004 trial indicated that the gel reduced HIV infection rates by between 6% and 39%. The gel was found to be safe and there was no evidence of tenofovir resistance or an increase in experiencing side effects. It was also found that tenofovir gel provides protection against HSV-2 (herpes simplex virus 2) infections in women (Abdool Karim et al., 2015).

The FACTS 001 study (done between 2011 and 2014), which was a much larger study than the CAPRISA 004 trial, showed disappointing results. This study found no difference in the HIV-infection rate in young women who received the tenofovir gel and the rate of infection in young women given a placebo gel (Rees et al., 2015). The authors conclude that 'this method of prevention is simply not suitable for young women' who find it difficult to adhere and use the gel every time they have sex. Another possible reason provided at the International Aids Conference in 2016, is that certain bacteria in the vagina may deactivate tenofovir.

The South African Medical Research Council (SAMRC) in partnership with international organisations developed the dapivirine vaginal ring that can be safely used by women to protect them from HIV infection. The ring slowly releases dapivirine (an antiretroviral drug) over time and it can provide protection for a month at a time. In 2016 two studies (ASPIRE and the Ring study) showed a significant modest reduction in HIV (from 27% to 31%) among women, and the ring was also deemed as safe and acceptable to women. The studies found that women over the age of 25 years were 61% less likely to acquire HIV compared to women of the same age using the placebo ring. No protection was observed among young women between 18 and 21 years – probably because they did not use the ring correctly (Ramjee, 2016).

Researchers doubt whether a microbicide will ever be able to provide 100% protection against HIV. Nonetheless, it is likely that condoms, when used

consistently and correctly, will provide better protection against HIV and other STIs than microbicides alone.

## Enrichment: Did you know the following about microbicides?

Did you know that…

- Antiretroviral-based microbicides (like the tenofovir gel microbicides or the dapivirine ring) aim to prevent HIV infection in the same way as PrEP (or pre-exposure prophylaxis).
- As an **ethical** obligation, all microbicide trials provide condoms and prevention counselling to all participants.
- Most volunteers must be HIV negative when they start participating in the trials. It is however also necessary to test the safety of the gel in women who are already infected.

**Glossary**

**Ethical** Related to what is good and right to do.

### 3.5.2.3 Antiretroviral treatment as prevention

The use of antiretroviral therapy to prevent HIV infection is referred to as 'Treatment as Prevention' or TasP. Treatment as prevention is based on the principle that antiretroviral therapy reduces HIV in the blood, semen, cervical fluids and rectal fluids to very low levels (also called 'undetectable' levels). Low levels of HIV reduce an HIV-infected individual's risk of transmitting the virus to a sex partner or to an infant during or after pregnancy. Treatment as prevention is currently used in the following instances:

- mother-to-child transmission;
- heterosexual discordant couples;
- post-exposure prophylaxis (PEP and nPEP); and
- pre-exposure prophylaxis.

## Enrichment: What is the difference between PEP and nPEP?

**PEP** or post-exposure prophylaxis is short-term antiretroviral treatment taken after exposure to HIV, for example in the occupational setting or after sexual assault.

**nPEP** is post-exposure prophylaxis for non-occupational exposure. Research on nPEP is currently underway among men who have sex with men (MSM) where the uninfected partner receives ARVs after sex with an HIV-infected partner.

#### Mother-to-child transmission

The use of antiretrovirals is a well-proven method to prevent HIV infection from a mother to her baby. Testing pregnant women and starting ART immediately on those who test HIV positive reduces mother-to-child transmission of HIV to about 98%.

#### Heterosexual discordant couples

The US National Institutes of Health (NIH) conducted a study in 2011 (the HPTN 052 study) where they immediately initiated ART in the infected partners

in heterosexual discordant couples. A discordant couple is a couple where one partner is HIV infected and the other is not. The results of the HPTN 052 study showed that treatment of the infected partner (regardless of CD4+T cell counts) led to 96% decrease in the risk of HIV transmission to the uninfected partner (Monater, 2011). In 2013, the WHO recommended treatment for all HIV-infected people living with uninfected partners.

### Post-exposure prophylaxis (PEP and nPEP)

Post-exposure prophylaxis (PEP) is short-term antiretroviral treatment taken after possible exposure to HIV. The use of post-exposure prophylaxis is well-known as treatment for healthcare workers who may have been exposed to HIV-infected body fluids in an occupational setting. PEP is also used to treat people who may have been exposed to HIV during a single event, for example rape, sexual assault, unprotected sex or sharing drug injecting equipment.

Research on post-exposure prophylaxis for non-occupational exposure (or nPEP) is currently underway among men who have sex with men. This involves ARV treatment for HIV-uninfected men after having sex with an infected partner. For nPEP to be successful, ARVs should be administered as soon as possible after sex. It is doubtful, however, that men will realise soon enough after exposure that they may be at risk of contracting HIV.

### Pre-exposure prophylaxis (PrEP)

Pre-exposure prophylaxis (or PrEP) is based on the principle of HIV-uninfected people taking ARVs before exposure to HIV to prevent infection. An example of PrEP in another (non-HIV) context is malaria tablets which are taken before exposure in an effort to prevent malaria. Truvada® is an example of an antiretroviral drug used as PrEP in the HIV context. Research shows a 44% to 73% reduction (depending on adherence levels) in the incidence of HIV infection among men who have sex with men (MSM) receiving a daily oral dose of Truvada®, combined with safer sex practices (Bekker & Rebe, 2013; Grant et al., 2010). Researchers believe that PrEP can reduce the risk of HIV transmission by up to 92% if it is taken correctly with high adherence levels. PrEP will probably benefit groups with high rates of infection, such as sex workers, people who inject drugs and MSM. Truvada® was approved in December 2015 for use in South Africa. In June 2016, the South African Department of Health started providing PrEP to sex workers in 10 sex worker programmes. Future plans are to provide PrEP intervention to all vulnerable young women.

## Enrichment: Treatment as Prevention

The reasoning behind Treatment as Prevention is based on the fact that a high viral load has a higher HIV transmission risk than a low viral load. If the HIV-infected person is treated with ARVs (regardless of CD4+T cell counts and viral loads), the viral load will be low, and the chances of transmitting the virus to an HIV-negative partner (or baby in the case of a pregnant woman) will thereby be reduced. Some researchers believe that if all HIV-infected people in a specific community receive ART, their collective viral loads will be low, which makes the chances of infecting

others in that same community much lower. New infections in that community will thus be reduced. Global treatment policy is currently to treat all HIV-infected persons, regardless of CD4+T cell count. For example, the Joint United Nations Programme on HIV/AIDS (UNAIDS) adopted the 90-90-90 global targets for antiretroviral therapy (ART) with the aim of testing 90% of all HIV-infected people, with 90% of those on ART, and 90% of those on ARVs achieving viral suppression. This approach is not without challenges. It is for example especially problematic to treat whole communities in resource-poor settings, and cost, sustainability, poor healthcare services, non-adherence to the medications and the development of resistance are only some examples of challenges facing such an approach.

### 3.5.2.4 HIV vaccines

It is widely accepted that our only hope for eradicating the HIV epidemic is an effective HIV vaccine. But how far are we in our search for an effective, preventative HIV vaccine? Before discussing this issue, we first need to know a bit more about vaccines in general.

A vaccine is a harmless substance that creates an immune response similar to that following an infection. It is used to build immunity or resistance to a later 'real' infection. We can say that a vaccine is a substance that 'teaches' the body to recognise and defend itself against future infections by bacteria and viruses that cause disease. The development of vaccines relies on the principle that the immune system is specifically activated by the protein components (or antigens) of an organism. The body does not have to be exposed to the dangers of the organism itself: the immune response (that is, the development of antibodies and/or killer T cells) can be activated by administering only the relevant proteins (antigens) of the organism. A successful vaccine will enable the body to stop or immobilise an invading organism (such as a virus). It is important to note that a vaccine is not a cure. It prevents infection or slows disease progression.

Vaccines have been around for thousands of years. One of the earliest examples of a vaccine comes from the Mano people of Liberia, who used to take fluid from smallpox sores and scratch it into the skin of an uninfected person using a thorn (Introducing HIV/Aids vaccines, 2002). The first modern vaccine was developed by Edward Jenner much later, in 1796, when he used matter from cowpox pustules to protect individuals from smallpox. (The word 'vaccine' is derived from the Latin word for 'cow'.) By the end of the nineteenth century, Louis Pasteur succeeded in producing vaccines for cholera, anthrax and rabies. Because of vaccines, diseases such as tetanus, polio, smallpox, diphtheria, pertussis (whooping cough), rubella (German measles) and mumps have decreased rapidly, and millions of lives are saved annually. Vaccines are also available for influenza, chickenpox, hepatitis A and B and tuberculosis. Some vaccines prevent cancer, for example immunising babies against hepatitis B prevents liver cancer, while the vaccine against the human papilloma virus (HPV) (a sexually transmitted virus) may protect against cervical and rectal cancer.

There are three basic strategies or designs for making vaccines (Kahn, 2005: 28):

- the use of live attenuated pathogens (the live pathogen is first weakened to reduce or eliminate its potential to cause disease);

- the use of killed whole organisms (which are then no longer able to multiply); and
- the use of purified proteins or polysaccharides. Genetic engineering has made it possible to make vaccines from just a small part of the pathogen (purified proteins). Making vaccines from just a part of the pathogen rather than the whole pathogen or a weakened form of pathogen eliminates the small but real risk that the vaccine could cause the very disease it should prevent. HIV vaccine research is based on this design.

Vaccines attempt to mimic the following two processes in which the immune system interacts with an infection:

- The humoral (or antibody) response is the response where the immune system (or the B lymphocytes) produces antibodies that recognise a specific pathogen in the blood and neutralise (or block) its activity before it can infect the body's cells.
- The cellular response is the response where **white blood cells** such as CD4+T cells and CD8+ (or killer T cells) are formed after the pathogen has infected some of the body's cells. The role of these white blood cells is to recognise and destroy infected cells so that the pathogen cannot multiply and spread to other cells (see Figure 2.4 in Chapter 2).

**Glossary**

**White blood cells** These are the fighter blood cells of the body. Whenever an organism invades, they rush to the scene and deal with it in a variety of ways. They either surround and eat it (see phagocytes) or they produce protective antibodies that will overpower the invading organism.

**Humoral immunity** Immunity involving the production of antibodies by the B lymphocytes.

The ultimate HIV vaccine will need to stimulate both a humoral and a cellular response. The **humoral immunity** needs to produce antibodies to prevent HIV from entering human cells. The **cellular immunity** needs to stimulate killer T cells to seek out, attack and destroy any human cells that have become infected with HIV. It is further important for a vaccine to prevent or eradicate the establishment of latent reservoirs that allow HIV to hide in resting memory CD4+T cells (Alchin, 2014; Siliciano, 2014). The ultimate vaccine will probably also stimulate a mucosal immune response of the mucous linings of the genital tract, anus and gut.

So far, vaccine development has been hampered by various challenges. These include the fact that scientists are not sure about what immune responses are needed and which components of the virus must be targeted to protect people against HIV infection. The high genetic diversity of the virus, its ability to hide (or cover) the places on its surface (epitopes) where antibodies could attach, and the flexibility of HIV which hinders antibody recognition, are all factors that make it difficult to develop a vaccine. Current vaccine research focuses on the development of vaccine candidates that elicit strong cellular immune responses (to stimulate cytotoxic or killer T cell responses) as well as humoral responses (stimulating the development of neutralising antibodies).

An easy way to remember these two processes of vaccine development is to distinguish between preventive and therapeutic vaccines. Preventive vaccines (based on the humoral responses and the development of antibodies) will hopefully protect uninfected people if they are exposed to HIV in the future. Therapeutic vaccines will be given to people who are already infected with HIV to help control their infection, or to slow down progression of the disease.

HIV vaccine research started in the 1980s. Although there have been small, ongoing victories since then, it is generally believed that we are still many years away from a vaccine for HIV. It is taking so long to develop a vaccine because, apart from the specific challenges posed by HIV, history has shown that vaccine

development in general takes many years to complete. For example, it took 47 years to develop the polio vaccine, 46 years to develop a vaccine for measles and 33 years to develop a vaccine for HPV (the human papilloma virus).

### 3.5.3 Structural intervention

Behavioural and biomedical interventions will not be successful if we do not also give attention to structural interventions. Structural interventions are necessary where social, political and economic structures (including the physical environment) make people vulnerable to HIV infection and restrict their access to prevention, treatment and care. Many sub-Saharan African countries still have laws that criminalise activities associated with HIV infection, such as laws against sex work, drug use and homosexuality. Safer sex or safer drug use practices and services are therefore often not available or accessible to people in these **marginalised groups**. Poverty, migration and poor living environments aggravate the problem further.

Stigma and **discrimination** make people more vulnerable to HIV and they impact negatively on all our prevention, treatment, care and support interventions. Women in Africa are often dying of Aids or are transmitting the virus to their babies because they were too ashamed or too afraid to go for HIV testing and to access antiretroviral therapy. In addition, even if they are on ARVs, they often do not adhere to their medications out of fear of discrimination. In one South African study, women who could not achieve optimum ARV adherence levels explained that they had to hide their ARVs from boyfriends, husbands, family members or friends; they feared violence or rejection; they could not ask for time off from work to go to clinics because their employers did not know that they were on ARVs; and they had nobody to support them (Van Dyk, 2010).

Structural interventions will have to address the reduction of stigma and discrimination as well as violations of human rights. Everything that we gain in terms of behavioural and biomedical interventions might be lost if stigma, discrimination and violation of human rights prevent those most in need of these interventions from accessing it.

**Note**

Stigma is not about information and training. It is about addressing people's deepest fears and concerns beyond rational arguments.

## 3.6 Conclusion

Aids is a very serious disease that has and can have devastating effects on individuals and communities alike. Fortunately, we now know exactly how the virus is spread and what we can do to prevent and manage HIV infection. However, prevention is a complex issue. Consequently, if we are to control the epidemic, far more than just condoms and antiretroviral therapy will be needed. Indeed, fundamental issues, such as poverty, social injustice, disempowerment of women, neglect of women's and children's rights, myths, negative attitudes and discrimination will all have to be tackled to stem the HIV and Aids tide. In this respect, we discuss symptoms and diseases associated with HIV in the next chapter.

## Test your understanding

1. Why is it relatively easy for HIV to gain entry through the linings of the genital and anal tracts?

2. Give reasons why the presence of STIs makes a person more vulnerable to HIV infection.
3. List the physiological and social reasons why women are more susceptible to HIV infection than men.
4. How safe is it to receive a blood transfusion in South Africa? Motivate your answer.
5. When does drug usage become a high-risk behaviour in terms of HIV infection?
6. What is the risk of HIV infection after accidental exposure to contaminated blood, and which factors increase the risk?
7. How can the chances of HIV transmission be reduced during breastfeeding?
8. Name and discuss the criteria for replacement feeding.
9. What is meant by the 'combination HIV prevention' approach? Draw a mind map to show all the HIV-prevention interventions in this approach.
10. What is a microbicide and what do we hope to achieve with an HIV microbicide?
11. What does the latest research on male circumcision reveal in terms of HIV prevention for men?
12. What is the function of a vaccine? (In other words, how does it work?)
13. Name and critically discuss the various ways ART can be used to prevent HIV infection (antiretroviral treatment as prevention).

## Reference list

Abdool Karim, S.S., Abdool Karim, Q., Kharsany, A.B., Baxter, C., Grobler, A.C., Werner, L., Kashuba, A., Mansoor, L.E., Samsunder, N., Mindel, A., & Gengiah, T.N. 2015. Tenofovir Gel for the Prevention of Herpes Simplex Virus Type 2 Infection. *The New England Journal of Medicine* 373(6): 530–539.

Abdool Karim, S.S. & Baxter, C. 2010. New prevention strategies under development and investigation. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/ AIDS in South Africa* (2nd edn.) (pp. 268–282.) Cape Town: Cambridge University Press.

Abdool Karim, Q. & Frohlich, J. 2000. Women try to protect themselves from HIV/AIDS in KwaZulu-Natal, South Africa. In M Turshen (Ed.). *Women's health in Africa*. Lawrenceville, NJ: Africa World Press.

Alchin, D.R. 2014. HIV vaccine development: an exploratory review of the trials and tribulations. *Immunologic Research* 60(1): 35–37.

Andersson, N., Foster, H., Mitchell, S., Scheepers, E. & Goldstein, S. 2007. Risk factors for domestic violence: national cross-sectional household surveys in eight southern African countries. *BMC Women's Health* 7(11): 1–13.

Auvert, B., Taljaard, D., Lagarde, E., Sobngwi-Tambekou, J., Sitta, R., & Puren, A. 2005. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. *PLoS Medicine* 2(11): 1549–1676.

Bailey, R.C., Moses, S., Parker, C.B., Agot, K., Maclean, I., Krieger, J.N., Williams, C.F., Campbell, R.T., & Ndinya-Achola, J.O. 2007. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* 369(9562): 643–656.

Bekker, L., & Rebe, K. 2013. Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection. *Southern African Journal of HIV Medicine* 13(2): 40–55.

Brinton, L.A., Reeves, W.C., Brenes, M.M., Herrero, R., Gaitán, E., Tenorio, F., et al. 1998. The male factor in the etiology of cervical cancer among sexually monogamous women. *International Journal of Cancer* 1989;44:199-203.

Centres for Disease Control. 2013. Infection control. Retrieved on 17/9/2015 from: http://www.cdc.gov/oralhealth/infectioncontrol/faq/bloodborne_exposures.htm

Coovadia, H. 2010. Mother-to-child transmission (MTCT) of HIV-1. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 201–215). Cape Town: Cambridge University Press.

De Coninck, Z., Feyissa, I.A., Ekström, A.M., & Marrone, G. 2014. Improved HIV Awareness and Perceived Empowerment to Negotiate Safe Sex among Married Women in Ethiopia between 2005 and 2011. *PLoS ONE* 9(12): e115453. doi:10.1371/journal.pone.0115453

Grant, R.M., Lama, J.R., Anderson, P.L., et al. 2010. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine* 363: 2587–2599.

Gray, G.E., McIntyre, J.A., Jivkov, B. & Violari A. 2001. Preventing mother-to-child transmission of HIV-1 in South Africa. Recommendations for best practice. *Southern African Journal of HIV Medicine* 4: 15-26.

Gray, R.H., Kigozi, G., Serwadda, D., Makumbi, F., Watya, S., Nalugoda, F., Kiwanuka, N., Moulton, L.H., Chaudhary, M.A., Chen, M.Z., Sewankambo, N.K., Wabwire-Mangen, F., Bacon, M.C., Williams, C.F., Opendi, P., Reynolds, S.J., Laeyendecker, O., Quinn, T.C., & Wawer, M.J. 2007. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* 369(9562): 657–666.

Heyns, A., & Swanevelder, J.P. 2010. Safe blood supplies. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/ AIDS in South Africa* (2nd edn.) (pp. 226–239). Cape Town: Cambridge University Press.

Introducing HIV/AIDS vaccines. 2002. Brochure developed by the South African HIV Vaccine Action Campaign (SA HIVAC). Cape Town: SA HIVAC.

Kahn, P. (Ed.). 2005. *AIDS vaccine handbook: global perspectives* (2nd edn.) New York: AIDS Vaccine Advocacy Coalition (AVAC).

Leggett, T. 2010. Intravenous drug use in South Africa. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/ AIDS in South Africa* (2nd edn.) (pp. 240–249). Cape Town: Cambridge University Press.

Minister Aaron Motsoaledi: Health Department Budget Vote 2017/17. (2016). Retrieved on 26/5/2016 from: http://www.gov.za/speeches/debate-health-budget-vote-national-assembly-10-may-2016-dr-aaron-motsoaledi-minister-health%20

Monater, J. S.G. 2011. Treatment as prevention – a double hat-trick. *Lancet* 378: 208–209.

Morris, L. & Cilliers, T. 2010. Viral structure, replication, tropism, pathogenesis and natural history. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 87–96). Cape Town: Cambridge.

National Department of Health, South Africa. 2015. *National Consolidated Guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults*. Pretoria: Department of Health, South Africa.

Parry, C., Petersen, P., Dewing, S., Carney, T., Needle, R., Kroeger, K., & Treger, L. May. 2008. Rapid assessment of drug-related HIV risk among men who have sex with men in three South African cities. *Drug and Alcohol Dependence* 95(1-2): 45–53.

Patterson, B.K. et al. 2002. Susceptibility to human immunodeficiency virus-1 infection of human foreskin and cervical tissue grown in explants culture. *American Journal of Pathology* 161(3): 867–873.

Ramjee, G. (2016). Pioneering HIV prevention research. *Mail & Guardian*, February 26 to March 3: 25.

Rees, H., Delany-Moretlwe, S.A., Lombard, C., Baron, D., Panchia, R., Myer, L., Schwartz, J.L., Doncel, G.F., & Gray, G. 2015. *FACTS 001 Phase III Trial of Pericoital Tenofovir 1% Gel for HIV Prevention in Women.* 2015 Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, Washington, USA, Abstract number: 26LB.

SAHIVSOC. 2014. Male Medical Circumcision in South Africa. Retrieved on 10/11/2016 from: http://sahivsoc2014.co.za/wp-content/uploads/2014/10/Fri_Dino_Rech%20Medical%20Male%20Circumcision.pdf

Schoub, B.D. 1999. *AIDS and HIV in perspective. A guide to understanding the virus and its consequences* (2nd edn.). Cambridge: Cambridge University Press.

Shisana, O., Rehle, T., Simbayi, L.C., Zuma, K., Jooste, S., Zungu, N., Labadarios, D., Onoya, D. et al. 2014. *South African National HIV Prevalence, Incidence and Behaviour Survey*, 2012. Cape Town: HSRC Press.

Siegfried, N., Muller, M., Deeks, J.J. & Volmink, J. 2009. Male circumcision for prevention of heterosexual acquisition of HIV in men (Review). *The Cochrane Library* 2: 1–39.

Siliciano, R.F. 2014. Targeting reservoirs to clear and cure. Nature Medicine 20(5): 480–481.

Skafte, I., & Silberschmidt, M. 2014. Female gratification, sexual power and safer sex: female sexuality as an empowering resource among women in Rwanda. *Culture, Health & Sexuality* 16(1): 1–13 http://dx.doi.org/10.1080/13691058.2013.815368

South African National Blood Services (SANBS). 2014. SANBS Annual Report. Retrieved on: 16/09/2015 from http://www.sanbs.org.za/PDFDocuments/SANBS_AnnualReport_2014_ONLINE-VERSION.pdf

Spielman, A. & D'Antonio, M. 2002. *Mosquito.* London: Faber and Faber.

United Nations Programme on HIV/AIDS (UNAIDS). 2011. *UNAIDS terminology guidelines*. Geneva.

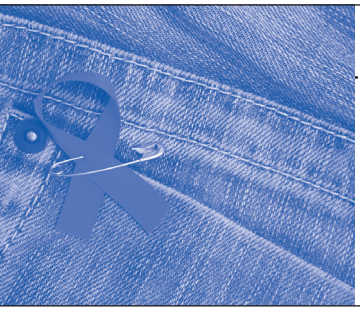
Van Dyk, A.C. 2010. Treatment adherence following national antiretroviral rollout in South Africa. *African Journal of AIDS Research* 9(3), 235–247.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (pp. 8–9). Cape Town: Nasionale Boekhandel Bpk.

Wamai, R.G., Morris, B.J., Bailey, R.C., Klausner, J.D., & Boedicker, M.N. 2015. Male circumcision for protection against HIV infection in subSaharan Africa: the evidence in favour justifies the implementation now in progress. *Global Public Health* 10(56): 639–666.

World Health Organization (WHO). 2015. *Blood safety and availability*. Retrieved on: 16/09/2015 from http://www.who.int/mediacentre/factsheets/fs279/en/

World Health Organization (WHO). 2016. *Guideline updates on HIV and infant feeding: The duration of breastfeeding and support from health services to improve feeding practices among mothers living with HIV.* Geneva: WHO.



# Chapter 4

# HIV-associated symptoms and diseases

Alta van Dyk

### Signs that Raka is nearby

*... and he barely noticed*
*how the terror-struck beasts were milling,*
*gathering in herds,*
*the tiny ones down at his feet*
*with fearful eyes tumbling in haste*
*through the tough, high grass, their pointed*
*black noses*
*all wrinkled with fear in the flight*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- explain the relationship between the CD4+T cell count, the viral load and the stages of infection;
- describe the different stages of HIV infection and the course of the disease;
- recognise the major symptoms and opportunistic infections associated with HIV infection in adults and children;
- describe and understand the link between HIV and TB;
- describe and understand the link between HIV and STIs;
- compile a checklist describing the symptoms and management of TB for an HIV clinic;
- recognise the main symptoms of STIs; and
- discuss the various ways to prevent STIs.

## Chapter outline

  - Chemoprophylaxis
  - Immunisation
- Tuberculosis
- Sexually transmitted infections

As a result of the unique way that HIV attacks and disarms the immune system, all the body's defence mechanisms are neutralised when a person becomes infected with HIV. When this happens, the body can no longer protect itself against other infections and diseases. As a result, all kinds of bacteria, fungi, protozoa and viruses can invade the body because they encounter no resistance. Some kinds of cancer also use this opportunity to take root and spread in the HIV-infected body that is now defenceless. In other words, we can say that HIV opens the body's protective gates (its immune system) and lets in all kinds of infections and diseases.

The health of an HIV-infected individual therefore depends on the condition of his or her immune system at any particular given time. As we noted in Chapter 2, HIV attacks and kills mainly the CD4+T cells. Therefore, if we measure the actual number of CD4+T cells, we have a very accurate indicator of the current status of the HIV-infected person's immune system. This count, called the CD4+T cell count, is also the best predictor of how easily opportunistic infections will be able to take root in an HIV-infected person. However, **CD4+T cell count tests** are not always available in resource-poor countries. Consequently, in 2007 the World Health Organization (WHO) developed (and is continuously revising) clinical staging and immunological classification guidelines of HIV to help healthcare practitioners in the clinical management of HIV, especially in areas that have limited laboratory capacity.

**Glossary**

**CD4+T cell count test** The laboratory test most commonly used to estimate the level of immune deficiency in HIV-infected individuals by 'counting' the CD4+T cells.

## 4.1 CD4+T cell count, viral load and stages of HIV infection

There is a particular relationship between a person's viral load and their CD4+T cell count. Viral load and CD4+T cells have an inverse 'seesaw' relationship. This means that a higher viral load is reciprocated by a lower CD4+T cell count, because the virus destroys the CD4+T cells. Conversely, a lower viral load is reciprocated by a higher CD4+T cell count, because if there are fewer viruses in the blood, the immune system gets a chance to build up CD4+T cells again. (See Figure 4.1 on page 85.) Consequently, taken together, the person's viral load and CD4+T cell count can predict the pace of their journey towards the final stage of Aids.

We will look at the WHO clinical staging in greater detail later on in this chapter.

**Glossary**

**Disease progression** The extent to which an HIV-infected person gets sick with opportunistic infections and diseases.

The viral load a person has, combined with the CD4+T cell count in their blood, determines their **disease progression**. As noted above, if a person has a high viral load and a low CD4+T cell count, it makes it easier for a wide range of infections to attack their body. Similarly, the development of full-blown Aids (when the person has advanced or severe symptoms), ultimately resulting in death, happens much more quickly with a high viral load than a low one. Conversely, someone infected with HIV, but who has a low viral load and a high CD4+T cell count, is able to stay healthy for many years, because their immune system is strong enough to fight off infections. Antiretroviral therapy is the best way to assist the immune system to fight HIV, to boost CD4+T cell production and to prolong life.

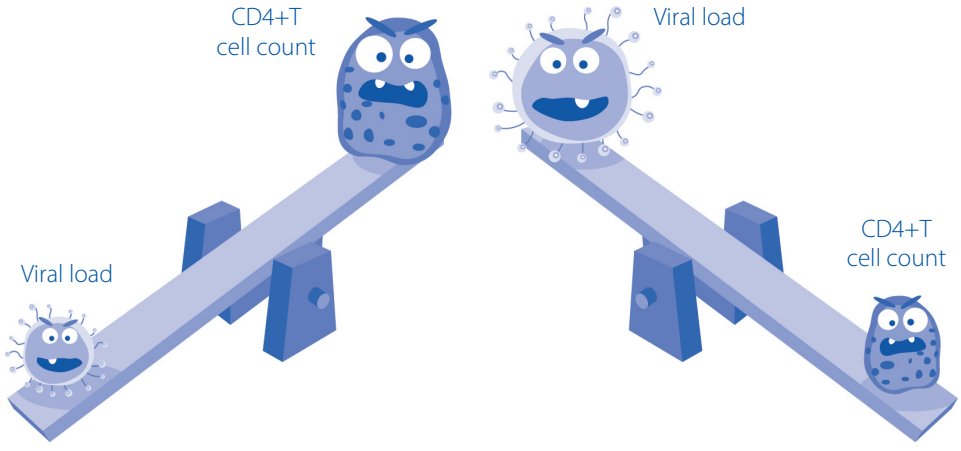



**Figure 4.1** The seesaw relationship between viral load and the CD4+T cell count

Figure 4.2 shows the relationship between a person's CD4+T cell count, their viral load and the stages of HIV infection during the course of an *untreated* HIV infection. Note that the relationship between the CD4+T cells, the viral load and stages of infection is not as definite and absolute as illustrated; they can vary from time to time. For example, the CD4+T cell count can decrease and the viral load increase in response to infections (such as flu), acute illness or recent vaccinations.

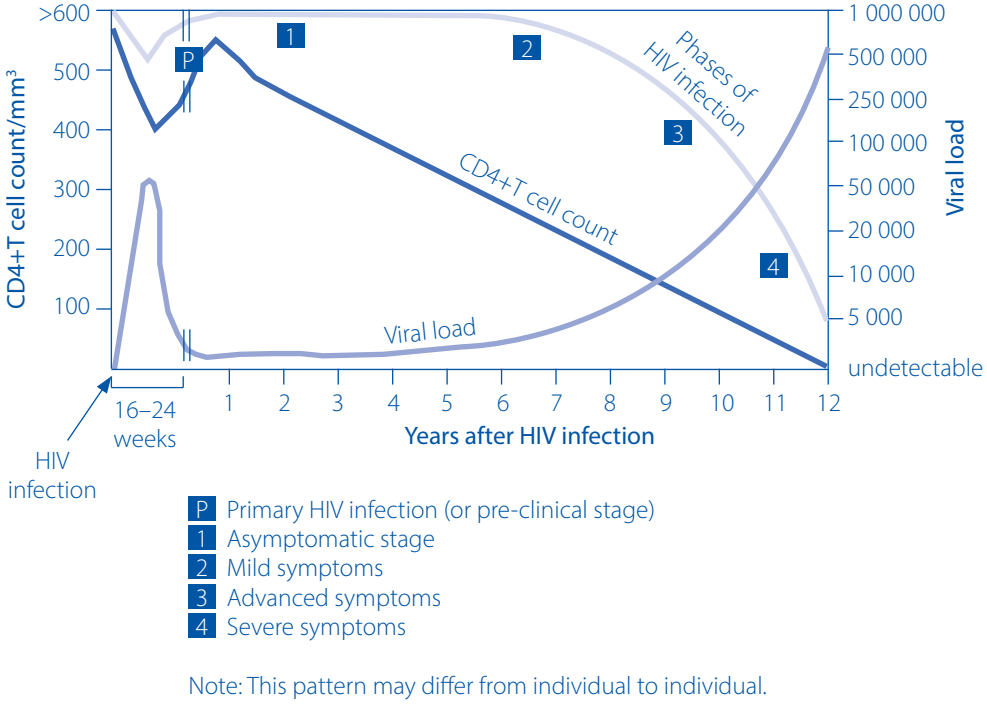



**Figure 4.2** The relationship between CD4+T cell count, viral load and stages of infection in a person with untreated HIV infection

**Note**

The main purpose of any effort to manage the health of an HIV-infected person is to enhance the functioning of the immune system by lowering the viral load and increasing the CD4+T cell count as much as possible. Although there are many ways to keep the immune system healthy, the best way to do this is with the help of antiretroviral therapy.

The WHO guidelines document is titled: 'WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children'. It is available at http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf

### Activity

Figure 4.2 on page 85 shows the relationship between the CD4+T cell count, the viral load and the progression of diseases without antiretroviral intervention.

- Use a red pen to draw new lines on this figure to show what will happen to the CD4+T cell count and the viral load if the patient starts taking ARVs as soon as possible after having been infected with HIV.
- Explain briefly what will happen with disease progression.

## 4.2 The stages of HIV infection

The World Health Organization developed a four-stage clinical staging and immunological classification system for adults, adolescents and children under 15 years old with HIV infection. The clinical staging system is useful for **baseline assessment**, assessment during wellness management, antiretroviral therapy initiation, and monitoring of patients on antiretroviral therapy, as well as in the prevention and management of opportunistic infections, for example when to start co-trimoxazole prophylaxis and other HIV-related interventions. As illustrated in Figure 4.2, the clinical stages of HIV infection are related to the survival, **prognosis** and progression of clinical disease in adults and children who are not receiving antiretroviral therapy (WHO, 2007: 11).

The clinical status of a person with HIV infection can be reversed and improved, using treatment with strong and effective **antiretroviral therapy regimes** that repress the viral load and boost immune recovery with an increase in CD4+T cells. The WHO recommends that clinical staging should also be done on people who are receiving antiretroviral therapy to guide decision-making processes, especially in resource-poor areas where CD4+T cell counts are not available. Clinical staging for people on antiretroviral therapy should, however, not be used during the first 24 weeks of antiretroviral treatment. Symptoms shown during this initial phases of antiretroviral therapy may largely be due to **immune reconstitution** or the toxicity of antiretroviral therapy, and may not be a true reflection of the person's clinical stage.

There are four WHO clinical stages of established HIV infection, based on the HIV-associated symptoms of each stage. These clinical stages are:

- Clinical stage 1: Asymptomatic
- Clinical stage 2: Mild symptoms
- Clinical stage 3: Advanced symptoms
- Clinical stage 4: Severe symptoms

There is also a 'pre-clinical' or very early stage of HIV infection which is called **primary HIV infection**. Primary HIV infection as well as the four clinical stages are now discussed in greater detail. Figure 4.3 on page 88 provides a visual summary of the stages. Refer to it when you read sections 4.2.1 to 4.2.5.

### Glossary

**Baseline assessment** An evaluation done when a person is first diagnosed with HIV infection that can be used later for comparisons.

**Prognosis** The most probable course or progress of a medical condition.

**Antiretroviral therapy regimes** A course, schedule, plan or routine of antiretroviral therapy describing what medications a patient should take and how often.

