For ICRC health staff

HIV
AIDS

EVERYTHING
you need to know

Edwin Louvel, MD & Frederic Stauffer, MD
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Worldwide, the global HIV/AIDS epidemic continues to expand. Africa, as well as Asia, is making little headway in the fight against AIDS, despite all prevention campaigns and the wider availability of life-prolonging drugs. Very few countries have been able to reduce their HIV-infection rate.

The first ICRC HIV/AIDS project, dealing with HIV preventive measures in favour of prisoners, started in Burundi in 2001. In 2004, the ICRC introduced a programme to improve access to HIV/AIDS preventive and curative measures in favour of its staff members. Later, in April 2004, the Institution took an official stand and included the fight against HIV/AIDS among its operational objectives and activities.

It is also recognized that there is a need to internally increase and improve knowledge of the scientific facts about HIV/AIDS in order to enhance our approaches.

The aim of this book is to facilitate access to basic scientific information on HIV/AIDS for ICRC health delegates confronted by issues related to the disease. Some of the chapters might also be useful or interesting to delegates who do not have any medical background.

But why an additional book when there are already so many publications available? Despite our extensive research, we did not find a simple and at the same time scientifically solid referral textbook dealing with all aspects of HIV/AIDS. There is a great deal of publications on the subject, but most of them are always highly specialized and targeting specific topics.

This is the gap we identified as our starting point. The idea was not to write an additional original textbook, which would have been beyond our competence and expertise but to provide the reader with a summary of our readings, encompassing all fields of HIV/AIDS. It starts with a brief overview of virology and epidemiology, goes on to describe HIV/AIDS clinical features and case management for adults and children, then proceeds with information on different HIV-related diseases and their treatment. The book insists also on HIV/AIDS prevention, emphasizing the importance of cultural references while, the last chapter stresses the importance of monitoring and evaluation in any HIV/AIDS project or programme.

Many sources were consulted, among them are: WHO, UNAIDS, CDC, Johns Hopkins University, IRC, FHI, USAID and University of Geneva.
Eventually, we would like to mention that by choice we did not want to deal with ICRC-related HIV/AIDS activities, for instance, in detention, in dealing with sexual violence or our preventive and curative activities for ICRC staff. Separate documents already exist and more will probably come out in the future.
Information to users

To make the book as user-friendly as possible, the reader will find many figures, tables and boxes used to illustrate the text.

The tables and figures are an integral part of the text and should be read in order to get a clear understanding of the topic dealt with.

The boxes are not an integral part of the text and it is possible to skip them over without losing any essential or major explanation. They contain examples, general information or additional scientific facts for those who are interested to learn more about a specific topic.

At the end of each chapter, the reader will find some of the main references (reports, guidelines or books) used during the writing of the book. They can be referred to on the CD-ROM attached to the book, just by clicking the corresponding link.

More web-based resources, especially those that are regularly updated, can be consulted on the internet by clicking on the corresponding link to be found on the last chapter of the CD-ROM version of the book. They will enable the reader to be informed on the rapid developments in the field of HIV/AIDS.

Taking into account the fast advances in scientific knowledge as well as the rapid evolution of case management, the authors will strive to regularly update this manual.
We are thankful to Dr Jacqueline Avril, head of the ICRC staff health unit, human resources department, and to Dr Hervé le Guillouzic, head of the health unit, assistance division, for their support and encouragements all along the writing of the book.

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<th>Full Form</th>
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<td>Acquired immunodeficiency syndrome</td>
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<tr>
<td>ANC</td>
<td>Ante natal care</td>
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<td>ART</td>
<td>Antiretroviral therapy</td>
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<td>ARV</td>
<td>Antiretroviral</td>
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<tr>
<td>BCC</td>
<td>Behaviour change communication</td>
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<td>BSS</td>
<td>Behavioural surveillance survey</td>
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<tr>
<td>bid</td>
<td>Twice a day</td>
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<tr>
<td>CBC</td>
<td>Complete blood count</td>
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<tr>
<td>CDC</td>
<td>U.S. Centres for Disease Control and Prevention</td>
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<td>CIA</td>
<td>Central Intelligence Agency</td>
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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<td>CNS</td>
<td>Central nervous system</td>
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<td>CYP</td>
<td>Cytochrome P</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>DOTS</td>
<td>Directly observed treatment – short course</td>
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<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
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<tr>
<td>FDC</td>
<td>Fixed-dose combination</td>
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<td>FHI</td>
<td>Family Health International</td>
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<td>FI</td>
<td>Fusion inhibitor</td>
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<td>GIPA</td>
<td>Greater involvement of people with HIV/AIDS</td>
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<tr>
<td>gp</td>
<td>Glycoprotein</td>
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<td>GPA</td>
<td>Global programme on AIDS</td>
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<td>HAART</td>
<td>Highly active antiretroviral therapy</td>
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<td>HAV</td>
<td>Hepatitis A virus</td>
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<td>HBV</td>
<td>Hepatitis B virus</td>
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<td>HCV</td>
<td>Hepatitis C virus</td>
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<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>IDU</td>
<td>Injecting drug user</td>
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<td>IDP</td>
<td>Internally displaced person</td>
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<td>IEC</td>
<td>Information, education, communication</td>
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<td>IgG</td>
<td>Immunoglobulin G</td>
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<td>INH</td>
<td>Isoniazid</td>
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<tr>
<td>Abbr.</td>
<td>Description</td>
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<tr>
<td>KAPB</td>
<td>Knowledge, attitudes, practices and behaviours</td>
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<tr>
<td>IFN</td>
<td>Interferon</td>
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<tr>
<td>IL</td>
<td>Interleukin</td>
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<tr>
<td>INR</td>
<td>International normalised ratio</td>
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<tr>
<td>IPT</td>
<td>Intermittent preventive treatment</td>
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<td>IRC</td>
<td>International Rescue Committee</td>
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<td>IRIS</td>
<td>Immune reconstitution inflammatory syndrome</td>
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<td>LTR</td>
<td>Long terminal repeat</td>
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<tr>
<td>MAC</td>
<td><em>Mycobacterium avium</em> complex</td>
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<tr>
<td>M&amp;E</td>
<td>Monitoring and evaluation</td>
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<tr>
<td>MSM</td>
<td>Men who have sex with men</td>
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<td>MTCT</td>
<td>Mother-to-child transmission</td>
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<tr>
<td>NNRTI</td>
<td>Non-nucleoside reverse transcriptase inhibitor</td>
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<tr>
<td>nPEP</td>
<td>Non-occupational post-exposure prophylaxis</td>
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<tr>
<td>NRTI</td>
<td>Nucleoside reverse transcriptase inhibitor</td>
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<tr>
<td>NtRTI</td>
<td>Nucleotide reverse transcriptase inhibitor</td>
</tr>
<tr>
<td>OI</td>
<td>Opportunistic infection</td>
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<tr>
<td>oPEP</td>
<td>Occupational post-exposure prophylaxis</td>
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<tr>
<td>PAP smear</td>
<td>Papanicolaou smear</td>
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<td>PBMC</td>
<td>Peripheral blood mononuclear cell</td>
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<tr>
<td>PCP</td>
<td><em>Pneumocystis jerovici</em> (formerly <em>carinii</em>) pneumonia</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<tr>
<td>PI</td>
<td>Protease inhibitor</td>
</tr>
<tr>
<td>PLHA/PLWHA</td>
<td>People living with HIV/AIDS</td>
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<tr>
<td>PMTCT</td>
<td>Prevention of mother-to-child transmission</td>
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<tr>
<td>PTB</td>
<td>Pulmonary Tuberculosis</td>
</tr>
<tr>
<td>qd</td>
<td>Every day</td>
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<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
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<tr>
<td>RPR</td>
<td>Rapid plasma regain</td>
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<tr>
<td>SGBV</td>
<td>Sexual and gender-based violence</td>
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<tr>
<td>SIV</td>
<td>Simian immunodeficiency virus</td>
</tr>
<tr>
<td>SP</td>
<td>Sulfadoxine-pyrimethamine</td>
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<tr>
<td>STD/STI</td>
<td>Sexually transmitted disease/infection</td>
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<tr>
<td>TB</td>
<td>Tuberculosis</td>
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<tr>
<td>TBA</td>
<td>Traditional birth attendant</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>--------------</td>
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<tr>
<td>TLC</td>
<td>Total lymphocyte count</td>
</tr>
<tr>
<td>TNF</td>
<td>Tumor necrotic factor</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
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<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>VCT</td>
<td>Voluntary counselling and testing</td>
</tr>
<tr>
<td>VDRL</td>
<td>Venereal disease research laboratory</td>
</tr>
<tr>
<td>VL</td>
<td>Viral load</td>
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<tr>
<td>WB</td>
<td>Western blot</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</table>
THE ORIGINS OF HIV

Human immunodeficiency virus (HIV) is part of a group of viruses called lentiviruses. Lentiviruses other than HIV have been found in a wide range of nonhuman primates. These other lentiviruses are known collectively as simian (monkey) immunodeficiency viruses (SIVs).

It is now generally accepted that HIV is a descendant of simian immunodeficiency virus. Certain SIVs bear a very close resemblance to HIV-1 and HIV-2, the two types of HIV.

HIV-2 corresponds to a SIV found in the sooty mangabey monkey, sometimes known as the green monkey, which is indigenous to western Africa.

HIV-1, the more virulent strain of HIV, was until very recently more difficult to place. In February 1999, the study of a frozen tissue from a chimpanzee found that the simian virus it carried (SIVcpz) was almost identical to HIV-1. The chimpanzee came from a sub-group of chimpanzees known as *Pan troglodytes troglodytes*, which were once common in west-central Africa.

This shows that these chimpanzees were the source of HIV-1, and that the virus at some point crossed species from chimpanzees to human. However, it was not necessarily clear that chimpanzees were the original reservoir for HIV-1 because chimpanzees are only rarely infected with SIVcpz.

Most probably, wild chimpanzees became infected simultaneously with two simian immunodeficiency viruses which combined to form a third virus capable of infecting humans and causing AIDS.
The researchers discovered that the chimpanzee virus was an amalgam of the SIV infecting red-capped mangabeys and the virus found in greater spot-nosed monkeys. They believe that the hybridisation took place inside chimpanzees that had become infected with both strains of SIV after hunting and killing the two smaller species of monkey.

Figure 1.1. From left to right: chimpanzee, red-capped mangabey, spot-nosed monkey

How could HIV have crossed species?
It has been known for a long time that certain viruses can pass from animals to humans, and this process is referred to as zoonosis.

The most commonly accepted theory is that of the “hunter”. HIV could have crossed over from chimpanzees to humans as a result of chimpanzees being killed and eaten or their blood getting into cuts or wounds on the hunter.

Some other controversial theories, such as the oral polio vaccine theory, the contaminated needle theory, the colonialism theory, or the Central Intelligence Agency (CIA) theory, have contended that HIV was transferred through medical experiments.

Box 1.1 | Time of HIV-1 origin
Studying the subtype of virus of some of the earliest known instances of HIV-1 infection can help to provide clues about the time of origin and the subsequent evolution of HIV in humans.

Three of the earliest known instances of HIV-1 infection are:
- A plasma sample taken in 1959 from an adult male living in what is now the Democratic Republic of Congo.
- HIV-1 found in tissue samples from an American teenager who died in St. Louis in 1969.
- HIV-1 found in tissue samples from a Norwegian sailor who died around 1976.

Analysis in 1998 of the plasma sample from 1959 was interpreted as suggesting that HIV-1 was introduced into humans around the 1940s or the early 1950s, which was earlier than had previously been suggested. Other scientists have suggested that it could have been even longer, perhaps around 100 years or more ago.
HIV-1 AND HIV-2

HIV was identified as the cause of AIDS by Robert C. Gallo and Luc Montagnier in 1983.

There are two types of HIV that can be distinguished genetically and antigenically: HIV-1 and HIV-2.

Both types are transmitted by sexual contact, through blood, and from mother to child, and they appear to cause clinically indistinguishable AIDS. However, it seems that HIV-2 is less easily transmitted, and the period between initial infection and illness is longer in the case of HIV-2.

HIV-1

HIV-1, the cause of the current pandemic, can be found worldwide. There are many sub-types of HIV-1.

Box 1.2 | HIV-1 groups and sub-types.

There are three groups of HIV-1, M (main), N (new) and O (outlier).

Based on nucleotide sequence analyses of the Env and Gag genes, it has been found that there are at least ten different HIV-1 subtypes (clades) within the M group - these are designated A to J. The major one in North America, Latin America and the Caribbean, Europe, Japan and Australia is type B. Most sub-types are found in sub-Saharan Africa with A and D found at the highest rates in central and eastern Africa and C in eastern and southern Africa. Type C is also the predominant form in India. Type E is found in Thailand and central Africa, type F in Brazil and Romania, type G in Russia and Gabon, while type H is found in Zaire and in Cameroon. Subtype I is found in Cyprus.

Mosaics between different clades, called circulating recombinant forms (CRF), are more and more frequently found.

There is some evidence from laboratory studies that different HIV-1 subtypes can be transmitted by different routes. For example, type B found in western countries, may be transmitted more effectively by homosexual intercourse and via blood (as in intra-venous drug use) whereas types C and E may be transmitted more via a heterosexual route. This is because types C and E replicate better in Langerhans’ cells found in the mucosa of the cervix, vagina and penis while type B replicates better in the rectal mucosa. It also appears that type E is more readily transmitted between sexual partners than type B.

Type O HIV-1 is mostly found in Cameroon and Gabon.

Type N, discovered in 1998 Cameroon, is extremely rare.
HIV-2
The relatively uncommon HIV-2 is concentrated in West Africa — where HIV-1 remains predominant — and is rarely found elsewhere.

Box 1.3  | HIV-2 distribution

West African nations with a prevalence of HIV-2 of more than 1% in the general population are Cape Verde, Ivory Coast, Gambia, Guinea-Bissau, Mali, Mauritania, Nigeria, and Sierra Leone. Other West African countries reporting HIV-2 are Benin, Burkina Faso, Ghana, Guinea, Liberia, Niger, Sao Tome, Senegal, and Togo.