**Immune reconstitution** This is often seen in cases of immune suppression (such as with HIV infection) in which the immune system begins to recover due to ARVs. But, instead of getting better, the patient initially gets sicker because the immune system has now restored enough (thanks to the ARVs) to respond to a previously acquired opportunistic infection with an overwhelming inflammatory response. The symptoms of this infection now become felt. The condition is called **immune reconstitution inflammatory syndrome** (or IRIS)

### 4.2.1 Primary HIV infection

Primary HIV infection is the very early stages of HIV infection, or the period between initial infection and the time that antibodies to HIV are detectable. Primary HIV infection begins immediately after seroconversion has taken place. Most HIV-infected people in the primary stage of infection are asymptomatic, but some develop acute retroviral syndrome two to six weeks after exposure to HIV. Acute retroviral syndrome is characterised by 'flu-like' symptoms, such as a headache, pharyngitis (a sore throat), muscle and joint pains, mild fever, fatigue or tiredness, lymphadenopathy (swelling of the lymph nodes), gastrointestinal symptoms and skin manifestations (for example, a rash). This symptomatic phase usually persists for about two to four weeks, although lymphadenopathy often persists for longer.

The HIV viral load (or HIV RNA level) is usually very high during the primary phase and can be more than 100 000 copies/ml (see Figure 4.2). This is because of very rapid multiplication and replication of the virus after infection. Or, to use our war metaphor, the enemy wants to send in as many of its soldiers as possible so that they can overrun the local soldiers (CD4+T cells) before they are detected.

Because there are so many infectious viruses in the blood in the primary phase of infection, the HIV-infected individual is highly infectious during this phase. However, it is not possible to say exactly at what point after exposure to the virus (or actual infection) the person becomes infectious to others. Remember that the viruses replicate at a tremendous rate before the immune system has had enough time to develop an immune response or to develop enough antibodies to be detected by HIV antibody tests (see 'The window period' on page 57. Also see the 'Frequently Asked Question' box on page 132.).

The viral levels reach a steady state 16 to 24 weeks after infection, when the immune system has developed HIV antibodies and tries to fight the virus. A lower viral burden at this stage indicates a better outlook or prognosis for the patient.

Primary HIV infection can be identified by recent appearance of HIV antibodies in the blood, but it should be noted that it can take from 25 days to several months after infection for seroconversion to take place. Primary HIV infection can also be diagnosed by identifying HIV proteins in the blood, such as HIV RNA, HIV DNA and/or the HIV p24 antigen. HIV RNA can be detected within 10 days of infection and p24 antigen within between 15 and 20 days. Many countries follow the World Health Organization's recommendation to start antiretroviral therapy as soon as possible (already during primary infection, if possible) to protect the immune system, to lower the viral load, to limit the size of the HIV viral reservoir and to decrease HIV transmission during this time of heightened infectiousness.

| Stage | Primary HIV infection | 1 Asymptomatic | 2 Mild symptoms | 3 Advanced symptoms | 4 Severe symptoms |
|---|---|---|---|---|---|
| Disease progression |  |  |  |  |  |
| CD4+T cells | Decreasing | >500 cells/mm$^3$ Decreases by 50 to 80 cells/mm$^3$ per year | 350 to 499 cells/mm$^3$ | 200 to 349 cells/mm$^3$ | Fewer than 200 cells/mm$^3$ or <14% |
| Viral load | First weeks: very high | Reaches a steady state 16 to 24 weeks after infection | Increasing | Increasing rapidly/high | Very high |
| Symptoms | Flu-like or none | None or persistent generalised lymphadenopathy | Minor | Major symptoms; opportunistic diseases | Aids with severe infections, opportunistic diseases and cancers |
| Performance | Normal activity | Normal activity | Normal activity despite symptoms | Bedridden for less than 50% of the day during preceding month | Bedridden for more that 50% of the day during preceding month. Difficult to work |

4 to 6 weeks — 6 years — 9 years — 12 years

death

Approximate time in years

Note: A normal CD4+T cell count is 500 to 1500 cells/mm$^3$.

**Figure 4.3** HIV/Aids timeline and symptom progression in a person with untreated HIV infection

## Frequently Asked Questions

### What are lymph nodes, and why are they swollen during primary HIV infection?

The lymphatic system is one of the body's defences against infection. The lymphatic system consists of a network of vessels throughout the body. Lymph nodes (small masses of tissue) are found at various places along these vessels. Some lie deep within the body and others lie near the skin where we can feel them (e.g. behind the ears, in the groin and in the armpits). Harmful particles and bacteria that enter the body are filtered out by the lymph nodes. Lymph nodes represent a very important part of the immune system because they produce the white blood cells (phagocytes and lymphocytes) that fight infection. When a person is infected by an organism, the lymph nodes are usually quick to respond by producing white blood cells to fight the infection, among other things, by making antibodies. When the lymph nodes are doing their job and the phagocytes (e.g. macrophages) and lymphocytes (e.g. CD4+T cells, CD8+T cells and B cells) are fighting the infection and trying to stop it from spreading, the lymph nodes may swell and become painful. These swellings are then often called swollen 'glands', although it is strictly speaking not the glands, but the lymph nodes that are swollen.

### Why is the viral load so high in primary HIV infection?

When a foreign organism enters the body, the immune system needs time to react and to launch a proper counter-attack. It takes two to three weeks (or longer) for the immune system to make enough white blood cells and antibodies to attack or neutralise invading organisms. When HIV attacks the immune system of an HIV-negative person, the body of this person has no immune response (e.g. antibodies against HIV) and needs time to get to know the enemy. (We call this time the window period.) During this time, HIV attacks and infects as many cells as possible. This leads to a very high viral load in the blood as well as a low CD4+T cell count. As soon as an immune response has developed, the immune system can fight back, and this is the point where the CD4+T cell count increases and the viral load drops dramatically (see Figure 4.2 on page 85). Unfortunately, the immune system is not able to keep up the fight against HIV without the help of antiretroviral therapy.

### Why does the viral load drop so dramatically after about 16 weeks of infection?

As can be seen in Figure 4.2, the viral load in the blood decreases dramatically 16 to 24 weeks after infection. This is because of the huge fight put up by the immune system, which has now had time to develop effective virus-specific immunity. A close look at Figure 4.2 reveals that the CD4+T cell count is increasing again at this point. But the immune system is facing a total and prolonged onslaught from HIV. It cannot keep up its defences indefinitely. The virus will win in the end if the immune system does not receive help in the form of antiretroviral therapy to repress virus production.

### What does it mean when we say that the viral load is 'undetectable'?

Viral loads can vary from 'undetectable' levels to values exceeding two to three million copies/ml of blood. 'Undetectable' means that the viral load in the blood is lower than the bottom limit of detection for a particular test that is being

used. In earlier years, the lowest level of viruses that could be detected by tests, was 10 000 copies/ml. Today we have ultra-sensitive tests than can test down to 25 to 50 viral copies/ml. An **undetectable viral load** does not mean that the person is no longer infected with HIV. The virus is still in the body, but at very low levels.

### Glossary

**Undetectable viral load** When the viral level (or the number of viruses) in the blood is too low for the HIV viral-load test to pick it up. This means that the person is still infected with HIV but that the number of viruses in the blood is very low. A person with an undetectable viral load is much less infectious than a person with a high viral load.

**Asymptomatic stage** The first clinical stage of HIV infection when an infected person displays no symptoms. Nonetheless, the virus remains active in the body and it continues to damage and undermine the person's immune system. The **asymptomatic latent stage** is usually associated with a CD4+T cell count larger than 500 cells/mm$^3$.

## 4.2.2 Clinical Stage 1: Asymptomatic

The first clinical stage of HIV infection is the **asymptomatic stage**. In this stage, most infected individuals show no symptoms. They often are not even aware that they are infected with HIV in this stage, and may therefore without their knowledge infect other sex partners. Even though the infected person is unaware of being infected, the virus is active in the body during this stage, weakening and destroying the person's immune system. Often, the only indication of HIV infection during the asymptomatic stage is a positive HIV test.

HIV-infected individuals can remain healthy for a long time, show no symptoms and carry on with their work in a normal way. The only symptom that is sometimes seen in Clinical Stage 1 is **persistent generalised lymphadenopathy** or PGL. PGL is diagnosed when the lymph nodes are swollen or enlarged to more than one cm in diameter, and when they occur in at least two sites, for example, the neck, below the jaw, or in the armpits, and if they persist for three months or more.

Some people can be HIV-positive for many years without showing any signs of clinical disease, whereas others can quickly develop symptoms, with their health declining rapidly. Most people with untreated HIV infection have a CD4+T cell count that drops by approximately 50 to 80 cells/mm$^3$ per year during the asymptomatic stage.

Clinical Stage 1 (asymptomatic) is associated with a CD4+T cell count >500 cells/mm$^3$ in adults and children older than five years. The normal CD4+T cell count in healthy, HIV-negative individuals varies between individuals, but it is approximately 500 to 1 500 cells/mm$^3$. Although the viral load usually declines and then levels off to a steady state during the asymptomatic phase, HIV is still very active in the lymph nodes (see the Enrichment box 'The titanic struggle in the so-called "silent phase"' below).

### Enrichment: The titanic struggle in the so-called 'silent phase'

The clinical calmness of the asymptomatic stage of HIV infection deceptively conceals the titanic struggle that is taking place in the person's body between rapidly replicating HIV and the frantic attempts of the CD4+T cell population to replenish the vast number of cells destroyed by the virus. Studies of untreated HIV-infected people have demonstrated that in the clinically asymptomatic (or 'silent') stage of infection, up to a billion virus particles are produced and destroyed daily while, at the same time, about two billion CD4+T cells are destroyed by the virus every day and need to be replaced by new cells. These findings illustrate not only the danger of the virus, but also the truly remarkable capacity of the body's immune system to resist, even temporarily, this immense viral onslaught. After reaching

very high levels in the first weeks after infection, the viral load usually reaches a steady state four to six months after infection. This steady state is because of the immune response, which helps to prevent HIV viral replication.

The symptoms described in this chapter are for persons aged 15 years or older. See Table 4.2, page 97 for symptoms associated with HIV infection in children younger than 15 years

## 4.2.3 Clinical Stage 2: Mild symptoms

In the second or **minor symptomatic stage** of infection, mild symptoms of HIV disease usually begin to show. This stage begins when people with HIV infection start to present with one or more of the symptoms listed below:

- Moderate, unexplained weight loss (less than 10% of presumed or measured body weight). Assessment of body weight in pregnant women needs to consider the expected weight gain of pregnancy.
- Recurrent upper respiratory tract infections (current event plus one or more in the last six-month period) such as sinusitis, otitis media (ear infection), tonsillitis and pharyngitis (sore throat).
- Herpes zoster (also called 'shingles') is a viral infection caused by the same virus that causes chickenpox. **Herpes zoster** affects nerve cells and is characterised by skin rash (tiny blisters) on the face, limbs or body that is very painful. It can also affect the eyes, and causes blurred vision and pain. Shingles can be very severe in people with depressed immune systems. Treatment (with the antiviral Ciclovir®) should be accessed as soon as possible.
- Angular cheilitis is cracks or splits on the lips and in the corner of the mouth (which are not the result of iron and vitamin deficiency), and it is often caused by fungi. It usually responds well to antifungal treatment.
- Oral ulcers that recur (two or more episodes in the last six months). The ulcers are often accompanied by inflammation and a yellow-grey pseudo-membrane.
- Papular pruritic eruptions (PPE) are characterised by an itchy rash that occurs on the legs, often with marked post-inflammatory pigmentation.
- **Seborrhoeic dermatitis** is an itchy scaly skin condition that mainly affects areas that are hairy, such as the scalp, face, upper trunk and groin.
- Fungal nail infections of the fingers are characterised by a red and swollen nail bed that is painful or a when the nail separates from the nail bed of the fingernail.
- Prurigo, or chronic itchy skin.
- Minor mucocutaneous manifestations.

Clinical Stage 2 (mild symptoms) is usually associated with a CD4+T cell count of between 350 and 499 cells/mm$^3$. This is an indication of mild immunosuppression. The individual in Stage 2 of HIV infection is usually able to carry on with his or her normal activities, despite being symptomatic.

### Glossary

**Minor symptomatic stage**
The second clinical stage of HIV infection, when minor and early symptoms of HIV disease begin to manifest. The minor symptomatic stage is usually associated with a CD4+T cell count of 350 to 499 cells/mm$^3$.

### Note

Shingles is also seen in HIV-uninfected (usually older) adults, probably as a result of excessive stress and other immune depressive conditions.

Papular pruritic eruptions, seborrhoeic dermatitis and fungal nail infections are also seen in individuals who are not HIV infected.

## 4.2.4 Clinical Stage 3: Advanced symptoms

More advanced symptoms and opportunistic infections begin to appear in the **advanced symptomatic stage** as the immune system continues to deteriorate in persons with untreated HIV infection. At this stage, the CD4+T cell count becomes very low, whereas the viral load becomes very high (see Figure 4.2). Signs of more severe HIV-related diseases begin to appear. These signs and symptoms

### Glossary

**Advanced symptomatic stage**
The third clinical stage of HIV infection, when signs of very severe HIV-related diseases and opportunistic infections start to manifest, with a continuously deteriorating immune system. The major symptomatic stage is usually associated with a CD4+T cell count of 200 to 349 cells/mm$^3$.

**Opportunistic infections**
Opportunistic infections are when a person gets sick from microorganisms that – in the presence of a healthy immune system – do not normally become pathogenic (in other words, make a person sick). A healthy immune system will take care of these pathogens and kill them before they can make us sick. But when an immune system is unable to defend the body, opportunistic infections will 'take any opportunity' (hence the name) to attack the body successfully.

are usually because of overgrowth of some of the body's natural flora with fungal infections and reactivation of old infections such as TB and herpes. They are also caused by uncontrolled multiplication of HIV itself in untreated individuals. More frequent and severe **opportunistic infections** occur as the immune deficiency progresses.

The following symptoms usually indicate advanced immune deficiency:

- Unexplained severe weight loss (more than 10% of presumed or measured body weight). The face thins, while the waist and extremities become noticeably thin and the body mass index is often less than 18.5 kg/m$^3$.
- Unexplained **chronic diarrhoea** that persists for more than one month.
- Unexplained persistent fever (above 37.6 °C) or intermittent or constant night sweats, for longer than one month which often do not respond to antibiotics or antimalarial agents. Malaria must be excluded in areas with a high incidence of malaria.
- Persistent and recurrent **oral *Candidiasis*** (or thrush) is a common sign of immune deficiency and it does not usually occur unless the CD4+T cell count is quite low at around <200 cells/mm$^3$). It is usually painful or tender and does not respond to local antifungal treatment.
- **Oral hairy leukoplakia** is fine, small linear patches on the lateral borders of the tongue. It usually occurs on both sides of the tongue and it does not scrape off.
- Pulmonary tuberculosis (TB) (current) characterised by chronic symptoms (lasting at least two to three weeks) such as shortness of breath, chest pain, productive cough, blood in the sputum (haemoptysis), fatigue, weight loss, fever and night sweats.
- Severe bacterial infections such as pneumonia, meningitis, empyema (infection of the pleural or lung space), pyomyositis (infection of skeletal muscles), bone or joint infection, meningitis, bacteraemia and severe **pelvic inflammatory disease** can appear. These infections are accompanied by fever and symptoms that localise the infection. They usually respond well to antibiotics.
- Acute necrotising ulcerative stomatitis, gingivitis or periodontitis. These conditions are characterised by bad odour, ulcers, loose teeth, spontaneous bleeding, severe pain in the mouth and rapid loss of bone and/or soft tissue.
- Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 x 10$^9$ per litre) or chronic trombocytopaenia (<50 x 10$^9$ per litre).

TB is the most common opportunistic infection in sub-Saharan Africa and will therefore be discussed in more detail later on in this chapter.

Clinical Stage 3 (advanced symptoms) is usually associated with a CD4+T cell count of between 200 and 349 cells/mm$^3$. This is an indication of advanced immunosuppression.

## 4.2.5 Clinical Stage 4: Severe symptoms

In the final stage of HIV disease, called the **severe symptomatic stage**, the symptoms become severe and more acute. More persistent and untreatable opportunistic conditions and cancers begin to manifest themselves and the immune system deteriorates exponentially (see Figure 4.2). HIV-related organ damage is also common at this stage of HIV disease.

Any of the following symptoms, conditions or opportunistic infections can occur in this stage, as well as any of the symptoms or opportunistic infections mentioned in the previous stages:

**Glossary**

**Severe symptomatic stage**
The fourth clinical stage of HIV infection, when the symptoms of HIV disease become more acute. Patients become infected by relatively rare and unusual organisms that do not respond to antibiotics and more persistent and untreatable opportunistic conditions and cancers begin to manifest. Aids patients usually have a very high viral load and severe immune deficiency with a CD4+T cell count of less than 200 cells/mm$^3$ or <14%.

- **HIV wasting syndrome** is experienced when unexplained weight loss of more than 10% of body weight and visible thinning of the face, waist and extremities with obvious wasting (body mass index <18.5), together with either unexplained chronic diarrhoea (loose or watery stools three or more times daily) lasting more than one month or fever or night sweats for more than one month, without other cause and with a lack of response to antibiotics or antimalarial agents. Malaria must be excluded in areas where it occurs.
- *Pneumocystis jiroveci* pneumonia or PCP is often seen in patients with Aids. Pneumocystis pneumonia is an infection of the lungs caused by a fungus, *Pneumocystis jiroveci*. It is characterised by a continual dry, non-productive cough that started recently (within the past three months), shortness of breath and sometimes painful breathing, weight loss and fever. There should be no evidence of bacterial pneumonia.
- Recurrent severe bacterial pneumonia (characterised by cough, fast and difficult breathing, chest pain and fever) for two or more episodes in the past six months. Bacterial pneumonia is a very common opportunistic infection in sub-Saharan Africa. It usually responds well to antibiotics.
- Chronic herpes simplex virus (HSV) infections affect the labial, genital or anorectal areas. It is characterised by severe and progressive painful lesions reported for more than one month. HSV is usually recurrent with a history of previous episodes.
- Oesophageal candidiasis is caused by oral ***Candida*** – a fungus. It is characterised by chest pain and difficulty in swallowing food and fluids (dysphagia). **Oesophageal candidiasis** is a very common opportunistic infection in southern Africa and responds well to antifungal treatment.
- **Extrapulmonary/disseminated TB** is tuberculosis that occurs outside of the lungs. The most commonly affected sites are the lymph nodes, pleural cavities, the heart, the meninges (brain), vertebral bodies (bone), kidneys and synovial tissue of the joints. Extrapulmonary TB is characterised by weakness, weight loss, persistent fever and night sweats. The symptoms further depend on the organs involved. Extra-pulmonary TB usually responds well to standard anti-TB treatment.
- Kaposi's sarcoma, a rare form of skin cancer, is characterised by a painless reddish-brown or bluish-purple swelling on the skin and mucous membranes (e.g. in the mouth). Kaposi's sarcoma can also occur in the gastrointestinal tract and lungs. It responds well to treatment but it can develop into invasive open lesions and cause death if not treated.
- Cytomegalovirus infection is caused by the **cytomegalovirus** (CMV), a common inhabitant of the human body. CMV can cause severe opportunistic infections in immune-depressed individuals, such as retinitis, an inflammation of the retina of the eye, which in many cases leads to blindness. CMV is a common cause of severe and often lethal pneumonia and it also targets the gastrointestinal tract. CMV is often excreted in the urine, saliva, semen, cervical secretions, faeces or breastmilk of immune depressed patients. CMV infections usually occur when the CD4+T cell levels fall below 50 cells/mm$^3$.
- Central nervous system (CNS) toxoplasmosis is a protozoal infection of the brain. It is characterised by fever, headache, focal neurological signs, convulsions and reduced level of consciousness. Cats are the major host of *Toxoplasma gondii*, the organism that causes the disease. It usually responds within 10 days to specific treatment.

**Glossary**

**HIV wasting syndrome**
Unexplained weight loss of greater than 10% of body weight and visible thinning of face, waist and extremities, plus either unexplained chronic diarrhoea (lasting more than one month) or unexplained prolonged or intermittent fever for one month or more.

**Note**

According to the WHO (2007) case definition of advanced HIV infection (including Aids), the clinical criteria for diagnosis of advanced HIV in adults and children older than 15 years with confirmed HIV infection, are: Diagnosis of any stage 3 or stage 4 condition and/or CD4+T cell count less than 350mm$^3$.

- **HIV encephalopathy** is a neurological abnormality which is characterised by a range of symptoms, including poor concentration, tremors, headaches, confusion, memory loss, loss of vision and seizures. Cognitive and motor functioning also deteriorate, disabling the patient and interfering with activities of daily living. In order to exclude other infectious causes, lumbar puncture should be conducted.
- Extrapulmonary cryptococcosis (including meningitis) is a fungal infection in the central nervous system. It causes fever, severe headache, nausea, vomiting, neck stiffness, mental status changes, seizures, confusion and behavioural changes. *Cryptococcus* infections can also occur in the lungs. It responds well to cryptococcal therapy.
- Disseminated non-tuberculous mycobacteria (DNTM) infections are characterised by non-specific clinical symptoms such as progressive anaemia, fatigue, diarrhoea, weight loss, fever and night sweats. Non-tuberculous mycobacteria are other mycobacteria which do not cause TB. They often cause pulmonary diseases resembling TB.
- Progressive multifocal leukoencephalopathy (PML) is a rapidly progressive and often fatal viral infection of the brain. It is characterised by headache, fever, memory loss, changes in mental status, cortical blindness, speech difficulty, partial paralysis and seizures.
- Chronic cryptosporidiosis (infection with protozoa) with chronic diarrhoea which is often profuse and watery (for more than one month) with weight loss, abdominal pain, nausea and vomiting.
- Chronic isosporiasis is an intestinal infection caused by the protozoan parasite *Cystoisospora belli*. It is often seen in immune compromised individuals with symptoms lasting over one month. Symptoms include watery diarrhoea, abdominal pain, anorexia, and low-grade fever.
- Disseminated mycosis refers to any infection or disease caused by fungi (e.g. histoplasmosis or coccidiomycosis). Non-specific symptoms include a cough, shortness of breath, fever, skin rash, anaemia and weight loss.
- Recurrent non-typhoid *Salmonella* bacteraemia is characterised by non-specific symptoms such as headaches, fever, sweats, weight loss, diarrhoea and anorexia.
- Lymphoma (cerebral or B cell non-Hodgkin) is cancer of the lymph nodes and it usually presents with enlargement of the lymph nodes or lymphadenopathy, enlargement of the spleen (**splenomegaly**) or the liver (**hepatomegaly**). Lymphoma also affects the brain.
- Invasive cervical carcinoma is cancer of the cervix and it is caused by the human papilloma virus (or HPV). It is characterised by a vaginal discharge that will not stop, bleeding after sexual intercourse or inter-menstrual bleeding that is unresponsive to antibacterial or anti-fungal treatment, and cervical lesions. Because HIV infection may increase the risk of cervical cancer (due to infection by HPV) it is important to do a pap smear of the cervix on all HIV-infected women every one to two years. An HPV vaccine is available for young women (and young men) to prevent infection by the human papilloma virus (see page 121).
- Atypical disseminated leishmaniasis is a disease caused by the protozoan parasite *Leishmania*. It is usually transmitted by the bite of an infected sandfly. Symptoms are malaise, chronic fever, weight loss, enlargement of the liver and

spleen, as well as pancytopenia (abnormal deficiency in all blood cells – red, white and platelets). If left untreated, leishmaniasis is nearly always fatal.
- Symptomatic HIV-associated nephropathy (kidney disease).
- Symptomatic HIV-associated cardiomyopathy (disease of the heart muscles).

Clinical Stage 4 (severe symptoms) is associated with very high viral loads and CD4+T cell counts lower than 200 cells/mm$^3$. This is an indication of severe immunosuppression.

## Enrichment: YouTube videos

You will find the following YouTube videos interesting. They will also support your learning.
- To watch a video on the differences between HIV, Aids and opportunistic diseases, click on the link: http://goo.gl/x75Xyi
- The following online library provides images and photographs of Aids-related diseases. You can use them to help you identify many Aids-related diseases. Click on the following website: http://www.aids-images.ch. Choose a disease by clicking on the alphabetic list. For example, if you want to know what Kaposi's sarcoma looks like, click on K and then search for 'Kaposi's sarcoma'. Note that you can also use the images in this online library to make PowerPoint slides.
- The following website is also very useful if you are looking for a definition of any HIV-related condition: https://aidsinfo.nih.gov/ (go to the 'Glossary' section), or go directly to: https://aidsinfo.nih.gov/education-materials/glossary

Table 4.1 summarises the WHO clinical staging of HIV and Aids for adults and adolescents. This table provides a useful summary of the stages of infection and can be used in resource-limited settings to manage HIV infection.

**Table 4.1** WHO clinical staging of HIV and Aids for adults and adolescents with confirmed HIV infection (15 years and older)

| **Clinical Stage 1** |
|---|
| • Asymptomatic<br>• Persistent generalised lymphadenopathy (PGL) |
| **Clinical Stage 2** |
| • Moderate unexplained weight loss (<10% of presumed or measured body weight)<br>• Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)<br>• Herpes zoster<br>• Angular cheilitis<br>• Recurrent oral ulcerations<br>• Papular pruritic eruptions<br>• Seborrhoeic dermatitis<br>• Fungal fingernail infections |

*continued*

| Clinical Stage 3 |
|---|
| • Unexplained severe weight loss (>10% of presumed or measured body weight)<br>• Unexplained chronic diarrhoea for longer than one month<br>• Unexplained persistent fever (above 37.6 °C) intermittent or constant for longer than one month<br>• Persistent oral candidiasis (thrush)<br>• Oral hairy leukoplakia<br>• Pulmonary tuberculosis (currently)<br>• Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)<br>• Acute necrotising ulcerative stomatitis, gingivitis or periodontitis<br>• Unexplained anaemia (haemoglobin <8 g/dl), neutropenia (neutrophils <0.5 x $10^9$ per litre) or chronic thrombocytopenia (platelets <50 x $10^9$ per litre) |
| **Clinical Stage 4** |
| • HIV wasting syndrome<br>• *Pneumocystis* pneumonia<br>• Recurrent severe bacterial pneumonia<br>• Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)<br>• Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)<br>• Extrapulmonary tuberculosis<br>• Kaposi's sarcoma<br>• Cytomegalovirus infection (retinitis or infection of other organs)<br>• Central nervous system toxoplasmosis<br>• HIV encephalopathy<br>• Extrapulmonary *Cryptococcosis* including meningitis<br>• Disseminated non-tuberculosis *Mycobacterium* infection<br>• Progressive multifocal leukoencephalopathy<br>• Chronic cryptosporidiosis (with diarrhoea)<br>• Chronic isosporiasis |
| • Disseminated mycosis (coccidiomycosis or histoplasmosis)<br>• Recurrent non-typhoidal *Salmonella* bacteraemia<br>• Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours<br>• Invasive cervical carcinoma<br>• Atypical disseminated leishmaniasis<br>• Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy |

(Source WHO, 2007: 15–16)

## 4.3 Symptoms of HIV infection in children

The clinical course of HIV infection in children is very different from that in adults. The time lapse between infection and the onset of Aids is usually much shorter in children than it is in adults, and most infected infants develop the disease during the first year of life. The mortality rate is especially high in Africa where it is estimated that the upper end of mortality in HIV-infected children is

in the region of 55% by two years of age, 90% by three years and 98% by five years without antiretroviral intervention (Coovadia, 2010: 202).

Table 4.2 summarises the WHO clinical staging of HIV and Aids for children younger than 15 years. The WHO clinical staging should be used to evaluate the wellness of children, at initiation of antiretroviral treatment and at follow-up visits to assess children on antiretroviral therapy.

If you want to know more about the infections or diseases mentioned, go to page 91 to 95 where adult symptoms are discussed, or go to the following website: https://aidsinfo.nih.gov/

**Table 4.2** WHO clinical staging of HIV and Aids for infants and children (aged under 15 years) with confirmed HIV infection

| **Clinical Stage 1** |
|---|
| • Asymptomatic<br>• Persistent generalised lymphadenopathy (PGL) |
| **Clinical Stage 2** |
| • Unexplained persistent hepatosplenomegaly (enlarged liver and spleen)<br>• Papular pruritic eruptions<br>• Fungal nail infections<br>• Angular cheilitis (splits or cracks at the angle of the mouth – not iron or vitamin deficiency)<br>• Lineal gingival erythema (LGE)<br>• Extensive wart virus infection<br>• Extensive molluscum contagiosum<br>• Recurrent oral ulcerations<br>• Unexplained persistent parotid enlargement<br>• Herpes zoster<br>• Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis or tonsillitis) |
| **Clinical Stage 3** |
| • Unexplained moderate malnutrition or wasting not adequately responding to standard therapy<br>• Unexplained persistent diarrhoea (14 days or more)<br>• Unexplained persistent fever (above 37.5ºC intermittent or constant) for longer than one month<br>• Persistent oral candidiasis (thrush) after first 6–8 weeks of life<br>• Oral hairy leukoplakia<br>• Acute necrotising ulcerative gingivitis or periodontitis<br>• Lymph node tuberculosis<br>• Pulmonary tuberculosis (TB)<br>• Severe recurrent bacterial pneumonia<br>• Symptomatic **lymphoid interstitial pneumonitis** (**LIP**)<br>• Chronic HIV-associated lung disease including bronchiectasis<br>• Unexplained anaemia (haemoglobin <8 g/dl), neutropenia (neutrophils <0.5 x $10^9$ per litre) and/or chronic thrombocytopenia (platelets <50 x $10^9$ per litre) |

*continued*

**Clinical Stage 4**

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- *Pneumocystis* pneumonia
- Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous for longer than one month) or visceral at any site
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (CMV): retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month
- Central nervous system (CNS) toxoplasmosis (after one month of life)
- Extrapulmonary cryptococcosis (including meningitis)
- HIV encephalopathy
- Disseminated endemic mycosis (coccidiomycosis or histoplasmosis)
- Disseminated non-tuberculosis mycobacteria infection
- Chronic cryptosporidiosis (with seborrhei)
- Chronic isosporiasis
- Cerebral or B cell non-Hodgkin's lymphoma
- Progressive multifocal leukoencephalopathy (PML)
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

(Source WHO, 2007: 17–18)

**Note**

An HIV-antibody test done on infants who are younger than 18 months may not be reliable because it can react to the HIV antibodies that the mother transfers to the baby during pregnancy. An HIV PCR (or viral test) should be done in children younger than 18 months to diagnose HIV infection.

The IMCI (Integrated Management of Childhood Illness) approach is that all children should be screened routinely for HIV. According to the WHO (2007: 39), a presumptive diagnosis of severe HIV disease among infants and children aged under 18 months in situations where virological testing is not available should be made in the following circumstances:

- the infant is confirmed as **HIV antibody-positive**; and
- diagnosis of any Aids-indicator conditions can be made; or
- the infant is symptomatic with two or more of the following: oral thrush, severe pneumonia or severe sepsis.

Other factors that support the diagnosis of severe HIV disease in an HIV-seropositive infant are recent HIV-related maternal death or advanced HIV disease in the mother, as well as CD4+T cell levels <20%. According to WHO (2015) guidelines, all HIV-infected children (especially children under the age of 10 years), no matter what their CD4+T cell counts or clinical staging, should be given antiretroviral therapy immediately.

## Enrichment: Immune status in children.

The immune status of adults is measured by using absolute CD4+T cell counts, which range from 500 to 1 500 cells/mm$^3$. The absolute CD4+T cell count in infants who are healthy and not infected with HIV is considerably higher than the CD4+T cell count in uninfected adults. However, the cell count in infants slowly declines to adult levels by the age of approximately six years old. The CD4+T cell count in young children (<5 years old) also tend to vary a lot. The WHO (2007) therefore recommends that the measurement of the CD4+T cells percentage (%CD4+T cells) should be used in young children. While the absolute CD4+T cell count is the number of CD4+T cells per ml$^3$, the CD4+T cell percentage is the percentage of the lymphocyte population that is CD4+T cells.

$$\%\ CD4+T\ cells = \frac{\text{Number of CD4+T cells}}{\text{Total number of lymphocytes}}$$

A CD4+T cell percentage of <14% is considered to correspond to the same degree of immunosuppression as an absolute CD4+T cell count of <299 cells/ml$^3$ (US Department of Health and Human Services, 2014: 99).

# 4.4 Prevention of opportunistic infections

Opportunistic infections and diseases that result from a depleted immune system are the primary cause of death in people with HIV infection. It therefore makes sense to prevent these infections from occurring (or re-occurring) by initiating early preventative measures.

The best way to prevent opportunistic infections is to strengthen the immune system with antiretroviral therapy. It is believed that the use of antiretroviral therapy can reduce opportunistic infections by approximately 80% (Maartens, 2010: 479). In this section, we look at three ways to prevent opportunistic infections:

- by preventing exposure;
- by providing chemoprophylaxis; and
- by immunisation.

It should however be noted that even with the use of antiretroviral therapy – especially if ART started late – opportunistic infections can continue to occur in patients whose immune systems remain suppressed.

## 4.4.1 Preventing exposure

Using the methods outlined below can help prevent exposure to infectious agents:

- Assuring a safe water supply. Many infections causing chronic diarrhoea (e.g. microsporidiosis) are waterborne and this can have serious consequences for people with depressed immune systems.
- Ensuring proper food hygiene. Food should be properly prepared and hygienically handled and stored to avoid salmonella, toxoplasma gondii and other serious infections.

Note that these methods will be explored in greater detail later on in this book.

- Preventing exposure to tuberculosis. This can be done with proper education and by improving living conditions. TB exposure should also be prevented in clinics and hospitals where sputum is handled, especially TB hospitals.
- Controlling malaria vectors. This is especially important in areas with a high occurrence of malaria.
- Encouraging safer sex practices. Safer sex practices are necessary to prevent re-infection with HIV or other sexually transmitted infections (STIs).

## 4.4.2 Chemoprophylaxis

Chemoprophylaxis is the use of antimicrobial agents to prevent opportunistic infections. Criteria for chemoprophylaxis are generally based on CD4+T cell counts. A low CD4+T cell count is usually a sign of immune deficiency. It can also be an indication that the person will develop opportunistic infections. Some opportunistic infections can, however, strike when the CD4+T cell count is quite high (e.g. 500 cells/mm$^3$).

We no longer consider the prevention of opportunistic infections in isolation, but follow specific WHO or national guidelines to prevent opportunistic infections (National Department of Health, 2015a: 93–100). Chemoprophylaxis includes:

- Co-trimoxazole preventive therapy (CPT);
- Cryptococcus (Crypto) screening and treatment; and
- Isoniazid preventive therapy (IPT).

### Terminology: The difference between *primary prophylaxis* and *secondary prophylaxis*

It is important to distinguish between *primary prophylaxis* and *secondary prophylaxis*. The purpose of primary prophylaxis is to prevent an opportunistic infection that has never occurred in the patient before. The purpose of secondary prophylaxis is to prevent the re-occurrence of infection, which means that the person has had the infection before. Examples of opportunistic infections that tend to re-occur in people with depressed immune systems are herpes simplex virus ulcers, oesophageal candidiasis, tuberculosis, bacterial pneumonia, salmonella infections and *Pneumocystis jiroveci* pneumonia (or PCP).

Tuberculosis usually occurs when the CD4+T cell counts are less than 350 cells/mm$^3$. Most other opportunistic infections occur if the count of CD4+T cells is lower than 200 cells/mm$^3$ (e.g. *Pneumocystis jiroveci* pneumonia, candidiasis and herpes simplex infections). The least virulent pathogens like cryptococcus and cytomegalovirus (CMV) occur when CD4+T cell counts are below 50 cells/mm$^3$.

### 4.4.2.1 Co-trimoxazole preventive therapy (CPT)

Co-trimoxazole preventive therapy (CPT) is an intervention that is simple, well tolerated and cost effective, and can both extend and enhance the quality of life of HIV-infected people. Co-trimoxazole (trimethoprim-sulfamethoxazole) is a broad-spectrum antimicrobial agent that targets various bacteria, fungi and protozoa. It should be implemented as an integral component of HIV care, including for those on antiretroviral therapy. Co-trimoxazole is safe to use in pregnancy.

Co-trimoxazole prophylaxis greatly reduces the amount of time HIV-infected individuals have to stay in hospital. In addition, it is associated with a 25% to 46% reduction in mortality among individuals infected with HIV in sub-Saharan Africa (Date, Vitoria, Granich, Banda, Fox & Gilks, 2010). Co-trimoxazole, furthermore, decreases the incidence of numerous opportunistic infections, such as:

- *Pneumocystis jiroveci* pneumonia;
- toxoplasmosis;
- malaria;
- bacterial pneumonia;
- bacteraemia; and
- isosporiasis.

All HIV-infected adolescents and adults who are in WHO stages 2, 3 or 4 (see Table 4.1), as well as all individuals (including children) with HIV/TB co-infection should be started on co-trimoxazole. It should also be offered to all **HIV-exposed** infants (aged between four and six weeks, or at their first encounter with the healthcare system) born to mothers with HIV infection. This treatment should continue until it is possible to exclude HIV infection.

Co-trimoxazole can be discontinued in patients on antiretroviral therapy when the CD4+T cell count has risen above 350 cells/mm$^3$ and remains above that level for at least six months (Aurum Institute & CDC/PEPFAR, 2015: 19). Co-trimoxazole is generally well-tolerated and the most common side effect is a skin rash in which case treatment may be continued if the rash is mild. Treatment can be interrupted and then reintroduced when the rash is better. Treatment should be stopped if the person has hepatitis, fever or mucous membrane lesions, for example in **Stevens-Johnson syndrome**.

Because most countries in Africa have used co-trimoxazole widely as treatment for common infections, co-trimoxazole resistance among some pathogens has increased. Co-trimoxazole is, for example, less effective against malaria in central and southern Africa because of pathogen resistance.

**Glossary**

**HIV-exposed** Refers to a person who was exposed to HIV (for example a baby born to an HIV-infected mother), but it is not certain if they are HIV-infected themselves. A test has to be done to determine an HIV-exposed person's HIV status (positive or negative).

Follow the National Department of Health (2015a) guidelines for co-trimoxazole preventive therapy in HIV-infected infants and children. Refer to the Enrichment box on page 104 for the web address.

### 4.4.2.2 Cryptococcus (Crypto) screening and treatment

Cryptococcus is a type of fungus that is found in the soil and it is associated with bird droppings. If inhaled, it can cause an infection in the lungs. It can spread to other parts of the body, for example causing **cryptococcal meningitis**. This infection is often seen in people with immune deficiencies.

All HIV-positive adults with CD4+T cell counts <100 cells/mm$^3$ should be screened for the cryptococcal antigen (CrAg) *before* antiretroviral therapy is started. People who had cryptococcal meningitis previously do not need to be screened. If CrAg screening is positive without any evidence of meningitis, oral fluconazole is given and antiretroviral therapy can be started after two weeks of antifungal treatment. If CrAg screening is positive with evidence of meningitis, the person is hospitalised for two weeks with intravenous antifungal treatment. Antiretroviral treatment can be started after four to six weeks of antifungal treatment. Fluconazole is teratogenic (causing birth defects) and should not be given to women who are pregnant.

Consult the 'National Consolidated Guidelines' for eligibility criteria for IPT. See page 160 for the web address.

### 4.4.2.3 Tuberculosis prophylaxis (Isoniazid preventive therapy or IPT)

Tuberculosis is the life-threatening opportunistic infection that is most frequent in people with HIV infection. Clinical trials have shown that tuberculosis prevention (also called Isoniazid Prevention Therapy or IPT) can reduce the overall risk of TB in people with HIV infection by 33% (Date et al., 2010: 2). It was further found that IPT had the greatest effect on HIV-infected individuals who also had a positive tuberculin skin test (TST) with a TB risk reduction of 64%. The World Health Organization recommends that IPT should only be offered to HIV-infected people who are TST positive. If the tuberculin skin test is not available when IPT is started, the test must be done within one month of starting IPT. If the TST is negative, IPT should be discontinued unless the person is on ARVs, in which case IPT should be continued for 12 months. TST status should be re-assessed annually, until it becomes positive. CD4+T cell counts are no longer used to initiate TB preventive therapy.

#### Frequently Asked Questions

**What is a tuberculin skin test (TST)?**

Tuberculin is a protein extracted from the organism that causes TB, namely *Mycobacterium* tuberculosis. This tuberculin protein is used in a skin test to determine if a person has been exposed to tuberculosis. The tuberculin preparation (also called PPD or purified protein derivative) is usually injected into the skin (intradermal). If a reaction is seen at and around the site of injection (e.g. swelling or hardening of the site of injection), the test is positive.

**What does a positive TST mean?**

A positive TST means that the person has been exposed to (or infected by) TB bacilli (but it does not necessarily mean that the person has active TB or TB disease). A TST will also be positive when a person was vaccinated with BCG.

**What does a negative TST mean?**

A negative TST means that the person has never been exposed to TB before. However, a negative tuberculin skin test does not exclude TB. Various conditions may cause a false negative reaction, such as HIV infection, malnutrition, cancer or severe disseminated TB, or viral infections like chicken pox or measles.

It is extremely important to make sure that the patient does not have **active TB** before starting preventive therapy. The reason for this is to avoid giving a single anti-TB drug (Isoniazid) to patients who need a full treatment regime (see the Enrichment box below).

#### Glossary

**Active TB** Active TB is the opposite of latent (or inactive) TB. In latent TB, a person has TB infection, but the bacilli *(M. tuberculosis)* lie dormant in the body without causing disease so that the infected person has no symptoms and is not contagious. However, when the TB becomes active, the person becomes sick and can spread the TB to others. TB can be latent from a few weeks to many years after infection.

## Enrichment: Why Isoniazid Preventive Therapy (IPT) should not be offered to patients with active TB

Isoniazid Preventive Therapy should never be offered to patients with active TB. Why is this so? Isoniazid given as a single drug is strong enough to *prevent* TB, but it is definitely not strong enough on its own to treat TB. Patients with active TB (with symptoms such persistent cough, weight loss, night sweats and fever) are never

treated with only one drug (isoniazid), but always with a combination of different drugs. To treat a patient with active TB with only one drug (such as isoniazid) will encourage the TB bacilli to become resistant to the effects of the drug. This same drug will then have no effect on the TB bacilli when used in the future, and the patient will remain sick and infective to other people.

Every person who is living with HIV must be screened for TB whenever visiting a healthcare facility or making contact with a healthcare practitioner. Symptom-based TB screening is sufficient to exclude active TB among adults and adolescents living with HIV (National Department of Health, 2015a: 93). The symptoms of tuberculosis for TB symptom screening are in Table 4.3. If any ONE of the symptoms listed in Table 4.3 is present, the patient must be further investigated for active TB disease. A child with TB symptoms (any ONE of the symptoms) and a history of recent (<12 months) close contact with a person diagnosed with infectious TB should be regarded as having TB until proven otherwise.

**Table 4.3** TB symptom screening (National Department of Health, 2015a: 93)

| TB symptom screen (adolescents/ adults/pregnant women | TB symptom screen (infants and children) |
|---|---|
| Current cough of any duration | Current cough |
| Persistent fever of more than two weeks | Persistent fever of more than two weeks |
| Unexplained weight loss of >1.5kg in a month, or failure to gain weight (pregnant women) | Fatigue/reduced playfulness |
| Drenching night sweats | Poor weight gain |

The recommended regime for TB prevention therapy for adults, adolescents and pregnant women is as follows (Department of Health, 2015a: 95):

- isoniazid (INH) 5 mg/kg/day (maximum 300 mg/day);
- pyridoxine (Vitamin B6) 25 mg per day to prevent **peripheral neuropathy** (a disease of the peripheral nerves that can be a side effect of INH).

The recommended regime for children is as follows:

- isoniazid (INH) 10 mg/kg/day (crushed and dissolved in water or multi-vitamin syrup)
- pyridoxine (Vitamin B6) daily for six months if the child is HIV-positive or malnourished. (<5 years old: 12.5 mg daily; ≥5 years of age: 25 mg daily.

Secondary preventive therapy (offering IPT to prevent TB in people who have had active TB before) may be given to adults (excluding children and people who had multidrug-resistant and extreme multidrug-resistant TB) if documented proof of bacteriological cure of TB is provided. In such a case (where previous TB is cured), IPT may be started immediately after completing TB treatment (National Department of Health, 2015a: 94).

A small minority of patients on isoniazid develops hepatitis, and treatment should be stopped if a patient is nauseous, vomits or develops jaundice. People with liver diseases or who abuse alcohol should not be offered isoniazid preventive therapy.

## Enrichment: Prevention and management of opportunistic infections

If you need to know more about the prevention and management of opportunistic infections (e.g. **eligibility criteria** and medication dosages for adults, adolescents, children and infants) download the following document:

- National Consolidated Guidelines for PMTCT and the management of HIV in children, adolescents and adults (Chapter 10: Prevention and management of opportunistic infections) at: http://www.sahivsoc.org/upload/documents/ART%20Guidelines%2015052015.pdf
- You can also download the following app on your smartphone: 'HIV Clinical Guide'.

**Glossary**

**Eligibility criteria** Before a person can be treated for a certain condition, the person must fulfil certain criteria before he or she qualifies for the treatment, or is eligible to receive the treatment.

## 4.4.3 Immunisation

Immunisation is a proven method to prevent infectious diseases, and it should be offered to HIV-infected people where appropriate. HIV-infected people with severe immune depression should not receive vaccinations with live organisms. Vaccine responses are also poor when people have a CD4+T cell count <200 cells/mm$^3$ and should in some cases not be given.

### 4.4.3.1 Adults

This information is based on: 'HIV and Immunizations' (in the USA). Retrieved from: https://aidsinfo.nih.gov on 23 October 2016. Consult your local national vaccination policies and adapt where necessary.

Read more about HPV and Gardasil® on page 121.

The following vaccinations should be considered for all HIV-infected adults (US Department of Health and Human Services, 2016):

- Hepatitis B virus vaccination (HBV). Hepatitis B is also a sexually transmitted infection like HIV infection. The vaccine should not be given to people with active hepatitis.
- Influenza (flu) vaccination (injectable) must be given every year.
- Human papilloma virus (HPV) vaccination (Gardasil®) is recommended for young girls and women aged nine to 26 years. HPV vaccination should not be given during pregnancy.
- Polysaccharide pneumococcal vaccine for the prevention of pneumonia should be given soon after HIV diagnosis. If CD4+T cell count is <200 cells/mm$^3$ when the vaccine is given, immunisation should be repeated when CD4+T cell count is ≥200 cells/mm$^3$.
- Tetanus, diphtheria and pertussis (Tdap) as a single vaccine that protects against these three diseases. The tetanus and diphtheria (Td) vaccine should be repeated every 10 years.

The following vaccinations are recommended for some HIV-infected individuals:

- Hepatitis A virus vaccination (HAV). It is recommended for healthcare practitioners, men who have sex with men, people who inject drugs, people with chronic liver disease, haemophiliacs and people travelling to certain parts of the world.

- *Haemophilis influenzae* type B vaccine to prevent bacterial meningitis. The necessity of this vaccine should be discussed with healthcare providers.
- Measles, mumps and rubella (MMR). It should not be given to HIV-positive adults with CD4+T cell counts <200 cells/mm$^3$ or to people who are HIV symptomatic.
- Meningococcal vaccine for bacterial meningitis is recommended for college students, military recruits and people who travel to certain parts of the world.
- Varicella vaccine for prevention of chickenpox. It should not be given to HIV-positive adults with CD4+T cell counts <200 cells/mm$^3$ or to pregnant women.

#### 4.4.3.2 Children

Children with *asymptomatic* HIV infection should be fully immunised. No vaccines are **contraindicated** in HIV-infected children who are asymptomatic. Children with *symptomatic* HIV infection should not receive BCG (Bacillus Calmette-Guérin, an anti-TB vaccine), OPV (oral polio vaccine), Rotavirus vaccine (RV) or measles vaccine.

The Expanded Programme on Immunisation in South Africa (EPI-SA) (National Institute for Communicable Diseases, 2016) recommends vaccination for HIV-infected children as follows:

- **BCG** anti-TB vaccine should be given to all HIV-infected babies at birth who do not show symptoms of HIV infection. It should under no circumstances be given to HIV-infected children or children of unknown HIV status who show symptoms consistent with HIV disease (see the Frequently Asked Question box on page 106). BCG should also not be given to a baby whose mother had TB. BCG immunisation gives up to 80% protection against the progression of TB infection to active TB disease. However, the main benefit of BCG is protection against the development of serious extra-pulmonary forms of TB such as TB meningitis and miliary TB in children. Babies born to mothers who are on anti-TB treatment or who have extensive resistant and multidrug-resistant (XDR and MDR) tuberculosis, should not receive BCG. They should be put on TB prophylaxis (IPT) and followed up for BCG later.
- The oral polio vaccine (OPV) should be given to all HIV-infected babies who do not show symptoms of HIV infection. OPV is made of live attenuated viruses and cannot be given to babies with depressed immune systems.
- DTaP-IPV-Hib-HBV vaccine provides prevention against diphtheria, tetanus, acellular pertussis, poliomyelitis, haemophilus influenza type B (Hib) and hepatitis B combined. All HIV-infected children (asymptomatic as well as symptomatic) should receive this vaccine. Note that the polio vaccine in this injectable format is made of inactivated polio virus and is therefore safe for use in symptomatic HIV-infected children.
- Rotavirus vaccine (RV) protects children from gastroenteritis caused by the rotavirus. Symptomatic HIV-infected children should not receive the rotavirus vaccine.
- The measles vaccine should be given to asymptomatic HIV-infected children and not to children who show symptoms of HIV infection.
- Pneumococcal conjugated vaccine (PCV) prevents pneumococcal infections. It can be given to all HIV-infected children (asymptomatic as well as symptomatic).
- Td vaccine (tetanus and reduced strength diphtheria vaccine) can be given to all HIV-infected children (asymptomatic as well as symptomatic).

**Glossary**

**Contraindicate** Suggest or indicate that a specific therapy (drugs or other treatment) should not be used in the diagnosed case.

**Note**

- BCG should be given at birth. It should not be given to children older than one year.
- OPV should be given at birth and again at six weeks. It should not be given to babies older than 10 weeks of age.
- DTaP-IPV/-Hib-HBV is given at six, 10 and 14 weeks and then again at 18 months of age.
- RV is given at six and 14 weeks of age. RV should not be given to children older than 24 weeks.
- Measles vaccine should be given at six and 12 months of age. The measles vaccine must not be administered with any other vaccine.
- PCV is given at six and 14 weeks and again at nine months.
- Td vaccine should be given at six years and again at 12 years.

- Tetanus toxoid vaccine (TT) or Td should be given after each trauma episode (unless there is proof that it was given in the preceding five years.) TT can be given to all children with HIV infection (asymptomatic as well as symptomatic).

There are no drug interactions between antiretroviral drugs and the vaccines discussed above. Children who are well controlled on ARV therapy can be vaccinated at the discretion of their physician.

### Enrichment: A change in the measles vaccination schedule

The measles vaccination product and schedule was changed in December 2015. The previously used product Rouvax® is no longer available and has been replaced by MeasBio®. MeasBio® must be administered at the age of six months and again at 12 months. (The Rouvax® measles vaccine was administered at nine and 18 months of age.) The MeasBio® measles vaccine may not be administered with any other vaccine. The schedule change (six and 12 months) allows the measles vaccine to be given as the only vaccine at the scheduled visit (National Institute for Communicable Diseases, 2016: 11).

### Frequently Asked Question

**Why should BCG, OPV, RV and measles vaccine not be given to symptomatic HIV-infected children?**

Some vaccines (like BCG, the oral polio vaccine, the rotavirus vaccine and the measles vaccine) are prepared from a weakened or attenuated form of the live virus or bacteria causing the infection. BCG, for example, is prepared from a weak form of the TB bacillus (*Mycobacterium tuberculosis*). If this weakened form of the TB bacillus is injected into a baby with an already weakened immune system, it can lead to very serious adverse effects associated with vaccines. The same goes for other vaccines made from live attenuated microorganisms.

## 4.5 Tuberculosis

Tuberculosis is the most serious and most common opportunistic infection in HIV-positive people, especially in sub-Saharan Africa. Between 50 and 60% of people who are HIV positive, and who get infected with TB, will develop active TB. The risk of active TB in an HIV-positive person is 10% per year compared to a lifetime risk of 10% in a healthy individual (National Department of Health, 2014: 8). Because of this well-established link between TB and HIV, it is vital that healthcare practitioners are well informed about TB and to recognise its symptoms when they see it.

### 4.5.1 Transmission of tuberculosis

A microorganism, the bacillus *Mycobacterium tuberculosis*, causes tuberculosis, which is an infectious disease. When people with pulmonary or respiratory tract TB sneeze, cough, speak or sing, they spray airborne particles (droplet nuclei) that

contain *M. tuberculosis*. These airborne particles enter the body of a susceptible person when he or she breathes in. In this way, TB is spread from one person to another. *M. tuberculosis* usually affects the lungs, but, using the bloodstream, the lymphatic system or the airways, it can spread from the lungs to almost any part of the body.

**Pulmonary TB** (in the lungs), which is the infectious form of TB, is also the most common form, occurring in over 80% of people who become infected with TB. Extra-pulmonary TB results from the spread of the disease to other areas, most commonly the pleura, lymph nodes, meninges (of the brain), spine, joints, genitourinary tract, intestines and pericardium (of the heart), kidneys, bones or abdomen. While TB in these sites may cause serious illness, the infected person is not likely to transmit the disease unless they also have TB of the lungs.

The possibility of *M. tuberculosis* being transmitted is determined by three factors:

- how many organisms are expelled into the air;
- what the concentration is of the organisms in the air (determined by the volume of the space and its ventilation determines this); and
- for how long an exposed person breathes the contaminated air.

A single cough can produce 3 000 TB droplet nuclei, while a solitary sneeze can release up to a million droplets. Yet, inhalation of between only 10 to 200 droplets is enough to cause infection (National Department of Health, 2014: 8). TB droplet nuclei are so tiny that air currents in any indoor space can keep them airborne for as long as four hours. The droplets are also minute enough to reach the alveolar spaces inside the lungs, where the nuclei replicate.

Healthcare practitioners should protect themselves by wearing tightly fitting masks that have a high filtration efficiency. They should also teach patients who have active TB to cover their mouths and noses when they cough or sneeze.

## 4.5.2 Primary and post-primary (secondary) TB

TB develops in two stages in the human body, namely primary and post-primary (or secondary) TB. The *primary stage of infection* occurs when an individual is exposed to TB bacilli for the first time. This usually occurs in childhood, but can also occur to a previously unexposed individual at any age. **Primary TB infection** is usually asymptomatic, and the immune system brings this original infection under control. In these circumstances, the only evidence of infection is a positive tuberculin skin test (TST) between four and five weeks after the person was infected. In contrast with most other infectious agents, the TB bacillus usually remains dormant or latent in the body for a number of years. The TB-infected person shows no symptoms of TB during this dormant phase of infection and he or she can also not infect others. Among those who do become infected, most (90%) will never become ill with TB. HIV of course changes this picture completely.

The *post-primary (or secondary) stage* of TB results from endogenous (from within) reactivation of latent infection, or from exogenous (from outside) re-infection. TB reactivation from within happens when the immunity of the host is suddenly weakened or compromised during the latent phase of infection. This can happen when a person is subject to continuous malnutrition, or when the immune system is suppressed, for example by HIV, stress, cancer or diabetes. The TB bacilli

**Glossary**

**Primary TB infection** The primary stage of TB infection occurs when a person is exposed to TB bacilli for the first time. A person usually does not show any symptoms of TB and the immune system controls the infection.

**Glossary**

**Post-primary TB** Also called secondary TB, this refers to re-infection with the TB bacilli. This can happen when a latent infection is reactivated (for example when the immune system is depressed) or when the person is re-infected by someone with active TB.

immediately begin to multiply and this multiplication leads to the second stage of the disease. In most cases, **post-primary TB** affects the lungs, but it can spread to almost any part of a person's body. Sputum smears are usually positive. If the person's body can recover from this illness, the TB bacilli once again revert to dormancy. Approximately one third of the world's population (including most South Africans) carry latent tuberculosis infection.

## 4.5.3 Symptoms of TB

The four main symptoms of pulmonary (lung) TB are (also see Table 4.3):
- persistent cough for two weeks or more (if the person is HIV-infected, cough of any duration);
- fever for more than two weeks;
- unexplained weight loss (more than 1.5 kg in a month); and
- drenching night sweats.

Healthcare practitioners should screen every patient for TB at every contact by asking questions about these four screening symptoms. If any ONE of these symptoms is present, the patient should be further investigated for TB. In addition, healthcare practitioners must know about the patient's background, because if the patient has had contact with someone who has TB, the chances of the patient being diagnosed with TB increases.

Other symptoms of tuberculosis are:
- sputum production which may occasionally be blood stained;
- loss of appetite, malaise, tiredness;
- shortness of breath and chest pains; and
- new palpable lymphadenopathy.

In children the presence of any three or more of the following features is suggestive of tuberculosis and should be further investigated:
- TB symptoms (cough, fever, failure to thrive, weight loss);
- physical signs suggestive of TB;
- positive tuberculin skin test (TST); and
- chest X-ray findings suggestive of TB.

## 4.5.4 Diagnostic tests for TB

Although there are many tests available to diagnose tuberculosis, only tests that are more generally used in sub-Saharan Africa are discussed here. These tests are:
- smear microscopy;
- culture methods; and
- molecular testing (PCR based assays).

The usefulness of the tuberculin skin test (TST) and chest X-rays as diagnostic tests of TB will also be discussed.

#### 4.5.4.1 Smear microscopy

One of the oldest tests to diagnose tuberculosis is a sputum examination for acid fast bacilli (AFB) through a microscope. There are two staining methods we can use to observe acid-fast bacilli: the Ziehl-Neelsen staining method or fluorescent auramine staining. These methods involve the spreading of a sputum specimen on a slide, staining by one of these methods and microscopic examination. Results of about 80% of smear tests are usually available within 48 hours. Positive results (i.e., acid-fast bacilli are detected) mean that the patient is has **smear-positive TB**. Sputum smear microscopy has a low sensitivity especially in HIV-positive individuals and children (and thus often show false negative results). It can also not determine **drug-resistance**.

#### 4.5.4.2 Culture methods

Culture methods are **more sensitive** than smear microscopy. As a result, they can detect a higher proportion of TB cases among people with TB symptoms. Culture involves the inoculation of a culture medium (e.g. solid medium or agar) with a sputum specimen, and incubation of the culture until growth of TB bacilli is either observed or not.

Culture, however, as a diagnostic technique is expensive. It is also slow, taking between four and six weeks of incubation before it shows either a positive or a negative reaction. Patients could be inappropriately treated during this waiting period, with drug-resistant strains continuing to spread, and resistance becoming amplified (National Department of Health, 2014).

Nonetheless, culture is an important diagnostic tool in HIV-positive patients with smear-negative pulmonary TB, diagnosis of difficult extra-pulmonary TB and diagnosing TB in children. Culture is also used for drug susceptibility testing, for example in people at high risk of drug-resistant TB.

#### 4.5.4.3 Molecular testing

Two different **PCR** technologies are available in South Africa for the diagnosis and management of tuberculosis:

- GeneXpert (GXP) is useful for rapidly diagnosing TB and for rapid screening of Rifampicin resistance.
- The Line Probe assay is useful for drug resistance confirmation and detects resistance to both Rifampicin and Isoniazid. The Line Probe assay provides rapid diagnosis of drug-resistant TB and results should be available within 48 hours in a laboratory and within seven days in health facilities.

The WHO recommends GeneXpert to replace smear microscopy as the first-line diagnostic test for TB and many countries in sub-Saharan Africa (including South Africa) already use it. The Xpert MTB/RIF rapid TB test, a fully-automated, cartridge-based diagnostic molecular test, uses the nucleic acid amplification technique (NAAT) to identify *Mycobacterium tuberculosis* DNA and resistance to rifampicin. The test is very easy to use and basically involves the transfer of liquefied sputum to a cartridge which is then loaded into the GeneXpert device for the assay. The results should be available within two hours in the laboratory and within 48 hours in healthcare facilities. An important advantage of the test is that it can simultaneously detect MTB and Rifampicin resistance from one specimen.

**Glossary**

**Smear-positive TB** Indicates a patient with active TB with large numbers of TB bacilli in the lungs. Such a person is likely to spread TB to other people.
**More sensitive** If one test is more sensitive than another test, it means that the more sensitive test is more likely to give a positive diagnosis than the less sensitive test.

**Glossary**

**PCR** Polymerase chain reaction, or PCR, is a laboratory technique used to make multiple copies of a segment of DNA. The PCR is a very sensitive and fast method to detect microbial pathogens in clinical specimens such as a blood sample. It is, for example, used to diagnose HIV infection and tuberculosis.

**Requirements for smear microscopy, culture and GeneXpert**

- Smear microscopy requires 10 000 TB bacilli/ml of sputum for a positive result.
- Culture requires only 10–100 TB bacilli/ml of sputum for a positive result.
- GeneXpert requires 130 TB bacilli/ml of sputum for a positive result.

(National Department of Health, 2014: 21.)

**Note**

A positive TST test indicates that a person was in contact with a TB patient and is therefore *infected* with TB, but it does not necessarily mean that the person has *active* TB disease. The bacilli can be dormant and the person healthy.

TB is the most common opportunistic disease to attack people with HIV infection in Africa. However, not all people with TB are co-infected with HIV. It is dangerous to assume this connection between TB and HIV because it can easily stigmatise people with TB and drive individuals with TB symptoms underground. People with TB may fear that others will say they 'have Aids' and so they might keep their symptoms secret, not seek medical help, spread the infection further into the community and die.

The Xpert MTB/RIF test can only be used for diagnosis and not for monitoring treatment, as it cannot differentiate between live and dead bacilli. A small proportion of Rifampicin resistance detected by the test may not correlate with physiological resistance, leading to discordance between Xpert and DST results or clinical outcome (National Department of Health, 2014: 23.) Xpert MTB/RIF is a more sensitive test than smear microscopy. It is therefore possible for a TB patient to be Xpert MTB positive but smear negative (see box below).

### 4.5.4.4 Tuberculin skin test

The tuberculin skin test (TST) is the most commonly used test for identifying previous infection with *M. tuberculosis*. A positive reaction on this test does not distinguish between *latent* infection and *active* tuberculosis. The test indicates hypersensitivity to proteins of the TB bacillus, as a result of either infection with *M. tuberculosis* or as induced by BCG vaccination. The tuberculin skin test is therefore not a good diagnostic indicator of TB – especially in adults in communities where TB is common. Tuberculin skin tests should, for example, not be used in South Africa (and other African countries) to diagnose TB, because most people living in Africa may have been exposed to TB and may therefore test positive on tuberculin skin tests. In the South African mines, for instance, 97% of mineworkers test positive on tuberculin skin tests because of previous exposure to TB bacilli. A negative tuberculin skin test does not automatically eliminate TB.

A strongly positive tuberculin skin test >5mm in a child aged under five years signals recent infection, which is a risk factor for progression to disease. If other factors are present, such as contact with a TB patient, signs and symptoms of TB and X-ray changes, the child should be further investigated and treated with TB medications. A negative tuberculin skin test, however, does not eliminate the possibility of TB in children. Various conditions, such as HIV infection, malnutrition, severe viral infections (e.g. measles or chickenpox), cancer, immunosuppressive drugs (e.g. steroids) or severe disseminated TB, may suppress the tuberculin test and provide a false negative result.

## Enrichment: How to do a tuberculin skin test and how to interpret the results

The YouTube video shows you how to do a tuberculin skin test, how to read the test, how to measure the induration and how to interpret the results. https://www.youtube.com/watch?v=bR86G-itrTQ

An induration looks like this:


(Source: http://www.funscrape.com/Image/33362/Tuberculosis+Skin+Test.html)

A TST is positive when the diameter of the induration is ≥ 5 mm in a person who is HIV positive, malnourished or who has a severe illness. In all other cases (HIV negative), including previous BCG immunisation, a TST is assessed as positive when the diameter of the induration is ≥ 10 mm.

In a child under five years or an HIV-infected child of any age, a positive skin test indicates recent infection and is a risk factor for progression to disease. In the presence of other features such as a history of a TB contact, signs and symptoms of TB and chest X-ray changes, a positive tuberculin skin test is suggestive of TB disease in children.

Children under the age of five years, HIV-infected children of any age and HIV-infected adults, who have a positive skin test and no symptoms or signs of TB, should be put on TB prophylaxis for six months (National Department of Health, 2014).

#### 4.5.4.5 Chest X-rays

Chest X-rays are convenient and quick. However, relying on chest X-rays as the main method of confirming a diagnosis of TB is often questionable. Many diseases (such as PCP and viral and fungal diseases) imitate TB on chest X-rays, which can lead to an incorrect diagnosis. In addition, X-rays can show lung fibrosis or destruction because of old TB, thereby leading to over diagnosis and incorrect treatment of pulmonary TB. Chest X-rays are, however, necessary in patients who cannot produce sputum or who have negative Xpert results and are HIV-positive, or where extra pulmonary TB (e.g. pleural effusions and pericardial TB) is suspected. Chest X-ray findings must thus be interpreted in the light of the patient's history and clinical findings (National Department of Health, 2014: 25).

### 4.5.5 Treatment of TB

TB can be completely cured in almost every case of infection if the patient completes a course of antibiotic treatment. Active TB is usually treated with the simultaneous administration of a combination of drugs that destroy the infective organisms. The following drugs are used in different combinations to kill the TB bacilli and to cure TB:

- isoniazid (H);
- rifampicin (R);
- pyrazinamide (Z);
- ethambutol (E); and
- streptomycin (S).

Healthcare practitioners use standardised treatment protocols with fixed-dose combination (FDC) medicines to treat adults and children with TB. Because treatment or **drug regimens** change from time to time, the specific combinations, dosages and durations of anti-TB medications are not given here (see the box on specific treatment regimens for adults and children on the right).

The standard, first-line treatment regimen for all patients is made up of an intensive phase lasting two months and a continuation phase lasting four months.

**Specific treatment regimens for adults and children**

For specific treatment regimens for adults and children, see the South African National TB Management Guidelines (the most recent version available). You can either search for the information on the Internet, or you can request it from: The Director General, Department of Health, Private Bag X828, Pretoria, 0001.

**Glossary**

**Drug regimen** A course, schedule, plan or routine of therapy describing what medications a patient should take and how often.

The fixed-dose combination tablets (RHZE) that is used during the intensive phase to kill the tubercle bacilli rapidly, consists of the four drugs:

- isoniazid (H);
- rifampicin (R);
- pyrazinamide (Z); and
- ethambutol (E).

Within about 10 to 14 days after starting treatment, patients become less infectious and their symptoms decrease. In the continuation phase, fixed-dose combinations of two drugs (isoniazid and rifampicin or RH) are used over a period of four months. These drugs eliminate the remaining bacilli and prevent any subsequent relapse. The fixed-dose combination of drugs should be taken for seven days a week for the full period of treatment (six months) (National Department of Health, 2014: 41).

The treatment of extra-pulmonary tuberculosis is the same as for pulmonary disease. In cases of severe or complicated disease (e.g. meningitis, TB in the bones or miliary TB), it may be necessary to extend treatment to nine months (two months' intensive treatment and seven months for the continuation phase).

### Enrichment: More information on tuberculosis

- If you need more information on tuberculosis, download the following document: Managing TB in A New Era of Diagnostics, Version 3, 2016 at: http://www.auruminstitute.org/index.php?option=com_phocadownload&view=category&id=3&Itemid=263
- Download the 'TB Clinical Guide' app on your smartphone.

## 4.5.6 TB and HIV

An HIV-infected person with a deficient immune system has a much greater risk of developing TB or of having a latent infection reactivated. In addition, the mortality rate from TB is significantly higher in people who are co-infected with HIV. Furthermore, tuberculosis often causes the number of CD4+T cells to reduce while it simultaneously increases the infected person's viral load, which can accelerate the progress of HIV infection to Aids. HIV-infected people also have a much greater chance of developing extra-pulmonary TB and disseminated (or miliary) TB which comes from the widespread blood-borne distribution of TB bacilli. TB is also more difficult to diagnose in HIV-infected people as immunosuppression progresses. HIV-infected people with a low CD4+T cell count may not be able to mount an immune response to a tuberculin skin test, so the skin test will give a false negative result. Sputum smears may also be negative and chest X-rays can be unreliable. Such false results lead to non-diagnosis, non-treatment and death.

HIV-infected people are treated for TB in exactly the same way as HIV-uninfected people with TB. All TB/HIV co-infected patients require antiretroviral therapy irrespective of CD4+T cell count. Antiretroviral treatment is determined by whether the patient develops TB whilst on ART or whether the patient presents with TB before commencing ART.

See Chapter 6 on p. 159 for more about TB and ART.

### 4.5.7 Side effects of TB medicines

All TB patients should be monitored for side effects of the medication, and patients and their family should be educated on how to recognise the symptoms of the common side effects of TB medicines and to report them as soon as they develop. Healthcare practitioners must ask patients about the symptoms listed below at every follow-up visit:

- burning, numbness and tingling sensation in the feet;
- joint pains;
- anorexia;
- nausea;
- abdominal pain;
- skin rash with/without itching;
- changes in the colour of urine;
- impaired vision;
- yellowing of eyes; and
- confusion.