Angola and Mozambique are other African nations where the prevalence of HIV-2 is more than 1%.

Seroprevalence data suggest that HIV-2 originated in Guinea-Bissau. It has recently been hypothesized that the independence war (1963 — 1974) in this former Portuguese colony played a critical role in the early dissemination of HIV-2.

WHAT CAUSED THE EPIDEMIC TO SPREAD SO SUDDENLY?

There are a number of factors that may have contributed to the sudden spread of the epidemic including international travel, the blood industry, and widespread injecting drug use.

International travel
The role of international travel in the spread of HIV was highlighted by the case of ‘Patient Zero’. Patient Zero was a Canadian flight attendant who travelled extensively worldwide. Analysis of several of the early cases of AIDS showed that the infected individuals were either direct or indirect sexual contacts of the flight attendant. These cases could be traced to several different American cities demonstrating the role of international travel in spreading the virus. It also suggested that the disease was probably the consequence of a single transmissible agent.

The blood industry
As blood transfusions became a routine part of medical practice, this led to the growth of an industry to meet this increased demand for blood. In some countries paid donors were used, including intravenous drug users. This blood was then sent worldwide.

Also, in the late 1960’s haemophiliacs began to benefit from the blood clotting properties of a product called Factor VIII. However, to produce the coagulant, blood from thousands of individual donors had to be pooled. Factor VIII was then distributed worldwide making it likely that haemophiliacs could become exposed to new infections.
Injecting drug use
The 1970s saw an increase in the availability of heroin following the Vietnam War and other conflicts in the Middle East, which helped stimulate a growth in intravenous drug use. This increased availability together with the development of disposable plastic syringes and the establishment of ‘shooting galleries’ where people could buy drugs and rent equipment provided another route through which the virus could be passed on.

HIV TRANSMISSION

Geographic and socioeconomic factors influence which modes of transmission predominate. In some countries more than one of the modes of HIV transmission below is responsible for the HIV/AIDS epidemic.

Modes of transmission

HIV can be transmitted

- By sexual contact: male-to-female, female-to-male, male-to-male, and female-to-female
- Through exposure to blood: blood transfusion, intravenous drug use (IDU) through needle-sharing, needle stick accidents
- From mother to child: in utero, during labour and delivery, during postpartum through breastfeeding.

HIV cannot be transmitted

- By casual contact: for example, hugging, shaking hands, sharing food and utensils, sneezing or coughing
- By surface contact: for example, toilet seats
- From insect bites: for example, from mosquitoes or fleas.

<table>
<thead>
<tr>
<th>Table 1.1</th>
<th>Estimated risk of HIV transmission following different types of exposure</th>
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</thead>
<tbody>
<tr>
<td><strong>Type of exposure to an infected source</strong></td>
<td><strong>Estimated risk</strong></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>90%</td>
</tr>
<tr>
<td>Needle-sharing exposure – drug use</td>
<td>0.67%</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>0.5%</td>
</tr>
<tr>
<td>Percutaneous needlestick</td>
<td>0.3%</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>0.1%</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>0.065%</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>0.05%</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>0.01%</td>
</tr>
</tbody>
</table>
Factors increasing the risk of transmission

**Biological factors**
High viral load (initial stage of infection and more advanced stages); susceptibility of recipient; inflammation or disruption of genital or rectal mucosa; lack of circumcision in heterosexual men; sex during menstruation (increasing a woman’s risk); presence of an ulcerative or non-ulcerative STD; viral properties.

**Socioeconomic factors**
Social mobility (HIV/AIDS follows the routes of trade); stigma and denial (stigma prevents HIV-infected people from seeking care and from taking preventive measures); people in conflict (violence, displacement, rape); cultural factors (for example, a woman cannot question her husband’s extramarital affairs, cannot negotiate condom use and cannot refuse to have sex); gender roles (for example, in many cultures men are socialised and encouraged to have many sexual relationships); poverty (poor people lack access to information needed to understand and prevent HIV/AIDS); drug use and alcohol consumption (these lower a person’s inhibitions and impair judgment, which may result in risky behaviour; injecting illicit drugs frequently involves the sharing of needles and injection equipment, increasing the risk of HIV transmission.)

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**Box 1.4 | Why mosquitoes cannot transmit AIDS**

- Mosquitoes that ingest HIV-infected blood digest that blood within 1-2 days and completely destroy any virus particles that could potentially produce a new infection.
- Mosquitoes do not ingest enough HIV particles to transmit AIDS by mechanical contamination. Crushing a fully engorged mosquito containing HIV infected blood would not begin to approach the levels needed to initiate infection.
- Mosquitoes are not flying hypodermic needles. The mosquito delivers salivary fluid through one passage and draws blood up another. As a result, the food canal is not flushed out like a used needle, and blood flow is always unidirectional.

**Box 1.5 | Plausible biological explanations for a connection between HIV infection and lack of circumcision**

The tissue of the internal foreskin absorbs HIV up to nine times more efficiently than female cervical tissue, mainly because it contains epidermal dendritic cells (Langerhans cells) in much greater quantities than the cervix or other genital tissue (including other parts of the penis). In addition, the internal foreskin has a mucosal surface, as opposed to the more hardened skinlike surface of the external foreskin. This mucosal surface is particularly susceptible to tears and abrasions, and, consequently, infection by STDs and HIV.
Prevalence is the proportion of a defined population infected at any one given point in time.

Incidence is the proportion of a defined population becoming infected in a given period of time (usually per annum).

Schematic illustration of HIV epidemic stages

In an endemic steady state the prevalence of infection is the product of incidence and the mean duration of the infection. However, in an epidemic situation, the relationship between prevalence and incidence varies as the epidemic ages.

The rate of spread of HIV depends upon the basic reproductive number \((R_0)\), the number of new infections caused by one infectious individual in an entirely susceptible population. The reproductive number at time \(t\) \((R_t)\) then alters as illustrated, as the epidemic progresses.

At the beginning of the epidemic’s growth phase, HIV incidence and HIV prevalence are likely to grow exponentially in the population at risk.

As the epidemic grows, the number of people who are susceptible to HIV infection will decrease in the population at risk. At the same time, the proportion of contacts of those infectious with other members of the population who have already been infected will increase. This effect reduces the reproductive rate of the infection and will slow the growth of incidence. Eventually, HIV incidence will decline while HIV prevalence continues to grow.

It is only when mortality of those infected increases that prevalence decreases or levels off. If the mortality rate of those infected is greater than the incidence of new infection then prevalence will decline until the two balance and prevalence remains constant.
EPIDEMIC SURVEILLANCE

UNAIDS/WHO epidemic states
For the purposes of surveillance, UNAIDS and WHO suggest a classification that describes the epidemic by its current state: low level, concentrated, or generalized. This typology recognizes that a country may shift from one state to another over time. It is important to stress, however, that such a shift is by no means an inevitable progression.

Box 1.7 | Low level, concentrated, and generalised epidemic

**Low level epidemic**
Although HIV infection may have existed for many years, it has never spread to significant levels in any sub-population. Recorded infection is largely confined to individuals with higher risk behaviour: e.g. sex workers, drug injectors, men having sex with other men. This epidemic state suggests that networks of risk are rather diffuse (with low levels of partner exchange or sharing of drug injecting equipment), or that the virus has been introduced only very recently.

Numerical proxy: HIV prevalence has not consistently exceeded five percent in any defined sub-population.

**Concentrated epidemic**
HIV has spread rapidly in a defined sub-population, but is not well-established in the general population. This epidemic state suggests active networks of risk within the sub-population. The future course of the epidemic is determined by the frequency and nature of links between highly infected sub-populations and the general population.

Numerical proxy: HIV prevalence consistently over five percent in at least one defined subpopulation. HIV prevalence below one percent in pregnant women in urban areas.

**Generalized epidemic**
HIV is firmly established in the general population. Although sub-populations at high risk may continue to contribute disproportionately to the spread of HIV, sexual networking in the general population is sufficient to sustain an epidemic independent of sub-populations at higher risk of infection.

Numerical proxy: HIV prevalence consistently over one percent in pregnant women.

Second generation surveillance
Goals of second generation surveillance systems are:
- A better understanding of HIV prevalence trends over time
- A better understanding of the behaviours driving the epidemic in a country
- A surveillance more focused on sub-populations at highest risk of infection
A flexible surveillance that moves with the needs and state of the epidemic
A better use of surveillance data to increase understanding and to plan prevention and care.

**Box 1.8 | Second generation surveillance systems**

**Second generation systems look at behaviour as well as HIV infection**
Traditional surveillance systems tracked HIV infection or other biological markers of risk such as STIs. Since HIV infection among adults must be preceded by one of a limited number of behaviours, such as unprotected sex with an infected partner or injection with contaminated needles, we know that if these behaviours change, there will be a change in the spread of HIV. Second generation surveillance systems monitor risk behaviours, using them to warn of or explain changes in levels of infection. Thus, second generation surveillance uses data from behavioural surveillance to interpret data gathered from sero-surveillance efforts.

**Second generation systems are tailored to the type of epidemic**
As the diversity of HIV epidemics becomes more apparent, it also becomes evident that there is no “one-size-fits-all” surveillance system. Efficient surveillance of a predominantly heterosexual epidemic in a country where one adult in six is infected will differ radically from surveillance in a country where HIV infection is growing rapidly in drug injectors but has yet to spread to the general population. In general, surveillance systems can be divided into three broad types directly related to the type of epidemic:

- In *generalised* epidemics, surveillance systems concentrate on monitoring HIV infection and risk behaviour in the general population.
- In *concentrated* epidemics, surveillance systems monitor infection in groups at high-risk of infection and pay particular attention to behavioural links between members of those groups and the general population. They might ask, for example, whether male sex workers have wives or girlfriends, or whether drug users finance their habit through sex work. In these situations, surveillance systems also monitor the general population for high-risk sexual behaviour that might lead to rapid spread of the virus if it were introduced.
- In *low-level* epidemics, surveillance systems focus largely on high-risk behaviours, looking for changes in behaviour which may lead to a burst of infection. Such changes have recently been recorded in several Eastern European countries, for example, where a surge in injecting drug use was followed by very rapid growth in HIV infection.

**Second generation systems use data in ways that maximise their power to explain the epidemic**
A classic antenatal clinic (ANC) surveillance system may show that HIV prevalence among women 15-49 years attending ANCs rose rapidly from 0 to 12 percent over eight years, and then levelled off. In the rising phase the upward trend meant more new infections (increasing HIV incidence), probably at all ages. But once the curve flattens out, the explanatory power of that single figure is lost. Prevalence may be unchanged for any number of reasons: because as many women are dying as are becoming newly infected, for example, or because many infected women are no longer becoming pregnant and so have dropped out of the pool of women tested at sentinel sites.
Box 1.8 Second generation surveillance systems... contd.

Some of these problems of interpretation can be reduced by concentrating analysis to women in the youngest age groups, who are less subject to biases of mortality or reduced fertility and whose infection is more likely to reflect recent trends in the epidemic. Analysing the ANC data together with data from other sources, such as general population surveys or behavioural surveys, also increases the explanatory power of sero-surveillance systems. The need to focus on young women in antenatal clinics was acknowledged several years ago when WHO/GPA designated two of its prevention indicators to HIV and sero-syphilis prevalence among women 15-24 years.

Second generation systems make the best possible use of resources

By concentrating surveillance in areas where it provides the most information and tailoring systems to a country’s capacity, second generation surveillance ensures that money and expertise are used as efficiently as possible. For example, sentinel sites are carefully chosen to provide reliable information from a minimum number of sites, while sampling for behavioural data collection takes sentinel sites into account so that strong inferences can be made in comparing behavioural and serological data sets.

Strengthened surveillance systems also make an effort to ensure that all data gathered are actually used, something which, perhaps surprisingly, has not been the case in the past. Syphilis data from ANC clinics have rarely been analysed for surveillance purposes, for example. Despite the association between HIV and TB, TB surveillance data are rarely included in HIV surveillance reports.

THE WORLD EPIDEMIC AT A GLANCE

Table 1.2 | Global estimates end of 2005. UNAIDS/WHO

<table>
<thead>
<tr>
<th>Number of people living with HIV</th>
<th>Total</th>
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<table>
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</thead>
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<tr>
<td>Children under 15 years</td>
<td>0.57 million</td>
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</table>
Figure 1.2. **Adults and children estimated to be living with HIV in 2005. UNAIDS/WHO**

![World map showing HIV burden by region]

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Virology and immunology

Human immunodeficiency virus (HIV) is the causative agent of AIDS (Acquired Immuno Deficiency Syndrome).

HIV is a lentivirus (“slow” virus), a class of retrovirus. Retroviruses are RNA viruses that must make a DNA copy of their RNA in order to replicate. Replication is mediated by an enzyme called reverse transcriptase.

HIV disease is characterized by a gradual deterioration of immune function. Most notably, crucial immune cells called CD4+ T cells are eventually disabled and killed during the typical course of infection.

HIV STRUCTURE

Figure 2.1. Viral structure
Viral envelope and surface glycoprotein

HIV has a diameter of 1/10,000 of a millimetre and is spherical in shape. The outer coat of the virus, known as the viral envelope, is composed of two layers of lipids, taken from the membrane of a host cell when a newly formed virus particle buds from the cell.

Embedded in the viral envelope are 72 copies of a complex HIV glycoprotein (frequently called “spikes”) that protrudes through the surface of the virus.

This glycoprotein (gp 160), known as Env, consists of a cap made of three molecules called gp 120, and a stem consisting of three gp41 molecules that anchor the structure in the viral envelope.

Gp120 is the protein that interacts with a receptor on the cell to be infected. Gp41 is the fusogen that is exposed after gp120 has bound to the cell.

Internal structural proteins

A HIV protein called p17, or matrix protein, lines the inner surface of viral membrane to which it is attached by covalently bound myristic acid.

The bullet-shaped inner core or capsid, is made of 2000 copies of another viral protein (p24).

The capsid surrounds two single strands of HIV RNA, each of which has a copy of the virus's nine genes. The two HIV RNAs are stabilized by the nucleocapsid proteins (p7 & p9).