While the clinic can treat minor side effects symptomatically, it must refer patients with major side effects to a hospital immediately.

### 4.5.8 Adherence to treatment

Tuberculosis treatment can only be successful if patients adhere to the treatment by taking a complete and uninterrupted course of the appropriate drug therapy. This means taking every dose of medication, seven days a week for the full prescribed period. Patients, their families and the community as a whole face very serious consequences if patients do not finish their prescribed treatment as required. These consequences include the following (National Department of Health, 2014: 51):

- prolonged illness and disability for the patient;
- continued TB transmission in the community because of the infectivity of the patient;
- development of drug-resistant TB; and
- the possibility of death.

Tuberculosis is a complex disease that has biological, economic, personal and cultural implications for the patient. Healthcare practitioners should give consideration to the many factors that can adversely influence treatment outcomes and support patients to adhere. The directly observed treatment (DOT or **DOTS**) strategy should be implemented in clinics, workplaces and communities to enhance compliance with TB treatment. The DOT strategy uses treatment supporters to watch TB patients swallow each dose of medicine for the complete required treatment period in a sensitive way that supports the patient's needs. This close monitoring and supervision of patients helps to ensure that they comply with their treatment. It also functions to assist in the early detection of adverse side effects resulting from the medication. The treatment supporter can be a healthcare practitioner, a trained community health or workplace worker, a family member or friend, or anyone that the patient trusts. Apart from motivating patients to take their medication, treatment supporters also remind patients to get their medication

**Glossary**

**DOTS** DOTS (directly observed treatment short course) is a strategy to help patients adhere to medications such as anti-tuberculosis medication. The DOTS strategy uses patient observers to watch patients (such as TB patients) swallow each dose of medicine, for the complete treatment period. Read more about the effectiveness of DOT on the next page.

Adherence to treatment (TB and HIV) is discussed in more detail in Chapter 6.

from the clinic in time, to plan for when they go on holiday and to make sure that they never run out of TB medication. Adherence counsellors should also be appointed to provide structured education and counselling to patients and to assist with specific adherence problems.

## Enrichment: Does directly observed therapy (DOT) really work?

Karumbi and Garner (2015) evaluated DOT compared to self-administered therapy in people on TB treatment or on TB prophylaxis (to prevent active disease). They also compared the effects of different forms of DOT (DOT at home versus DOT in a health facility). They did a systematic review of 11 trials with 5 662 participants from various countries, including South Africa. DOT was performed by various people, including nurses, community health workers, family members and former TB patients. The authors found that TB cure was low with self-administration across all studies (41% to 67%) and direct observation DID NOT provide a solution to poor adherence to TB treatment. DOT also did not improve treatment completion when compared to self-treatment. There was also little or no difference in cure or treatment completion when DOT at home by family members or community health workers was compared to DOT at a health facility.

Karumbi and Garner (2015) concluded that DOT did not provide a solution to poor adherence in TB treatment. They suggested that policymakers should reconsider strategies that depend on direct observation, given the large resource and cost implications of DOT.

### 4.5.9 Drug-resistant tuberculosis

The *M. tuberculosis* bacilli have developed resistance against various anti-tuberculosis drugs, which means that the standard anti-tuberculosis drugs can no longer be used for patients who are infected with resistant strains of the bacilli. These resistant strains are transmitted to other susceptible people who inhale the resistant bacilli. The standard TB drugs will also not work for them. We are currently dealing with various categories of drug-resistant TB, including the very serious **extensive drug resistant TB** (XDR-TB) (See Table 4.4).

Multidrug-resistant tuberculosis is a problem created by people because it is mainly the result of human error, for example patient non-adherence, stock-outs due to bad management of drug supply, prescription errors, insufficient counselling and support of patients, and inadequate contact tracing and follow-up of MDR cases.

**Table 4.4** Drug-resistant TB categories and definitions

| Drug-resistant TB category | Definition |
|---|---|
| Rifampicin resistant TB (RR-TB) | Resistance to rifampicin, with or without resistance to other TB medicines. This maybe mono-, poly-, multi- or extensive drug resistance. |

*continued*

| Drug-resistant TB category | Definition |
|---|---|
| Multidrug-resistant TB (MDR-TB) | Resistance to at least both rifampicin and isoniazid. |
| Extensive drug-resistant TB (XDR-TB) | Resistance to any fluoroquinolone (a second-line drug) and to at least one of the three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug-resistance). |
| Mono-resistant TB | Resistance to one of the first-line TB medicines (rifampicin, isoniazid, pyrazinamide or ethmbutol). |
| Polydrug-resistant TB | Resistance to more than one first-line TB medicines. This excludes resistance to both rifampicin and isoniazid. |

(Source: National Department of Health, 2014: 75)

The time to diagnosis of RR-TB and MDR-TB has been greatly reduced with the introduction of rapid diagnostic tools (Xpert MTB/RIF). It is however always important to assess the clinical condition of the patient and not to rely only on a laboratory test. If a laboratory test is inconsistent with the clinical data, the test should be repeated.

Patients with MDR-TB should be referred to MDR-TB treatment initiation sites for standardised MDR-TB treatment. MDR-TB patients are hospitalised until they are confirmed as being non-infectious, with further outpatient management and counselling.

Extensive drug-resistant TB (XDR-TB) is enormously difficult and very expensive to treat because it is resistant to most, if not all, drugs available for treating the infection. The mortality rates of XDR-TB are very high, at over 90%. The only viable way to control XDR-TB is through prevention. According to Churchyard and Corbett (2010: 464) at least half of the MDR-TB cases (including XDR-TB) in South Africa are thought to be due to nosocomial transmission (transmission in healthcare facilities). This highlights the need for strict tuberculosis infection control measures in hospitals and other facilities. Like regular tuberculosis, MDR-TB (including XDR-TB) is spread through the air (airborne) by, for example, sneezing or coughing. As with regular TB, not all people who inhale the MDR-TB bacilli will become infected. It is estimated that one MDR-TB case could infect 20 people, but only two would develop active TB.

## Frequently Asked Questions

### XDR-TB: Where did it start?

Extensive drug-resistant TB (or XDR-TB) was first diagnosed in Tugella Ferry, a rural town in KwaZulu-Natal in 2005. Of the 53 patients infected with XDR-TB bacilli, 52 died on average 16 days after diagnosis. Patients who were HIV infected and on ARVs also died. By October 2006, over 200 XDR-TB cases were diagnosed in Tugella Ferry – the highest number at any single hospital on the planet (Bateman, 2015: 18). This number rose to 500 cases in 2009, with 98% of those patients being HIV positive. The crisis at Tugella Ferry gave rise to the first MDR hospital in Greytown, KwaZulu-Natal.

**What happens if a patient with MDR-TB or XDR-TB refuses treatment or hospitalisation?**

According to Section 7 of the National Health Act 61 of 2003, a health service may not be provided to a user without the user's informed consent or without the informed consent of family or a designated person in cases where the patient is not in a state to make a decision. In the case of MDR-TB and XDR-TB, it is important for patients to be treated with anti-TB drugs and/or to be hospitalised, not only to protect the patient but also to protect the community. So what happens if a patient with drug-resistant TB refuses treatment or hospitalisation? The patient and family should be counselled about the importance of treatment and/or hospitalisation and their concerns should be addressed. Patients should understand the implications of not taking the treatment on their health and on that of others. If necessary, the patient should be referred to a psychologist and social worker, and the district coordinator should be informed about the situation. If the patient or family still refuses treatment or hospitalisation, the facility manager may approach the local Magistrates office to obtain a court order to enforce treatment and/or hospitalisation. Section 7 of the National Health Act 61 of 2003 makes provision for forcibly treating patients if the failure to treat the person or group of people, which includes the user, could result in a serious risk to public health.

## 4.6 Sexually transmitted infections

Although sexually transmitted infections (STIs) are not opportunistic infections, their strong association with HIV makes it necessary to discuss them here. Sexually transmitted infections constitute a major public health problem in southern Africa, and South Africa has one of the highest STI rates in the world.

People with STIs – especially those with genital ulcers (e.g. in patients with chancroid, syphilis and herpes) are especially susceptible to HIV infection. The concentration (number) of HIV is also very high in genital discharges and secretions, which are increased by STIs. Abnormal discharges result in inflammation of the genital tract causing the migration of millions of T lymphocytes and macrophages to the site of the infection. As we mentioned earlier, these cells have special receptors on their surfaces to which HIV attach. In addition, HIV infection is able to change the natural history of other STIs and may make them more severe and difficult to treat. The probability of HIV transmission is generally greater when the STIs are symptomatic than when they are asymptomatic.

Most non-viral STIs are curable and preventable. It is therefore important for healthcare practitioners to identify people with STIs, to treat them, and to refer them for HIV testing after counselling.

### Enrichment: Condoms and sexually transmitted infections

When used consistently and correctly, latex condoms are very effective in preventing the transmission of HIV. In addition, using them correctly and consistently can reduce the risk of transmission of gonorrhoea, chlamydia and trichomoniasis.

Furthermore, they can assist in the reduction of the risk of transmission of genital herpes, syphilis, chancroid and HPV (human papilloma virus), but only when the condom covers and protects the infected areas. Latex condom use has also been linked to a reduction in the risk of HPV-associated diseases, for example cervical cancer.

### 4.6.1 Diagnostic versus syndromic management of STIs

The ideal approach in the management of STIs is to establish a definitive diagnosis of the STI by identifying the causing organism, and to treat the infection with absolute precision. This approach is called the *diagnostic approach*. The diagnostic approach is very difficult to follow in southern Africa because of its dependence on laboratory support. Laboratories with sophisticated techniques and facilities are rarely available in remote or rural areas. Waiting for laboratory results to confirm a diagnosis also delays the test results. Because it is often not possible for patients to return for test results at a later stage, the STI goes untreated and the danger of infecting sex partners remains.

A more practical alternative for the management of STIs in Africa is the *syndromic approach*. Syndromic management of STIs involves recognising patient symptoms and clinical signs (or a syndrome) and prescribing treatment for the major causes of that syndrome. A syndrome can be defined as a combination of symptoms or complaints. The syndromic approach enables healthcare practitioners who lack specialised skills and access to sophisticated laboratory tests to treat most symptomatic infections effectively during a patient's first clinic visit.

The following are the most important STI-related syndromes discussed in the STI Management Guidelines (National Department of Health, 2015b):

- vaginal discharge syndrome (VDS);
- lower abdominal pain (LAP);
- male urethritis syndrome (MUS);
- scrotal swelling (SSW);
- genital ulcer syndrome (GUS);
- bubo; and
- balanitis/balanoposthitis (BAL)

**Syndromic management of STIs** offers several advantages: it is easy to use; it is inexpensive; it does not require highly trained STI specialists; it does not require laboratory support; and it allows treatment of the infection at the time of the first visit with no delays or need for a return visit. The treatment recommended covers the whole range of infections known to cause the syndrome, and the success rates are high. For example, if a certain syndrome is known to be caused by either gonorrhoea or chlamydia, the syndromic approach requires medications that will treat both conditions. A disadvantage of the syndromic approach is overtreatment of patients, who may receive more drugs than are actually necessary. This approach also does not address the problem of people with asymptomatic infection who do not come for treatment.

**STI screening**

STI screening should be done at all healthcare visits. It is possible to prevent STIs and many can be treated. However, early access to care is important because it helps to prevent further transmission between partners or from a mother to her child. It also decreases the risk of STI-related complications. STI screening should include the following three questions of all persons aged 15–49 years, regardless of clinical presentation (National Department of Health, 2015b: 4):

- Do you have any genital discharge?
- Do you have any genital ulcers?
- Has/have your partner(s) been treated for an STI in the last eight weeks?

## Enrichment: Sexually Transmitted Infections Management Guidelines

The discussion that follows will not deal in depth with treatment regimens, because these are changed from time to time. Consult the Sexually Transmitted Infections Management Guidelines (2015: 6 – 12) or later versions) for more detail. This document can be downloaded from: http://www.sahivsoc.org/upload/documents/STIguidelines-1-28-15(LC).pdf

**Treatment of vaginal discharge syndrome**

Vaginal discharge syndrome is treated with a combination of antibiotics to treat for gonorrhoea, chlamydia, trichomoniasis and bacterial vaginosis. Topical anti-yeast medication is used to treat candidiasis if the patient is also complaining of vulval itching and/or curd- or cheese-like discharge. (See Sexually Transmitted Infections Management Guidelines, 2015 (or later versions) for details on treatment.)

## 4.6.2 Vaginal discharge syndrome (VDS)

Vaginal discharge is usually caused by STIs such as gonorrhoea, chlamydia, trichomoniasis, genital candidiasis and bacterial vaginosis. Here we look at trichomoniasis, genital candidiasis and bacterial vaginosis.

### 4.6.2.1 Trichomoniasis

Trichomoniasis in women produces vaginitis and cystitis (bladder infection), although to a lesser extent. If the infection is mild, only a slight discharge may be noticed. If it is extremely severe or acute, patients may complain of a profuse, thin, offensive-smelling white, yellow or yellow-green discharge which sometimes looks frothy. When more closely examined, acute inflammation of the vulva and inner thighs is often visible and the wall of the vagina walls and the cervix are usually covered in a thin discharge. The mucous surfaces may be observed to be extremely red after the discharge has been removed.

### 4.6.2.2 Genital candidiasis

Genital candidiasis (thrush) usually occurs in women and manifests as infections of the vagina and vulva. Genital candidiasis is often found in association with HIV infection. The symptoms in women are irritation of the vulva and vaginal discharge, but many women may be symptom-free. The discharge is usually scant and watery, but it can be copious, thick and white (like cottage cheese) in severe cases. The vulva may be red and swollen and it may have cracks (fissures).

### 4.6.2.3 Bacterial vaginosis

One of the most important causes of vaginal discharge is bacterial vaginosis or non-specific vaginitis. It is shown by a grey, vaginal discharge that is sticky, homogeneous and, usually, bad-smelling. Bacterial vaginosis is not associated with itchiness (pruritus), painful urination (dysuria) or painful sexual intercourse (dyspareunia). The main complaint is the discharge itself, which often is copious and is usually described as having a fishy odour. Women with discharge from the vagina sometimes also show symptoms of pelvic inflammatory disease or PID (see Lower abdominal pain below).

## 4.6.3 Lower abdominal pain (LAP)

The spread of microorganisms from the vagina and cervix to the uterus, fallopian tubes and pelvic organs causes lower abdominal pain. This syndrome is often

caused by gonorrhoea, chlamydia or anaerobes. It is characterised by severe lower abdominal pain and a typical gait, which includes slow walking and grasping of the lower abdomen. The patient often has a bad-smelling vaginal discharge and a high temperature (fever). A gynaecological history should be taken to exclude pregnancy, missed period, recent delivery and termination of pregnancy or miscarriage – in which cases the woman should be referred for gynaecological or surgical assessment.

**Treatment of lower abdominal pain syndrome**

Lower abdominal pain syndrome is usually treated with a combination of antibiotics used for the treatment of gonorrhoea, chlamydia and anaerobes. If vaginal discharge is also present, refer to the treatment protocol for vaginal discharge syndrome. HIV testing should be emphasised.

### 4.6.4 Male urethritis syndrome (MUS)

The common causes of male urethritis are gonorrhoea and chlamydia (or non-gonococcal urethritis). Patients with urethritis complain of urethral discharge (or discharge from the penis) or dysuria (painful or difficult urination). In most cases, the discharge is an abnormal, yellow, white or greenish colour. It is also often profuse and purulent (containing pus). Rectal gonococcal infection is common in men who have sex with men, and it may present with rectal discharge and a burning pain in the rectum. Gonococcal pharyngitis (throat infection) often occurs in both sexes after oral-genital contact (oral sex). Although candidiasis usually occurs in women, it can be found in men, particularly men who have not been circumcised. It often occurs in men with HIV-infection. Typically, both the foreskin and the area underneath it, are very red and sore. In some cases, there is a yellow discharge under the foreskin. In addition, the skin of the penis and scrotum, as well as the skin around the anus, may become red, itchy and quite sore.

**Treatment of male urethritis syndrome**

Male urethritis syndrome is treated with a combination of antibiotics for gonorrhoea and non-gonococcal urethritis. HIV testing, as well as tracing and treatment of the partner(s), is important in male urethritis syndrome.

### 4.6.5 Scrotal swelling (SSW)

Men with STIs often report having acute pain in the testes, accompanied by scrotal swelling and tenderness (epididymo-orchitis). This is usually caused by gonorrhoea and chlamydia (or non-gonococcal urethritis). Apart from treatment with antibiotics, scrotal support and pain relief should also be offered if necessary. The patient should be referred for HIV testing. If torsion (testes rotated and elevated) is expected or if the person has other non-tender swelling that is not the result of sexual activity, he should be referred to a surgeon urgently.

**Treatment of scrotal swelling**

Scrotal swelling is treated with a combination of antibiotics used to treat gonorrhoea and non-gonococcal urethritis.

### 4.6.6 Genital ulcer syndrome (GUS)

A thorough and proper understanding of genital ulcer disease is vital to decrease the incidence of HIV because (as we noted earlier) open lesions and ulcers contribute to the spread of HIV infection. Genital sores or ulcers can be with or without pain. Most genital ulcers are caused by syphilis, genital herpes and chancroid. Open lesions and ulcers are most commonly found on the glans penis and penile shaft in men, and on the labia, vulva and vaginal walls or cervix in women. Anal and rectal syphilis ulcers are also commonly seen in men who have sex with men.

Genital ulcers are usually accompanied by enlarged lymph nodes in the groin area. These enlarged nodes can become very painful and precipitate pustule formation in some cases of chancroid. In Africa, chancroid (followed by syphilis) is the most common cause of genital ulceration. Chancroid has also been found to be a major co-factor in the heterosexual transmission of HIV in developing countries. It is therefore extremely important to be able to diagnose and treat chancroid as

**Treatment of genital ulcers**

Genital ulcers are usually treated with a combination of antibiotics plus aciclovir for genital herpes. Individuals often present with STIs that cause genital ulcerations or sores as well as genital discharge. Such cases should be treated with a combination of medication.

accurately and as quickly as possible. The patient should also be examined for Bubo (see next section) and HIV testing should be emphasised.

## Enrichment: Genital herpes

Herpes simplex (genital herpes) is very common, especially in individuals with HIV infection. The herpes simplex virus causes herpes. The infection is lifelong, it is recurrent, and ulcers will reappear periodically throughout an infected person's life. It recurs most frequently when a person is ill or is suffering from stress, or around the time of menstruation. Herpes simplex presents with small blister-like sores that commonly blend to form larger sores. Genital herpes is extremely painful, but it usually settles after about two weeks. In patients with HIV infection, herpes may occur more frequently, be more severe and painful, and remain active for longer. The 2012 Antenatal HIV and HSV Survey showed an exceptionally high prevalence of HSV-2 in HIV-positive women in comparison with HIV-negative women, with 89.1% of HSV-2 among HIV-positive women compared to 42.5% among HIV-negative women. HSV-2 status was therefore a strong indicator of HIV status among the antenatal women who participated in the study (National Department of Health, 2012: 6).

While herpes simplex (which is caused by a virus) cannot be treated with antibiotics, genital ulcers can be suppressed with aciclovir. Lesions should be kept clean and dry, using talcum powder and pain relief should be offered if necessary.

### 4.6.7 Bubo

**Treatment of bubo**

Bubo is treated with a combination of antibiotics.

Inguinal bubo is a tender, enlarged lymph node in the groin area, resulting from absorption of infective material. It is caused by early syphilis or lymphogranuloma venereum and the patient usually complains of swollen lymph nodes which can be very painful. Hernia or femoral aneurysm should be excluded before making a diagnosis of Bubo. Apart from treatment with antibiotics, the lymph node can be aspirated in a sterile manner if bubo is fluctuant. The process could be repeated every 72 hours as necessary. HIV testing should be emphasised.

### 4.6.8 Balanitis/balanoposthitis (BAL)

**Treatment of balanitis**

An anti-fungal cream should be applied 12 hourly for seven days. If there is a copious amount of watery pus beneath the foreskin, an antibiotic should be added (usually a single-dose injection).

See STI Management Guidelines, 2015b: 19 for treatment guidelines (National Department of Health, 2015b).

Balanitis is an infection of the glans penis characterised by thrush on the foreskin and head of the penis. It is caused by candidiasis. If a patient complains of an itchy glans and/or foreskin of the penis (without an ulcer or urethral discharge) and soreness, the condition should be managed by retracting the foreskin and washing the area with a water-filled syringe (soap should be avoided while the area is inflamed). Anti-fungal cream and antibiotics should be used as necessary. If the foreskin cannot be retracted, the patient should be referred to a surgeon. All patients with Balanitis should be offered circumcision.

More than one STI syndrome can occur, for example MUS (male urethritis syndrome) plus SSW (scrotal swelling) and it should be treated accordingly. Table 4.5 on pages 124–126 gives a summary of all the major sexually transmitted infections.

## Frequently Asked Questions

### What are human papilloma viruses (HPV)?

Human papilloma viruses are DNA-based viruses that infect the skin and mucous membranes. There are more than 100 different types of HPVs and some of them cause benign (not malignant) skin warts or papillomas that can be transmitted by casual skin-to-skin contact. A separate group of about 30 HPVs is transmitted sexually, and some of them can cause **genital warts**. Approximately a dozen HPVs that are sexually transmitted can result in the development of cancer of the cervix, as well as in cancer of the vulva, anus and penis. HPV infection is a required factor in the development of almost all cases of cervical cancer. A cervical pap smear is used to diagnose HPV infection. If a woman is infected with HPV, the pap smear will show cellular abnormalities. Pre-cancerous lesions will then be targeted and removed surgically, before the development of invasive cervical cancer.

### Is there a vaccine against HPV?

Two HPV vaccines, Gardasil® and Cervarix®, were approved for use by the FDA (Food and Drug Administration) in the USA in 2006 and 2007 and by the Medicines Control Council (MCC) of South Africa in 2008. They are effective only when used as prophylaxis and should therefore be administered before exposure to HPV. The ideal age for vaccination is before having sex for the very first time (sexual debut). Both vaccines can be administered to girls from nine years of age. Gardasil® and Cervarix® are effective as protection against at least 70% of cervical cancers. Gardasil® also protects against 90% of genital warts caused by HPV and is therefore also approved for boys nine years and older (Richter, 2015). Gardasil® can be administered to girls and boys aged 9 to 13 years and Cervarix® to girls aged 9 to 14 years. In April 2014 the National Department of Health in South African implemented a school-based HPV vaccination programme for all girls aged nine years and older in Grade 4 public schools. Internationally, Cervarix® is approved for use in women up to the age of 45 years, and Gardasil® up to the age of 45 years in women and 26 years in men. Although women already infected with a virus that is included in the vaccine will not benefit from that part of the vaccine, they could benefit from the other vaccine virus types in the vaccine. Because the vaccine does not protect women against all the HPV types, women are encouraged to continue to having regular pap smear testing after they have received the vaccine.

### What is a pap smear test and how often should it be done?

A **pap smear test** is a painless test where cells are taken from the cervix. The sample is then placed on a glass slide so that the cells can be examined under a microscope to look for abnormal cells indicating cervical cancer. The pap smear can also be used to test for HPV. The South African HPV Advisory Board recommends that women begin having pap smears when they become sexually active or turn 21 each year until the age of 30, and then every three years after the age of 30. All HIV-infected women in South Africa, whatever their age or antiretroviral therapy status, are allowed a free pap smear when they are diagnosed with HIV, if they have not had a pap smear in the previous 12

months. They can then also have a free pap smear every three years if normal, or earlier if not. At the time of writing (2016) no commercial tests are available to ascertain HPV infection in men.

### 4.6.9 General points in managing STIs

Apart from treating patients with STIs using a syndromic approach (or a diagnostic approach where possible), healthcare practitioners should also do the following:

- Make services accessible and user friendly. Integrate STI services with other primary care and HIV services, and try to provide clinic services at convenient times, for example during weekends and in the evenings.
- Avoid stigma, blame and negative attitudes towards patients. Treat the patient with **respect** and consideration for his or her dignity.
- Always be on the lookout for other STIs, and treat if present.
- Encourage the person to be tested for HIV.
- Counsel the person on compliance to medications and risk reduction.
- Counsel the person on safer sex practices and promote and provide condoms. Condoms should be used until the infection is fully healed, and thereafter to prevent re-infection.
- Sex partners should be notified and treated.
- Take blood for RPR and VDRL (syphilis tests).
- Encourage the patient to return for a follow-up visit, especially if treatment does not cure the infection.
- If the syndromic treatment fails, refer the patient to a skilled STI (sexual health) practitioner or a clinic for further investigation through the diagnostic approach (e.g. serological tests or swabs).

### 4.6.10 Failure of syndromic treatment

If syndromic treatment fails, the following should be considered:

- The medication may not have been taken properly and completely.
- The sexual partner may not have been treated, and the patient is being re-infected.
- The STI may be resistant to the medication the patient is taking.
- The patient may be immune-suppressed due to HIV infection, and therefore may need prolonged or more aggressive STI treatment.
- Herpes infection may have an unusual appearance, especially in the presence of HIV, or it may be secondarily infected. Also, remember that herpes does not respond to the usual syndromic protocols (because herpes is caused by a virus).

## 4.7 Conclusion

HIV attacks the immune system and, as the person's immune system becomes weaker, various infections and diseases may present themselves. You have learned more about these infections and diseases in this chapter, and you have also learned how these infections could be prevented or treated. But to manage HIV infection properly, it is imperative to diagnose it as early as possible. The diagnosis of HIV infection will be discussed in the next chapter.

## Test your understanding

1. What does seroconversion mean and how long after infection does seroconversion usually take place?
2. When is the HIV viral load at its highest?
3. Name the main symptoms of an HIV-infected person during each one of the four stages.
4. Describe the relationship between the viral load and the CD4+T cell count during the different stages of HIV infection.
5. Discuss three ways to prevent opportunistic infections.
6. List the main symptoms of pulmonary (lung) tuberculosis.
7. Discuss the two stages of TB development in the human body.
8. Illustrate the difference between treatment of TB and prevention of TB in patients with HIV infection.
9. Why do HIV and STIs often go hand-in-hand?

**Table 4.5** Sexually transmitted infections

| Infection | How do you get it? | Causing agent | How long before the disease manifests itself? | What are the symptoms? | How is it treated? | What are the effects of no treatment? |
|---|---|---|---|---|---|---|
| Candida (thrush, yeast) | Men: Sexual contact<br>Women: Frequently acquired infection from the bowel, where *Candida albicans* naturally occurs | Fungal infection caused by *C. albicans* | | Women: Thick, white discharge, swelling of vulva, painful and frequent urination, itching around the genitals<br>Men: Swelling, redness, itching of the penis. Can cause balinitis in men and, rarely, urethritis | Vaginal cream or pessaries | Extreme discomfort; babies may develop oral or genital thrush |
| Chancroid | Sexual contact | *Haemophilus ducreyi* | Less than one week | Multiple painful ulcerations erupting from intradermal abscesses<br>Ulcers bleed easily<br>Ulcers often confused with other STI ulcers | Antibiotics | Abscess formation of the lymph nodes<br>Inguinal ulceration |
| Chlamydia | Sexual contact | *Chlamydia trachomatis* | One to three weeks | Women: Pelvic pain, vaginal discharge, painful and frequent urination, bleeding after sexual intercourse (Sometimes no symptoms at all)<br>Men: Discharge from penis, painful urination, scrotal swelling (Sometimes no symptoms at all) | Antibiotics | Severe infection of reproductive organs<br>Men: Sterility<br>Women: LAP; tube pregnancy and infertility<br>Infection can be passed on to babies |
| Genital molluscum contagiosum (GMC) | Sexual and non-sexual transmission | Molluscum virus | Two weeks to six months | Papules on genital or other parts of the body (skin infection) | Tincture of iodine BP applied to core of lesions<br>ART strengthens the immune system to fight the virus | Secondary bacterial skin infections and severe symptoms |
| Genital warts | Sexual contact and skin-to-skin contact with genital warts | Human papilloma virus (HPV) | One to six months | Small, painless bumps grow on the genitalia, with slight itching or burning<br>They may be on the vulva, vaginal walls and cervix in women and on the urethra in men<br>Peri-anal and rectal warts often seen<br>There may be no outward signs<br>Determined with pap smear | Patient-applied therapy for external warts; can also be removed by burning, freezing and minor surgery<br>A vaccine is available to prevent HPV | Grow large and spread<br>Lead to cervical cancer<br>Infection can be passed on to babies |

*continued*

| Infection | How do you get it? | Causing agent | How long before the disease manifests itself? | What are the symptoms? | How is it treated? | What are the effects of no treatment? |
|---|---|---|---|---|---|---|
| Gonorrhoea (drip, clap, dose) | Sexual contact | *Neisseria gonorrhoeae* | One to ten days | Women: Most women have pelvic pain, painful urination, vaginal discharge or fever<br>Men: Painful urination, discharge or drip from penis or no symptoms at all | Antibiotics | Vaginal infection<br>Severe damage to reproductive organs may lead to infertility in women and sterility in men<br>Heart trouble; skin disease<br>Infection can be passed on to babies |
| Hepatitis B | Sexual contact, body fluids, e.g. blood, semen, vaginal fluid and saliva | Hepatitis B virus | Two to five months (average three months) | Stage 1: Flu, fatigue, weight loss, painful joints<br>Stage 2: Jaundice, skin and whites of eyes are yellow<br>Stage 3: Gradual recovery<br>Fatality rate varies: 1–10% | Adequate fluids, rest, nutrition; a vaccine can be given to prevent hepatitis B | Associated with liver cancer<br>Can lead to death<br>Infection can be passed on to babies |
| Genital herpes (blisters) | Sexual contact, with direct contact with sore (oro-genital or purely genital) | Herpes simplex virus | Two to 20 days (usually one week) | Onset: Itching or burning; fever, malaise, and painful lymph nodes with primary infections<br>Painful blisters break into open sores<br>Sores can be found on the mouth or sex organs | Once infected, the virus stays in body – no cure<br>Aciclovir may provide relief | Sores will go away without treatment, but often reappear when the person is ill or stressed. Infection can be passed on to babies |
| Neonatal conjunctivitis | Acquired from infected mother as the infant passes through the birth canal | Bacterial or viral, e.g. chlamydia, gonococcal | First month of life | Red eyes, thick pus and swelling of eyelids | Antibiotics: oral, IV, drops or ointments | Corneal ulcerations; blindness |
| Non-gonococcal urethritis (NGU) | Sexual contact | Number of causative organisms (usually no specific causative agent) | One to three weeks | Women: Frequent painful urination and a discharge<br>Men: Painful and frequent drip or discharge from penis, painful urination. Often symptom-free in men | Antibiotics | Infertility |
| Non-specific urethritis (NSU) | Sexual contact and can be caused by chlamydia | Depends on cause of NSU | | Men: Burning while urinating; discharge from the penis<br>Women: Few symptoms | Antibiotics | Severe infection of organs, infertility |

*continued*

| Infection | How do you get it? | Causing agent | How long before the disease manifests itself? | What are the symptoms? | How is it treated? | What are the effects of no treatment? |
|---|---|---|---|---|---|---|
| Pelvic inflammatory disease (PID) (also called LAP or lower abdominal pain) | Sexual contact, can be caused by gonorrhoea or chlamydia | Caused by ascending spread of microorganisms from vagina to pelvic organs. Mainly *N. gonorrhoeae* | | Fever, nausea, vomiting, low abdominal pain, pain during intercourse, pain during menstruation, profuse vaginal discharge, typical PID gait (slow walking, grasping of lower abdomen) | Antibiotics | Sterility, abscesses on tubes |
| **Pubic lice** (crabs) | Sexual contact, close physical contact Using the same clothing or bed | Infestation by the crab louse *(Phthirus pubis)* | Immediately | Infestation mostly confined to pubic and peri-anal areas, but might spread to thighs, chest, axillae, eyelashes and eyebrows. Never the scalp. Lice feed on blood. Chief symptom is itching due to bites. Crawling lice and small eggs (nits) on hair or clothing | Special shampoos or lotions. All clothing and bedding must be washed in hot, soapy water. Dead lice and nits are removed with fine-toothed comb | Skin irritation and secondary infections due to scratching |
| **Scabies** (itch) | Sexual contact, close physical non-sexual contact (families, schools, overcrowded conditions) | Parasitic mite, *Sarcoptes scabiei*, poverty and poor standards of hygiene contribute to spread | Four to six weeks symptom free after infection, but infectious to others | Itching at night. Red lines in the skin as the female mites burrow. Ulcers develop after scratching. Sites commonly affected are the genital area, lower abdomen, buttocks, inner thighs, finger webs, axillae, but rarely the head and neck | Special cream and preparations that should be applied to whole body, except head and neck. All clothing and bedding to be washed before applying. Repeat after three days | Spread all over body. Secondary infections as a result of scratching. Extremely severe manifestations of the disease may be seen in patients co-infected with HIV |
| Syphilis (the pox) | Sexual contact | *Treponema pallidum* | Stage 1: Nine to 90 days Stage 2: Three to six months Stage 3: Over two years after acquiring disease | Stage 1: A painless sore called a chancre Stage 2: Fever, headache, malaise, general rash, general lymphadenopathy Stage 3: Very ill. The cause is not easy to find. Late syphilis phase not infectious | Antibiotics (superficial lesions of early syphilis (Stages 1 and 2) are infectious; those of late syphilis are non-infectious) | Severe infection, infertility, skin diseases, arthritis, baby can be born blind, deaf or stillborn; heart, blood vessel and brain damage |
| Trichomoniasis (trich) | Sexual contact | *Trichomonas vaginalis*, which is a flagellate protozoan | One week | Women: Copious, thin, offensive white, yellow or greenish frothy discharge. Acute inflammation of vulva, perineum, inner thighs and itching around genitals. Sometimes cystitis. In many cases symptom-free Men: Urethritis and balanitis, but mostly symptom-free | Flagyl | Fever and infection of organs. Pass infection on to baby. Can cause prostatitis and very rarely, epididiymitis |

# Reference list


Aurum Institute & CDC/PEPFAR. 2015. *Managing HIV: A clinician's tool.* Johannesburg: Arum Institute.

Bateman, C. 2015. Tugela Ferry's extensively drug-resistant tuberculosis – 10 years on. *South African Medical Journal* 105(7): 517–20.

Churchyard, G., & Corbett, E. 2010. Tuberculosis and HIV. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.). (pp. 457–478). Cape Town: Cambridge.

Coovadia, H. 2010. Mother-to-child transmission (MTCT) of HIV-1. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 201–215). Cape Town: Cambridge University Press.

Date, A.A., Vitoria, M., Granich, R., Banda, M., Fox, M.Y., & Gilks, C. 2010. Implementation of co-trimoxazole prophylaxis and isoniazid preventive therapy for people living with HIV. *Bulletin of the World Health Organization*, 88(4): 253–259.

Karumbi, J., & Garner, P. 2015. Directly observed therapy for treating tuberculosis. *Cochrane Database Systematic Reviews* 29(5): CD003343. DOI: 10.1002/14651858.CD003343.pub4

Maartens, G. 2010. Prevention of opportunistic infections in adults. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 479–488). Cape Town: Cambridge University Press.

National Department of Health, South Africa. 2012. *The 2012 National Antenatal Sentinel HIV & Herpes Simplex Type-2 Prevalence Survey in South Africa.* Pretoria: National Department of Health.

National Department of Health, South Africa. 2014. *National Tuberculosis Management Guidelines.* Pretoria: National Department of Health.

National Department of Health, South Africa. 2015a. *National Consolidated Guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults.* Pretoria: Department of Health, South Africa.

National Department of Health, South Africa. 2015b. *Sexually Transmitted Infections Management Guidelines*, Pretoria: National Department of Health.

National Institute for Communicable Diseases. 2016. *Communicable Diseases Communiqué* 15(1). Retrieved on 28 August 2016 from: http://www.nicd.ac.za/assets/files/NICD%20Communicable%20Diseases%20Communique_Jan2016_final%20pdf.pdf

Richter, K. 2015. *Implementation of HPV vaccinations in South Africa.* Public Health Association of South Africa. Retrieved on: 19/10/2015 from https://www.phasa.org.za/implementation-hpv-vaccination-south-africa/

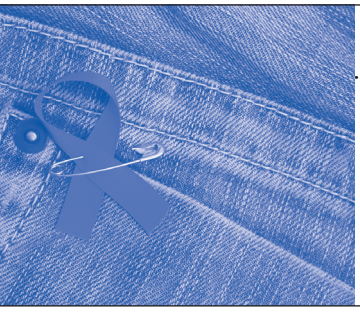
U.S. Department of Health and Human Services. 2016. *HIV and immunization.* Aids Info. Retrieved on: 23/10/2016 from https://aidsinfo.nih.gov/contentfiles/Recommended_Immunizations_FS_en.pdf

U.S. Department of Health and Human Services, Health Resources and Services Administration. 2014. *Guide for HIV/AIDS Clinical Care.* Rockville, MD: U.S. Department of Health and Human Services.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (p. 14). Cape Town: Nasionale Boekhandel Bpk.

World Health Organization (WHO). 2007. *WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-related Disease in Adults and Children.* Geneva: World Health Organization.

World Health Organization (WHO). 2015. *Guidelines on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV.* Geneva: World Health Organization.



# Chapter 5

# HIV tests

Alta van Dyk

### Definite signs of Raka's presence

*Then the men saw of his strength*
*by the signs in the bush:*
*this must be his work when the black buffalo bull ...*
*lies stiff in the morning on the footpath*
*where its bulk has cracked at the knees …*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- explain the difference between HIV-antibody tests and HI viral tests;
- counsel people about HIV tests and explain the implications of test results;
- explain to a client what is meant by the window period; and
- explain the testing algorithm to a mother whose baby (younger than 18 months) has been exposed to HIV.

## Chapter outline

- HIV testing as a diagnostic tool
- HIV antibody tests
- HIV virus tests
- HIV counselling and testing algorithms
  - Adolescents and adults
  - Children younger than 18 months
  - Children 18 months and older

After Montagnier discovered HIV in 1983 and Gallo demonstrated its propagation in cell culture, the great search for a test to diagnose HIV began. This effort was especially driven by blood banks, which urgently needed a test to screen blood. Gallo's laboratory played a huge role in the development of HIV diagnostic tests, and the first kits for antibody testing became available in April 1985. Later that year, commercially produced HIV diagnostic tests were licensed by the Food and Drug Administration (FDA) of the United States.

**Glossary**

**Diagnostic tool** A device (like a test) that can be used to establish the nature or the cause of a disease.

**Sensitivity of a test** The sensitivity of a test is that percentage of infected individuals who are detected by the test.

**Specificity of a test** The specificity of a test is that percentage of non-infected individuals who have a negative test result.

## 5.1 HIV testing as a diagnostic tool

The first commercially produced HIV diagnostic tests were designed on the ELISA (enzyme-linked immunosorbent assay) principle, which is the most widely used test for detecting viral antibodies in the blood. Earlier ELISA tests lacked specificity, which means that they frequently gave positive results for individuals who were not infected. However, major advances in the design of these tests have now improved them to a level of very high sensitivity and specificity. HIV testing as a **diagnostic tool** became much more sophisticated with the development of tests that can identify virus antigens or viral nucleic acids in the blood.

**Frequently Asked Question**

**What is meant by the 'sensitivity' and 'specificity' of tests?**

The two factors that determine the accuracy of a serological (blood) test are sensitivity and specificity. The **sensitivity of a test** is its ability to pick up very low levels of antibodies (its ability to detect HIV positivity and not give false negative results). The **specificity of a test** is its ability to disregard the presence of antibodies that are not specific to HIV. In other words, it can differentiate specific HIV antibodies from other cross-reacting non-specific antibodies (i.e. its ability to demonstrate HIV negativity and not give false positive results). Specificity and sensitivity are usually expressed as percentages.

### 5.1.1 Why test for HIV?

There are various reasons why HIV testing is carried out:

- to screen donated blood;
- to research the transmission patterns and prevalence of the virus;
- to diagnose HIV infection in individuals;
- to monitor the progress of the infection;
- to monitor responses to antiretroviral therapy (viral-load tests); and
- to detect drug failure.

Previously, the main purpose of HIV testing was to diagnose or confirm suspected HIV infection in people who experienced certain symptoms or diseases. Nowadays, it is recommended that people make routine use of HIV counselling and testing (HCT) services to find out their HIV status. It is hoped that people who know that they are sero-negative will be motivated to use preventive measures to prevent future infection, and that people who are sero-positive will apply prevention methods and access care, support and treatment.

### 5.1.2 Diagnostic approaches

There are two main approaches to diagnosing HIV:

- identification of the virus; and
- detection of an immune response to HIV.

### 5.1.2.1 Identification of the virus

Some tests can detect the p24 viral antigen in blood, while other tests can detect viral nucleic acids in the blood. Nucleic acid tests (also called NAT) can detect proviral DNA in the cells, or viral RNA in fluids.

### 5.1.2.2 Detection of an immune response to HIV

The immune system reacts in two ways on HIV infection, namely production of antibodies (a humoral reaction) and a cellular response including specific CD4+T cell responses or cytotoxic cell responses. Antibody tests are generally used to diagnose HIV infection. CD4+T cell and cytotoxic cell counts are not used for diagnostic purposes but to assess the health of the immune system.

**A combination test**

A combination test is also available which is based on the detection of HIV antibodies, as well as p24 virus antigens. We call these tests 'fourth generation' ELISA (EIA) tests and they are particularly useful for detecting early HIV infection with a window period of 16 days. Figure 5.1 illustrates all the HIV diagnostic tests, as well as their general uses. Refer to this figure while reading the next sections.

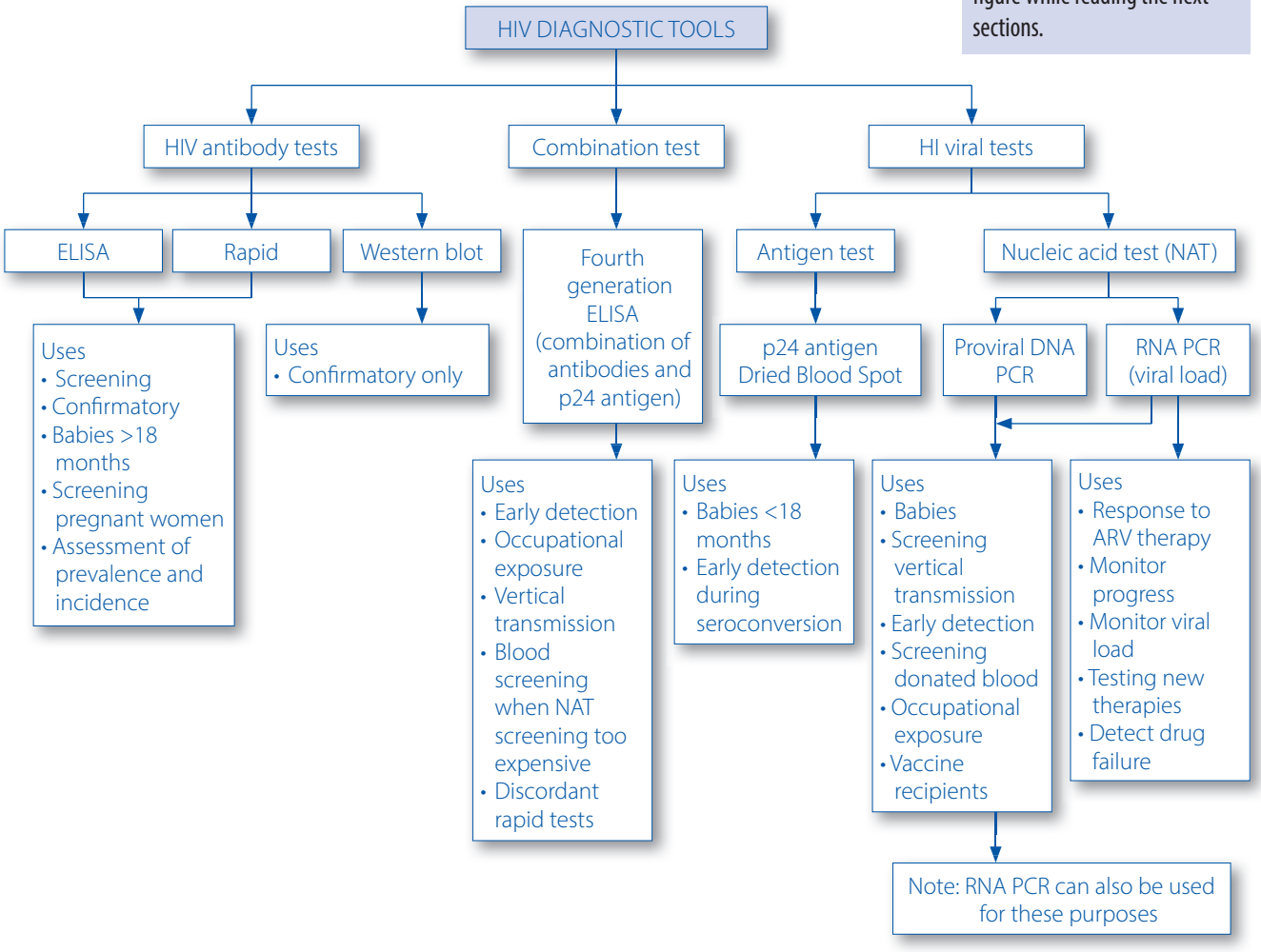



**Figure 5.1** HIV diagnostic tools and their uses

## 5.2 HIV-antibody tests

HIV-antibody tests are usually done on blood (whole blood, serum and plasma). However, HIV antibodies can also be detected in other body fluids such as saliva and urine. Some of the most well-known HIV-antibody tests are the Rapid HIV-antibody test, the ELISA (EIA) and the **Western Blot tests** (which is only used in some cases as confirmatory test).

HIV-antibody tests cannot trace the virus in the blood, but they react to the HIV antibodies that are formed when the immune system attempts to protect the body against the virus. An antibody test becomes positive only after the host (or HIV-infected person) has mounted an immune response, and has seroconverted. The ELISA antibody tests can detect antibodies to both HIV-1 and HIV-2, as well as antibodies to the known variants of HIV-1. The ELISA and Western Blot tests are done in a laboratory. The ELISA test is also available in a rapid format, which does not require laboratory facilities.

**Glossary**

**Western Blot test** A blood test that detects the antibodies to HIV infection. It is sometimes used to confirm an ELISA test that has produced a (HIV) positive result.

### 5.2.1 The ELISA antibody test

The ELISA HIV-antibody test is currently the most commonly used and popular HIV test. It is both inexpensive and widely available. In addition, it is reliable and highly sensitive, and produces hardly any **false negative results**. The latest generation ELISA tests has shortened the window period tremendously. While the first-generation ELISA tests took about 45 days to show positivity, third-generation tests can detect antibodies three weeks (approximately 22 days) after infection, while fourth-generation tests can detect antibodies after approximately 16 days.

An HIV-antibody positive test should always be confirmed by a second confirmatory test to exclude the occurrence of a **false positive result**. False positive results are rare if both the screening and confirmatory tests are positive. If the ELISA (or rapid) test results are negative and there is reason to believe that the person has been exposed to HIV, the test should be repeated within three to four weeks.

**Glossary**

**False negative result** A false negative result means that the patient is infected with HIV, but the test result is negative.
**False positive result** A false positive result means that the test result is positive, but the person is actually HIV negative.

**Frequently Asked Question**

**What is the window period?**

The window period is the period between HIV infection and the appearance of antibodies that can be detected by antibody tests (when antibody tests will give positive results). If we say that the window period for a third-generation ELISA antibody test is 22 days, it means that the test will only show positive after this period. If the test is conducted during the window period (i.e. before before 22 days are up), it could provide false negative results. This means that although the virus is present in the person's blood, the test is not able to detect any antibodies. The tests will indicate, incorrectly, that the person is not infected. An antibody test will become positive only after the host has mounted the initial immune response namely to develop antibodies. The window period is usually much shorter for tests that detect the presence of the virus itself. Virus tests do not have to wait for the immune system to form antibodies, but respond to the presence of the actual virus particles (antigens or nucleic acids). The individual is already infectious during the window period and so could unintentionally infect other people.

## 5.2.2 Rapid HIV-antibody tests

The ELISA tests are also available as rapid tests (or rapid assays). **Rapid HIV-antibody tests** can be performed outside a laboratory (in places such as clinics, consulting rooms, in the field during mass testing, or at the workplace), and the results are usually available within ten minutes. Body fluids used for rapid tests are whole blood, serum or oral fluid. Rapid HIV-antibody tests are easy to use (they involve a prick of the finger with a lancet), less invasive, not expensive, easily transported and can be stored at a whole range of temperatures (4°C to 30°C). The rapid tests are robust and very reliable if used correctly. The tests can be performed and read by non-laboratory personnel such as healthcare practitioners with adequate training and experience. All positive rapid HIV-antibody test results should be confirmed with a second rapid test (from a different manufacturer), and if the second rapid test result is indeterminate, a laboratory-based ELISA antibody test should be done. A new development in rapid testing is the availability of a confirmatory rapid kit that contains multiple antigens. This test is performed in the same manner as the rapid screening test. It produces reaction profiles similar to the Western Blot test (Puren, 2010: 103).

### 5.2.2.1 Home test

Rapid HIV diagnostic home-kit tests are available, but people should use them with extreme caution. It is not advisable for people to conduct the home test if they have not had proper **pre-HIV test counselling** and **post-HIV test counselling** because of the potentially serious consequences for individuals who discover their HIV status without support. The results, furthermore, can be wrong if:

- the person does not follow the testing instructions exactly;
- the test kit was not stored at the requisite temperature;
- the kit is older than the expiry date shown; and
- a poor quality test kit is used.

There are suggestions that all home test kits should include a telephone number that can be called at any time to guide a person in doing the test and to provide telephone counselling. Anybody who uses a home test and obtains a positive result should always get subsequent laboratory test confirmation of the result.

**Glossary**

**Pre-HIV test counselling** Counselling people before they are tested to prepare them for the HIV test, and to educate them about HIV infection and safer sex.

**Post-HIV test counselling** Counselling people to discuss the results of their HIV test. Post-HIV test counselling is always done individually, and the nature of the counselling depends on the result of the test.

**Saliva rapid tests** These tests detect the presence of HIV antibodies in saliva. It takes about 20 minutes to indicate whether HIV antibodies are present in the saliva.

### Enrichment: How a rapid HIV home test is done

If you want to see how a rapid HIV home-test is done, go to: https://www.youtube.com/watch?v=7JxMUjI2hGY
Note that this is also what the rapid HIV test used by healthcare workers looks like.

### 5.2.2.2 Saliva test

Test that detect the presence of HIV antibodies in saliva are called **saliva rapid tests**. OraQuick® is an example of such a test. Saliva testing has a number of advantages over blood testing:

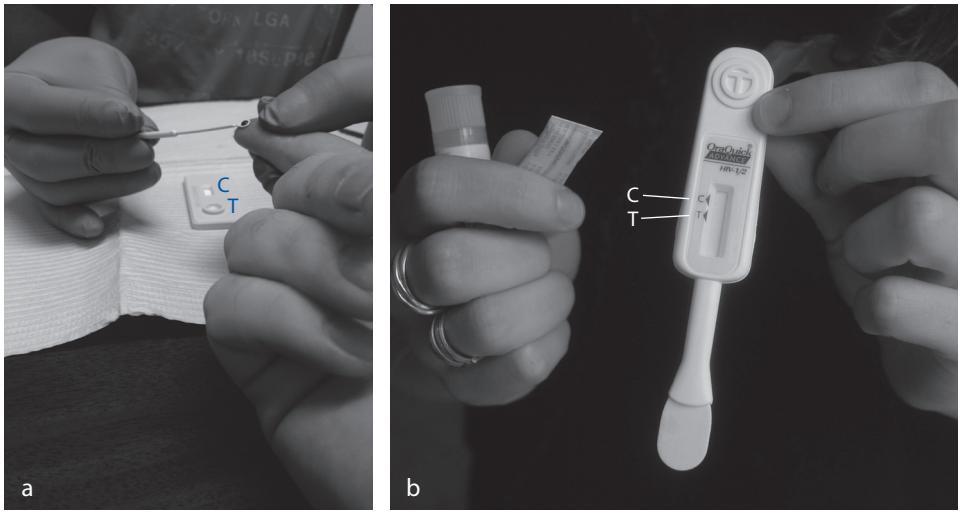
- Is is very easy to use.
- It is not as intrusive as blood testing.
- It is painless.

- It avoids the potential hazard of the person doing the test sustaining a needlestick injury.
- It can be used in situations where it is difficult to take blood, for example in children and intravenous drug users whose veins are often difficult to access.

The saliva is usually collected by placing an absorbent pad under the tongue, or by wiping a testing device around the upper and lower gums and between the cheek and teeth. The device is usually inserted into a vial that contains a developing solution and it takes about 20 minutes to indicate whether or not HIV antibodies are present in the saliva. The sensitivity of saliva tests is good, but positive results must be confirmed by conventional ELISA testing on blood before a person can be diagnosed as HIV positive. The saliva test is often used in **unlinked, anonymous surveillance studies**, and it also offers opportunities for home testing. Saliva tests are not recommended for home use without proper pre- and post-test counselling. Figure 5.2 shows pictures of the rapid HIV-antibody tests that require blood or oral fluids. Both can test for HIV-1 and HIV-2.

**Glossary**

**Unlinked, anonymous surveillance studies** A survey involving HIV testing of people (like pregnant women or youth) to determine HIV prevalence (the percentage of people living with HIV at a specific time). Surveillance tests are anonymous, which means that names are not attached to the tests. They are also unlinked, which means that test results cannot be linked to a specific person. Surveillance studies are mainly used for research purposes.




- For (a) a drop of blood is placed at the tip of the test collector – or in the 'sample' circle.
- For (b) saliva is collected by wiping the device between cheek and teeth (or under tongue).
- A few drops of reagent are added to the drop of blood (a) or the device is inserted into a vial (b) to help the test to work.
- The fluid will diffuse along the strip where reactions with antigens will occur (both tests).
- A red line must appear next to the 'C'. This is a built-in quality control reagent to control for technical errors.
- If the test is reactive (positive) a red line will appear next to the 'T' or test on the test collector.
- If the test result is negative, no line will appear next to the T.

**Figure 5.2** Rapid HIV-antibody test kit requiring (a) blood and (b) oral fluid.

**Frequently Asked Question**

**If a saliva test can diagnose HIV infection, does it also mean that saliva can spread HIV?**

This question can best be answered by making a clear distinction between antibodies in saliva and actual HIV in saliva. HIV antibodies are abundant in saliva, but the concentration of the actual virus is extremely low. The saliva (or oral) test is based on detecting the antibodies in the saliva, not the virus. The viral concentration in saliva is so low that transmission through kissing, for example, is highly unlikely. (Blood in saliva may of course increase infectivity.)

### 5.2.3 The Western Blot antibody test

The Western Blot test is an antibody test that relies on the development of antibodies to give an HIV positive result. The Western Blot test is more expensive and less widely available than the ELISA. It is never used as a screening test (to diagnose HIV infection), but only as a confirmatory test which is used under special circumstances. The use of the Western Blot as a confirmatory test usually depends on the preferences of the laboratory doing the testing. A combination of ELISA and rapid tests are usually used as confirmatory tests. They are less expensive than the Western Blot test but are as reliable. The testing algorithms used in South Africa are discussed in Section 5.4.

## 5.3 HIV virus tests

HIV tests detect particles of the actual virus in the blood, and do not rely on the development of antibodies. Diagnosis of HIV infection using viral tests is based on the following:

- detection of viral antigens such as p24 (a core protein of the virus);
- detection of viral nucleic acid (the genome of the virus either in its RNA form in fluids, or in its proviral DNA form in cells); and
- isolation of the virus in lymphocyte cell culture. (This process is **cumbersome** and seldom used for diagnostic purposes.)

The p24 antigen test and the HIV PCR techniques are two of the most well-known HIV viral tests. Because these tests detect actual HIV particles in the blood, they yield a positive result much sooner after infection (usually within 11 to 16 days) than do the ELISA, Western Blot or rapid tests. The p24 antigen test detects the p24 antigen in fluids (see Figure 2.5 on page 36 for the position of p24 antigens). The main function of the HIV PCR technique is to detect the virus nucleic acid in its RNA or DNA form (see Figure 2.6 on page 40 for the positions of the viral RNA and proviral DNA). A HIV PCR technique that detects proviral DNA is called a **qualitative PCR technique**, while a HIV PCR technique that detects viral RNA is called a **quantitative PCR technique** (or a viral-load test). Nucleic acid techniques (NAT) are so sensitive that they can detect as little as one fragment of the nucleic acid of HIV in 100 000 host cells (Schoub, 1999: 141).

**Glossary**

**Cumbersome** Slow and complicated.

**Qualitative PCR technique** A test that detects proviral DNA in infected cells. This test is used for diagnostic purposes, which means that if the test picks up proviral DNA in a blood sample, that the person is infected with HIV.

**Quantitative PCR technique** A test that detects viral RNA in body fluids. This test is used after diagnosis and during ARV treatment to measure the viral load or amount of viruses in a particular body fluid.

### 5.3.1 The HIV p24 antigen test

The **HIV p24 antige**n test detects the predominant HIV antigen (p24) in the blood. The p24 antigen is the main protein of the core of the virus and can usually be detected in the blood shortly (±16 days) after initial HIV infection. The sensitivity of the p24 antigen test during early infection (during seroconversion) is useful in certain clinical situations where early detection is important (e.g. for newborn babies or for screening of blood and tissue donations). The p24 test is sensitive only during the very early phase of HIV infection when the viral load is high. After that, the p24 antigens slowly decline because of **antigen-antibody complex formation**. Standalone p24 tests are now superseded by the fourth-generation ELISA tests which offer a combination of p24 and antibody testing. Fourth-generation tests are thus more useful than p24 tests alone for early detection of HIV infection.

**Glossary**

**Antigen-antibody complex formation** This means that the immune system produces antibodies which eliminate the p24 antigens. The p24 test is therefore only sensitive early on in infection when there are still many p24 antigens (before the immune system kills them).

#### 5.3.1.1 The dried blood spot (DBS) test

The **dried blood spot** (**DBS**) plasma p24 antigen test is a convenient way to test for HIV infection in young babies (see Figure 5.3). The test reacts to the p24 antigens in the baby's blood (and not to antibodies). The test is performed by pricking the heel of a baby's foot and by blotting drops of blood onto filter paper. The filter paper is then sent to a laboratory where an ELISA-based procedure is used to detect p24 antigens. The DBS is especially useful in resource-poor settings because it is:

- inexpensive;
- easy to use;
- not very invasive for the patient; and
- not very hazardous for healthcare practitioners to handle.

The DBS is also easier to transport and to store than liquid blood specimens. In addition, a DBS sample further has a longer lifespan (some sources say six weeks) with reduced need for refrigeration. Furthermore, the DBS has high levels of sensitivity and specificity.

**Figure 5.3** The dried blood spot test

We now discuss tests that detect nucleic acids of the virus. Virus nucleic acid techniques (NAT) are used to detect proviral DNA (a qualitative PCR technique) and viral RNA (a quantitative PCR technique).

If you think back to Chapter 2, you will remember that proviral DNA is formed in an infected CD4+T cell after reverse transcription has taken place.

## 5.3.2 Proviral DNA detection

A qualitative PCR (polymerase chain reaction) technique is used to detect the presence of proviral DNA in cells. This test is also called a HIV DNA PCR technique. The DNA PCR is especially useful when someone needs an early diagnosis, for example for post-exposure prophylaxis or to screen for vertical transmission from a mother to her baby. The test is also used to:

- diagnose babies younger than 18 months;
- exclude existing HIV infection in rape survivors before starting ART;
- screen donated blood; and
- test HIV vaccine recipients for HIV infection.

The estimated window period for a DNA PCR test is 16 days.

## 5.3.3 Viral RNA detection

A quantitative PCR technique (also called a RNA PCR) detects the presence of viral RNA in fluids. This procedure is not used for general diagnostic purposes, but it can be used in early detection of HIV infection, for example in newborn babies (vertical transmission) or after occupational exposure. (RNA may be detected within five days of infection.) The RNA PCR is mainly used after diagnosis to monitor viral RNA levels. It is a quantitative measure of how many viral copies there are in the blood (expressed as copies/ml of fluid) – hence the name 'viral-load test'. The RNA PCR is mainly used to:

- measure the response to antiretroviral therapy (is the viral load decreasing?);
- monitor progress;
- test new therapies; and
- detect drug failure.

In most cases, the viral load is a reliable indicator of the infected patient's prognosis.

### Enrichment: Using a metaphor from nature to remember the two main classes of HIV tests

The following metaphor from nature might help you to remember the two main classes of HIV tests. You know that there are animals in the veld when you see their spoor (or footprints) or when you see the animals themselves. Well, HIV tests work the same. They either look for the spoor (HIV antibodies) or for the animals themselves (HIV). Fourth-generation ELISA tests can do both: they can detect the spoor (antibodies) as well as the animal (the p24 antigens).

**Frequently Asked Question**

**Will participants in vaccine trials test positive on an HIV-antibody test?**

A person who has received an HIV vaccine and takes an HIV-antibody test (such as ELISA, rapid tests and Western Blots) will test false positive. A vaccine stimulates the immune system to develop antibodies against a specific antigen and these antibodies will be detected by current tests. The vaccine participant will therefore have a false positive result. Specific ELISA tests need to be developed that can distinguish between responses to vaccines, and real infections. Vaccine trial participants should be counselled about this and they should be referred back to their trial sites for HIV counselling and testing if they suspect HIV infection. Vaccine trial participants who are HIV negative will test negative on NAT (nucleic acid) tests. In short: Vaccine participants will have HIV antibodies in their blood, but not the virus itself.

## 5.4 HIV counselling and testing algorithms

The National Department of Health has provided recommended HIV testing algorithms (protocols) for the following individuals and groups in their policy guidelines for HIV counselling and testing (National Department of Health, 2015: 20–35):

- adolescents and adults (including pregnant and breastfeeding women);
- children younger than 18 months of age; and
- children older than 18 months of age.

### 5.4.1 HIV counselling and testing for adolescents and adults

The recommended algorithm for HIV counselling and testing (HCT) for adolescents and adults, including pregnant and breastfeeding women (see Figure 5.4 on page 140) is as follows (National Department of Health, 2015: 21):

- A group information session should be offered to all clients to outline the benefits of HCT (HIV counselling and testing). If there are pregnant women in the group, the benefits for the baby should also be addressed.
- The group session should be followed up with an individual information session to address any additional questions and concerns, and to clarify any misunderstandings. An HIV test should be offered to the client.
- When written or verbal consent has been obtained, a rapid HIV-antibody test should be carried out with a finger prick using an approved testing kit.
- If the first test is negative (non-reactive), the client is considered to be HIV uninfected. The client should receive appropriate post-test counselling and should be encouraged to repeat the test three months after the negative result to exclude the possibility of the window period. The client should be educated about the window period and HIV risk reduction behaviour. The client should also be offered HIV prevention services, such as medical male circumcision or condoms.

- Pregnant and breastfeeding women who test negative should be considered part of the PMTCT (prevention-of-mother-to-child-transmission) programme and be offered routine repeat HIV testing as well as TB screening throughout pregnancy, labour and breastfeeding as well as at the six-week EPI (immunisation) visit. They must also be counselled on correct and consistent use of condoms, on recognising TB symptoms and on safe feeding for the baby. It was found that approximately 4% of pregnant women in South Africa who initially test HIV negative in early pregnancy later test HIV positive in the same pregnancy.
- People in the general population (as well as men who have sex with men and sex workers) who test HIV negative, should repeat testing every six to 12 months, depending on their risk behaviour. Sexually active adolescents should also be tested every six to 12 months or more frequently if they have new sexual partners or if they practise unprotected intercourse. Adults and adolescents who were exposed to HIV, should be tested after six to 12 weeks to make provision for the window period. Families of HIV-infected people should be tested as soon as possible after the family member is diagnosed.
- If the first rapid HIV-antibody test is positive (reactive), a confirmatory test (second rapid test) should be performed immediately, from a second finger prick and utilising a different rapid test kit product. Results should not be given before the confirmatory test, if one is to be done. A person is considered to be HIV infected if the second rapid test is also positive.
- Give the results and provide post-test counselling in the language of choice of the client. TB screening should be done on the same day (if not done before) as well as HIV education, CD4+T cell count, clinical staging and other tests, as necessary.
- If a pregnant or breastfeeding woman tests HIV positive on the second rapid test, she should start with antiretroviral therapy on that same day. All other clients who test HIV positive, should start with ART (regardless of their CD4+T cell counts) as soon as they are ready to adhere to the medication.
- If the two rapid tests have **indeterminate results** (or discordant results), blood should be drawn from a vein and sent to a laboratory for an ELISA antibody test. This should be explained to the client. The results of the ELISA test should be considered confirmatory.
- If blood is sent to the laboratory for an ELISA test, the client should be asked to return within five days for the results. The importance of coming back for the results should be emphasised.
- Pregnant women who refuse to be tested after the individual information session must be offered post-refusal counselling. HIV counselling and testing as well as TB symptom screening should be continuously offered at every visit in a non-coercive way. Unbooked women reporting in labour must be counselled and tested for HIV at the earliest opportunity during labour and if possible, be provided with antiretroviral therapy.

Do you remember which symptoms to look for during TB screening? If not, revise them on page 103 (Table 4.3).

**Glossary**

**Indeterminate result** Rapid test results are indeterminate if the first rapid test is positive and the second rapid test is negative.

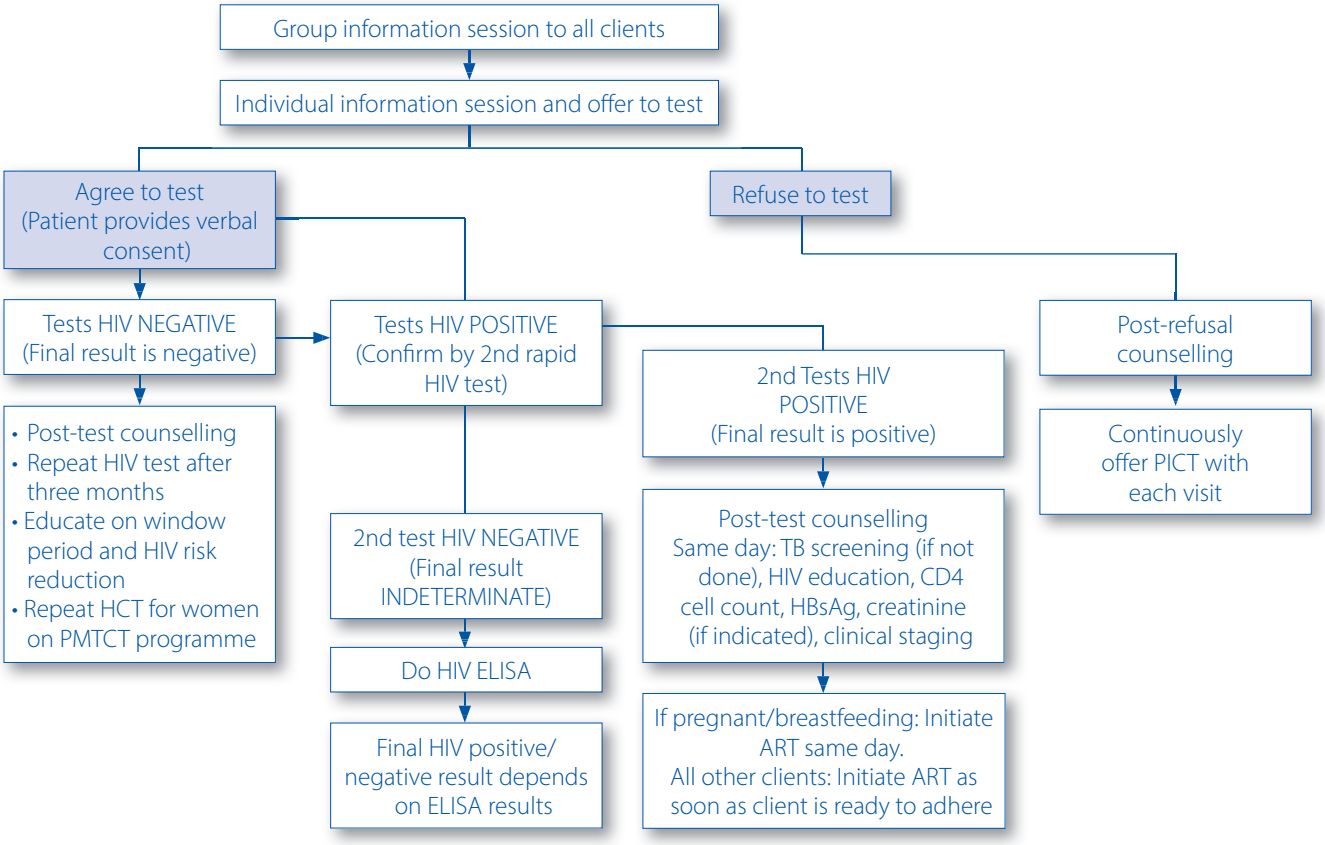



**Figure 5.4** HIV counselling and testing algorithm for adolescents and adults, including pregnant and breastfeeding women (National Department of Health, 2015: 21).