The reverse transcriptase (p51/p66) and the integrase (p32) enzymes bind to the HIV RNAs.

The viral protease (p11) occupies the space between the matrix and the virus core.

HIV GENOME

The HIV-1 proviral genome (Figure 2.2) contains 9 genes. It is flanked at both its ends by long terminal repeats (LTRs).

Figure 2.2. HIV Genome
HIV LIFE CYCLE: A MULTIPLE STEPS PROCESS

Viral replication is a dynamic and quick process able to produce up to ten billions new particles per day which the immune system has to clear.

The virus replication cycle can be divided into the following steps: HIV entry into CD4+ target cell (with the following sub-steps: attachment, binding and fusion); reverse transcription; integration; transcription; translation; assembly; and budding.
**HIV entry into CD4+ target cell**

Infection typically begins when an HIV particle, which contains two copies of the HIV RNA, encounters a cell with a surface molecule called cluster designation 4 (CD4). Cells carrying this molecule are known as CD4 positive (CD4+) cells.

First, one or more of the virus gp120 molecules attaches tightly to CD4 molecule(s) on the cell’s membrane. The *attachment* of gp120 to CD4 results in a conformational change in the gp120 molecule allowing it to bind to a second molecule on the cell surface known as a co-receptor or chemokine receptor.

Figure 2.3. **Virus entry into the CD4+ cell**

The *binding* of surface gp120, CD4, and the chemokine receptor produces an additional radical conformational change in gp41. This allows gp 41 to insert into the target cell membrane, leading to the *fusion* of virus and target cell’s surface. After fusion is complete, the viral payload can be delivered and the process of hijacking the cell and turning it into an HIV factory is well on the way.

Studies have identified multiple co-receptors for different types of HIV strains. In the early stage of HIV disease, most people harbour viruses that use, in addition to CD4, a receptor called CCR5 to enter their target cells.

With disease progression, the spectrum of co-receptor usage expands in approximately 50 percent of patients to include other receptors, notably a molecule called CXCR4.
The co-receptors, also called chemokine receptors, include the CXC (CXCR1-5) family and the CC (CCR 1-9) family.

The difference in chemokine receptors that are present on the CD4 target cells explains how different strains of HIV may infect cells selectively, e.g.:

- Macrophage trophic (M-trophic) strains interact with the CCR5 chemokine receptor. CCR5 is expressed on macrophages and other antigen presenting cells but also on lymphocytes homing to the periphery, particularly those trafficking to the gut or genital tract. Typically, viruses isolated at primary infection are CCR5-using viruses.

- Lymphocyte trophic (T-trophic) strains interact selectively with the CXCR4 chemokine receptor. CXCR4-using virus is more likely to induce syncytia and infect memory T-cells. Typically, virus isolated late in the disease process uses CXCR4.

Dual tropic HIV strains, able to interact with more than one chemokine receptor do also exist.

In about 5% of the Caucasian population (especially in Northern Europe), a gene deletion (delta 32) prevents expression of the CCR5 receptor on the cell membrane. The result is that homozygous individuals exposed to M-trophic strains are protected from infection, while infected heterozygous individuals present a slower progression to both AIDS and death.

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**Figure 2.4. HIV life cycle**

**Reverse transcription**

The conversion of viral RNA into proviral DNA, mediated by the viral enzyme reverse transcriptase (RT), occurs in the cytoplasm of the target cell and is a crucial step in viral replication cycle.
Once reverse transcription has resulted in the synthesis of a double stranded HIV DNA, the viral RNA is degraded by the viral ribonuclease enzyme.

The replication of retroviruses is error prone and is characterized by a high spontaneous mutation rate. In average, reverse-transcription results in 1 to 10 errors per genome and per round of replication. These mutations can lead to the formation of replication-incompetent viral species, but can also be the cause of drug resistance.

As a consequence, many variants of HIV develop in an individual, some of which may escape destruction by antibodies or killer T cells. Additionally, different strains of HIV can recombine to produce a wide range of variants or strains.

Integration
The newly made HIV DNA (double strain) moves to the cell’s nucleus, where it is spliced (integrated) into the host’s DNA with the help of HIV integrase. HIV DNA that enters the DNA of the cell is called a provirus.

Transcription
For a provirus to produce new viruses, RNA copies must be made that can be read by the host cell’s protein-making machinery. These copies are called messenger RNA (mRNA), and production of mRNA is called transcription, a process that involves the host cell’s own enzymes.

Viral genes in concert with the cellular machinery control this process: the Tat gene, for example, encodes a protein that accelerates transcription. Genomic RNA is also transcribed for later incorporation in the budding virus.

Translation
Once processed in the host cell’s nucleus, HIV m-RNA and HIV genomic RNA are transported into the host cell cytoplasm. HIV regulatory proteins are critical to this process.

In the cytoplasm, the provirus co-opts the host cell’s protein making machinery to produce long chains of viral proteins and enzymes using HIV m-RNA as a template.

Assembly and budding
Newly made HIV core proteins, enzymes and genomic RNA gather just inside the cell’s membrane, while the viral envelope proteins aggregate within the membrane.
An immature viral particle forms and buds off from the cell, acquiring an envelope that includes both cellular and HIV proteins from the cell membrane.

During this part of the viral life cycle, the core of the virus is immature and the virus is not yet infectious.

The long chains of proteins and enzymes that make up the immature viral core are now cleaved into smaller pieces by a viral enzyme called protease. This step results in infectious viral particles.

**HIV & IMMUNE SYSTEM**

**First contact between HIV and the immune system: the dendritic cells**
Dendritic cells are important antigen-presenting cells that present the pathogens to T lymphocytes in lymphoid tissues. They can be found in the skin, the submucosal tissue of the genito-urinary tract, the respiratory tract, the gut, and in the blood stream.

Epidermal dendritic cells (Langerhans cells) may be among the first cells to encounter HIV at mucosal surfaces and have the capability of shuttling the virus in the lymph nodes which contain high concentrations of CD4+ T cells.

HIV actively replicates within the lymph nodes, where large amounts of virus become trapped in networks of specialized cells with long, tentacle-like extensions. These cells are called follicular dendritic cells. They act like flypaper, trapping invading virus and holding them until the initiation of an immune response, i.e. the activation of CD4+ T cells.

**Humoral and cell-mediated immune responses**
Activated CD4+ T cells stimulate B lymphocytes, the generators of humoral immunity, to produce antibodies (immunoglobulins). Although antibody levels are high, neutralizing antibody response against HIV is not strong, and is rapidly followed by the emergence of viruses resistant to the neutralizing activity of these antibodies.

CD4+ T cells also participate in the stimulation and recruitment of another subset of T cells, the CD8+ T cells, through the production of cytokines. These CD8+ T cells are able to target and lyse virally infected cells by recognizing foreign antigens bound by host proteins.
**Box 2.3 | T lymphocytes & cytokines**

**T lymphocytes (T cells)** originate from the bone marrow and mature in the thymus. Two types of T cells are responsible for the cell-mediated immunity: the CD4+ T cells which express CD4 antigen and the CD8+ T cells that express CD8 antigen.

- CD4+ T-cells (or helper T-cells) are the heart of the immune system, responsible for co-ordination of immune response. This regulator has multi-functional roles, primarily executed through the coordinated release of cytokines and direct cell surface interactions involving co-stimulatory molecules. CD4+ T cells, through expression of interleukin (IL)-2, provide help for the activation and maturation of CD8+ T cells. Interferon (IFN-γ) activates macrophages, increasing their capacity to kill intracellular pathogens. Interleukins such as IL-4 and IL-6 are essential for the coordinated production of antibodies from B cells.

- CD8+ T cells belong to two groups:
  - Suppressor T cells that inhibit or suppress immune responses
  - Cytotoxic or killer T cells which attack cancerous cells and cells infected with viruses

**Role of CD4 cells in coordination of immune response**

Cytokines are non-antibody proteins released by cells that act as intercellular mediators especially in immune response.

While greater quantities of certain cytokines such as Tumor Necrotic Factor-alpha and interleukin 6 (IL-6) are secreted during HIV infection, other cytokines with key roles in the regulation of normal immune function may be secreted in decreased amounts.

For example, CD4+ T cells may lose their capacity to produce interleukin 2 (IL-2), a cytokine that enhances the growth of other T cells and helps to stimulate other cells’ response to invaders. Infected cells also have low levels of receptors for IL-2, which may reduce their ability to respond to signals from other cells.
Following initial infection with HIV, the rapid emergence of CD8+ T-cell responses is associated with a decrease in plasma levels of HIV. However, despite high levels of HIV-specific CD8+ T cells, sustained suppression of viral replications is rarely achieved. Viral mutations that render infected cells undetectable by cytotoxic T cells, and evidence that HIV-specific CD8+ T cells may be dysfunctional, may explain this incomplete viral suppression.

**Loss of CD4+ T cells**

Although other cells can be infected, CD4+ T cells are the major cell type that is infected by the virus. 98% of the total body store of lymphocytes reside in lymphatic tissue scattered throughout the body, mainly in the intestine tract, while only 2% circulate in the peripheral blood. There is a massive depletion of intestine lymphocyte CD4 T cells during the acute HIV infection.

HIV only infects activated CD4+ T cells. The fact that HIV targets HIV-activated CD4 T cells leads to a relentless decline of T4 cells that are specific to HIV, thereby depleting the arm of the immune system that controls replication of the virus.

When HIV has critically depleted the CD4+ T cell population, the body can no longer launch a specific immune response and becomes susceptible to many opportunistic diseases that characterise AIDS.

**Box 2.4 | How HIV destroys or disables CD4+ T cells?**

A number of mechanisms may occur simultaneously in an HIV-infected individual.

**Direct cell killing.** Infected CD4+ T cells may be killed directly when large amounts of virus are produced and bud off from the cell surface, disrupting the cell membrane, or when viral proteins and nucleic acids collect inside the cell, interfering with cellular machinery.

**Apoptosis.** Infected CD4+ T cells may be killed when the regulation of cell function is distorted by HIV proteins, probably leading to cell suicide by a process known as programmed cell death or apoptosis. Apoptosis is closely correlated with the aberrant cellular activation seen in HIV disease.

Uninfected cells also may undergo apoptosis. Investigators have shown in cell cultures that the HIV envelope alone or bound to antibodies sends an inappropriate signal to CD4+ T cells causing them to undergo apoptosis, even if not infected by HIV.

**Innocent bystanders.** Uninfected cells may die in an innocent bystander scenario. HIV particles may bind to the cell surface, giving them the appearance of an infected cell and marking them for destruction by killer T cells after antibody attaches to the viral particle on the cell. This process is called antibody dependent cellular cytotoxicity.

**Cytolytic T cells** also may mistakenly destroy uninfected cells that have consumed HIV particles and that display HIV fragments on their surfaces. Alternatively, because HIV envelope proteins bear some
Viral reservoirs
Most of the T cells in the body are in a resting state; approximately half are naive cells (cells that have not yet responded to any foreign antigen), and the remainder are memory cells (cells that have previously responded to some antigen). The cells circulate throughout the lymphoid tissues until they encounter an antigen that they recognize, after which they proliferate, and carry out their functions. Some of the cells survive and revert back to a resting state as long-lived memory T cells, cells that allow the host to respond quicker to the same antigen in the future.

In HIV infection, the virus replicates in activated CD4+ cells and tends to kill them very quickly. However, some of the activated cells can become infected as they are in the process of reverting back to a resting state, resulting in a stably integrated viral genome in a long-lived memory T cell. These resting T cells, protected from the cytopathic effects of massive viral replication, constitute a significant reservoir of latent HIV that may be activated to complete the replication cycle upon activation of the host cell.

The incapacity of current antiretroviral therapies to eradicate virus in resting CD4+ cells and the long half life of these cells make unlikely the prospect of a cure for HIV infection in the near future.

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Comprehensive care and support

Comprehensive care and support package to people living with HIV/AIDS (PLHA) should strive to meet their overall needs, i.e. their medical, psychological, social and economic needs.

Because of its pervasive presence, stigmatisation and discrimination associated with HIV/AIDS acts as a major barrier to care and support.

KEY ELEMENTS

Comprehensive care and support for HIV/AIDS should include counselling and testing, HIV prevention, clinical care, psychological and socioeconomic support.

Meeting the needs of PLHA and their family members requires the collective effort of many facilities and organizations, both clinic- and community-based. It also necessitates a solid referral network of providers (Figure 3.1).

STIGMA AND DISCRIMINATION

Stigma

Stigma has been described as “a dynamic process of devaluation that significantly discredits an individual in the eyes of others”.

Stigma is not unique to HIV. It has been seen throughout history in relation to other diseases such as sexually transmitted diseases, leprosy, mental illness, etc.
Stigma can be experienced internally (internal or self-stigma) or externally (as in discrimination). Internal stigma refers to the personal shame associated with HIV/AIDS and the fear of being discriminated against on account of the illness.

Factors contributing to HIV/AIDS-related stigma include:

- The fact that HIV/AIDS is a life-threatening disease
- People are afraid of contracting HIV
- HIV is associated with socially improper forms of sex (such as sex between men) and injecting drug use
- People living with HIV/AIDS are often thought of as being responsible for having contracted the disease
- Religious or moral beliefs that lead people to conclude that having HIV/AIDS is the result of a moral fault that deserve punishment
- Limited recognition of stigma.
**Discrimination**

Discrimination (or “external” stigma) is the unfair and unjust treatment of an individual based on his or her real or perceived HIV status.

In addition to being a violation of human rights in itself, discrimination directed at people living with HIV or those believed to be HIV-infected, leads to the violation of other human rights, such as the rights to health, dignity, privacy, equality before the law, and freedom from inhuman, degrading treatment or punishment.