## 5.4.2 HIV counselling and testing for children younger than 18 months

The recommended algorithm for HIV testing for children younger than 18 months (See Figure 5.5 on page 141) is as follows (Department of Health, 2015: 27):

- Check every child's HIV status at every health care visit. If the mother is HIV negative, repeat HIV testing of the mother at the six weeks EPI (immunisation) visit and then three monthly throughout breastfeeding.
- If the mother is HIV negative, it is not necessary to test the baby unless it shows symptoms at any time.
- If the mother is HIV positive, the baby should be tested with an HIV PCR test at birth, at 10 weeks or 18 weeks, or any other time indicated. Testing of HIV-exposed infants at birth would ensure that more HIV-infected infants access testing and would enable early initiation of treatment. This should improve health outcomes and reduce infant mortality.
- If the baby tests HIV positive on the HIV PCR test, a second confirmatory PCR should be done. Antiretroviral therapy should be started immediately while waiting for the confirmatory results.
- If the results of the HIV PCR tests are indeterminate, HIV PCR should be repeated and a viral-load test should be done at the earliest possible opportunity.

- If the HIV PCR test result is negative, the child is uninfected. If the mother is still breastfeeding, HIV testing should be repeated six weeks after **cessation** of breastfeeding.
- HIV-exposed infants (babies born to HIV-infected mothers) who are HIV PCR negative six weeks after stopping breastfeeding should have a confirmatory rapid test at 18 months of age. Infants of newly diagnosed HIV-positive breastfeeding mothers must receive an age-appropriate HIV test (HIV PCR if <18 months; HIV rapid test ≥18 months) and ART should be initiated immediately until results are available

**Glossary**

**Cessation** The ending or the process of ending an activity.

See ART protocol in cases of both a negative and positive result in the Consolidated Guidelines of the National Department of Health (2015: 27).

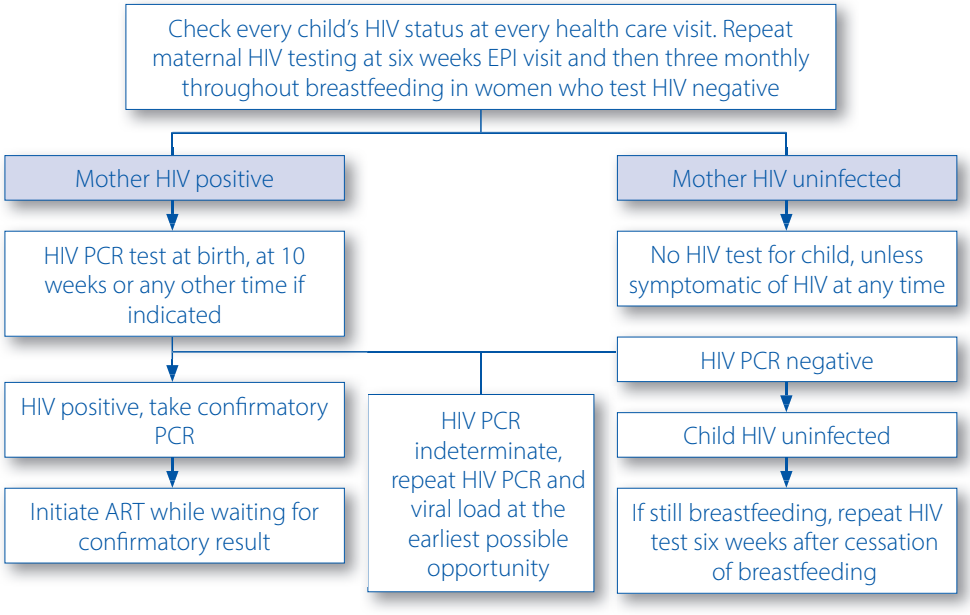



**Figure 5.5** HIV counselling and testing algorithm for children younger than 18 months (National Department of Health, 2015: 27).

## Frequently Asked Question

### Which HIV tests should be used on babies?

HIV-antibody detection tests cannot tell the difference between a mother and her baby's antibodies. Healthcare practitioners, therefore, cannot use HIV-antibody tests, such as ELISA or rapid tests, to test babies who are younger than 18 months' old to diagnose HIV infection. In babies younger than 18 months, it is not clear whether the baby or the mother produced the antibodies in the baby's blood. During pregnancy the mother's antibodies (against all the diseases that the mother has been exposed to, or was vaccinated against) pass across the placenta from the mother to her unborn baby (passive immunity). These antibodies protect the baby against diseases in the first six months of the baby's life. The same happens with HIV antibodies. They pass from the HIV-infected mother across the placenta to the foetus. These maternal antibodies can stay in the baby for as long as 18 months and will show up on an HIV ELISA antibody (or rapid) test. This means that, up to the age of 18 months, a baby who got the antibodies but not the virus from the mother can test HIV-antibody positive without actually being infected.

The HIV PCR test should be used to test infants who are less than 18 months' old for HIV infection. Not only is this test able to detect HIV genes in human cells (and does not rely on the presence of HIV antibodies); it is also extremely sensitive (98.8%) and highly specific (99.4%) from six weeks of age. In the public health sector in South Africa, it is recommended that all babies, whose mothers are HIV positive, are tested with the DNA PCR test either at birth, at 10 weeks or at 18 weeks, or at any other time if indicated. All infants who test PCR positive should have a second HIV PCR test in order to confirm the PCR result. In addition, ART should be initiated on the same day.

### 5.4.3 HIV counselling and testing for children of 18 months and older

All HIV-exposed children should be tested with a rapid HIV test (the same test that is used for adults) at 18 months of age. The recommended algorithm for HIV testing of children of 18 months and older is as follows (National Department of Health, 2015: 29):

- Every child's HIV exposure status should be checked at every health care visit. Breastfeeding mothers who test HIV negative, must have a repeat test three monthly.
- If the mother was HIV uninfected in the last three months, it is not necessary to test the child.
- If the mother is HIV positive, the child should be screened with the rapid HIV test. If the rapid HIV test is negative, the child is uninfected provided there are no clinical signs of HIV. If still breastfeeding, the child should again be tested for HIV six weeks after cessation of breastfeeding.
- If the rapid HIV test is positive, a confirmatory rapid HIV test (with a different rapid test) should be done. If the confirmatory rapid HIV test is also positive, the child is infected with HIV.
- If the rapid HIV test is positive and the confirmatory rapid test is negative, an HIV ELISA test should be done. If the HIV ELISA test is negative, the child is HIV uninfected. If the HIV ELISA test is positive, the child is HIV infected.
- All HIV-infected children should start with ART as soon as possible after diagnosis, irrespective of their CD4+T cell count. If the child is younger than five years, ART should be initiated immediately.
- Healthcare practitioners must check with every HIV-exposed child older than 18 months if they received the rapid HIV test at 18 months. If the exposed child was not tested at 18 months, an HIV rapid test must be done whatever the age of the child.

An age-appropriate test should be done at all times under the following circumstances:

- on request of the parents, if the child's father or a sibling is HIV positive;
- on the death of the mother, father or a sibling, if any were HIV positive; and
- when the mother's HIV status is unknown, her whereabouts are unknown, or she is unavailable to be tested.

Children should also be tested if they show clinical signs suggestive of HIV infection, if they have acute, severe illness, tuberculosis or a history of TB treatment,

if they are at risk of sexual assault, or if a woman with unknown or HIV-positive status wet-nursed or breastfed them. Children who are potential candidates for fostering or adoption should also be tested with an age-appropriate HIV test.

## Enrichment: HIV testing for abandoned babies

Although healthcare practitioners do not use HIV rapid antibody tests to diagnose HIV infection in babies younger than 18 months old, they can be used to test abandoned babies younger than 18 months to find out if the baby was exposed to HIV or not. A positive HIV rapid test result means that the baby has HIV antibodies, indicating that the abandoned baby's mother was HIV positive. To find out if the baby is infected with HIV, an HIV PCR test should be done. If the HIV PCR is positive, infant ART should be started immediately. If the baby's HIV-antibody test result is negative, it means that not only was the baby's mother uninfected (she was not HIV positive), but also that the baby had no exposure to HIV.

Figure 5.6 provides a schematic presentation of the recommended HIV testing algorithm for infants older than 18 months.

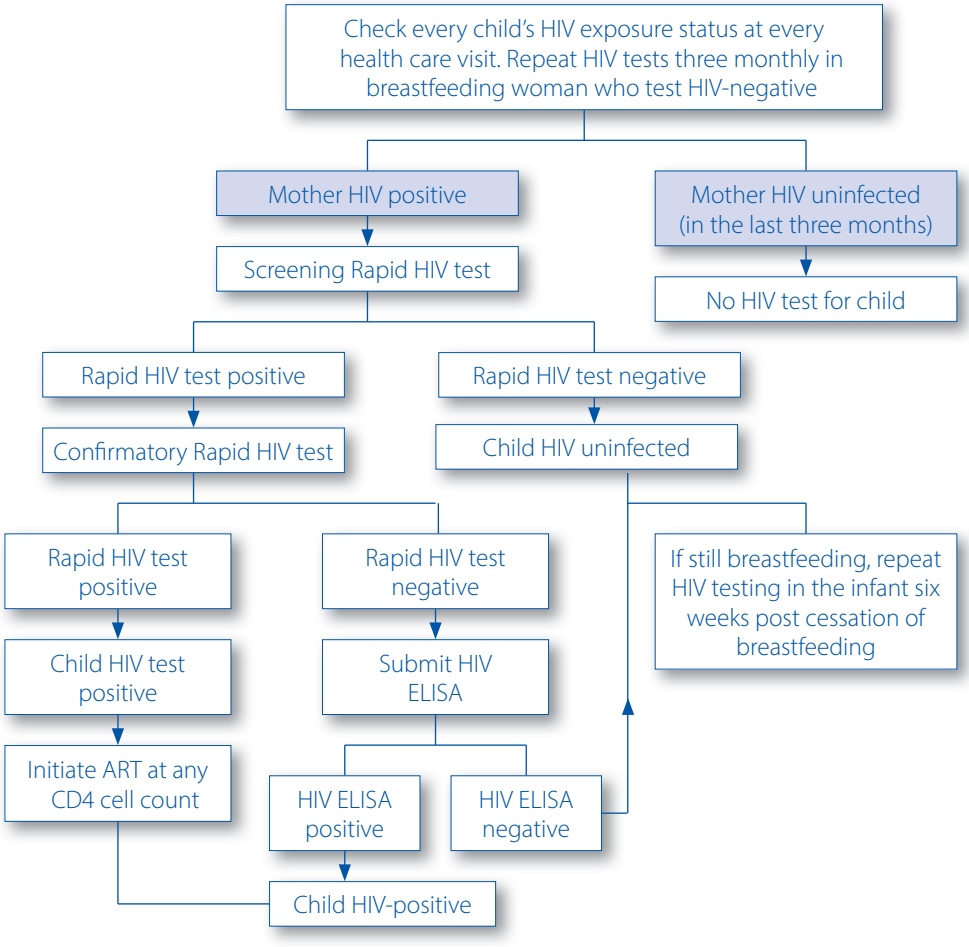



**Figure 5.6** Algorithm for testing children older than 18 months (National Department of Health, 2015: 29).

**Glossary**

**Mandatory** Compulsory or required by law.

**Age of consent**

A child of 12 years and older may consent to HIV testing.

Pre- and post-HIV test counselling are discussed in Chapter 13. Legal and ethical aspects of HIV testing are discussed in Chapter 22.

Clients must always have pre-HIV test counselling before being tested for HIV infection and post-HIV test counselling after being tested. Children should also be counselled, if they are sufficiently mature to understand the implications of the HIV test. Informed consent and confidentiality are **mandatory**.

## 5.5 Conclusion

The early diagnosis of HIV infection is vital for the HIV-infected individual as well as for the community. Timely treatment with antiretroviral therapy not only saves individual lives, it also lowers the chances of spreading the virus to other people in the community. The management of HIV infection with antiretrovirals will be discussed in the next chapter.

## Test your understanding

1. Compile a table that shows the main differences between the rapid HIV-antibody tests and HIV tests.
2. What is meant by the 'window period'?
3. What are the implications of the window period for the diagnosis of HIV infection?
4. Why is the use of rapid HIV-antibody tests not suitable to test babies who are younger than 18 months old?
5. What is meant by an indeterminate test result? What advice would you give to a client with an indeterminate test result?
6. Circle the correct phrases in the following sentence:
   The HIV DNA PCR is a [6.1 qualitative/quantitative] test which is used to [6.2 diagnose HIV infection/count the viral load], while the HIV RNA PCR test is a [6.3 qualitative/quantitative] test used to [6.4 diagnose HIV infection/count the viral load].
7. Describe the HIV testing algorithm for adolescents and adults (including pregnant and breastfeeding women).
8. Describe the HIV testing algorithm for babies younger than 18 months, as well as for babies older than 18 months.

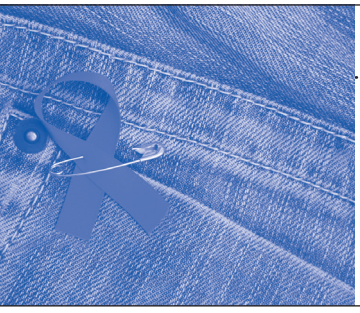
## Reference list

National Department of Health, South Africa. 2015. *National Consolidated Guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults*. Pretoria: Department of Health.

Puren, A.J. 2010. HIV diagnosis. In S.S. Abdool Karim & Q. Abdool Karim (Eds.). *HIV/AIDS in South Africa* (2nd edn.) (pp. 97-116). Cape Town: Cambridge University Press.

Schoub, B.D. 1999. *AIDS and HIV in perspective. A guide to understanding the virus and its consequences* (2nd edn.). Cambridge: Cambridge University Press.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (p. 7). Cape Town: Nasionale Boekhandel Bpk.



# Chapter 6

# Antiretroviral therapy (ART)

Alta van Dyk

### Delaying Raka

*... but behind him*
*he heard a frantic snarl and pursuing steps*
*as he turned ... the great thing stopped dead*
*in his tracks and, grimacing, withdrew,*
*fierce but afraid, and half perplexed ...*

From: *Raka* by NP Van Wyk Louw (1968).

## Learning outcomes

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

- explain the importance of a CD4+T cell count and a viral load;
- explain to a client what the four goals of ART are;
- devise a personal plan for a client to help him or her adhere to ART;
- draw a picture to show to a colleague how a virus can develop drug resistance; and
- explain the protocol that should be followed before a rape survivor can receive ARVs as post-exposure prophylaxis.

## Chapter outline

- Clinical assessment
- Goals of ART
- Classes of ARVs and their mechanisms of action
- Antiretroviral drugs available in southern Africa
- Guidelines for the use of ART
- Adverse effects of ART
- How to know if ART is effective
- When to change treatment
- The development of drug-resistant viruses
- Adherence to ART
- Prevention of mother-to-child transmission
- Post-exposure prophylaxis after occupational exposure
- PEP after rape or sexual assault
- Pre-exposure prophylaxis

We have made much progress in management and treatment of HIV infection since the early 1980s, when so little about this new disease was known. The first antiretroviral drug, AZT (zidovudine), was approved for use in 1987, and in 1994 antiretroviral therapy (ART) was used for the first time to prevent a mother from transmitting HIV to her child, although this only started happening in South Africa in 2002. The big turnaround began in 1995 when the use of triple-drug therapy or HAART (highly active antiretroviral therapy) was introduced. HAART changed the status of Aids from a disease without much hope to that of a manageable disease. The lives of thousands of HIV-infected South Africans changed for the better when the South African government made antiretroviral therapy publicly available in 2003.

This chapter focuses primarily on antiretroviral therapy and the guidelines for treatment used in South Africa. Other aspects of the management of HIV infection, such as strengthening of the immune system and managing specific symptoms and HIV-related diseases, are discussed in Chapter 20.

## 6.1 Clinical assessment

It is critical to do a full clinical assessment of a patient's health after a HIV-positive diagnosis has been determined. In order to monitor any changes in the patient's health, he or she should undergo regular check-ups (at least every six months if healthy, but more frequently if he or she has symptoms).

The following should be done at every clinic visit (Aurum Institute & CDC/FEPFAR, 2015: 5):

- WHO staging (see Table 4.1 on page 95);
- CD4+T cell count;
- screening for TB symptoms;
- screening for STIs;
- screening for pregnancy;
- mental health screening;
- screening for **comorbidities** and non-infectious diseases including hypertension and diabetes;
- pap smears for women, as indicated in policy;
- assessment of eligibility for ART and IPT (to prevent TB), if the patient is not yet on ARVs; and
- monitoring adherence if the patient is already on ARVs.

If any health problems are identified with clinical assessment or screening, it should be managed as follows:

- Prescribe IPT if eligible (to prevent TB).
- Manage comorbidities and **intercurrent illnesses**.
- Provide family planning advice and contraception as needed.
- Counsel on nutrition, a healthy lifestyle and how to avoid transmission of HIV to sexual partners and children.
- Provide support for **disclosure** and partner notification.
- Advise HIV-infected individuals to come back whenever they experience problems with their health.

**Glossary**

**Comorbidity** When a patient simultaneously has two or more chronic diseases or conditions; additional diseases co-occurring with the primary disease.
**Interrcurrent illness** When an illness occurs during the progress of another illness
**Disclosure** When a person shares personal information with another person, e.g. being HIV positive.

- If a patient is ready for initiation of antiretroviral therapy, further assessment (e.g. blood tests such as serum creatinine to assess renal function, full blood count, fasting cholesterol and triglycerides) should be done as necessary.

### 6.1.1 CD4+T cell count and viral load

In order to manage HIV infection and opportunistic infections, it is important to monitor the individual's CD4+T cell lymphocyte count (or percentage of CD4+T cells in children), as well as the viral load in the blood on an ongoing basis.

CD4+T cell counts are important to:
- assess the status of the immune system;
- indicate when prevention or treatment of opportunistic infections and diseases should start or stop; and
- indicate when to start antiretroviral treatment in countries that still use the CD4+T cell count as indication of when to initiate ART.

A viral-load test (RNA PCR) is important to:
- assess how severe the HIV infection is (or its prognosis) by telling us how far the immune system has been eroded;
- measure the response of the patient to antiretroviral therapy; and
- detect antiretroviral resistance.

The viral load is usually undetectable after six months of antiretroviral treatment.

## 6.2 Goals of ART

Antiretroviral therapy has the following four primary goals:
1. *Virological goal:* to reduce the HIV viral load as much as possible – preferably to undetectable levels – for as long as possible.
2. *Immunological goal:* to restore and/or preserve immunological function so as to improve immune functioning, reduce opportunistic infections and delay the onset of Aids.
3. *Therapeutic goal:* to improve the quality of the HIV-infected patient's life.
4. *Epidemiological goal:* to reduce HIV-related sickness and death (morbidity and mortality) and to reduce the impact of HIV transmission in the community.

The four goals of ART can be achieved by suppressing the replication of the virus as strongly and for as long as possible, through the indefinite use of treatment that is both tolerable and sustainable. In so doing, the CD4+T cell lymphocyte count usually increases progressively with partial restoration of the immune system, which, in turn dramatically reduces both the morbidity and mortality associated with HIV infection (Southern African HIV Clinicians Society, 2012: 114).

Antiretroviral therapy is used mainly:
- to treat established HIV infection; and
- to prevent HIV transmission, such as the prevention of mother-to-child transmission, post-exposure prophylaxis (e.g. in cases of occupational exposure, rape or sexual assault) and as pre-exposure prophylaxis or PrEP.

Figure 6.1 illustrates the two main uses of ART. Use the diagram when you read this chapter to put the work in context.

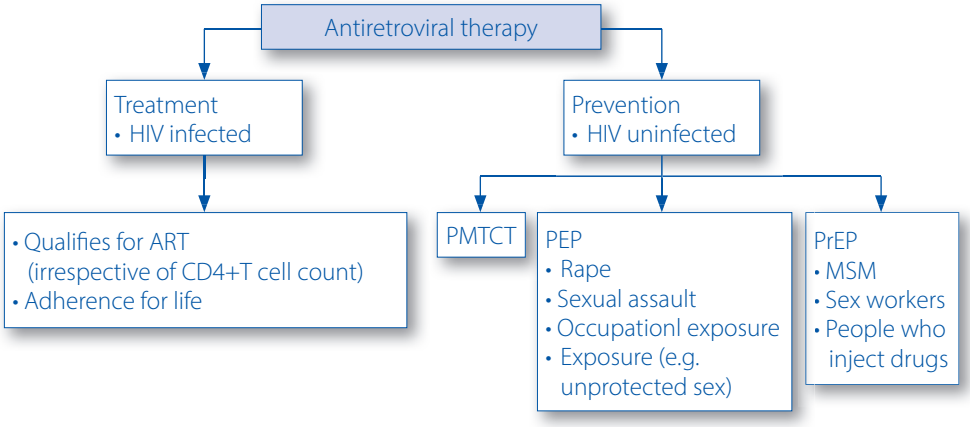



**Figure 6.1** The main uses of antiretroviral therapy

## 6.3 Classes of ART and their mechanisms of action

In Chapter 2 we explained how HIV infect CD4+T cells by attaching to the cell's receptors, by then entering the cell and finally, by using viral enzymes to take over the cell and to replicate themselves. Antiretroviral drugs are designed to block these actions of the virus. To fully understand the different classes of ARVs and their mechanisms of action, it is first necessary to revise what we know about the viral enzymes:

- *Reverse transcriptase enzymes* are vital for completing the early stages of HIV replication by transforming viral RNA into proviral DNA.
- *Protease enzymes* are required for the assembly of new viral RNA and viral proteins, and for the maturation of fully infectious new viruses that bud from the CD4+T cells.
- *Integrase enzymes* assist with HIV DNA integration into the nucleus of the CD4+T cell.

There are currently four classes of antiretroviral drugs that interfere with (or inhibit) the viral enzymes mentioned above, and one class that inhibits entry into the host cell:

- nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs and NtRTIs);
- **non-nucleoside reverse transcriptase inhibitors** (**NNRTIs**);
- protease inhibitors (PIs);
- integrase inhibitors; and
- entry inhibitors.

The effect of the different classes of antiretroviral drugs on HIV will now be discussed as illustrated by Figure 6.2 on page 149. Use this figure to follow the discussion.

### 6.3.1 Reverse transcriptase inhibitors (NRTIs and NNRTIs)

The reverse transcriptase inhibitors (both the NRTIs as well as the NNRTIs) interrupt the lifecycle of HIV by interfering with the reverse transcriptase enzyme during the early replication of the virus (see Figure 6.2, A). NRTIs mimic the normal building blocks of DNA, while NNRTIs inhibit reverse transcriptase directly. Both these interferences with the reverse transcriptase enzyme prevent the virus from changing its RNA into proviral DNA.

### 6.3.2 Protease inhibitors (PIs)

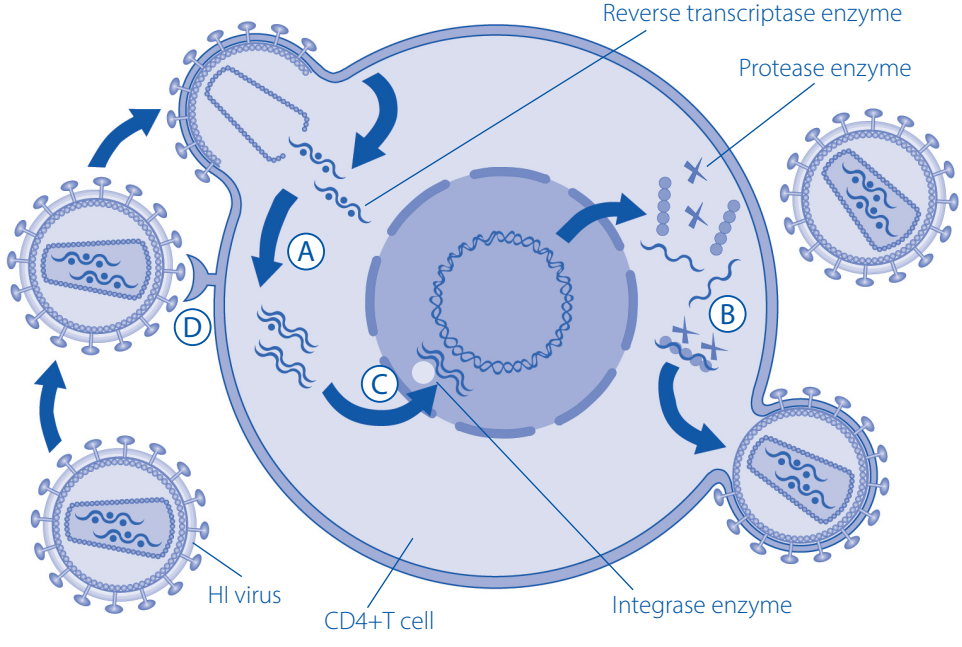
The protease inhibitors (PIs) inhibit the creation of new viruses by 'paralysing' the protease enzyme. In this way, the PIs prevent newly replicated HIV from the infected cells from being assembled and released (see Figure 6.2, B).

### 6.3.3 Integrase inhibitors (In STIs)

Integrase inhibitors interfere with the integrase enzyme and prevent HIV DNA to integrate into the nucleus (or core) of the CD4+T cell. The virus is therefore unable to replicate because it cannot be integrated into the host cell's DNA (see Figure 6.2, C). Integrase inhibitors are also called integrase strand transfer inhibitors (or InSTIs).

### 6.3.4 Entry inhibitors

Entry inhibitors stop HIV from entering the host cell by affecting the interaction between the virus and the cell (see Figure 6.2, D). They bind to the viral protein p41, which stops these viral proteins from forming stable interactions with the CD4+T cell. Some entry inhibitors bind to CCR5 co-receptors to prevent gp120 to bind to the CD4+T cell.




A. Drugs interfere with the reverse transcriptase enzyme and prevent the transformation of viral RNA into proviral DNA
   - Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)
   - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
B. Drugs interfere with the protease enzyme and prevent the formation of new viruses
   - Protease inhibitors (PIs)
C. Drugs interfere with the integrase enzyme and prevent integration of viral DNA into the cell's nucleus
   - Integrase inhibitors (In STIs)
D. Drugs block entry of HIV into the cell
   - Bind to viral gp41 or gp120
   - Bind to CD4 receptors
   - Bind to CCR5 co-receptors

**Figure 6.2** The effect of antiretroviral drugs on HIV

## Activity

A classroom project

- If you are a teacher, make (or ask the children in your class to make) a model from different coloured clays or plasticine to demonstrate the interaction between HIV and a CD4+T cell.
- To see a YouTube video on how ARVs work, go to the following website: https://www.youtube.com/watch?v=UuszI8l0B2w
- Use the model to explain to the children what antiretroviral drugs do to the virus.

The classes of ARVs discussed above and what they do are summed up in Table 6.1.

**Table 6.1** Classes of ARVs and their mechanisms of action

| Classification of ART | Abbreviation | Mechanism of action | Specific action |
|---|---|---|---|
| Nucleoside & nucleotide reverse transcriptase inhibitors | NRTIs/NtRTIs | Reverse transcriptase inhibition | Mimics the normal building blocks of HIV DNA, preventing transcription of viral RNA to DNA |
| Non-nucleoside reverse transcriptase inhibitors | NNRTIs | Reverse transcriptase inhibition | Directly inhibits reverse transcriptase |
| Protease inhibitors | PIs | Protease inhibition | Inhibits final maturation stages of HIV replication, resulting in formation of non-infective viral particles |
| Integrase inhibitors (also called integrase strand transfer inhibitors) | InSTIs | Inhibition of viral integration | Prevent the transfer of proviral DNA strands to the host cell's chromosomal DNA |
| Entry inhibitors | | Entry inhibition | Bind to viral gp41 or gp120 or host cell CD4+ receptors or CCR5 receptors to prevent entry into the host cell. |

(Source: Based on Southern African HIV Clinicians Society, 2014: 122)

## 6.4 Antiretroviral drugs available in southern Africa

Table 6.2 below gives a summary of the antiretroviral drugs currently available in southern Africa. There are different **fixed-dose combinations** (FDCs) available which reduce the burden of taking multiple pills and help individuals to adhere to their medications. New treatments for clinical use become available regularly, and healthcare workers are advised to contact the Southern African HIV Clinicians Society for the most current version of treatment guidelines. The treatment guidelines are available on their website (http://www.sahivsoc.org). Dosages, side effects and special requirements are provided in Table 6.8 at the end of this chapter.

**Table 6.2** Antiretroviral agents available in southern Africa

| Classification of ART | Antiretroviral medication |
|---|---|
| Nucleoside/Nucleotide reverse transcriptase inhibitors (NRTI / NtRTI) | • Tenofovir (TDF) (NtRTI)<br>• Lamivudine (**3TC**)<br>• Emtricitabine (FTC)<br>• Abacavir (ABC)<br>• Zidovudine (AZT)<br>• Stavudine (d4T)<br>• Didanosine (**ddI**) |
| Non-nucleoside reverse transcriptase inhibitors (NNRTI) | • Efavirenz (EFV)<br>• Nevirapine (NVP)<br>• Rilpivirine (RPV)<br>• Etravirine (ETV) |
| Protease inhibitors (PI) | • Atazanavir (ATV)<br>• Lopinavir/ritonavir (LPV/r) (Boosted PI)<br>• Darunavir (DRV)<br>• Saquinavir (SQV) (rarely used)<br>• Indinavir (IDV) (rarely used) |
| Integrase inhibitors (InSTI) | • Raltegravir (RAL) |
| Entry inhibitors CCR5 blocker | • Maraviroc (MVC) |

**Glossary**

**Fixed-dose combination** Also known as FDC, a fixed-dose combination is two or more active pharmaceutical ingredients combined in a single dosage form, for example one tablet or capsule. Antiretroviral as well as TB treatment is available in fixed-dose combinations. Compliance to treatment has been greatly improved since the availability of FDCs (a person now has to take only one pill instead of three to four pills, as in the past).

## 6.5 Guidelines for the use of ART

The Southern African HIV Clinicians Society (2014) recommends that HIV patients should be given antiretroviral regimens that are maximally suppressive in order to achieve the best clinical results and to prevent **resistance**. Highly active antiretroviral therapy (HAART) with three antiretroviral agents is therefore recommended for optimal results. A combination of three different antiretroviral drugs has been shown to produce the best effects in terms of both viral suppression and reducing the development of drug-resistant viruses.

Effective combination therapy attacks the virus at different levels (in the case of first-line regimens, sites A and B as shown in Figure 6.2 on page 149). Different

**Glossary**

**Resistance** Resistance happens when the medication taken for treatment of a condition (e.g. HIV infection) can no longer prevent the resistant virus from replicating (making more copies of itself).

FDCs are becoming increasingly available. They are recommended as they reduce the pill burden and have the potential to improve adherence.

**Frequently Asked Question**

**What is meant by a drug 'regime'?**

The word 'regime' in this sense refers to a course or schedule of therapy or treatment. A drug regime therefore means the medication schedule, plan or routine that a patient will have to follow.

## 6.5.1 When to start antiretroviral therapy

Two randomised controlled trials (INSIGHT START Study Group, 2015 and TEMPRANO ANRS 12136 Study Group, 2015) investigated the optimal timing of ART in HIV-infected patients with high CD4+T cell counts. These studies found significant individual clinical benefits from starting ART immediately in patients with CD4+T cell counts higher than 500 cells/mm$^3$, rather than deferring until a certain lower CD4+T cell threshold or clinical indication was met. The conclusion of these studies is that early ART initiation can potentially reduce both HIV incidence and morbidity. Based on these finding, the Southern African HIV Clinicians Society decided to adjust the ART guidelines for adults as follows (Meintjes et al., 2015: 3):

- All patients diagnosed with HIV infection should be initiated on lifelong ART. The CD4+T cell count and clinical stage of the patient should no longer be a consideration in the decision to start ART.
- For patients who are asymptomatic with CD4+T cell counts >350 cells/mm$^3$, additional time (weeks to a few months) can be spent counselling and preparing the patient for lifelong ART with good adherence before starting. In those with CD4+T cell counts <350 cells/mm$^3$ (and especially <200 cells/mm$^3$), or with clinical indication for starting, there should not be undue delay.
- Within ART programmes, it is important to factor in that the absolute benefit of ART is much greater at lower CD4+T cell counts (there is a mortality benefit at CD4+T cell counts <350 cells/mm$^3$ (Severe, et al., 2010). Therefore, planners and clinicians should prioritise and fast-track those with low CD4+T cell counts (especially <200 cells/mm$^3$); this is particularly relevant where there are ART shortages or anticipated **stock-outs**.

**Glossary**

**Stock-out** A situation when an item (e.g. an essential drug) is not available (out of stock).

The World Health Organization's recommendations on when to start ART among people living with HIV, are provided in Table 6.3. These guidelines are also followed by the South African Department of Health.

**Table 6.3** WHO recommendations on when to start ART among people living with HIV

| Target population | Specific recommendations |
|---|---|
| Adults (>19 years) | ART should be initiated in all adults living with HIV irrespective of CD4+T cell count. |
| | As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO Clinical Stage 3 or 4) and individuals with CD4+T cell count ≤350 cells/mm$^3$. |
| Pregnant and breastfeeding women | ART should be initiated in all pregnant and breastfeeding women living with HIV irrespective of CD4+T cell count, and should be continued lifelong. |
| Adolescents (10 to 19 years old) | ART should be initiated in all adolescents living with HIV irrespective of CD4+T cell count. |
| | As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO Clinical Stage 3 or 4) and adolescents with CD4+T cell count ≤ 350 cells/mm$^3$. |
| Children (1 to <10 years old) | ART should be initiated among all children one to <10 years old living with HIV, irrespective of CD4+T cell count. |
| | As a priority, ART should be initiated in all HIV-infected children <2 years old and those with severe or advanced HIV clinical disease (WHO Clinical Stage 3 or 4) and children with CD4% <25% (if younger than five years old) or with CD4+T cell count ≤350 cells/mm$^3$ (if five years and older). |
| Children (<1 year old) | ART should be initiated in all children living with HIV younger than one year old, irrespective of CD4+T cell count. |

(Source: WHO Guidelines, 2015: 13)

To summarise ART initiation guidelines: All adults, pregnant and breastfeeding women, adolescents, children and babies should be initiated on ART irrespective of their CD4+T cell count. Before initiating ART, patients (or caretakers of children with HIV) should be counselled (see 6.5.2 on the next page) and special attention should be given to ARV adherence. The patient must be ready to start taking ARVs for the rest of his or her life.

In some cases, it will be necessary to prioritise (or fast-track) initiation of ART, for example in adults, adolescents and children with severe or advanced HIV clinical disease (WHO Clinical Stage 3 or 4) and individuals with CD4+T cell count ≤ 350 cells/mm$^3$. Initiation of ART should also be prioritised in all children younger than two years old (see Table 6.3).

The policy to initiate ART irrespective of CD4+T cell count is not without critique, especially in developing countries with failing health services. Financial cost, adequate planning of drug supply, health service capacity and infrastructure to avoid stock-outs should all be taken into consideration.

## 6.5.2 Counselling before ART initiation

To take antiretrovirals is a major decision for HIV-infected individuals – something that healthcare workers often lose sight of. It is extremely important to counsel every individual who is eligible for antiretroviral therapy on the following aspects (Aurum Institute & CDC/FEPFAR, 2015: 8):

- Provide information on HIV, including:
  - transmission;
  - **pathogenesis**;
  - prognosis.
- Provide information on ART including:
  - that ART is lifelong;
  - why 100% adherence is important;
  - ART side effects.
- Discuss safer sex and reproductive health including:
  - consistent condom use;
  - family planning and contraception;
  - pregnancy and how to prevent mother-to-child-transmission (MTCT).
- Encourage disclosure to partner and/or other household members.
- Encourage identifying a treatment buddy and/or becoming involved in a support group.
- Ensure that contact details of patient and treatment buddy are available.
- Formulate a treatment plan with each patient specifying:
  - storage of medication;
  - strategies for missed doses;
  - integration of medication into daily routine;
  - follow-up visits.

**Glossary**

**Pathogenesis** The way in which a disease develops.

## 6.5.3 Choice of drug regime

Before we discuss the antiretroviral regime that is prescribed for individuals with HIV infection, it is necessary to understand the difference between an individualised and a standardised drug regime approach.

### 6.5.3.1 Individualised versus standardised drug regime approach

The traditional approach when selecting a drug regime for an HIV-infected patient in a developed country is to choose a combination of suitable drugs that best suit this specific individual's requirements and preferences. This is called an **individualised drug regime.** An individual approach is, unfortunately, not always possible in developing countries. In developing countries, health systems often lack adequately trained workers who can manage the complexity of HIV treatment. In addition, the health systems may not always have suitable monitoring facilities. The World Health Organization (WHO) therefore advocates a **standardised drug regime** approach that simplifies antiretroviral treatment but does not compromise the outcomes of the treatment offered or its quality.

When treatment is standardised, it means that a decision-making body (such as a country's health department) decides on specific drugs (e.g. two specific NRTIs and one specific NNRTI) to prescribe to all HIV-infected patients who qualify for treatment and who are first-time users of ART. The Southern African

**Glossary**

**Individualised drug regime** Medication (or a combination of medications) that is prescribed with a specific individual and his or her needs in mind.

**Standardised drug regime** A decision-making body decides beforehand which medications to prescribe for a specific condition. All patients with HIV infection who are first-time users of ART, will thus be treated with the same medication regime. This is often done in developing countries.

HIV Clinicians Society lists the following advantages of the standardised drug regime approach (Southern African HIV Clinicians Society, 2005):

- It simplifies training for and education of providers and patients.
- It simplifies monitoring of side effects and toxicity.
- Patterns of resistance are easier to predict.
- Sequence of drug combinations is predictable and standardised which assist in the mass obtaining and prescribing of drugs.
- The numbers of drugs to obtain and manage are limited.

### 6.5.3.2 ART for adults and adolescents ≥15 years

The first line of treatment for pregnant and breastfeeding women (adolescent and adult), as well as all other adults and adolescents – as recommended by the WHO and implemented by the South African National Department of Health – consists of two NRTIs plus one NNRTI. Regimes that include FDCs that are taken only once daily are preferred. The favoured regimen used in the public sector for first-line treatment is:

> TDF (tenofovir) + 3TC (lamivudine) OR FTC (emtricitabine) + **EFV** (efavirenz).

Protease inhibitors (PIs) and integrase inhibitors (integrase strand transfer inhibitors or InSTIs) are not recommended for first-line use because they are expensive and are not as well tolerated in the long term as NNRTIs. However, intolerance of or contraindications to NNRTIs may necessitate the use of PIs and InSTIs. An affordable InSTI may in future be included in first-line treatment. PIs are currently used in second-line treatment and InSTIs in third-line treatment in the public sector.

There is broad **cross-resistance** against the NNRTIs currently available, and resistance to any single NNRTI prevents any other (currently available) NNRTIs in that class of drugs from being used. However, resistance to one NRTI or PI does not necessarily make all the ARVs in that class of drugs **redundant.** It is an ongoing research challenge to find new categories of drugs and the most suitable combination of drugs for various groups of patients with their distinct needs. It is a further challenge to eliminate treatment failure and determine how to assess the likelihood that a patient will develop resistance to antiretroviral drugs.

The antiretroviral first-line regime for adolescents 15 years or older and adults, including pregnant and breastfeeding women, is outlined in Table 6.4.

**ART abbreviations**

Use this quick reference box to see what the ART abbreviations that we will use in the following sections mean:

| | | |
|---|---|---|
| FDC | = | Fixed-dose combination (one pill containing a combination of ARVs) |
| TDF | = | Tenofovir (NtRTI) |
| 3TC | = | Lamivudine (NRTI) |
| FTC | = | Emtricitabine (NRTI) |
| ABC | = | Abacavir (NRTI) |
| AZT | = | Zidovudine (NRTI) |
| EFV | = | Efavirenz (NNRTI) |
| NVP | = | Nevirapine (NNRTI) |
| LPV/r | = | Lopinavir/ritonivir (boosted PI) |
| D4T | = | Stavudine (to be changed to TDF) |
| ddI | = | Didanosine (to be changed to ABC) |

**Glossary**

**Cross-resistance** Resistance to one antiretroviral drug resulting in resistance to other drugs in the same class.

**Redundant** No longer useful or required; useless or superfluous.

**Table 6.4** First-line ART regimes for adolescents ≥15 years and adults (including pregnant and breastfeeding women)

| Criteria | Regimen | Comments |
|---|---|---|
| • Adolescents ≥15 years and weighing ≥40kg.<br>• Adults<br>• All HIV/TB co-infection<br>• All HIV/HBV co-infection<br>• Women who are pregnant, breastfeeding or within one year **postpartum**. | TDF + 3TC (or FTC) + EFV provide as FDC (fixed-dose combination). | Replace EFV with NVP in patients:<br>• with significant psychiatric comorbidity or intolerance to EFV<br>• where neuropsychiatric toxicity of EFV may impair daily functioning (e.g. nightshift workers). |
| Adults and adolescents on d4T (stavudine) (d4T must be discontinued in all patients)* | Change d4T to TDF. | • Switch to TDF if virally suppressed and the patient has normal creatinine clearance, even if d4T is well tolerated.<br>• If VL>1 000 copies/ml, manage as treatment failure and consider switching to second line. |
| Adolescents weighing <40kg (<15 years) | ABC + 3TC + EFV (as three individual drugs) | |
| Pregnant adolescents:<br>• >40kg<br>• <40kg | • initiate FDC (TDF+FTC+EFV), regardless of age<br>• prescribe three individual ARV drugs (ABC+3TC+EFV) | |
| If EFV contradicted (psychiatric problems, intolerance, impairment of daily function). | TDF + FTC (or 3TC) + NVP** | |
| If EFV and NVP contraindicated | TDF + FTC (or 3TC) + LPV/r | |
| If TDF contraindicated | ABC + 3TC +EFV | |
| If TDF and EFV contraindicated | ABC + 3TC + NVP | |

(Source: National Department of Health, 2015: 73)

**Glossary**

**Postpartum** After childbirth; after the birth of the baby.

**Note**

* **d4T** was used in previous treatment regimens and it is no longer a drug of preference because of severe toxicity in patients. Patients should no longer be on d4T and it should be replaced with TDF (tenofovir).
** Give Nevirapine only if CD4+T cell count <250 in women and <400 in men. Use LPV/r (instead of NVP) if CD4+T cell count ≥250 in women and ≥400 in men.

### 6.5.3.3 ART for adolescents aged 10 to 15 years

Adolescents who are infected with HIV fall into two categories: **perinatally** infected (through mother-to-child-transmission of HIV) or behaviourally infected (e.g. unsafe sex). There is however no difference in the treatment of the two groups of adolescents. ART first-line regimen for adolescents between 10 and 15 years is provided in Table 6.5.

**Glossary**

**Perinatally** Related to the period of time immediately before and after childbirth, usually measured in weeks.

**Table 6.5** ART first line regimes for adolescents 10 to 15 years

| Criteria | Regime | Comment |
|---|---|---|
| Weight <40kg or age <15 years | ABC + 3TC + EFV | • If adolescent weight <40kg, align with paediatric regimen.<br>• NVP can be used if EFV is contraindicated.<br>• Use TDF if creatinine clearance is >80ml/min with no proteinuria.<br>• If <80 ml/min, use ABC+3TC+EFV and adjust dosages according to renal dysfunction and discuss with an expert. |
| Weight ≥40kg and age ≥15 years | TDF + 3TC/FTC + EFV (Use fixed-dose combinations) | |

(Source: National Department of Health, 2015: 68)

### 6.5.3.4 ART for children

The standard first-line treatment for children is shown in Table 6.6. Doses are based on a child's weight, so it is therefore important to check the children's weight regularly and that they are being given the correct dose based on their weight. Maximum doses should, however, not be exceeded in older children and adolescents. Initially, a healthcare worker should see children once a month for regular follow-ups and monitoring. After they have stabilised, follow-up visits can be reduced to once every three to six months for children older than two years. Children younger than two years should go more regularly since they gain weight more quickly (National Department of Health, 2015: 61).

**Table 6.6** First-line ART regimens for children

| Criteria | Regimen | Comment |
|---|---|---|
| • Children <three years or<br>• older children weighing <10kg | ABC + 3TC + LPV/r | • Doses are based on child's weight and need to be adjusted as the child grows. |
| • Children three to 10 years and >10kg<br>• Adolescents 10 to 15 years or <40kg | ABC +3TC + EFV<br><br>Children who started on ABC/3TC/LPV/r before three years old must remain on same regime at three years of age or older | • Do not exceed maximum dosage.<br>• If adolescents weight <40kg, align treatment with children's regimen. |

*continued*

| Criteria | Regimen | Comment |
|---|---|---|
| Children on d4T | Change all d4T to ABC | • If VL* suppressed: change to ABC.<br>• If VL>1 000 copies/ml, manage as treatment failure.<br>• If VL 50–1 000 copies/ml, consult specialist. |
| Children on ddI | Change all ddI to ABC | • Change all regardless of VL. |

**Note**

* VL stands for viral load. Sufficient VL suppression is <50 copies/ml.

(Source: National Department of Health, 2015: 61)

## Support for children to adhere to ART

It is important to support the parents or caregivers of children on ART to understand the importance of adherence for the success of treatment in children. The following criteria should receive attention when working with the parents or caregivers of children on ART:

- Education and information regarding HIV and ART should be provided to parents or the caregiver of the child before commencing ART, on the following:
  - goals of therapy;
  - need for lifelong adherence;
  - prognosis of the condition (treated and untreated);
  - modes of action and adverse effects of the medication;
  - the risk and implications of drug resistance;
  - that all medications should be given as prescribed.
- There should be at least one caregiver who can be identified and is able to supervise the child's medication regimen. The social circumstances of vulnerable children (such as **orphans**) should be taken into account to enable them to receive ART when needed.
- Disclosure of the child's treatment to one other adult living in the same house should be encouraged. This person can then assist with the child's ART to make sure that the child adheres to the medication.
- The involvement and support of the family and community-based groups should be encouraged.
- The child's caregiver or parent should be motivated and committed to the child's lifelong therapy. Caregivers should understand that adherence involves giving every dose of medication, exactly as prescribed every day of every year.
- Caregivers or parents should be counselled to anticipate and plan for weekends away, schooling and other activities which could mean that doses are missed.
- Parents or caregivers should understand that poor adherence is the single most important factor associated with drug failure and resistance. Parents should understand that resistance implies loss of future treatment options for the child. Good adherence should be emphasised at each visit.

Parents or caregivers often understand adherence better if ART is compared to treatment of diabetes or **hypertension**, both of which may require lifelong therapy and where poor adherence is associated with disease progression. Healthcare workers should keep in mind that the doses of ART are likely to need modification at each visit as the child gains weight and grows. The child's medication dosage and weight should be monitored with a weight/dosage chart.

## 6.5.4 Use of ART in patients with TB

Tuberculosis is the opportunistic infection that most often occurs in HIV-infected patients. HIV-infected patients also have an increased risk of developing TB compared with the general population. It is preferable that public sector TB clinics manage TB because they follow the most recent WHO treatment regimes. Antiretroviral therapy for adults with simultaneous (concomitant or coexistent) TB will depend on whether the TB develops while the patient is on ART, or whether TB is diagnosed before starting ART. The following guidelines (Table 6.7) should be followed to treat patients with TB/HIV co-infection (National Department of Health, 2015: 102):

**Table 6.7** ART and TB treatment for adults with concomitant TB

| TB diagnosed while on ART | TB diagnosed before starting ART |
|---|---|
| • Start TB treatment immediately at standard doses.<br>• Continue ART throughout TB treatment.<br>• First-line ART regimen: Patient can remain on the regimen they are taking (unless they are on NVP, then EFV is preferred).<br>• Second-line ART regimen: The Lopinavir/**Ritonavir** (LPv/r) dose should be doubled (increase gradually from two tablets 12 hourly to four tablets 12 hourly) while the patient is on Rifampicin-based TB treatment.<br>• Monitor ALT (alanine transaminase) monthly.<br>• Reduce Lopinavir/Ritonavir to standard dose two weeks after TB treatment is completed. | • Start TB treatment first, at standard doses.<br>• Start with TB treatment first, followed by ART as soon as possible, preferably within eight weeks.<br>• If CD4 <50 cells/mm$^3$, initiate ART within two weeks of starting TB treatment, when the patient's symptoms are improving and TB treatment is tolerated.<br>• If CD4 >50 cells/ mm$^3$, initiate ART within two to eight weeks of starting TB treatment.<br>• First-line ART regimen: FDC is recommended: TDF + 3TC (or FTC) + EFV. |

(Source: Based on National Department of Health, 2015: 102)

**Note**

HIV-infected TB patients qualify for lifelong ART, regardless of CD4+T cell count.

## 6.5.5 Drug interactions

There are many **drug interactions** between ARVs and other medications, as well as interactions between specific ARVs themselves. A drug interaction occurs when one drug affects the activity of another drug when both are administered together. Healthcare workers should therefore always carefully consult the package inserts of ARV agents and coexistent (concomitant) medications to check whether or not there are any drug interactions. Patients should be encouraged to tell their healthcare workers of all medicines (including herbal medicines) that they are taking.

It is important to take note of drug interactions between antiretroviral therapy and TB medications (especially Rifampicin) since this can have serious effects on the health of the person who is co-infected with HIV and TB. EFV

**Glossary**

**Drug interaction** A drug interaction occurs when one drug affects the activity of another drug when both are administered together.

**Glossary**

**Virological failure** Virological failure occurs when ARVs fail to suppress HIV in the body. This is evident if a patient's viral load >1 000 copies/ml on at least two occasions two months apart, despite good adherence.

(Efavirenz) is the preferred NNRTI to be used together with Rifampicin. Patients with contraindications for EFV (e.g. psychosis) can use NVP (nevirapine) an alternative, but it does carry a higher risk of hepatitis and **virological failure** if it is used together with Rifampicin.

### Enrichment: Additional information on ART

If you need any information on ART that is not in this chapter (e.g. ART dosages, ARV dosage adjustments in renal failure or liver impairment, management of side effects, transition from paediatric to adult or adolescent regimens, re-initiation of patients previously on ART regimens, ART for pregnant adolescents, treatment failure, second-line ART, third-line ART, management of TB-HIV, paediatric HIV management, and management of TB co-infection) please consult the following sources:

- Managing HIV: A clinician's tool, 2015. Available at: http://www.auruminstitute.org/index.php?option=com_phocadownload&view=category&id=3&Itemid=263
- National Consolidated Guidelines, 2015. Available at: http://www.sahivsoc.org/practise-guidelines/national-dept-of-health-guidelines (or: http://www.sahivsoc.org/upload/documents/ART%20Guidelines%2015052015.pdf
- Download the 'HIV Clinical Guide' app on your smartphone.

## 6.6 Adverse effects of ART

**Glossary**

**Lactic acidosis** Acidosis is too much acid in the body. Lactic acidosis is due to the build-up of lactic acid in the body.

At the end of this chapter (Table 6.9) you will find a list of the antiretroviral drugs currently available in southern Africa, their dosages and pill burdens, as well their common side effects.

A critical factor in the success of treatment is how well the patient tolerates the antiretroviral drugs. ARVs often have side effects and occasional serious adverse effects. Adults more frequently have side effects than children. Individuals should be counselled about the milder side effects that they can expect in the first few weeks or months on ART, including diarrhoea, dizziness, mild nausea, vomiting, general malaise, peripheral neuropathy and nail discolouration. If the side effects are mild, ART should not be discontinued. Symptomatic therapy, counselling and monitoring of the condition should be implemented.

If the patient however experiences life-threatening side effects, for example severe drug-induced hepatitis, **lactic acidosis**, kidney toxicity, severe drug rash, pancreatitis or abacavir hypersensitivity reactions, an experienced HIV clinician should be consulted to manage the future treatment of the patient. The clinician will probably stop the NNRTIs, while continuing with the NRTIs for another week.

Many HIV-infected individuals on ART are also being treated for TB. Antiretroviral therapy and TB treatment have particular shared side effects. These are outlined in Table 6.8 on the next page.

**Table 6.8** Shared side effects of ART and TB treatment

| Side effects | ART | First-line TB treatment |
|---|---|---|
| Nausea and vomiting | ddI, AZT, PIs | Pyrazinamide |
| Hepatitis | NVP, EFV, PIs (especially when dose is increased to overcome rifampicin induction) | Rifampicin, INH, pyrazinamide |
| Peripheral neuropathy | d4T, ddI | INH |
| Neuropsychiatric side effects | EFV | INH |
| Renal toxicity | TDF | Rifampicin |
| Rash | NVP, EFV | Rifampicin, INH, pyrazinamide, ethambutol, streptomycin |

(Source: Aurum Institute & CDC/PEPFAR, 2015: 23)

Patients should be counselled about the possibility of **immune reconstitution inflammatory syndrome** (IRIS) that often occurs during the first three months of antiretroviral treatment (or TB treatment) particularly in patients with a CD4+T cell count <100 cells/mm$^3$. Although IRIS will be discussed in the next section, it should be noted that IRIS is *not a side effect* of antiretroviral therapy, but a *consequence of immune reconstitution* following treatment.

**Glossary**

**Immune reconstitution inflammatory syndrome** Abbreviated as IRIS, this is a condition in which the immune system begins to recover, but then responds with a massive inflammatory response (calling up large number of the 'soldiers' of the immune system) to an opportunistic infection the patient previously contracted, thereby – contrary to expectations – worsening the symptoms of the infection.

## 6.6.1 Immune reconstitution inflammatory syndrome (IRIS)

Have you heard of patients who complained that, instead of getting better after they started with ART that they actually got sicker? Or that an opportunistic infection, for which they are treated, like tuberculosis, is suddenly more severe after they started with ART? This is a typical example of IRIS (or immune reconstitution inflammatory syndrome). IRIS is a condition that is often seen in cases of immune suppression (such as with HIV infection) when the immune system starts recovering as a result of ARVs. But, instead of getting better, the patient initially gets sicker because the immune system has now been restored enough (thanks to the ARVs) to respond with an overwhelming inflammatory response to an opportunistic infection previously acquired. The symptoms of this infection now become felt.

When an HIV-infected patient is not on ARVs, the suppression of CD4+T cells by HIV causes the body's normal response to certain infections to decrease. Consequently, not only can this result in **subclinical infection**; it can also make it more difficult for the body to fight off the infection. In such a case, we can say that the immune system is so heavily under attack by HIV that it 'can't be bothered to fight any infections'. When the patient starts taking ARVs, the CD4+T cell count rapidly increases and a sudden increase of inflammatory response produces non-specific symptoms such as fever. Opportunistic infections that were there all the time can now suddenly emerge again because of the immune system which is

**Glossary**

**Subclinical infection** A level of infection that would normally produce symptoms is instead undetected.

once again fighting-fit. The most common treatment of IRIS is to treat the specific infections or diseases with infection-specific medications.

In South Africa, the most common presenting IRIS is TB. Approximately one third of patients who begin ART while on TB treatment will experience either a recurrence of their TB symptoms or worsened new manifestations. other manifestations of IRIS include rashes (such as zoster, herpes and others) and cryptococcal meningitis, as well as hepatitis B and C, that occur in the first weeks and months after initiation of ART. IRIS does not indicate drug failure or drug side effects, and it is not a reason either to stop ART or to change the ARV regimen. Careful counselling, however, is required to ensure that the patient understands this. It is however important to investigate alternative diagnoses, such as drug-resistant TB.

### Activity

**Visit your local pharmacy and ask the pharmacist for the inserts (or information pamphlets) for some of the antiretroviral drugs available.**

Read the information on the pamphlet (you can also access this information on the Internet) and make a summary in table form that includes the following:

- the name of the drug;
- the class or category of the medication (e.g. NRTI, NNRTI or PI);
- the contra-indications (e.g. can this drug be taken by pregnant women, or by patients with renal failure or with liver disease?);
- the dosage and directions for use;
- the possible side effects of the medication;
- the special precautions (e.g. does the manufacturer discuss negative interactions with other medications or herbal products?); and
- the special requirements (e.g. should alcohol be avoided, should certain foods be avoided, should the medicines be taken on an empty or a full stomach?)

## 6.7 How to know if ART is effective

The effectiveness of antiretroviral therapy should be monitored by looking at the viral load (VL). Viral load monitoring for first-line regimes for adolescents 15 years or older and adults is as follows (National Department of Health, 2015: 75):

- *If the viral load is <400 copies/ml:* Monitor VL 12 monthly and provide intensified adherence for patients whose VL is above 50 copies/ml.
- *If the viral load is between 400 to 1 000 copies/ml:* Assess and manage adherence carefully and repeat VL in 6 months and manage accordingly.
- *If the viral load is >1 000 copies/ml:* Assess adherence and provide intense adherence support. Repeat VL in two months and check HBV status and Hb. If VL <1 000 copies/ml, repeat in six months and then reassess. If the VL is still >1 000 copies/ml and adherence issues have been addressed, switch to second-line therapy after checking HBV status and Hb.

We know that a patient's ARVs are effective when the viral loads are low – preferably to undetectable levels <50 copies/ml. An increase in the viral load either indicates non-adherence or that the treatment is not working and that a patient's

drug therapy needs to be re-evaluated and changed. The CD4+T cell count is not a good indicator of ART failure and should not be used to indicate the effectiveness of ART. A patient with optimal **virological suppression** can in some cases have low CD4+T cell count responses and if the low CD4+T cell count is taken as evidence of ART failure, the ART regime will be inappropriately switched. Failure of ART should therefore be defined only on the basis of viral load, irrespective of the CD4+T cell response.

**Glossary**

**Virological suppression** The correct use of ARVs reduces or suppresses the replication and function of HIV to such an extent that the viral load can become undetectable, which means to levels <50 copies/ml.

## 6.8 When to change ART

Because there are only a limited number of drugs available, careful consideration should be given before changing antiretroviral therapy. It is a major step to change from a first-line ART regimen to a second-line ART regime. This is because drugs used in second-line regimens are often not as well tolerated as those in the first line. In addition, they are more expensive than first-line ART regimens (Southern African HIV Clinicians Society, 2014: 128).

Antiretroviral medication should be changed under the following circumstances:

- when the patient shows intolerance of the medication, despite adequate and appropriate treatment;
- when drug toxicity occurs; and
- when virological failure occurs, e.g. when, despite good treatment adherance, the viral load increases or shows an insignificant decline.

If the viral load (VL) is detectable, it is important to do adherence counselling. The SAHIV Clinician's Society (2014: 128) advise a switch to a second-line regimen without undue delay when two VL measurement have been >1 000 copies/ml, preferably with the measurements taken two to three months apart, with at least four weeks of an intensified adherence intervention in between. In patients with a low CD4+T cell count (<100 cells/mm$^3$) the process of changing ART should be expedited. If patients have persistently detectable VLs at low levels (200–1 000 copies/ml) for a prolonged period of more than one year, or if they have persistently low CD4+T cell counts (<100 cells/mm$^3$) together with low level VL despite adherence interventions, they should be switched to second-line ART.

When a patient shows intolerance towards a specific medication, the drug can be replaced with another drug in the same treatment regime. When virological failure occurs, the entire regime should be changed.

**Note**

When replacing one drug with another drug in the same treatment regime or when changing the entire drug regime, make sure you follow the Southern African HIV Clinicians Society or the DOH guidelines.

## 6.9 The development of drug-resistant viruses

The development of **drug resistance** is a serious problem, which can have dire consequences for future treatment. Consequently, it is imperative for healthcare workers to understand what drug resistance is and what must be done to prevent it. The development of drug-resistant organisms is not a new phenomenon and our first introduction to the problem of drug resistance was probably when we were urged to take all our antibiotic medication as a child (although the reason why was never explained to us). Although drug resistance will now be explained at the hand of HIV, the same basic principles apply for the development of drug-resistant organisms in tuberculosis and other diseases.

**Glossary**

**Drug resistance** If a patient does not take his or her medication as prescribed, or if an insufficient ART regime is prescribed, the concentration of drugs in the bloodstream will fall too low to keep the pathogen depressed and mutants will develop. The drugs will be ineffective against these mutants.

Two main factors influence the development of drug resistance in HIV. These are:
- the high genetic variability of HIV; and
- the relative 'fitness' of these variations in the presence of antiretroviral drugs.

In Chapter 2 we explained that the variability of HIV is mainly the result of the 'mistakes' that are being made by the reverse transcriptase enzyme when DNA copies are made from the viral RNA. We further explained that the RNA replication mechanism does not have a facility to 'proofread' for mistakes and to repair them. These mistakes or errors are called mutations. Many spontaneous genetic mutations of HIV arise every day – including changes in the enzymes that are targeted by the antiretroviral drugs. ARVs are made to 'fit' or to attach to the viral enzymes – much like a key that fits only into one specific lock. If these enzymes change (because they mutated), there is no way that the ARV (the key) will fit into the mutated enzyme (the lock). The ARV will thus be completely useless against the mutation.

What happens in the body if a person adheres completely to the ARV treatment regime? Every previously untreated HIV-infected person will have a lot of viruses in the blood. Most of these viruses will be **wild-type viruses**. There will also be mutant viruses, but they will be in the minority because they cannot compete with the dominant wild-type viruses. The mutations will thus naturally persist at very low levels in the blood. If the patient starts taking ARVs and adheres to the medications optimally, the wild-type viruses will be suppressed and they will not get the chance to reproduce. The mutants will also not increase because their levels are so low that the immune system will take care of them. The viral load will drop to undetectable levels and the immune system will get the chance to replenish itself. This is the ideal situation.

**Glossary**

**Wild-type virus** The wild-type virus is the most common or dominant form of HIV. Anything different from the wild type is considered a mutation. The 'pattern' of the wild-type virus is used to make ARVs.

## 6.9.1 Non-adherence and drug resistance

What happens when a patient either does not adhere to the medication or if the patient uses an insufficient ART regime (e.g. **monotherapy** with only one drug instead of three)? It is important to understand that the introduction of ART, which suppresses the wild-type virus, dramatically changes the virus population's ecology in the body. If this suppression is not sufficient (e.g. the patient is only on one drug) the majority of the wild-type viruses will be killed but viral suppression will not be sufficient. This means that there will be a sudden gain in mutations' 'fitness' because there will not be enough wild-type viruses left to compete against. The mutants will now replicate and become the dominant virus in this patient's body because the wild-type viruses are repressed by the ARVs. These mutations are drug resistant and the drugs will have absolutely no effect on them, because existing ARVs were not made to 'fit' these mutant viruses. This patient's treatment is compromised because the viral load is not sufficiently suppressed. When the healthcare worker realises the mistake of prescribing an inferior regime, it may be too late because none of the known ARVs (in a specific class) will 'fit the lock' of the mutants to stop them from replicating.

What happens when patients do not adhere to their treatment regime? To repress the wild-type virus sufficiently so that the virus cannot replicate and mutate, there should be enough ARVs in the bloodstream 24 hours a day. Levels of ARVs in the blood are high just after taking a dosage and low just before taking the next

**Note**

If combination ARV drugs are used consistently, viral replication is suppressed completely. When virus replication is suppressed, mutations cannot occur and resistance does not develop.

dosage. If a patient forgets to take his or her ARVs, the drug levels in the blood fall below the optimum level and this will give some viruses (both wild-type and mutations) the opportunity to escape and to produce new viruses – some of which will be mutations. If the patient starts taking ARVs again, the ARV blood levels will rise to optimum levels again and most HIV viruses will again be suppressed. However, the small number of viruses that have escaped during the period of non-adherence (and which formed mutants) will now be resistant to the action of the drugs. They will survive and replicate even though the patient is taking her or his ARVs again. Eventually, this resistance will lead to an increase in the quantity of viruses in the blood (high viral load). But, instead of having treatable, sensitive viruses, the patient will now have drug-resistant viruses which no longer respond to the drugs he or she is taking. Figure 6.3 on page 166 provides a simplified illustration of what happens in the body when a person does not adhere to his or her ARVs.

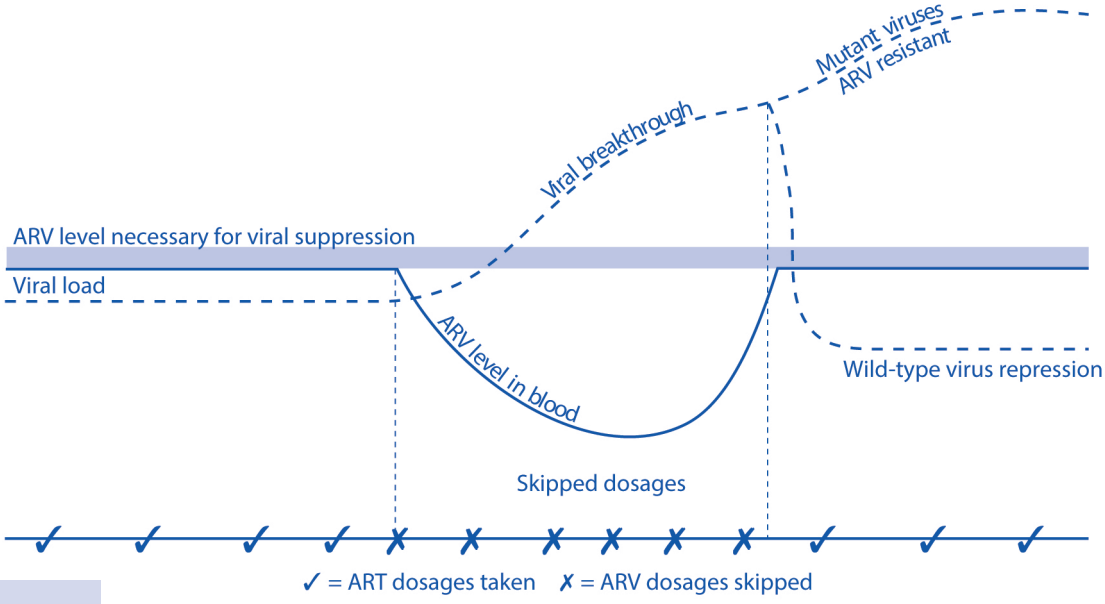
The development of drug-resistant viruses has serious consequences, not only for individual patients, but also, generally, for treatment. Resistance to one drug (specifically the NNRTIs) could, for example, lead to resistance to other drugs in that same class. This is known as cross-resistance and it means that, if the virus has developed resistance to one drug in a specific class (e.g. NNRTI category), none of the other NNRTIs will have an effect on the virus. It seriously compromises the treatment options of the patient. Resistant viruses also pose a significant public health challenge, because these resistant viruses are transmitted to other people. Resistance testing can be done to determine if individuals are resistant to specific medications.

## Enrichment: Resistance testing

There are two types of resistance tests:

- a genotypic assay; and
- a phenotypic assay.

Whereas the genotypic assays look directly at the genetic material of the HIV in a patient's blood and gives them information about the HIV drugs their virus is resistant to, phenotypic assays assess how well the HI virus is responding to specific medications in a particular environment that is controlled, such as a laboratory. For more information, see, for example: https://www.aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/understand-your-test-results/resistance-test/




**Note**

This is a very simplistic illustration of how drug resistance can develop if drug dosages are skipped. The process is, of course, more complex.

**Figure 6.3** The effects of non-adherence to an ARV regime

## 6.10 Adherence to ART

In the scientific community it is widely accepted that 90% is the minimum adherence level required to suppress the virus sufficiently, to prevent the danger of mutation, and to prevent drug resistant strains and drug failure from developing.

### 6.10.1 Reasons for non-adherence

**Glossary**

**Treatment fatigue** This means that patients get so tired of taking medication all the time that they simply stop.

There are many reasons why people often find it difficult to adhere to ART. Some of these reasons are (Van Dyk, 2011):

- *Person-centred or psychosocial barriers:* **Treatment fatigue;** forgetfulness; bad planning and running out of ARVs; sharing ARVs with friends; alcohol abuse; denial; depression; no personal intention to adhere (was coerced by healthcare workers or family to take ARVs); non-disclosure; no support from significant others; no treatment supporters and too ashamed to disclose to hospital personnel after emergency admission that they are on ART.
- *Relationship between patient and healthcare worker:* Lack of healthcare support; lack of sharing of information with the patient, e.g. about CD4+T cell counts and viral load; and no understanding of why they should adhere.
- *Practical problems:* Transport problems to the clinics; insufficient food to eat that meets ARV requirements; difficulty in advance planning to ensure an ongoing supply of ARVs, e.g. when going on holiday or away for work; cannot ask time off from work (non-disclosure); working shifts which makes ARV taking difficult; and muggings and robbery of ARVs.
- *Work-related issues:* Patients are often unable to attend clinic visits during the week. Clinics should therefore be flexible and run smoothly to avoid long waiting times. Evening clinics and adherence clubs should be offered.

- *Medication-related issues:* Difficult treatment regime to follow (if FDCs are not used); side effects; and pills too big to swallow.
- *Service-related barriers:* Hospitals and clinics not having enough stock; structure of clinics (e.g. separate HIV areas); healthcare workers on strike; poor discipline in clinics (e.g. bad service, early closure); and prisoners finding it difficult to get ARVs in prison.
- *Stigma:* Secrecy, fear and lies; hiding of pills; non-disclosure; no support groups because of secrecy; and fear of community rejection.
- *Health control:* No control over own health; fatalistic attitude ('Nothing I can do will make a difference'); and an external **locus of control** ('What happens to me is controlled by factors that I have no control over.').
- *Cultural aspects:* Using medicines from traditional healers with ARVs without disclosing to healthcare worker.
- *Conflict of opinion:* Healthcare providers, particular alternative health providers and some churches may have different opinions on use of ART, which may confuse the patient and lead to non-adherence.