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**Box 3.1 | Examples of discrimination against people living with HIV**

**In family and community settings**
- Ostracization such as the practice of forcing women to return to their kin upon being diagnosed HIV-positive, after the first sign of illness, or after their partners have died of AIDS
- Shunning and avoiding every day contact
- Verbal harassment
- Gossip
- Verbal discrediting and blaming
- Physical violence
- Denial of traditional funeral rites

**In institutional settings**
- Health care services: reduced standard of care, denial of access to care and treatment, HIV testing without consent, breaches in confidentiality including identifying someone as HIV-positive to relative and outside agencies, negative attitudes and degrading practices by health-care workers
- Workplace: denial of employment based on HIV-positive status, compulsory HIV testing, exclusion of HIV-positive individuals from pension scheme or medical benefits
- Schools: denial of entry of HIV-affected children, dismissal of teachers
- Prisons: mandatory segregation of HIV-positive individuals, exclusion from collective activities

**At national level**
- Compulsory screening and testing of groups and individuals
- Prohibition of people living with HIV from certain occupations and types of employment
- Isolation, detention and compulsory medical examination, treatment of infected persons
- Limitations on international travel and migration including HIV testing for those seeking work permits and the deportation of HIV-positive foreigners

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**Impact of stigma and discrimination**

Stigma and discrimination can act as barrier to care and treatment.
Negative attitudes about HIV also create a climate in which people become more afraid of the stigma and discrimination associated with the disease than of the disease itself.

When fear and discrimination prevail, people may choose to ignore the possibility that they may already be, or could become, HIV-positive. And they may decide not to take precautions to protect themselves for fear that in doing so they are associating themselves with HIV and having been ‘at risk’.

All of this helps to create an environment in which the disease can more easily spread.

**Tackling stigma and discrimination**

Interventions aiming to tackle stigma and discrimination should encompass the following elements:

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**Box 3.2 | Negative effects of stigma and discrimination on individuals, communities and health programme interventions.**

- Emotional stress and anxiety, self-deprecation, loss of hope, despair, depression, attempted suicide
- Isolation
- Problems in family relationships and friendships; increased inequities between those who are affected and those who are not
- Increased disability
- Participation restrictions (e.g., loss of job, economic dependency, inability to marry, lack of access to loans and credit) that may affect entire families and, in high prevalence areas, entire villages
- Concealment of the disease after diagnosis
- Preventive behaviours (condoms, discussing safer sex with a partner, PMTCT) not adopted
- Continued transmission of HIV
- Delay in presentation for treatment
- Poorer treatment prognosis; more complicated and more expensive treatment
- Lack of motivation to continue treatment, poor adherence, default on treatment, risk of drug resistance
- Increased burden on health services

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- Create greater recognition about stigma and discrimination
- Develop in-depth, applied knowledge about all aspects of HIV and AIDS through a participatory and interactive process
- Provide safe spaces to discuss the values and beliefs that underline stigma and discrimination
- Find common language to talk about stigma and discrimination
- Ensure a central role for people with HIV/AIDS as defined by the Greater Involvement of People with HIV/AIDS (GIPA) principles.
One of the most effective ways to break the cycle of stigma and discrimination is through ensuring people living with HIV can contribute to society. The best way to do this is to provide treatment to keep people healthier longer.

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HIV voluntary counselling and testing

HIV voluntary counselling and testing (VCT) has been shown to have a role in both HIV prevention and, for people with HIV infection, as an entry point to care.

VCT is the process by which an individual undergoes counselling enabling him/her to make an informed choice about being tested for HIV. This decision must be entirely the choice of the individual and he/she must be assured that the process will be confidential.

The expected outcomes are to reduce HIV transmission and acquisition, to improve access to medical, psychological and social care, as well as to legal support, to improve family planning, to facilitate MTCT interventions, to improve coping for people with HIV, to promote awareness, challenging stigma (societal benefits), and to improve adherence to ARVs and preventive therapies, coping with adverse effects.

COUNSELLING

Definition
HIV counselling has been defined as a confidential dialogue between a person and a care provider aimed at enabling the person to cope with stress and make personal informed decisions related to HIV/AIDS.

Counselling is not about advising, but about helping.
Objectives
The objectives of counseling are to prevent HIV transmission, to provide support to those who intend to be tested and to support people to cope with the test results.

Process
It includes an evaluation of personal risk of HIV transmission and facilitation of preventive behaviour. It consists of pre-test, post-test and follow-up counselling. HIV counselling can be adapted to the needs of the client/s: it can be for individuals, couples, families and children. The content and approach may vary considerably for men and women and with various groups, such as counselling for young people, men who have sex with men (MSM), sex workers, etc.

Pre-test counselling
HIV counselling should be offered before taking an HIV test. Ideally, the counsellor prepares the client for the test by explaining what an HIV test is, as well as by correcting myths and misinformation about HIV/AIDS. The counsellor may also discuss the client’s personal risk profile, including discussions of sexuality, relationships, possible sex and/or drug-related behaviour that increase risk of infection, and HIV prevention methods. The counsellor discusses the implications of knowing one’s sero-status, and ways to cope with that new information.

In case people do hesitate to take the test, it is recommended to give them 1 or 2 days to make up their mind. Nobody should feel under pressure of getting the test.

People who do not want pre-test counselling should not be prevented from taking a voluntary HIV test. However, informed consent from the person being tested is usually a minimum ethical requirement before an HIV test.

Post-test counselling
Post-test counselling should always be offered. The main goal of this counselling session is to help clients understand their test results and initiate adaptation to their sero-positive or negative status.

When the test result is negative
- Keep in mind that during the “window period” (approximately 3-6 weeks immediately after a person is infected), antibodies to HIV are not always detectable.
- While the client is likely to feel relief, the counsellor must emphasize several points. Counsellors need to discuss changes in behaviour that can help the client stay HIV-negative, such as safer sex practices including the use of condom and other methods of risk reduction.
- The counsellor must also motivate the client to adopt and sustain new, safer practices and provide encouragement for these behaviour changes. This may mean referring the client to ongoing counselling, support groups or specialized care services.
When the test result is positive

- The counsellor tells the client the result clearly and sensitively but in a straightforward way, providing emotional support and discussing how he/she will cope.

### Box 4.1 | Possible expressions of initial distress when learning a HIV+ status

- Some cry. This is a natural response. Give them time to cry.
- Persons who are shocked may appear to listen to you but do not take in anything that you say. They may fall quiet for a long time. The counsellor has to ask questions that may engage them.
- Some express anger. It is important that the counsellor does not take offence.
- Some become agitated. The counsellor must remain calm.
- Some may pass through a denial stage. Do not force the patients to face reality, because they might react with explosive emotions, becoming very anxious or aggressive. It is necessary to adopt a gradual and sensitive approach.
- Some might enter a stage of resignation or depression and further sessions are needed to support them. It might also be necessary to refer them to specialized units (psychology or psychiatry).

One of the aims of post-test counselling is to help persons to pass through these stages to reach an acceptance of their condition. This is likely to take more than one session, and some people may need several further sessions.

- Sharing a sero-positive result with a partner or trusted family member or friend is often beneficial and some clients may wish someone to be with them and participate in the counselling.
- Clients often forget what was said after they receive a positive result. Many will benefit from a second counselling session.
- It is not helpful to falsely reassure clients.
- It is often useful to propose supportive and problem-solving sessions following the disclosure of a positive result. The aim is to help the clients to reach and carry out decisions to enable them to cope with their problems.
- Crisis counselling: Following a positive result, some people will feel overwhelmed by problems (personal or linked to their family or community, etc.). They might feel anxious and helpless, or feel intensively threatened or react irrationally. Here, the aim of the counselling is to restore a sense of control.

### VCT AS AN ENTRY POINT TO PREVENTION AND CARE

VCT is an important entry-point to both HIV prevention and HIV-related care (Figure 4.1). People who test sero-positive can have early access to a wide range of services including medical care,
ongoing emotional support and social or legal support. People who test sero-negative can have counselling, guidance and support to help them remain negative.

**Figure 4.1. VCT and its links with other services**

**Box 4.2 | VCT uptake**

Although VCT play critical roles in HIV prevention by helping people to cope with the disease and avoid infecting others, less than 20% of people in Africa know their HIV status.

Free testing (and treatment) definitely increases the number of people volunteering to be tested.

**DEVELOPMENT OF VCT FOR SPECIFIC GROUPS**

When VCT services are being developed, consideration should be given to the different needs of the people attending.

**VCT for couples**

In case of sero-discordant test results, this can pose difficult challenges in the relationship. Counselling can help the couple overcome feelings of anger or resentment.

**VCT for children**

HIV-positive children have special counselling needs such as understanding and coping with their own illness, dealing with discrimination by other children or adults.
**VCT for the youth**
Influence of peer pressure (e.g., to take drugs or alcohol) and the development of their sexual and social identities are characteristics to be taken into account when dealing with teenagers.

**VCT for sex workers**
VCT for commercial sex workers need to be sensitive to the problems of stigma and illegality associated with commercial sex in many societies.

**VCT for injecting drug users**
Injecting drug use is a practice that is illegal and socially stigmatized in many cultures. VCT services that are part of such institutions may, therefore, be unlikely to attract drug-using clients. Counselling and prevention messages delivered by outreach workers, e.g., former drug users, are often perceived as being more credible and better accepted.

**SELECTION AND TRAINING OF COUNSELLORS**

A counsellor is an agent for change. Counselling is the principal means of slowing or stopping transmission of HIV infection. A counsellor knows about barriers that prevent and conditions that facilitate learning. He/she is able to communicate and share their knowledge meaningfully with others.

The physical environment is important. Counselling should take place in a comfortable and quiet room, where the necessary privacy conditions are fulfilled, creating the appropriate conditions for the counsellor to set a positive climate.

**Client expectations**
- To be listened to
- Not to feel alone
- To feel understood
- To get advice and support
- Empathic relationship

**Selection of counsellors**
Different categories of workers with different professional backgrounds can be trained as counsellors, e.g., primary health workers, psychologists, social workers, traditional birth attendants (TBAs), teachers, people living with HIV/AIDS, community workers, etc.
It is not enough, simply to have a caring personality. A counsellor needs to have qualities that should be identified during the selection process. Counsellors need to be good listeners, warm and caring, respected, not judging, well informed, motivated, resilient and familiar with the prevailing cultural context.

Training of counsellors
In addition, counselling requires training in specific skills (Table 4.1) that include: listening in an open and non-judgmental way, asking supportive questions, discussing options, encouraging clients to make their own informed decisions, giving accurate information, arranging follow up, etc.

A short (minimum 2 weeks) period of training in counselling can improve the skills and confidence of health care and social workers (Table 4.2). People are sometimes put on short (2 to 3 days) training courses without a serious selection process, for instance to fill up a course. This is one of the reasons why those trained in counselling often do not practise it or only for a few months.

After the initial training, counsellors should receive support and supervision in their work and participate in a further refresher-training workshop several months later.

Although there can be a great deal of satisfaction in providing support to people through counselling, it can also be very stressful. Counsellors can become emotionally exhausted or “burnt out.”

Table 4.1 | Skills to be mastered by counsellors

- Active listening
- Paraphrasing (rephrasing)
- Two ways communication
- Respect silence but be able to “re-launch” the dialogue
- Clarifying (some aspects, when necessary)
- Empathy (be a kind of mirror for the patient)
- Attention to the non verbal communication (body language, neurovegetative signs, etc.)
### Some of the essentials issues to be included in the training of counsellors

#### Why is it necessary to counsel before doing a HIV antibody test?

Pre-test counselling is necessary to enable the individuals to reach an informed decision about whether to have the test or not and, if they decide to have it, to prepare them for the result.

#### Why is it necessary for the client to make an informed decision?

Access to HIV/AIDS treatment, although becoming more and more possible, is far more complicated compared to STIs. Furthermore, there may be disadvantages of being tested. Therefore, it is important for the client to consider the advantages and disadvantages before deciding.

**Advantages:**
- Having the test may reduce the anxiety of not knowing whether they are infected.
- They will be in a better position to make decisions about the future (such as whether to become pregnant or not).
- If they are infected, opportunistic infections can be treated more quickly, and unnecessary tests avoided.
- If they are infected, they may be motivated to take up a healthier lifestyle.
- There may be benefits that they become entitled to if they are known to be HIV positive, e.g. social welfare services for PLWHA.
- Entry point to treatment (ARVs).

**Disadvantages:**
- If others learn that they are HIV positive, the clients may be stigmatized.
- They may be rejected by their partner or family.
- Women may lose financial support if their husband learns that they had a positive test result.
- Travel to other countries may be limited.

#### Why do people find AIDS a difficult disease to understand?

Many people do not know about the immune system. People often find it difficult to understand why different AIDS patients suffer from such different symptoms. It can be helpful to describe the immune system as the “defense army” of the body. HIV attacks the “soldiers” (white cells). It is easy to understand that diseases of the sexual organs can be spread sexually. But many find it hard to believe that HIV, which causes symptoms in other parts of the body, can be transmitted sexually. The fact that someone who is well can be infectious also causes confusion.

#### Confidentiality

Counsellors need to have a clear understanding of why confidentiality is so important and have to inform clients that everything that is said will remain confidential and that their HIV status will not be disclosed without their consent. Many people are afraid to seek HIV services because they fear stigma and discrimination from their families and community. VCT services should therefore always preserve individuals’ needs for confidentiality.
Table 4.2 Some of the essentials issues to be included in the training of counsellors... contd

Denial
It is also important for the trainees to have a clear understand of what denial means. Denial may be a powerful and unconscious influence on behaviour. Denial can prevent people from accepting an HIV test, coming back for results or seeking treatment. Denial can prevent people from telling their sexual partner about their infection or practicing safe sex to protect others, and may result in aggressive reactions toward counsellors and partners who raise these issues.

Stigma
HIV is highly stigmatized in many countries and people with HIV may experience social rejection and discrimination. This fear of rejection or stigma is a common reason for declining testing.

Discrimination
In some countries, people with HIV are subjected to discrimination at work or in education. Unless legislation is in place to prevent this, some people will be reluctant to undergo VCT.

Gender inequalities
Studies have also shown that women may be particularly vulnerable following VCT and in some cases have lost their homes and children or have been beaten or abused by their husbands/partners if their status became known.

References
- A guide to establishing voluntary counselling and testing services for HIV. FHI. 2002
- Basics AIDS counselling guidelines. Canadian international development agency. 2001
- Protecting the future. IRC. 2003
- The impact of voluntary counselling and testing. UNAIDS. 2001
- Voluntary counselling and testing (VCT). UNAIDS. 2000
HIV infection in adults and adolescents

On average, there is a period of 6 to 10 years from initial infection to clinical AIDS in adults.

About 10% of persons will rapidly progress to AIDS in 2 to 3 years following HIV infection, while about 10% have not progressed to AIDS even after 10 years.

There is no evidence that shows a failure of HIV-infected persons to evolve to clinical AIDS over time, though the speed at which this evolution occurs may vary greatly.

natural history of HIV-1 infection

The natural history of untreated HIV-1 infection in adults can be divided into the following stages:

- **Initial infection**
  - 2 – 3 weeks

- **Acute retroviral syndrome**
  - 1 – 2 weeks

- **Recovery and seroconversion**
  - 2 – 3 weeks

- **Asymptomatic chronic HIV infection**
  - 6 – 10 years

- **Symptomatic HIV infection**
  - 1 – 3 years
- Death
Natural history of HIV infection in a patient without antiretroviral therapy from the time of HIV transmission to death

The initial event is the acute retroviral syndrome, which is accompanied by a precipitous decline in CD4 cell counts and high concentrations of HIV RNA (viral load) in plasma. Clinical recovery is accompanied by a reduction in viral load, reflecting development of cytotoxic T-cell response. A viral set point is established within a few weeks to months after infection. Set points are thought to determine how long it will take for disease progression to occur. With continued infection, HIV RNA levels gradually increase.

Viral load as AIDS predictor

The slope of the CD4 cell decline depends on the viral load. The slope increases in late stage disease. Late stage disease is characterized by a CD4 count <200 cells/mm³ and the development of opportunistic infections, selected tumours, wasting, and neurological complications. In an untreated patient, the median survival after the CD4 count has fallen to <200 cells/mm³ is 3.7 years; the median CD4 count at the time of the first AIDS-defining complication is 60–70 cells/mm³; the median survival after an AIDS-defining complication is 1.3 years.
Acute retroviral syndrome

After an incubation period of two to three weeks, most cases present with an acute flu-like illness. Between 50 to 90% of the patients are symptomatic.

The most common symptoms are fever, lymphadenopathy, pharyngitis, rash, myalgia and/or arthralgia (Table 5.1).

Acute retroviral infection is not life–threatening.

**Table 5.1. Acute retroviral syndrome: Expected frequency of associated signs and symptoms**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fever</td>
<td>96%</td>
</tr>
<tr>
<td>• Lymphadenopathy</td>
<td>74%</td>
</tr>
<tr>
<td>• Pharyngitis</td>
<td>70%</td>
</tr>
<tr>
<td>• Rash (erythematous maculopapular; mucocutaneous ulceration)</td>
<td>70%</td>
</tr>
<tr>
<td>• Myalgia or arthralgia</td>
<td>54%</td>
</tr>
<tr>
<td>• Diarrhea</td>
<td>32%</td>
</tr>
<tr>
<td>• Headache</td>
<td>32%</td>
</tr>
<tr>
<td>• Nausea and vomiting</td>
<td>27%</td>
</tr>
<tr>
<td>• Hepatosplenomegaly</td>
<td>14%</td>
</tr>
<tr>
<td>• Weight Loss</td>
<td>13%</td>
</tr>
<tr>
<td>• Thrush</td>
<td>12%</td>
</tr>
<tr>
<td>• Neurologic symptoms (meningoencephalitis or aseptic meningitis; peripheral neuropathy or radiculopathy; facial palsy; Guillain–Barré syndrome; brachial neuritis; cognitive impairment or psychosis)</td>
<td>12%</td>
</tr>
</tbody>
</table>
The symptomatic phase of acute HIV-1 infection lasts between one and two weeks. The severity and duration of symptoms has prognostic implications, as severe and prolonged symptoms are associated with more rapid disease progression.

As the consequence of the non-specific nature of the symptoms, the diagnosis of acute infection is missed in the majority of cases, as other viral illnesses (“flu”) are often assumed to be the cause of the symptoms and there are no HIV-1-specific antibodies detectable at this early stage of infection.

However, an accurate early diagnosis of acute HIV-1 infection is important, as patients are highly infective (high viral load) and infection of sexual partners can be prevented.

**Seroconversion**

Seroconversion with detectable HIV antibody by laboratory testing accompanies the immune response, sometimes in as little as a week, but more often in three to six weeks after infection.

**Chronic infection**

A relative equilibrium between viral load and the host immune response is reached and individuals may have no clinical manifestations of HIV infection.

Despite the relative clinical latency, viral replication and CD4 cells turnover remain active with millions of CD4 cells and billions of virus produced and destroyed each day.

The analogy of a train on a track (Figure 5.1) can be helpful in illustrating the independent contributions of CD4+ count and HIV viral load in an individual. If the infected individual is imagined as being on that train travelling toward a clinical event — such as dying from AIDS — the CD4+ count provides information on the distance of the train from that destination, whereas the viral load provides information on the speed of the train in reaching the destination.

**Figure 5.1. Contributions of CD4 count and viral load towards a clinical event**
**Box 5.2 | Long-term non-progressors**

Long-term non-progressors are people who have been infected with HIV for more than 7 years, who have stable CD4$^+$ T cell counts above 600/mm$^3$ and have no history of symptoms and have not been taking anti-retroviral drugs. The CD4$^+$ T lymphocytes of these patients fall after primary infection and seroconversion but remain at normal levels thereafter, in some cases up to 15 years.

This seems to be a heterogeneous group of people whose long-term non-progressive disease results from a robust CD8$^+$ T cell immune response against HIV, a poorly replicative virus, or mutations in CCR5 co-receptors that HIV needs, along with CD4 antigen, to enter the cell.

---

**Advanced HIV/AIDS disease**

The WHO case definition of advanced HIV disease in adults and adolescents with confirmed HIV infection$^1$ include clinical stage 3 or stage 4 (Table 5.2) or any clinical stage and CD4 $<350$/mm$^3$.

AIDS is defined as clinical diagnosis of any stage 4 condition with confirmed HIV infection or severe immunological suppression (CD4 count $< 200$cells/mm$^3$) with confirmed HIV infection.

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**STAGING SYSTEM FOR HIV INFECTION**

**WHO clinical staging system**

The WHO has recently (2006) revised its HIV/AIDS clinical staging system (Table 5.2).

---

**Table 5.2 | Revised WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection. One condition is sufficient to define the stage.**

<table>
<thead>
<tr>
<th>Clinical stage I (Asymptomatic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic infection</td>
</tr>
<tr>
<td>• Persistent generalised lymphadenopathy (PGL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage II (Mild symptoms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unexplained moderate weight loss (&lt;10% of presumed or measured body weight)</td>
</tr>
<tr>
<td>• Recurrent respiratory tract infections (sinusitis, tonsilitis, otitis media, pharyngitis)</td>
</tr>
<tr>
<td>• Herpes zoster</td>
</tr>
</tbody>
</table>

---

$^1$ See Chapter 6 for WHO case definition for HIV infection
### Table 5.2 Revised WHO clinical staging of HIV/AIDS for adults and adolescents ... contd.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>III (Advanced symptoms)</td>
<td>Angular cheilitis, Recurrent oral ulcerations, Papular pruritic eruptions, Seborrhoeic dermatitis, Fungal nail infections</td>
</tr>
<tr>
<td>IV (Severe symptoms)</td>
<td>Unexplained severe weight loss (&gt;10% of presumed or measured body weight), Unexplained chronic diarrhoea for longer than one month, Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month), Persistent oral candidiasis, Oral hairy leukoplakia, Pulmonary tuberculosis, Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia), Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis, Unexplained anaemia (&lt; 8 g/dL), neutropenia (&lt;500/mm³) and/or chronic thrombocytopenia (&lt;50 ,000/ mm³), HIV wasting syndrome, Pneumocystis pneumonia, Recurrent severe bacterial pneumonia, Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month’s duration or visceral at any site), Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs), Extrapulmonary tuberculosis, Kaposi sarcoma, Cytomegalovirus infection (retinitis or infection of other organs), Central nervous system toxoplasmosis, HIV encephalopathy, Extrapulmonary cryptococcosis including meningitis, Disseminated non-tuberculous mycobacteria infection, Progressive multifocal leukoencephalopathy, Chronic cryptosporidiosis, Chronic isosporiasis, Disseminated mycosis (extrapulmonary histoplasmosis or coccidiomycosis)</td>
</tr>
</tbody>
</table>
Table 5.2 Revised WHO clinical staging of HIV/AIDS for adults and adolescents ... contd.

- Recurrent septicaemia (including non-typhoidal *Salmonella*)
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

**WHO immunological staging system**

CD4 cell count is useful for determining the degree of immunosuppression.

Where CD4 laboratory facilities are available, CD4 cell count should be used to support clinical and therapeutic decision-making.

Table 5.3 |  **WHO immunological staging of HIV Infection for adults and adolescents**

<table>
<thead>
<tr>
<th>Immunosuppression</th>
<th>CD4+ cells count (absolute or %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not significant</td>
<td>&gt;500/mm³</td>
</tr>
<tr>
<td>Mild</td>
<td>350 - 499/mm³</td>
</tr>
<tr>
<td>Advanced</td>
<td>200 - 349/mm³</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;200/mm³ or &lt;15%</td>
</tr>
</tbody>
</table>

**U.S. Centres for Disease Control and Prevention (CDC) staging system**

Box 5.3 |  **CDC HIV/AIDS Surveillance Case Definition for Adolescents and Adults (1993)**

<table>
<thead>
<tr>
<th>CD4+ T cells/mm³</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asymptomatic, acute primary HIV infection or persistent generalized lymphadenopathy</td>
<td>Symptomatic, not A or C conditions*</td>
<td>AIDS indicator conditions</td>
</tr>
<tr>
<td>&gt; 500</td>
<td>A1</td>
<td>B1</td>
<td>C1</td>
</tr>
<tr>
<td>200 - 499</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>&lt;200</td>
<td>A3</td>
<td>B3</td>
<td>C3</td>
</tr>
</tbody>
</table>

* Symptomatic conditions not included in category C that are: 1) attributed to HIV infection or indicative of a defect in cell-mediated immunity or 2) considered to have a clinical course or management that is complicated by HIV infection.
History and physical examination
Both history and physical signs (Table 5.4) should be collected at baseline and at each subsequent visit i.e. at least every 3 months.

History should include: HIV-specific information (first known HIV test, possible timing for HIV infection, understanding of HIV disease), risk assessment (substance abuse, sexual behavior), past medical history, and social history (housing, food sources, income, legal issues).
Laboratory testing

Laboratory testing (Table 5.5) should be done to confirm and stage the HIV disease, evaluate the general health status, identify the presence of concurrent conditions, guide the initiation of ART, and monitor therapeutic response and drug toxicities.

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV serologic test</td>
<td>Baseline</td>
<td>Confirmation of HIV+ status</td>
</tr>
<tr>
<td>Complete blood count (CBC)</td>
<td>Baseline, then every 3-6 months Repeat more often with bone marrow suppressive drugs such as AZT</td>
<td>Detection of anemia, leucopenia, and thrombocytopenia</td>
</tr>
<tr>
<td>CD4 count &amp; percentage</td>
<td>Twice at baseline, then every 3-6 months</td>
<td>HIV staging Guides initiation of ART Indicates risk of OIs and guides initiation of prophylaxis against OIs</td>
</tr>
<tr>
<td>Viral load</td>
<td>Twice at baseline Repeat at 6-month intervals (more frequently with initiation of ART)</td>
<td>Prognostic indicator Major indicator of therapeutic response</td>
</tr>
<tr>
<td>Chemistry panel(electrolytes, creatinine, liver enzymes)</td>
<td>Baseline, then every 6-12 months</td>
<td>Useful to monitor drug toxicities</td>
</tr>
</tbody>
</table>
Table 5.5  Standard laboratory tests ...contd.

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting lipids and fasting glucose</td>
<td>Baseline, then every year</td>
<td>Especially for patients on PIs</td>
</tr>
<tr>
<td>PAP smear</td>
<td>Baseline, at 6 months, then annually</td>
<td>Detects abnormal cell changes, dysplasia</td>
</tr>
<tr>
<td>Tuberculin skin test</td>
<td>Baseline if no history of TB or no prior positive test Repeat if initial test was negative and patient was exposed Repeat if CD4 count was &lt; 200 cells/mm³ on initial test but increases to &gt; 200 cells/mm³</td>
<td>Detect latent TB infection</td>
</tr>
<tr>
<td>VDRL or RPR</td>
<td>Baseline, then annually if patients sexually active</td>
<td>Syphilis screening</td>
</tr>
<tr>
<td>Hepatitis A serology</td>
<td>Baseline</td>
<td>Identifies candidates for HAV vaccine</td>
</tr>
<tr>
<td>Hepatitis B serology</td>
<td>Baseline</td>
<td>Detects past or ongoing infection Identifies candidates for HAB vaccine</td>
</tr>
<tr>
<td>Hepatitis C serology</td>
<td>Baseline Repeat if patient at risk (IDU)</td>
<td></td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em> IgG</td>
<td>Baseline Repeat if patient becomes symptomatic or CD4 count drops to &lt; 100 cells/mm³</td>
<td></td>
</tr>
<tr>
<td>CMV IgG</td>
<td>Baseline Repeat if CD4 count drops to &lt; 50 cells/mm³</td>
<td>Assessment of likelihood of CMV disease in late stage HIV infection.</td>
</tr>
</tbody>
</table>

References

- A guide to primary care of people with HIV/AIDS. US DHHS. 2004
- Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings. WHO. 2006
- WHO case definition of HIV for surveillance & clinical staging & immunological classification of HIV-related disease in adults and children. WHO. 2006
Laboratory assays

Diagnostic tests provide suggestive or/and confirmatory evidence of HIV infection. They are two types: antibody (serologic) and virologic tests.