It is important for healthcare workers to talk to their patients and to understand the factors in their lives that may affect adherence.

**Glossary**

**Locus of control** The extent to which individuals believe they can control events that affect them. People with an external locus of control believe they have no control over what happens to them, whereas people with an internal locus of control believe they are in control of their choices.

## 6.10.2 Strategies for improving adherence to ART

It is recognised that healthcare workers in southern Africa, who work in the HIV field, often work in very challenging and complex circumstances. It is however important for healthcare workers to understand fully the very dire implications of poor ARV adherence and, consequently, to make every effort to help their patients to adhere to their regimens. The following recommendations are made for healthcare workers to support their patients on ART to adhere:

- Evaluate the person's ability and intention to adhere. Patients who want to take ARVs must be committed, demonstrate insight, be well informed, and able to keep to a strict medication regime. If they do not show this commitment and readiness, prepare them for it before starting the regimen.
- Simplify treatment regimens by prescribing fixed-dose combination (FDC) regimes. FDCs have higher adherence levels.
- Identify the relevant barriers or challenges to adherence (personal, environmental, social or cultural) that specific patients may face and develop an individualised plan that supports the patient to reach and sustain optimum adherence levels.
- Ensure healthcare workers have been trained to recognise, manage or refer patients with problems that can impact seriously on adherence, such as mental health (e.g. depression) problems and substance (e.g. alcohol) abuse.
- Use teaching techniques, e.g. ask patients to repeat information (patients often do not listen because they are worried); use pamphlets and visual aids in the patient's language and describe how to take medication.
- Skills training (e.g. how to plan and manage ARVs; how to disclose ARV taking to potential sources of support (if it is safe to do so); how to negotiate for time off from work when necessary; how to disclose to sex partners; and adherence skills in cases where it is not safe to disclose to sex partners should form part of adherence support.

- Reminder strategies might help some patients to adhere, such as a radio or TV programmes, cell phones or alarm clocks.
- Healthcare workers should support patients to develop skills on how to cope with treatment fatigue and forgetfulness and help them to make specific adherence plans.
- Assist ARV users to deal with discrimination, stigma and negative attitudes. Create opportunities for the patient to talk about this. Patients often hide their ARVs out of fear that someone may find them.
- Ongoing patient education (individual and group) is a vital part of adherence counselling. Do they understand their treatment plan and expected clinic visits? Why they should adhere? Do they know what is meant by adherence? Do they understand why certain tests are done (e.g. CD4+T cell count and viral load)? Do they understand the logical connection between viral load suppression and clinical outcome?
- Patients should be made aware of possible side effects and to expect them in the first few weeks after starting ART. They should also be counselled to report side effects immediately when they occur so that action plans like treatment can be made.
- Healthcare workers should be advocates for their patients and use their influence to bring about policy changes to make life easier for their patients on ART (e.g. avoidance of stock-outs, and the policy of including food parcels and transport vouchers for patients who need them).
- Healthcare workers should accept the fact that many of their patients also visit traditional healers and the risks of medication interactions should be discussed with patients (without disrespecting the patient's cultural beliefs).
- Enhance patient–healthcare worker communication by expressing personal interest in the patient and by establishing respect and unconditional acceptance. Use positive reinforcement (e.g. praise adherence, share results of CD4+T cell counts and viral loads).
- Enlist the help of partners, family, friends, peers, support groups in the community, the church and allied healthcare workers, to reinforce adherence to treatment. Care should be taken in involving other people in communities where it is not safe to disclose (see Chapter 11).
- Encourage the patient to find a treatment supporter who is willing to help the patient to always get and take the medicines. A good treatment supporter should be someone the patient can trust, who keeps the patient's HIV status confidential, who lives in the patient's household or neighbourhood, who is a responsible and reliable adult, who is able to support the patient for a long time, who can remind the patient to go for follow-up visits and who can go with the patient to the clinic when necessary. If the patient refuses to involve a treatment supporter, accept that there might be good reasons for the refusal and assist the patient in other ways to adhere.
- Refer patients with financial problems to the relevant social service departments for assistance and disability grants. Poverty and food insecurity often lead to poor adherence and missed clinic visits.
- Missed appointments for medicine pick-ups are a powerful predictor of poor adherence and it should trigger immediate assessment.
- Conflict of opinions (e.g. the patient's church believes that ARVs should not be taken) should be addressed in an honest and non-judgemental way.

Adherence counselling is not a once-off occurrence. Patients often experience treatment fatigue. Patients also often stop taking their medications when they start feeling better. Recounselling and remotivation on a regular basis are therefore, extremely important.

**Frequently Asked Question**

**Can ARVs cure Aids?**

Although HIV infection can be treated with antiretrovirals to suppress the viral load, ARVs are not a cure for HIV infection or Aids. There is currently NO cure for HIV infection. The current emphasis in treating HIV is to keep the viral count at undetectable levels and to strengthen the immune system to keep the individual as healthy as possible for as long as possible, and to treat opportunistic infections.

Note that an HIV antibody test may be false negative in patients who have been on ART for a long time. Some patients may believe that they are 'cured' which is, of-course, not the case.

We have now reached the end of the discussion on ART as treatment for established HIV infections. The sections that follow will look at the uses of ART to prevent HIV infection from occurring (see Figure 6.1 on page 148).

## 6.11 Prevention of mother-to-child transmission

The use of ART has been shown to be the most important strategy in preventing mother-to-child transmission of HIV. Healthcare personnel at antenatal care clinics should provide all women attending antenatal care (as first-time attendees and those on follow-up visits) with routine information about HIV testing and the PMTCT programmes.

The National Department of Health aims for the PMTCT programme to reach all women before and during pregnancy, through labour and delivery, and through the postnatal period up to 18 months. The programme aims to identify and promote the health of HIV-positive mothers and their HIV-exposed infants, including the diagnosis, management and prevention of opportunistic infections (National Department of Health, 2015: 51).

The PMTCT programme consists of the following key components:

- Offer sexual and reproductive health services to all women of reproductive age.
- Offer HCT (HIV counselling and testing) to all pregnant women at the first antenatal visit. Repeat PICT (**provider-initiated counselling and testing**) for HIV-negative women every three months. Provide antenatal care and further management as necessary depending on the HIV status of the woman.
- Conduct management during labour and delivery as per HIV status. All HIV-negative women should be tested for HIV at labour or delivery regardless of when last they were tested.

**Glossary**

**Provider-initiated counselling and testing** Also known as PICT, this is HIV counselling and testing which is initiated and recommended by healthcare providers to all adults, youth and children attending healthcare facilities as a standard component of medical care.

- Provide postnatal care as necessary depending on the HIV status of the mother. Repeat PICT for HIV-negative women at EPI (immunisations) visits and three monthly throughout breastfeeding.
- All infants should be followed up and managed as per HIV status.

Mothers should be encouraged to breastfeed their infants exclusively during the first six months of life. They should introduce appropriate complementary foods from six months onwards and breastfeeding should continue until the infant is one year old.

All pregnant women, women who are breastfeeding their babies and women who are diagnosed with HIV infection postpartum, regardless of their feeding choice, are eligible for lifelong ART. Lifelong ART should be initiated on the same day that the woman tests positive, regardless of CD4+T count. If the woman has no contraindications for FDC and no TB symptoms, she can start with FDC (fixed-dose combination of TDF + 3TC (or FTC) + EFV) on the same day (see Table 6.4 on page 156).

### Enrichment: Management of pregnant women on ART

Consult the National Department of Health's Consolidated Guidelines, 2015 (or a more recent source) at: http://www.sahivsoc.org/practise-guidelines/national-dept-of-health-guidelines for more information on the management of pregnant women on ART, including the prevention and management of opportunistic infections.

Women who become pregnant while on lifelong ART should continue with their ARVs. The benefits of ART to prevent MTCT as well as the benefits of lifelong ART for the mother should be discussed with her. She should also be reassured about the safety of ART during pregnancy. The link between viral load and the risk of HIV transmission should be explained as well as the importance of frequent monitoring during pregnancy, including viral-load checks and partner testing.

## 6.11.1 Infant prophylaxis

**Glossary**

**HIV-exposed infant** A baby who was exposed to HIV (e.g. born to an HIV-infected mother) but is not necessarily infected with the virus.

Infant prophylaxis is the foundation of a post-exposure prophylaxis strategy. Antiretroviral prophylaxis that is given to all **HIV-exposed infants** soon after birth is effective in reducing MTCT, whether the mother is on ARVs or not. The following principles should be followed for infant prophylaxis (Aurum Institute & CDC/PEPFAR, 2015: 44; National Department of Health, 2015b):

- If the mother is on ART with VL <1 000 copies/ml, the baby should receive NVP at birth and then daily for six weeks.
- If the mother is initiated onto ART late in pregnancy (less than four weeks before delivery) or if she is diagnosed while in labour or within 72 hours of delivery, and she is breastfeeding, the baby should receive NVP daily for 12 weeks.
- If the mother is on ART and her VL >1 000 copies/ml, NVP plus AZT should be given for six weeks. An HIV PCR test should be performed on the baby at or shortly after birth.

- If a breastfeeding mother tests HIV-positive >72 hours post-delivery, the baby should start taking NVP plus AZT immediately. An infant PCR should be done and results should be reviewed in seven days. If PCR is negative, AZT can be stopped and the infant should continue to take NVP for 12 weeks. If PCR is positive, stop NVP and AZT and start urgently with ART regime for babies.
- If a non-breastfeeding mother is diagnosed HIV positive >72 hours post-delivery, no infant prophylaxis is necessary.
- If the maternal status is unknown including abandoned infants or orphans, give NVP immediately after birth and continue until HIV-exposure status is confirmed. Do an HIV rapid test and if the rapid test is positive (which means the infant is HIV exposed) continue NVP for six weeks. If the rapid test is negative, it means that the infant was not exposed and NVP can be stopped.

To see what the ART regime for babies is, see Table 6.6 on page 157.

All infants born to HIV-infected mothers should receive nevirapine daily for six weeks (15 mg if the birth weight is ≥2.5 kg and 10 mg if the baby weighs <2.5 kg). Infant prophylaxis should be started as soon after delivery as possible.

### Frequently Asked Questions

**What happens if an HIV-infected mother refuses ART prophylaxis for her baby?**

If a mother refuses ART prophylaxis for her baby, a counsellor must intervene and explain the risks of MTCT, as well as the ways in which ART prophylaxis can benefit the infant. If the mother still refuses prophylaxis for the baby, she should be advised of the infant's legal right to receive protection against acquiring HIV. According to the Children's Act, No. 38 of 2005, the best interest of the child shall be a primary consideration in all actions concerning children. With permission of the head of the facility, the necessary treatment can be provided to the infant.

**How do ART work to prevent mother-to-child transmission?**

The main function of ART taken by the mother is to lower the HIV concentration in her blood. The baby's chance of becoming infected during pregnancy and the birth process is much lower if the viral load in the mother's blood is low. If the mother takes antiretroviral drugs while she breastfeeds her baby, the effect is the same: ARVs reduce the viral load (or concentration of viruses) in the breast milk, so there is less chance that the baby will become infected.

## 6.12 Post-exposure prophylaxis after occupational exposure

Although the risk of contracting HIV after occupational exposure to HIV is low (0.3%), the risk of contracting hepatitis B and C is much higher. Everything possible should therefore be done to protect healthcare workers against occupational exposure to HIV and hepatitis infections. Research indicate that occupational exposure to HIV and the hepatitis virus in southern African countries is substantial (Karstaedt & Pantanowitz, 2001; Westermann et al., 2015). In a study among hospital workers in Uganda, more than half reported having experienced at least

one needlestick injury in the last year (Nsubuga & Jaakkola, 2005). A study on the practices of nurses in rural Limpopo in South Africa found that seven in 10 nurses reported previous needlestick injuries. Post-exposure prophylaxis or PEP was not available in all the healthcare facilities for exposed nurses to access (Delobelle et al., 2009).

PEP can significantly reduce the risk of HIV infection after percutaneous exposure to HIV-infected blood. PEP consists of antiretroviral therapy which must start as soon after the incident as possible (it must be within 72 hours after exposure) to reduce the chances of viral reproduction as much as possible. The efficacy of PEP after 72 hours is highly unlikely. PEP should not be offered to individuals who are already infected with HIV.

The following protocol should be followed in cases of occupational exposure to HIV-infected blood or other body fluids:

- Do a clinical assessment of the nature of the exposure (see the Enrichment box on page 173).
- Assess the healthcare worker's eligibility for PEP by doing a rapid HIV antibody test after pre-test counselling and informed consent. An ELISA test can also be used if a laboratory is close by. Results can usually be obtained within three hours in emergency cases.
- If the baseline test is HIV negative and the healthcare worker accessed help within 72 hours of the incident, a 28-day course of the following antiretrovirals should be offered (as recommended for adults and adolescents by the Southern African HIV Clinician's Society, 2015):
  - TDF (tenofovir) + 3TC (lamivudine) or FTC (emtricitibine) are the preferred backbone drugs for PEP, preferably as a fixed-dose combination.
  - The preferred third drug is raltegravir (RAL). The preferred drug in pregnancy is ATV/r (atazanavir/ritonavir).
- All PEP ARV regimes must be taken for a full 28 days.
- If the healthcare worker accesses treatment 72 hours after the incident, counselling and blood tests are offered, but PEP is not given. PEP does not have a prophylactic effect after 72 hours and resistance might develop if the person is indeed HIV infected and PEP is prescribed.
- If the baseline rapid test is HIV positive, PEP is not given under any circumstances. The healthcare worker should receive counselling and referral to appropriate service providers for further testing (e.g. CD4+T cell counts) and counselling to prepare the healthcare worker for lifelong ART. To give ARVs as PEP for 28 days to a person who already is HIV positive will not help. It might contribute to the development of resistant viruses, which may compromise the future treatment of the person.
- If PEP is given, provide information about the PEP guidelines and the possible side effects.
- Offer follow-up HIV testing three months after exposure and link healthcare worker to HIV treatment if necessary.
- Healthcare workers on ART should receive counselling to help them to adhere to the medication and to deal with the psychological turmoil and uncertainty after the diagnosis. They should also be prepared for possible side effects of the ARVs and treatment for side effects should be offered.

Also see the Clinician's Society Guidelines on PEP (updated in 2015) at: www.sahivsoc.org/Files/PEP%202015%20Guidelines.pdf

## Enrichment: Eligibility for post-exposure prophylaxis

Exposures that may warrant PEP:

- parenteral or mucous membrane exposure (sexual exposure and splashes to the eye, nose or oral cavity); and
- bodily fluids such as blood, blood-stained saliva, breast milk, genital secretions and cerebrospinal, amniotic, rectal, peritoneal, synovial, pericardial or pleural fluids.

Exposures that do not require PEP:

- when the exposed individual is already HIV positive;
- when the source is established to be HIV negative; and
- exposure to bodily fluids that do not pose a significant risk, like tears, non-blood-stained saliva, urine and sweat.

The list of exposures that may warrant PEP is not exhaustive and all cases should be assessed clinically and decisions made by healthcare workers as to whether exposure constitutes significant risk. The WHO (2014: 17) further recommends that in some settings with a high HIV prevalence or where the source is known to be at high risk for HIV infection, all exposure may be considered for post-exposure prophylaxis without risk assessment.

It is not only healthcare workers who are at risk of occupational exposure but also non-health workers, such as cleaners in hospitals, firefighters, police officers, teachers, sex workers, prison warders and bar bouncers. PEP is also not only provided to people exposed to HIV in the healthcare setting or after sexual assault but can also be used after unsafe sex, (e.g. casual unprotected sex, or in situations of condom breakage or where the condom slipped off during sex). However, ART should be used with care, and it should not be used routinely or frequently in place of general safer sex practices.

## Activity

**While working in a hospital as a counsellor, you notice that a volunteer caregiver is pricked by a needle which was left in the bed of a mentally very confused patient with Aids.**

How would you counsel the caregiver?

- The clinic gives the caregiver a 'starter pack' of antiretroviral drugs, but no information on how to use it. What advice would you give the caregiver?
- Make a wall poster indicating all the steps that healthcare workers should take after accidental exposure to HIV-infected blood in the healthcare situation. (See 'Management of accidental exposure to blood and other infectious body fluids' on page 573 to help you with this.)

### Enrichment: 'Starter' packs for PEP

Starter packs for PEP are used in many settings to facilitate rapid initiation of ART (e.g. after needlestick injuries, rape or sexual assault). A starter pack contains enough antiretroviral drugs for only three days and the person should be advised to get a prescription for the rest of the medication (or to get it from the hospital pharmacy or clinic) to complete the 28-day course. But will people do that? Ford and colleagues (2015) conducted a meta-analysis on data of 11 714 PEP initiations and they found that overall adherence were better when participants were offered a full 28-day course of PEP instead of only a starter pack. They also found higher completion rates when individuals were offered the full 28-day course. More than a quarter (28%) of individuals provided with a PEP starter pack failed to return for their subsequent appointment and thus did not take the full course of PEP. The conclusions of this study are that starter packs do not improve adherence to PEP and may result in lower adherence and completion rates.

## 6.13 PEP after rape or sexual assault

Because of the high incidence of violent crime in South Africa, healthcare workers are often called upon to treat the trauma that accompanies rape or sexual assault on adults and children. The risk of HIV infection after rape depends on factors such as the HIV status of the rapist, the viral load in the blood of the rapist, and the coexistence of STIs – especially ulcerations. The risk of HIV infection may also be higher in cases of violent rape and rape of children, because of the considerable physical trauma inflicted. Incidents of male rape (e.g. forced anal sex) are often reported, and counsellors should not underestimate this problem. Oral sex can also put the rape survivor at risk of HIV.

It is very important to begin prophylactic treatment with antiretroviral therapy as soon after the incident as possible (no later than 72 hours after the event, but preferably within the first hour or two) after the first act of penetration or attempted penetration. Children who are sexually assaulted or raped especially need to be treated with ART as soon as possible (within the first two hours) after the incident.

The same ART regime and medication dosages that are used after occupational exposure (see Section 6.12) are used for rape survivors. A combination of three drugs is preferable and it should be used for 28 days.

The rape survivor should be counselled and tested for HIV (with a rapid HIV antibody test or ELISA if emergency testing is available) before ART is started. The following protocol should be followed:

- If the rape survivor tests HIV positive on the rapid HIV antibody or the ELISA test, ART should not be given, because the person was not infected by the rape, but previously infected. Treating an already HIV-infected rape survivor (or healthcare worker after a needlestick injury) with short-term antiretroviral drugs may lead to drug resistance, which will compromise future treatment. The person should be referred for further counselling and preparation for lifelong ART.
- If the rape survivor tests HIV negative, start PEP immediately and inform the person about the PEP guidelines, e.g. to take every single dose of the

medication for the 28 days. If a starter pack is provided explain to the person how important it is to get the rest of the prescription filled (see the Enrichment box on page 174).

- Some sources suggest that, in cases where you have to wait for HIV test results for so long that the client loses his or her 72-hour opportunity, PEP should be started. If the HIV test is negative, continue with treatment for 28 days. If the HIV test is positive, discontinue treatment and refer the client for support counselling and preparation for lifelong ART. It is however seldom necessary to wait so long for test results with the general availability of rapid tests.
- Patients on PEP should be counselled about the possible side effects that the drugs might have on them. Adherence counselling is extremely important.
- Rape survivors should be counselled to go back for HIV antibody testing at three months to test for seroconversion.
- Counsel the rape survivor about practising safer sex for three months, until the next test is done.

The rape survivor is at risk not only of HIV infection, but also of other sexually transmitted infections such as syphilis, hepatitis B and hepatitis C. It is therefore important for rape survivors to be tested and treated prophylactically for STIs and to be vaccinated with hepatitis B vaccine. There is no known prophylaxis for hepatitis C. There is also a 'morning-after' pill that women can take to stop them from falling pregnant as a result of the rape.

In South Africa, rape survivors are provided with free antiretroviral drugs at public hospitals and clinics. If the drugs are not available, rape survivors should be advised to call the Aids Helpline (0800-012-322) to find out where they can get ART for free.

## Frequently Asked Questions

### Can children take antiretroviral drugs after sexual assault or rape?

Yes, children can (and should) take antiretroviral drugs for PEP. Although the 72-hour rule also applies to children, children should preferably be treated with ARVs as soon as possible after the incident. All children who come to the hospital or clinic within 72 hours of the incident (rape or sexual assault), and who are HIV negative, are offered a 28-day course of ARVs.

Children who come to the attention of medical personnel 72 hours after the incident, or children who are HIV infected, are not offered PEP. They and their parents or guardians are counselled and referred for follow-up care and counselling. ART should be initiated in children who test HIV positive irrespective of CD4+T cell count or CD4%.

It is important for children to receive PEP as soon as possible (within the first two hours if possible) after sexual assault. The reason for this is that rape or sexual assault on a child is usually accompanied by physical trauma or injury and bleeding, which are all factors conducive to the entry of viruses. Children older than 12 years do not require permission from their parents or guardians to have an HIV test or to take ARVs. Children younger than 12 years (with the maturity to understand) may consent to HIV testing, but not to ARV treatment. To take ARVs, they will need the consent of one of their parents, a guardian or the hospital superintendent. In emergency situations where a child younger than 12 years has been raped and needs urgent assistance, doctors should be guided by the best interests of their patients and their duty to give emergency medical treatment.

**How does ART work to prevent HIV infection after needlestick injuries or rape?**
If ART is given as soon as possible (within 72 hours) after rape or a needlestick injury there is a good possibility that the viruses that entered the body will be eradicated before they have a chance to attack CD4+T cells, replicate and establish themselves in the body. Remember that ART interferes with the replication mechanisms of HIV and prevents the virus from reproducing.

## 6.14 Pre-exposure prophylaxis

**Glossary**

**Serodiscordant couple**
A relationship in which one partner is infected by HIV, whereas the other is not. (A relationship in which both partners have the same HIV status is called a seroconcordant couple.)

The World Health Organization (2015: 14) recommends the following regarding HIV-negative individuals who are at substantial risk of HIV infections (e.g. **serodiscordant couples**, men who have sex with men, transgender women, sex workers, people who inject drugs and vulnerable young women):

*Oral PrEP (containing TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches.*

See Figure 3.1 in Chapter 3 for combination prevention approaches.

Truvada® (the ARV of choice for PrEP) consists of a combination of FTC (emtricitabine) and TDF (tenofovir). Note that oral PrEP should be used as part of combination prevention approaches. This means that the person should not only rely on PrEP, but should also use condoms.

## 6.15 Conclusion

Part 1 of this book is concerned largely with the physical aspects of HIV and Aids: how the virus is transmitted, what effect it has on the body, how it is diagnosed and how it can be treated. In the first part, we saw how the character of HIV infection has changed from being fatal to being manageable. The advent of antiretroviral drugs has brought hope to millions of HIV-infected people who would have died without them. Great advances have also been made in the use of ART as a means to prevent HIV infection. There is, however, still much to do and the relentless search for a vaccine is ongoing. Nonetheless, in the context of a cure for HIV infection still eluding us, one of our best strategies against the disease is to keep the virus out of the body. Part 2 of this book thus deals specifically with how to prevent HIV infection by changing people's current behaviour patterns that increase the risk of infection to behaviours that avoid such risk. In this respect, it outlines how children and adults can acquire the life skills necessary to prevent HIV infection.

## Test your understanding

1. What is the relationship between a person's immune status and his or her CD4+T cell count?
2. What does an increasing viral load in a person's blood signify?
3. Why are the CD4+T cell count and the viral load inversely related to each other?
4. What is the overall purpose of antiretroviral therapy (ART)?

5. Describe in your own words the effect of different kinds of antiretroviral drugs on HIV.
6. Why is highly active antiretroviral therapy (treatment with three drugs) recommended for the treatment of HIV infection?
7. When should antiretroviral drug therapy be initiated in an HIV-infected adolescent and adult?
8. What are the advantages of FDCs (fixed-dose combinations)?
9. Can antiretroviral medication eliminate HIV completely from the body?
10. How soon should antiretroviral therapy be started in the case of rape survivors? For which other diseases should the person be tested and treated?

**Table 6.9** Antiretroviral drugs mostly used by SA National Department of Health, dosages, contraindications and adverse drug reactions

| Generic name | Class of drug* | Recommended dosage | Contraindications/cautions | Common or severe adverse drug reactions |
|---|---|---|---|---|
| Tenofovir (TDF) | NtRTI | 300mg once daily (od) | • Avoid if:<br>– CrCl <50ml/min in non-pregnant adults<br>– CrCl <80ml/min in adolescents 15 to 19 years<br>– creatinine >85 µmol/l in pregnant women<br>• Caution in patients on other nephrotoxic drugs e.g. aminoglycosides (used in MDR-TB treatment)<br>• Risk of rebound hepatitis if discontinued in patients with chronic Hep B | • Nephrotoxicity (renal failure)<br>• Reduced bone mineral density<br>• Flatulence, nausea, diarrhoea, abdominal discomfort<br>• Hyperlactataemia/steatohepatitis (very low potential) |
| Zidovudine (AZT) | NRTI | 300mg twice daily (bd) | • Avoid if:<br>– Hb <8g/dL in non-pregnant adults and adolescents<br>– Hb <7g/dL in pregnant women | • Bone marrow suppression (anaemia, neutropenia)<br>• Headache, myalgia, nausea, fatigue – usually resolve two to four weeks after initiation<br>• Myopathy<br>• Lipoatrophy<br>• Medium potential for hyperlactataemia/ steatohepatitis |
| Abacavir (ABC) | NRTI | 300mg bd or 600mg od | • Avoid if:<br>– previous hypersensitivity reaction<br>– severe hepatic impairment | • Hypersensitivity reaction<br>• Rash<br>• Headache, nausea, vomiting diarrhoea<br>• Very low potential for hyperlactataemia/ steatohepatitis |
| Lamivudine (3TC) | NRTI | 300mg od | Risk of rebound hepatitis if discontinued in patients with chronic Hep B | • Generally well tolerated<br>• Headache, dry mouth<br>• Anaemia (pure red cell aplasia)<br>• Very low potential for hyperlactataemia/ steatohepatitis |
| Emtricitabine (FTC) | NRTI | 200mg od | | • Hyperpigmentation of palms and soles<br>• Headache, nausea, insomnia<br>• Very low potential for hyperlactataemia/ steatohepatitis |
| Stavudine (d4T) | NRTI | 30mg bd | Discontinue use in all patients | • Peripheral neuropathy<br>• Lipoatrophy<br>• Pancreatitis<br>• High potential for hyperlactataemia/steatohepatitis |
| Efavirenz (EFV) | NNRTI | • Weight ≥40kg–600mg nocte<br>• Weight <40kg–400mg nocte | • Avoid if:<br>– significant psychiatric morbidity<br>– intolerance to EFV<br>– neuropsychiatric effects may affect daily functioning e.g. shift workers<br>– severe liver disease | • Central nervous system (CNS) disturbances (vivid dreams, confusion, dizziness, drowsiness) – severity usually decreases within two to four weeks<br>• Mood changes<br>• Rash, hepatitis<br>• Hyperlipidaemia<br>• Gynaecomastia |

*continued*

| Generic name | Class of drug* | Recommended dosage | Contraindications/cautions | Common or severe adverse drug reactions |
|---|---|---|---|---|
| Nevirapine (NVP) | NNRTI | • 200mg od X 14 days, then 200mg bd<br>• Assess 14 days post-initiation, prior to increasing dose – if rash has occurred do not increase dose until resolved<br>• If rash does not resolve within another week, switch NVP to an alternative drug<br>• If treatment interrupted for >7 days, restart with once daily lead-in dosing | • Avoid if:<br>– CD4 count ≥250 cells/mm3 in women or ≥400 cells/mm3 in men (NVP reactions more common at higher baseline CD4 counts)<br>– significant hepatic impairment or active hepatitis B or C<br>• Caution with TB treatment | • Skin rash – mild to life-threatening<br>• Hepatitis – can be fatal<br>• Patients being initiated on NVP should be warned to return to the clinic immediately should they develop a rash, any significant muco-cutaneous reaction, fever, jaundice or abdominal pain |
| Lopinavir/ ritonavir (LPV/r) | Boosted PI | • 400mg/100mg (2 x 200/50mg tabs) bd<br>• Adjust dose if on TB treatment | • Avoid if:<br>– fasting cholesterol >6mmol/L | • Gastrointestinal (GIT) symptoms – diarrhoea, nausea, vomiting<br>• Dyslipidaemia<br>• Hepatitis<br>• Taste perversion<br>• Hyperglycaemia, diabetes<br>• Lipodystrophy |
| Atazanavir/ ritonavir (ATV/r) | PI | • 400mg od (only if ART-naïve) or 300mg ATV with RTV 100mg od (preferred)<br>• With TDF-300/100mg ATV/r od<br>• With EFV-400/100mg ATV/r od | • Avoid if:<br>– hypersensitivity<br>– severe liver impairment | • Unconjugated hyperbilirubinaemia, jaundice in minority of patients<br>• Hepatitis<br>• PR interval prolongation<br>• Renal stones (rare)<br>• Less potential for dyslipidaemia than other PIs |
| Raltegravir (RAL) | InSTI | 400mg (bd) | No contraindications documented | • Headache<br>• GI disturbance<br>• Hepatitis and rash (rare)<br>• Rhabdomyolysis (rare) |
| Maraviroc (MVC) | CCR5 blocker | 150mg, 300mg or 600mg (bd).<br>Doses depends on concomitant medication and interaction | • Avoid if:<br>– severe renal impairment or end-stage renal disease (CrCl <30 ml/min) in patients who are taking potent CYP3A inhibitors or inducers | • Rash<br>• Hepatitis<br>• Fever<br>• Abdominal pain<br>• Cough<br>• Dizziness<br>• Musculoskeletal symptoms (all rare) |

(Source: Managing HIV: A Clinician's tool, 2015: 10, 11. Available at: http://www.auruminstitute.org/index.php?option=com_phocadownload&view=category&id=3&Itemid=263)

**Notes to classes of ARVs in Table 6.9:*
*Nucleoside reverse transcriptase inhibitors (NRTIs) may be associated with lactic acidosis, hepatic steatosis and lipodystrophy.*
*Non-nucleoside reverse transcriptase inhibitors (NNRTIs) may be associated with rash (including Stevens-Johnson and toxic epidermal necrolysis).*
*All protease inhibitors (PIs) may be associated with metabolic abnormalities (including dyslipidaemia, hyperglycaemia, insulin resistance, lipodystrophy.*

## Reference list


Arum Institute & CDC/PEPFAR. 2015. *Managing HIV: A clinician's tool*. Johannesburg: Arum Institute.

Delobelle, P., Rawlinson, J.L., Ntuli, S., Malatsi, I., Decock, R., & Depoorter, A.M. 2009. HIV/AIDS knowledge, attitudes, practices and perceptions of rural nurses in South Africa. *Journal of Advanced Nursing 65*(5): 1061–1073. doi:10.1111/j.1365-2648.2009.04973.x

Ford, N., Shubber, Z., Calmy, A., Irvine, C., Rapparini, C., Ajose, O., Beanland, R.L., Vitoria, M., Doherty, M., & Mayer, K.H. 2015. Choice of antiretroviral drugs for postexposure prophylaxis for adults and adolescents: a systematic review. *Clinical Infectious Diseases* 60 (suppl 3): S170-S176.

INSIGHT START Study Group, Lundgren JD, Babiker AG, et al. 2015. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *New England Journal of Medicine* 373: 795–807.

PMID: 26192873, http://dx.doi.org/10.1056/NEJMoa1506816

Karstaedt, A.S. & Pantanowitz, L. 2001. Occupational exposure of interns to blood in an area of high HIV seroprevalence. *South African Medical Journal* 91: 57–61.

Meintjes, G., Black, J., Conradie, F., et al. 2015. Southern African HIV Clinicians Society adult antiretroviral therapy guidelines: Update on when to initiate antiretroviral therapy. *Southern African Journal of HIV Medicine* 16(1), Art. #428, 4 pages. http://dx.doi.org/10.4102/sajhivmed.v16i1.428

National Department of Health, South Africa. 2015. *National Consolidated Guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults*. Pretoria: Department of Health.

Nsubuga F.M. & Jaakkola M.S. 2005. Needle stick injuries among nurses in sub-Saharan Africa. *Tropical Medicine and International Health* 10(8), 773–781.

Severe, P., Juste, M.A., Ambroise, A., et al. 2010. Early versus standard antiretroviral therapy for HIV-infected adults in Haiti. *New England Journal of Medicine* 2010: 363:257–265. PMID: 20647201, http://dx.doi.org/10.1056/NEJMoa0910370

Southern African HIV Clinicians Society. 2012. Adult antiretroviral therapy guidelines. Retrieved on: 11/11/2012 from www.sahivsoc.org/

Southern African HIV Clinicians Society. 2014. Adult antiretroviral therapy guidelines. *Southern African Journal of HIV Medicine* 15(4):121–143. DOI:10.7196/SAJHIVMED.1130.

Southern African HIV Clinicians Society. 2015. Guideline on the management of occupational and non-occupational exposure to the human immunodeficiency virus and recommendations for post-exposure prophylaxis: 2015 update. *Southern African Journal of HIV Medicine.* DOI:10.4102/sajhivmed.v16i1.399

TEMPRANO ANRS 12136 Study Group, Danel C., Moh R., et al. 2015. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. *New English Journal of Medicine* 373: 808–822. PMID: 26193126, http://dx.doi.org/10.1056/NEJMoa1507198.

Van Dyk, A.C. 2011. Differences between patients who do and do not adhere to antiretroviral therapy. *Journal of the Association of Nurses in Aids Care* 22(4): 269–282.

Van Wyk Louw, N. P. 1941. *Raka.* In *Raka. English translation* by Dawes, A. 1968 (p. 4). Cape Town: Nasionale Boekhandel Bpk.

Westermann, C., Peters, C., Lisiak, B., Lamberti, M., & Nienhaus, A. 2015. The prevalence of hepatitis C among healthcare workers: a systematic review and meta-analysis. *Occupational and Environmental Medicine* 72: 880–888. doi:10.1136/oemed2015102879.

World Health Organization (WHO). 2014. Guidelines on post-exposure prophylaxis for HIV and the use of Co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: Recommendations for a Public Health Approach. *Supplement to the 2013 Consolidated Guidelines on the use of Antiretroviral Drugs for Treating and Preventing HIV Infection*. Retrieved on: 30/10/2015 from http://apps.who.int/iris/bitstream/10665/145719/1/9789241508193_eng.pdf?ua=1&ua=1

World Health Organization (WHO). 2015. Guidelines on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Retrieved on: 27/05/2016 from http://i-base.info/new-who-guidelines-for-when-to-start-art-and-use-of-prep-september-2015/