Prognostic tests help in monitoring the disease progression. They consist of: absolute CD4 cell count, CD4 percentage and viral load.

Resistance tests provide a measure of drugs resistance for HIV. Two methods are used: genotyping and phenotyping.

DIAGNOSTIC TESTS

Serologic tests
The detection of antibodies specifically recognizing HIV is the most common way to diagnose HIV infection in adults and children >18 months old.

Tests for antibodies to HIV do not establish the presence of HIV infection in infants < 18 months because of transfer of maternal antibodies to the foetus; therefore a virologic test should be utilized.

The antibodies are usually detectable within 3 to 6 weeks after infection, and almost all individuals seroconvert by 12 weeks. In very rare cases, antibodies may not be detected for months or years.

The time period between infection and the detection of antibodies is called window period.

Serologic testing is currently performed with a highly sensitive screening assay and confirmation of preliminary positive specimens with a highly specific confirmatory assay.
HIV antibody screening assays: Enzyme-Linked Immunosorbent Assay (ELISA)

A very sensitive test, but not entirely specific - can detect antibodies to antigens other than HIV, making it possible to give a false positive. A positive ELISA result means that the sample needs to be tested further by Western blot or a different ELISA test.

<table>
<thead>
<tr>
<th>HIV prevalence</th>
<th>0.1%</th>
<th>1%</th>
<th>5%</th>
<th>10%</th>
<th>30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative predictive value with one non-reactive test</td>
<td>100.0%</td>
<td>100.0%</td>
<td>99.9%</td>
<td>99.9%</td>
<td>99.6%</td>
</tr>
<tr>
<td>Positive predictive value with one reactive test</td>
<td>9.0%</td>
<td>50%</td>
<td>83.9%</td>
<td>91.7%</td>
<td>98.5%</td>
</tr>
<tr>
<td>Positive predictive value with two reactive tests</td>
<td>90.8%</td>
<td>99.0%</td>
<td>99.8%</td>
<td>99.9%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

**Box 6.1 | Sensitivity, specificity, predictive value**

**Sensitivity** is defined as the probability of testing positive if the disease is truly present.

**Specificity** is defined as the probability of testing negative if the disease is truly absent.

The **positive predictive value** of a test is the probability that the person is HIV-infected when the test is positive, expressed as a percentage.

The **negative predictive value** is the probability that the person is uninfected when the test is negative, expressed as a percentage.

Even with a very accurate test (high sensitivity and high specificity), in settings with a low HIV prevalence (e.g. <1%) the positive predictive value of a test may not be sufficiently high.

In general, the higher the prevalence of HIV infection in the population, the greater is the probability that a person testing positive is truly infected. With increasing HIV prevalence the proportion of false-positives decreases.

Conversely, the probability that a person with a negative test result is uninfected declines slightly as HIV prevalence increases.

It is necessary to conduct a second test if the first test is reactive, as this markedly increases the positive predictive value.

**Positive and negative predictive values at various HIV prevalences (calculated with a sensitivity and a specificity of 99%)**

HIV antibody screening assays: Enzyme-Linked Immunosorbent Assay (ELISA)

A very sensitive test, but not entirely specific - can detect antibodies to antigens other than HIV, making it possible to give a false positive. A positive ELISA result means that the sample needs to be tested further by Western blot or a different ELISA test.
**HIV antibody confirmatory assays: Western Blot (WB)**

The most common confirmatory assay for HIV antibody, the Western blot is considered the “gold standard” for HIV diagnostic testing.

A reactive WB demonstrates antibody to two of the three major bands. A nonreactive WB will have no detectable viral bands.

**Box 6.3 | Western Blot**

The virus is disrupted, and the individual proteins are separated by molecular weight via differential migration on a gel and blotted onto a membrane support. HIV serum antibodies from the patient are allowed to bind to the proteins in the membrane support, and patterns of reactivity can be visibly read. The three major viral bands for HIV are the core protein p24 and the two envelope proteins, gp41 and gp120.

Specimens that are repeatedly reactive by ELISA and reactive by the confirmatory assay are reported as positive for antibody to HIV.

Samples that are nonreactive by ELISA or repeatedly reactive by ELISA and nonreactive by the confirmatory assay are negative for antibody to HIV.

A WB in which serum antibodies bind to any other combination of viral bands is considered indeterminate, and a follow-up blood specimen should be obtained 1 month later for repeat HIV antibody testing.

Individuals with repeat indeterminate results may undergo further testing using molecular assays, such as Polymerase Chain Reaction (PCR), to help resolve infection status.
Rapid tests
Rapid test are easy to perform, easy to interpret and easy to store. They provide results in about 20-30 minutes. Sensitivity approaches 100 percent; specificity is >99 percent—analogous to ELISA screening tests.

Most rapid tests detect both HIV-1 and HIV-2 but most of these tests do not differentiate between them.

Figure 6.1. **WHO rapid testing strategy for diagnostic purpose**

The terms *reactive*, *nonreactive*, and *indeterminate* are used to describe the results of the screening and confirmatory assays. The terms *positive*, *negative*, and *inconclusive* are used to describe the final interpretation of results for a specimen.
Viral identification assays

HIV-1 DNA Polymerase Chain Reaction (DNA PCR)
DNA PCR is a sensitive technique used to detect specific HIV proviral sequences in DNA of patients’ peripheral blood mononuclear cells (PBMC).

Box 6.4  |  HIV DNA PCR
The individual’s peripheral blood mononuclear cells (PBMC) are harvested, cellular DNA is extracted, and target DNA is amplified using a very specific set of oligonucleotide primers. The reaction progresses through 30 to 35 cycles of denaturation, annealing, and synthesis of new DNA, ending with billions of copies of the target DNA.

This is the most sensitive (can detect 1 to 10 copies of HIV proviral DNA) and the preferred virologic method for diagnosing HIV infection in infants born to mothers infected with HIV-1 (refer to Chapter 8  *HIV Infection in Paediatrics*).

Two positive DNA PCR obtained on different days confirms HIV infection. Children < 18 months are uninfected if negative results occur in 2 or more DNA PCR when one is performed after 1 month of age and the other is performed after 4 months of age.

p24 antigen assay
The p24 antigen, one of the core proteins of the HIV capsid, can be detected in the serum of individuals as early as 16 days post-infection and prior to the detection of antibodies.

Ultrasensitive p24 assays, that have a specificity and sensitivity nearly comparable to PCR tests but are less expensive and technically less demanding, can be readily used in resource-poor settings for the diagnosis of HIV-exposed infants.

Viral culture
This assay is very specific but it is rarely used because it is expensive, labour-intensive, and less sensitive than antibody testing. A negative culture may be caused by technical problems, a defective virus, or the inability of the virus to replicate in culture.

Simplified WHO case definition for HIV infection

Adults and children 18 months or older
HIV infection is diagnosed based on:
  •  A positive HIV antibody testing (rapid or laboratory-based enzyme immunoassay). This is
usually confirmed by a second HIV antibody test (rapid or laboratory-based enzyme immunoassay) relying on different antigens or of different operating characteristics and/or
• A positive virologic test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virologic test obtained from a separate determination.

Children younger than 18 months
HIV infection is diagnosed based on:
• A positive virologic test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virologic test obtained from a separate determination taken more than four weeks after birth.

Positive antibody testing is not recommended for definitive or confirmatory diagnosis of HIV infection in children until 18 months of age.

PROGNOSTIC TESTS

Once a patient has been diagnosed as being HIV infected, tests need to be administered to help in evaluating and monitoring the clinical progression of the disease.

CD4⁺ count and percentage
The CD4⁺ cell count is important in determining the staging of HIV disease and for indicating the need for prophylaxis against opportunistic pathogens.

In addition, the CD4⁺ cell count continues to be used to assist in decisions regarding initiation or adjustment of ARV treatment.

Normal laboratory ranges are usually 500-1,400/mm³. CD4⁺ cell counts of < 200 cells/mm³ meet the case definition for AIDS.

Absolute CD4⁺ cell counts are calculated values that may fluctuate widely, especially in infants. As a result, HIV clinicians should measure and follow the CD4⁺ percentage in addition to the absolute count because the CD4⁺ percentage is a direct measurement and more reliable. A significant change in the absolute CD4⁺ cell count in the setting of a stable CD4⁺ percentage can assure both the patient and the clinician that immunologic stability is present.

Treatment decisions should not be made solely on the basis of a single CD4⁺ cell measurement obtained at a single point in time.
**HIV RNA PCR (Viral load)**

Viral load assays quantify the amount of HIV RNA circulating in the blood of an infected individual. Although total quantification includes cell-free virus, virus in infected cells in all compartments of the body, and integrated provirus, the easiest measurement of viral load is that of cell-free virus in an individual's plasma.

Because there are differences in the absolute copy number generated by different viral load assays, the same assay should be used to follow an individual's viral load.

The goal of ARV therapy is to suppress the HIV viral load as low as possible for as long as possible. Standard assays have a lower limit of detection of 400 copies/mL, and ultrasensitive assays may detect viral loads as low as 5 to 50 copies/mL.
Cohort studies strongly suggest that patients with viral loads <50 copies/mL have more sustained viral suppression than patients with viral loads between 50 and 400 copies/mL, and therefore the ultrasensitive assays may be more useful than standard viral load tests in predicting prolonged viral suppression and are recommended for monitoring patients who are receiving ARV therapy.

It is important to note that acute concurrent illness and/or recent vaccination may cause a transient rise in viral load.

<table>
<thead>
<tr>
<th>Copies/mL</th>
<th>$\log_{10}^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000,000</td>
<td>6.0</td>
</tr>
<tr>
<td>100,000</td>
<td>5.0</td>
</tr>
<tr>
<td>50,000</td>
<td>4.7</td>
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<tr>
<td>10,000</td>
<td>4.0</td>
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<td>5,000</td>
<td>3.7</td>
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<tr>
<td>1,000</td>
<td>3.0</td>
</tr>
<tr>
<td>100</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* $\log_{10}$ (base 10 logarithm) is the power to which 10 must be raised to produce a given number. For example, $10^3 = 1,000$; therefore, $\log_{10} 1,000 = 3$.

**RESISTANCE TESTS**

There are two general types of resistance testing assays: genotypic assays (i.e., HIV gene sequencing to detect mutations that confer HIV drug resistance) and phenotypic assays (i.e., drug susceptibility testing of plasma virus).

**Box 6.6 | Genotypic and phenotypic assays**

A **genotype assay** provides an indirect measure of drug resistance because it is based on detection of the mutations known to be associated with resistance. Genotype testing involves determining the sequence of the protease and reverse transcriptase regions of the HIV genome because these are the functions to which currently available ARV drugs are targeted.

The HIV RNA is isolated from a blood specimen and the protease and reverse transcriptase regions of the HIV genome are amplified and sequenced. This sequence is then compared with that of a drug-sensitive (wild-type) strain of HIV, and differences (mutations) present in the specimen sequence are noted.
Box 6.6 Genotypic and phenotypic assays ... contd

Currently available genotype assays require a minimum viral load in the range of 500 to 2,000 copies/mL, depending on the assay. Genotype assays generally require 2 weeks or less for results.

A phenotypic assay provides a relative measure of drug resistance. Phenotypic assays measure the ability of the population of virus circulating in HIV-infected patients to grow in the presence of a drug. Therefore, results from a phenotype test include the net effect of any and all resistance mutations.

In the phenotype assay, HIV RNA is isolated from plasma, converted into cDNA, and amplified by PCR. As in genotyping, the regions amplified are the protease and reverse transcriptase genes. This amplified material is inserted into a recombinant virus system whereby the susceptibility to different drugs can be tested.

Phenotypic assays have a minimum viral load requirement of 500 to 1,000 copies/ml and generally require 3 to 5 weeks for results.

References
- Diagnostic, prognostic and resistance tests for HIV. NYSDH. 2004
- Diagnostic, prognostic and resistance tests for HIV. Tables and recommendations. NYSDH. 2004
- Guidelines for laboratory test result reporting of human immunodeficiency virus type 1 ribonucleic acid determination. CDC. 2001
- Rapid HIV tests: Guidelines for use in HIV testing and counselling services in resource-constrained settings. WHO. 2004
- Use of TLC vs CD4 cell count. UCSF. 2006
- WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. WHO. 2006
Antiretroviral therapy in adults and adolescents

The most important goal of HIV antiretroviral therapy (ART) is to reduce the HIV viral load to as low as possible for as long as possible.

The other goals of antiretroviral therapy are to:
- Prevent HIV-related morbidity and mortality
- Prevent HIV transmission
- Avoid HIV resistance
- Preserve HIV treatment options.

ANTIRETROVIRAL DRUGS

Current antiretroviral drugs
The current 22 antiretroviral drugs (ARVs) belong to four distinct classes: the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs, NtRTIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs), the protease inhibitors (PIs), and the fusion inhibitors (FIs) (Table 7.1).

<table>
<thead>
<tr>
<th>Class</th>
<th>NRTIs &amp; NtRTIs (or “nukes”)</th>
<th>NNRTIs</th>
<th>PIs</th>
<th>FIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs (trade name in italic)</td>
<td>Abacavir (ABC) Ziagen</td>
<td>Delavirdine (DLV) Rescriptor</td>
<td>Amprenavir (APV) Agenerase</td>
<td>Enfuvirtide (ENF or T-20) Fuseon (for salvage therapy)</td>
</tr>
<tr>
<td></td>
<td>Didanosine (ddI) Videx</td>
<td>Efavirenz (EFV) Sustiva or Stocrin</td>
<td>Atazanavir (ATV) Reyataz</td>
<td>(for salvage therapy)</td>
</tr>
<tr>
<td></td>
<td>Emtricitabine (FTC) Emtriva</td>
<td>Nevirapine (NVP) Viramune</td>
<td>Fosamprenavir (F-APV) Lexiva</td>
<td></td>
</tr>
</tbody>
</table>

Table 7.1 | Current antiretroviral drugs
Table 7.1  Current Antiretroviral Drugs ... contd

<table>
<thead>
<tr>
<th>Class</th>
<th>NRTIs &amp; NtRTIs (or “nukes”)</th>
<th>NNRTIs</th>
<th>PIs</th>
<th>FIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs</td>
<td>Lamivudine (3TC) Epivir</td>
<td>Indinavir (IDV) Crixivan</td>
<td>Lopinavir/Ritonavir</td>
<td>Ritonavir (RTV or /r if used as booster) Norvir</td>
</tr>
<tr>
<td></td>
<td>Stavudine (d4T) Zerit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tenofovir (TDF) Viread</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zalcitabine (ddC) Hivid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zidovudine (AZT or ZDV) Retrovir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nelfinavir (NFV) Viracept</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ritonavir (RTV or /r if used as booster) Norvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Saquinavir SGC Fortovase</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Saquinavir HCG Invirase</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tipranavir (TPV Aptivus)</td>
<td></td>
</tr>
</tbody>
</table>

Box 7.1 | ARVs mechanism of action

NRTIs and NtRTIs are synthetic analogs that substitute a nucleoside in the reverse transcriptase (RT)
Fixed-dose combinations

Fixed-dose combinations (FDCs) are based on the principle of inclusion of two or more active pharmacological products in the same pill, capsule, tablet or solution.

The use of quality assured ARVs in FDCs presents the advantage of a reduced pill burden, leading to better adherence which, in turn, limits the emergence of drug resistance. Additionally, FDCs are generally much cheaper than separate dispensing drugs.

For instance, the FDC of d4T + 3TC + NVP, which is one of the regimens recommended as first-line therapy by WHO, allows an easy dosing (i.e., a single pill to be taken twice a day) for a cost not exceeding 140 US$/year (June 2006).

Evolution of ARVs regimen costs

The chart below shows the evolution of prices in the last six years of the main WHO recommended first-line regimens in developing countries.

Figure 7.1. Evolution of ART prices in developing countries
WHEN TO INITIATE ANTIRETROVIRAL THERAPY

The decision to start therapy depends on the risk-to-benefit ratio of treatment (Table 7.2).

### Table 7.2 | Benefits and risks of ART

**Benefits**
- Suppression of viral replication
- Preservation and/or restoration of immune function
- Improvement of overall health and prolongation of life
- Possible decrease in risk of viral transmission to others (including mother-to-child transmission)

**Risks**
- Adverse effects of the medications on quality of life
- Long-term drug toxicities, including potential fetal toxicity
- Development of HIV drug resistance that would limit future treatment options

The reduction in CD4 cells is the pivotal event of HIV disease that renders the patient susceptible to the unique opportunistic infections (OIs) and tumors that have come to be known as AIDS defining diagnoses.

The patient becomes vulnerable to these diseases when the CD4 cell count decreases from normal levels (500-1,500 cells/mm³) to <200 cells/mm³.

CD4 count < 200 cells/mm³ is the universally accepted threshold for initiating treatment.

### Table 7.3 | When to start therapy. WHO recommendations

<table>
<thead>
<tr>
<th>WHO clinical stage</th>
<th>CD4 count not available</th>
<th>CD4 count available</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Treat</td>
<td>Treat irrespective of CD4 count</td>
</tr>
</tbody>
</table>
| III                | Treat                   | - Consider treatment if CD4 count is below 350/mm³  
|                    |                         | - Start ART before CD4 drops below 200/mm³ |
| II                 | Do not treat            | - Consider treatment if CD4 count is below 350/mm³  
|                    |                         | - Start ART before CD4 drops below 200/mm³ |
|                   | Do not treat            | - Consider treatment if CD4 count is below 350/mm³  
|                    |                         | - Start ART before CD4 drops below 200/mm³ |
Patient readiness and acceptance may be the most important factor in the decision to start ART. ART is almost never an emergency!

Box 7.2 | Provider steps to treatment readiness

- Begin adherence assessment and counselling early in HIV care
- Determine barriers to accepting therapy
- Provide adequate education about the nature of adherence, as well as HIV and therapy
- Involve the patient in the development of a treatment regimen
- Address co-existing morbidities before initiating therapy when possible
- Start prophylactic treatment (co-trimoxazole) if needed
- Obtain patient informed consent to ART

**FIRST LINE REGIMEN**

The current standard for formulating a highly active antiretroviral therapy (HAART) recommends the use of two N(t)RTIs as backbone plus one NNRTI or one PI (or ritonavir-boosted PI).

- NNRTI-based regimens are the most widely prescribed combinations for initial therapy in naïve patients ( naïve patient: patient who has never received ARVs). Nevirapine and efavirenz have comparable efficacy when administered with two NRTIs as backbone (Table 7.4).

<table>
<thead>
<tr>
<th>Table 7.4</th>
<th>WHO recommended first-line ARV drugs for adults and adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>One dual N(t)RTIs backbone</strong></td>
<td><strong>+</strong></td>
</tr>
<tr>
<td>AZT or d4T or ABC or TDF</td>
<td>+</td>
</tr>
<tr>
<td>3TC or FTC</td>
<td></td>
</tr>
</tbody>
</table>

NVP: Maintain close observation over the first 12 weeks of therapy in women with CD4 > 250/mm³ or men with CD4 > 400/mm³ because of higher incidence of serious and even fatal hepatotoxicity.

EFV: Contraindicated in first trimester of pregnancy or in women with significant child-bearing potential due to its teratogenicity.

ABC: Not to be started at the same time as NVP (both can induce skin rash).
• PIs-based regimens remain an accepted standard-of-care for initial regimens but their high cost relative to NNRTI-based regimens makes their use more problematic in resource-limited countries.

• Triple N(t)RTI regimens as sole antiretroviral combination have less potent virologic activity than comparator NNRTI- or PI-based regimens. Triple NRTI regimen (such as AZT + 3TC + ABC or TDF) should only be used when NNRTI- or PI-based regimen may be less desirable due to concerns over toxicities or drug interactions.

• Regimen should be individualised based on the pros and cons of each combination such as pill burden, dosing frequency, toxicities, drug-drug interactions potential, co-morbid conditions, preservation of future therapeutic options (Table 7.5).

• Monotherapies and 2-NRTI regimens are not recommended due to rapid development of resistance and inferior antiretroviral activity when compared to triple combinations.

• NNRTIs are not active against HIV-2; triple N(t)RTIs are recommended as the first-line regimens for individuals living with HIV-2 alone.

### Table 7.5 | Class-based advantages and disadvantages

<table>
<thead>
<tr>
<th>Regimens</th>
<th>Class advantages</th>
<th>Class disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI-based</td>
<td>• Less fat maldistribution and dyslipidemia than PI-based regimens</td>
<td>• Low genetic barrier to resistance</td>
</tr>
<tr>
<td></td>
<td>• Save PI options for future use</td>
<td>• Cross resistance among NNRTIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Potential for cytochrome P450 drug interactions</td>
</tr>
<tr>
<td>PI-based</td>
<td>• Save NNRTI for future use</td>
<td>• Fat maldistribution, dyslipidemia, insulin resistance</td>
</tr>
<tr>
<td></td>
<td>• Longest prospective study data including data on survival benefit</td>
<td>• Cytochrome P450 3A4 inhibitors &amp; substrates</td>
</tr>
<tr>
<td>Triple N(t)RTI</td>
<td>• Save NNRTI and PI for future use</td>
<td>• Inferior virologic response</td>
</tr>
<tr>
<td></td>
<td>• Minimal drug–drug interaction</td>
<td>• Rare but serious cases of lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td></td>
<td>• Low pill burden</td>
<td></td>
</tr>
</tbody>
</table>

### FOLLOW-UP OF PATIENTS STARTING ART

Patients who start an ARV regimen should be seen at least twice within the first month to assess effectiveness, adherence, tolerability, and side effects of the regimen.

• At 2 weeks on a new regimen, check the following:
- CBC with platelets (especially for patients starting a zidovudine-containing regimen) to monitor for anemia
- Liver enzymes (especially for patients starting a nevirapine-containing regimen) to monitor for hepatotoxicity

- At 4-8 weeks on a new regimen, and every 3 months on a stable regimen, check the following:
  - CD4 cell count—to monitor initial CD4 response to therapy (note that CD4 response may lag behind virologic response)
  - HIV viral load—to monitor initial virologic response to therapy
  - CBC with platelets
  - Liver enzymes and renal function tests, glucose

- Patients should have lipid profiles checked at baseline and, if normal, every 4-6 months after starting ART. If results are abnormal, recheck every 3-4 months while on regimen.

### WHEN TO CHANGE THERAPY

Treatment can be changed for two main reasons: treatment failure or drug intolerance.

#### Treatment failure
Treatment failure can be defined clinically, immunologically, and/or virologically.

#### Clinical failure
Clinical progression can be defined as the occurrence or recurrence of HIV-related events (opportunistic infection or malignancy) after at least 3 months on ART and excluding immune reconstitution syndromes.

#### Immunologic failure
Mean increases in CD4 cell counts in treatment-naïve patients with initial antiretroviral regimens are approximately 150 cells/mm$^3$ over the first year.

Immunologic failure is characterized by failure to increase the CD4 count by 25-50 cells/mm$^3$ above the baseline count over the first 6 to 12 months of therapy, or a decrease to below the baseline CD4 count on therapy.

#### Virologic failure
The expectation for a naïve patient on ART is a 10-fold reduction (1log$_{10}$) at 1-4 weeks after starting treatment, a viral load < 400 c/mL after 16-24 weeks, and a viral load < 50 c/mL (i.e., viral load undetectable) after 48 weeks.
Virologic failure is defined as repeated HIV RNA > 400c/mL after 24 weeks or > 50 c/mL by 48 weeks, or repeated detection of HIV RNA after virologic suppression.

There are two causes for virologic failure:
- The HIV strain is resistant to one or more of the drugs in the regimen
- The drugs fail to reach the virus, which may be due to lack of adherence, drug interactions, or drug malabsorption. The most common cause is lack of adherence.

Isolated episodes of intermittent viremia, or blips (transient plasma HIV RNA levels of 50 – 200 copies/mL), do not predict subsequent virological failure.

### Box 7.3  |  Viral load reduction with ART in a patient with a starting viral load of 100,000 copies/mL (= 5 log_{10})

<table>
<thead>
<tr>
<th>log_{10} change</th>
<th>Percent decrease</th>
<th>Fold reduction</th>
<th>Resultant copy number</th>
<th>Resultant log_{10}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>50.0</td>
<td>2</td>
<td>50,000</td>
<td>4.7</td>
</tr>
<tr>
<td>0.4</td>
<td>60.0</td>
<td>2.5</td>
<td>40,000</td>
<td>4.6</td>
</tr>
<tr>
<td>0.5</td>
<td>66.0</td>
<td>3</td>
<td>33,000</td>
<td>4.5</td>
</tr>
<tr>
<td>0.6</td>
<td>75.0</td>
<td>4</td>
<td>25,000</td>
<td>4.4</td>
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<td>0.7</td>
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<td>1.0</td>
<td>90.0</td>
<td>10</td>
<td>10,000</td>
<td>4.0</td>
</tr>
<tr>
<td>1.5</td>
<td>96.8</td>
<td>32</td>
<td>3,200</td>
<td>3.5</td>
</tr>
<tr>
<td>2.0</td>
<td>99.0</td>
<td>100</td>
<td>1,000</td>
<td>3.0</td>
</tr>
<tr>
<td>2.5</td>
<td>99.7</td>
<td>316</td>
<td>300</td>
<td>2.5</td>
</tr>
<tr>
<td>3.0</td>
<td>99.9</td>
<td>1000</td>
<td>100</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Relation across virologic failure, immunologic failure, and clinical progression**

Virologic failure, immunologic failure, and clinical progression have distinct time courses and may occur independently or simultaneously. In general, virologic failure occurs first, followed by immunologic failure, and finally by clinical failure. These events may be separated by months or years.

**Drug intolerance**

Side effects of ARVs are common and highly variable in severity and implications.

Nausea is rather common and may become an impediment to adherence. Other side effects can be life threatening such as pancreatitis, hypersensitivity, Steven-Johnson syndrome, lactic acidosis, and hepatic necrosis (Table 7.6).
If the side effects preclude adherence or lead to serious medical consequences, different drugs must be substituted.

<table>
<thead>
<tr>
<th>Table 7.6</th>
<th>Adverse reactions associated with ARVs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N(t)RTIS</strong></td>
<td><strong>Class-specific adverse effects:</strong></td>
</tr>
<tr>
<td>ABC</td>
<td>Lactic acidosis with hepatic steatosis due to toxicity of N(t)RTIs on cellular mitochondria (rare)</td>
</tr>
<tr>
<td>ddI</td>
<td>Hypersensitivity reaction</td>
</tr>
<tr>
<td>FTC</td>
<td>Pancreatitits; Peripheral neuropathy; Nausea; Diarrhea</td>
</tr>
<tr>
<td>3TC</td>
<td>Minimal toxicity</td>
</tr>
<tr>
<td>d4T</td>
<td>Rapidly progressive ascending neuromuscular weakness (rare)</td>
</tr>
<tr>
<td>TDF</td>
<td>Peripheral neuropathy; Lipodystrophy; Pancreatitits; Hyperlipidemia</td>
</tr>
<tr>
<td>ddC</td>
<td>Asthenia; Headache; Diarrhea; Nausea; Vomiting; Nephrotoxicity</td>
</tr>
<tr>
<td>AZT</td>
<td>Bone marrow suppression (anemia, neutropenia); Gastrointestinal intolerance; Headache; Insomnia; Asthenia</td>
</tr>
</tbody>
</table>

| **NNRTIS** | **Class-specific adverse effects:** |
| DLV | Steven-Johnson syndrome (NVP ++); Rash; Hepatotoxicity (hepatitis or asymptomatic transaminase elevation) |
| EFV | Neuropsychiatric disturbances; Teratogenic |
| NVP | Hepatic necrosis (occurs with significantly higher frequency in female patients with CD4 counts > 250cells/mm³) |

| **PIs** | **Class-specific adverse effects:** |
| APV | Gastrointestinal intolerance: nausea, vomiting, diarrhea; Rash; Oral paresthesias |
| ATV | Hyperbilirubinemia; Prolonged PR interval |
| f-APV | Skin rash; Diarrhea; Nausea; Vomiting; Headache |
| IDV | Nephrolithiasis; Nausea; Hyperbilirubinemia |
| LPV/r | Nausea; Vomiting; Diarrhea; Asthenia |
| NFV | Diarrhea |
| RTV | Nausea; Vomiting; Diarrhea; Paresthesias; Asthenia; Taste perversion |
| SQV-HGC & SQV-SGC | Nausea; Diarrhea; Headache |

| **FIs** | **Class-specific adverse effects:** |
| ENF | Local injection site reactions (pain, erythema, induration); Hypersensibility reaction; Increase rate of bacterial pneumonia |

*Potentially life-threatening adverse effect*
SECOND LINE REGIMEN

In the setting of treatment failure:

- The entire regimen should be changed from a first to a second line combination regimen, with at least one drug from one new class. A new NRTIs backbone should be selected and the NNRTI substituted for a PI or vice versa (Table 7.7).
- In developed countries, HIV drug resistance testing should be performed to assist in selecting active drugs.

<table>
<thead>
<tr>
<th>NNRTI-based first-line regimen</th>
<th>Second-line regimen</th>
<th>Second-line N(t)RTIs backbone</th>
<th>+</th>
<th>One PI/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>(AZT or d4T) + (3TC or FTC) + NVP or EVF</td>
<td>ABC + (ddl or TDF) or TDF + 3TC* ± AZT</td>
<td>ATV/r or FPV/r or IDV/r or LPV/r or SQV/r</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF + (3TC or FTC) + NVP or EVF</td>
<td>ABC + ddl or ddl + 3TC* ± AZT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC + (3TC or FTC) + NVP or EVF</td>
<td>(ddl or TDF) + 3TC* ± AZT</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 3TC can be considered to be maintained in second-line regimen to reduce the viral fitness

Patients who failed on triple N(t)RTI regimens as sole antiretroviral combination should be offered a second-line regimen including NVP or EFV ± ddl + one PI/r.

**DRUG INTERACTIONS**

Drug interactions have become an increasingly complex challenge for clinicians treating HIV infected patients (Table 7.8).

In addition to the use of at least three ARV medications to treat HIV infection, patients are often receiving therapy for comorbid conditions and for prophylaxis of opportunistic infections.

Potential HIV drug-drug interactions should be taken into consideration when selecting an antiretroviral treatment. Moreover, review of drug interaction potential should be undertaken when any new drug is added to an existing ARV combination.
Table 7.8  |  Common mechanisms of drug interactions

<table>
<thead>
<tr>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interactions altering pharmacokinetics</strong></td>
<td></td>
</tr>
<tr>
<td>Absorption</td>
<td>Concurrent therapy (or food) results in an increase or reduction in drug absorption, thereby increasing or decreasing bioavailability</td>
</tr>
<tr>
<td>Indinavir taken with magnesium/ aluminum-containing antacids can reduce indinavir absorption</td>
<td></td>
</tr>
<tr>
<td>Distribution</td>
<td>Concurrent therapy leads to protein-binding displacement, altering the activity of either drug</td>
</tr>
<tr>
<td>Cotrimoxazole can displace warfarin from its protein-binding sites, increasing International Normalised Ratio (INR)</td>
<td></td>
</tr>
<tr>
<td>Metabolism</td>
<td>Therapy induces or inhibits CYP450 enzymes, thereby increasing or decreasing drug concentration</td>
</tr>
<tr>
<td>Rifampin can induce CYP450 3A4 and cause marked reductions in PI concentrations</td>
<td></td>
</tr>
<tr>
<td>Excretion</td>
<td>Concurrent therapy results in enhanced or decreased renal excretion of drug</td>
</tr>
<tr>
<td>Probencid taken with zalcitabine can reduce renal elimination of zalcitabine</td>
<td></td>
</tr>
<tr>
<td><strong>Interactions affecting pharmacodynamics</strong></td>
<td></td>
</tr>
<tr>
<td>Additive response</td>
<td>Concurrent therapy results in additive drug effect</td>
</tr>
<tr>
<td>Additive bone marrow suppression with concurrent use of zidovudine and ganciclovir</td>
<td></td>
</tr>
<tr>
<td>Synergistic response</td>
<td>Concurrent therapy results in an exponential increase in drug effect</td>
</tr>
<tr>
<td>Concurrent use of indinavir, lamivudine, and zidovudine results in their combined effect being greater than the sum of their individual effects</td>
<td></td>
</tr>
<tr>
<td>Antagonistic response</td>
<td>Concurrent therapy leads to reduced drug effect for both drugs</td>
</tr>
<tr>
<td>Concurrent use of zidovudine and stavudine reduces antiviral effect</td>
<td></td>
</tr>
</tbody>
</table>

Box 7.4  |  Cytochrome P450 enzyme and ritonavir-boosted PIs

The cytochrome P450 enzyme system is responsible for oxidative metabolism of many drugs. The enzyme responsible for the majority of drug metabolism, including NNRTIs and PIs, is the CYP450 isoenzyme. Drug therapy interacts with CYP450 enzymes in one of three ways: 1) through inhibition, 2) through induction, or 3) by acting as a substrate. Some medications may interact in more than one way and act as an inhibitor and inducer of different CYP450 enzymes.
ADHERENCE

Adherence may be defined as the extent to which a patient takes a medication in the way intended by a health care provider.

Nonadherence to medication, in general, is very common. Typical adherence rates for medications prescribed over long periods of time are approximately 50-75%.

Nonadherence to ART, likewise, is common in all groups of treated individuals.

The initial goal of ART is full and durable viral suppression. Full viral suppression allows for maximal reconstitution or maintenance of immune function and minimizes the emergence of drug-resistant HIV.
resistant virus selected by ongoing replication in the presence of antiretroviral drugs.

For most patients, near-perfect (>95%) adherence is necessary to achieve full and durable viral suppression. In practice, this degree of adherence requires a patient on a twice-daily regimen not to miss or substantially delay more than 3 doses of antiretroviral medications per month.

This degree of adherence requested for patients on ARVs is far greater than that commonly associated with other chronic diseases and is quite difficult for most patients to maintain over the course of a lifelong illness.

The most important intervention to promote adherence is making sure patients start medication only when they are ready and understand that the first HAART regimen has the best chance for long-term success!

**Box 7.5 | Factors that promote adherence**

**Patient-related factors**
- Absence of mental illness (depression, other psychiatric morbidity)
- Absence of drug or alcohol abuse
- Perceived ability to take medication as instructed
- Older age
- Higher literacy
- Strong social support network
- Adherence with medical appointments
- Stable housing
- Adherence with previous therapies
- Positive attitude toward efficacy of medication

**Medication-related factors**
- Fewer medications, fewer doses, and fewer pills
- Once a day regimen
- Fewer side effects
- Lack of dietary restrictions
- Shorter time on therapy
- Good “fit” of regimen into patient’s daily routine

**Health system-related factors**
- Trusting relationship with health care provider
- Patient education: patients understand their regimen, including food restrictions, patients understand the association of adherence and resistance
- Convenient access to primary medical care and medication
References

- A guide to primary care of people with HIV/AIDS. US DHHS. 2004
- Antiretroviral therapy for HIV infection in adults and adolescents in resource limited setting: Towards universal access. Recommendations for public health approach. WHO. 2006 Revision
- Antiretroviral therapy. NYSDH. Dec 2004
- Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. DHHS. May 2006
- Promoting adherence to antiretroviral therapy. AIDS Institute NYSDH
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- Untangling the web of prices reduction: A pricing guide for the purchase of ARVs for developing countries. MSF. July 2006
HIV infection in paediatrics

The best way to address paediatric HIV infection is to significantly reduce the proportion of children acquiring infection.

In developing countries where 95% of new infections in children are caused through mother-to-child transmission (MTCT), only 10% of pregnant HIV infected women have access to services to prevent MTCT.

Although the diagnosis of HIV infection in infants < 18 months is difficult and the treatment of paediatric AIDS complex, high mortality and morbidity among perinataly infected children should prompt early identification and enrolment in care of these children.

NATURAL HISTORY OF PAEDIATRIC HIV INFECTION

There are critical differences between the disease progression in children and in adults. Stemming largely from the lower efficiency of a child’s immature immune system, these differences result in much more rapid disease progression and a much shorter duration for each stage.

The most common symptoms of HIV/AIDS during infancy include poor growth, recurrent infections (particularly pneumonia), and severe diarrhoea.

Although disease manifestations vary considerably from child to child, most babies develop HIV-related symptoms by 12 months of age, and half of children infected during pregnancy or labour/delivery will die by their second birthday.
DIAGNOSIS OF HIV INFECTION IN INFANTS

While the diagnosis of HIV in adults is relatively straightforward, establishing the HIV infection status of an infant or young child <18 months is more complex.

Specialized virologic tests, not available in all resource-limited settings, are required to determine whether or not a baby has been infected with HIV.

**HIV antibody testing**

The HIV antibody is passively transmitted across the placenta during pregnancy, and all babies born to HIV-infected women will test HIV antibody positive at birth. However, the virus itself is not always transmitted and only some babies become infected.

At a minimum, maternal antibody is present in the baby’s blood for the first six months of life. After six months, levels of maternal HIV antibody fade, and babies who are not infected test negative for the HIV antibody by 18 months of life.

In contrast, babies who are infected with HIV produce their own HIV antibody, and their antibody tests remain positive for life. Any child 18 months or older with a positive HIV antibody test is infected with HIV.

---

**Box 8.1 | Predictors of disease progression**

**Predictors of disease progression in infants include:**
- Infecting viral dose (maternal viral load)
- Any infection before 4 months of life
- Infant peak viremia
- Low CD4 count and percent
- Rapid decline in CD4 count
- Clinical AIDS

**Maternal predictors of infant disease progression include:**
- Maternal viral load at time of delivery
- Maternal CD4 cell count (<200/mm³)
- Rapidly progressive maternal disease
- Maternal death, which is associated with a 2- to 5-fold increase in infant mortality when compared to infants born to mothers who survive
HIV antibody testing can be used to exclude HIV infection as long as the child ceased breast feeding at least three months prior to the test.

A child who has not breastfed for the past three months and whose HIV antibody test is negative is not infected with HIV.

While it would, therefore, be theoretically possible to defer paediatric diagnosis until 18 months of age and use the standard HIV antibody test, this approach is clinically unwise. HIV disease may progress very rapidly in infants — mortality at two years approaches 50 percent if HIV is not treated. Early identification and treatment of paediatric HIV disease can have a dramatic impact on outcome, and should be a priority whenever possible.

In summary:

- A positive HIV antibody test in a child of 18 months or older means the child is infected with HIV.
- A positive HIV antibody test in a child of less than 18 months does not help to distinguish the HIV-infected child from the HIV-uninfected child.
- A negative HIV antibody test three or more months after the cessation of breast feeding (or in a child who has never breast-fed) means that the child is not infected with HIV.
- A negative HIV antibody test in a child who is still breast feeding, or who recently stopped breast feeding is insufficient to exclude HIV infection. The test must be repeated at least three months after breast feeding ceases.

Virologic testing

In contrast to HIV antibody tests, specialized virologic tests can differentiate the infected baby from the uninfected baby during the first months of life.

The sensitivity and specificity of virologic tests is generally excellent but false positive or negative tests can occur.

All positive tests should be confirmed on a repeat specimen. Low viral loads (<10,000 copies/mL) are particularly likely to be false positives, as infants usually have very high levels.

Identically, two virologic tests after one month of age are required to confirm that a child is not HIV-infected.
WHO case definition for HIV infection in children
Refer to Chapter 6.

WHO STAGING SYSTEM FOR HIV INFECTION IN INFANTS AND CHILDREN

Clinical staging system
The WHO clinical staging system for children with confirmed HIV infection (Table 8.1) is now harmonized with the classification of disease for adults and adolescents.

Table 8.1 WHO clinical staging of HIV/AIDS for children with confirmed HIV infection. One condition is sufficient to define the stage

<table>
<thead>
<tr>
<th>Clinical stage I</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic</td>
</tr>
<tr>
<td>• Persistent generalized lymphadenopathy</td>
</tr>
</tbody>
</table>
### Clinical stage II

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Fungal nail infections
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis or tonsilitis)

### Clinical stage III

- Unexplained moderate malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
- Persistent oral candidiasis (after first 6-8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis or periodontitis
- Lymph node tuberculosis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (<8g/dL), and or neutropenia (<500/mm³) and or chronic thrombocytopenia (<50,000/mm³)

### Clinical stage IV (AIDS)

- 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, or meningitis but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Extrapulmonary tuberculosis
- Kaposi’s sarcoma
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after one month of life)
- HIV encephalopathy
Immunological staging system

Immunological staging for infants and children is very valuable to guide decision on initiation of ART, and wherever possible should be used in conjunction with clinical assessment. The immunological parameter can also be used to monitor responses to treatment.

The absolute CD4 count associated with a specific level of immune suppression tends to change with age, whereas the CD4 percentage related to immunological damages does not vary as much.

Therefore, the measurement of the CD4 percentage (= absolute number of CD4/mm³ times 100 divided by absolute number of lymphocytes/mm³) is recommended for younger children (<5 years).

Table 8.2 | WHO immunology classifications for paediatric HIV infection

<table>
<thead>
<tr>
<th>Immune Categories</th>
<th>&lt; 12 months</th>
<th>1 – 3 years</th>
<th>3 – 5 years</th>
<th>&gt; 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No suppression</td>
<td>&gt; 35%</td>
<td>&gt; 30%</td>
<td>&gt; 25%</td>
<td>&gt; 500/mm³</td>
</tr>
<tr>
<td>3. Advanced suppression</td>
<td>25 – 30%</td>
<td>20 – 25%</td>
<td>15 – 20%</td>
<td>200 – 349/mm³</td>
</tr>
<tr>
<td>4. Severe suppression</td>
<td>&lt; 25%</td>
<td>&lt; 20%</td>
<td>&lt; 15%</td>
<td>&lt;200/mm³ or &lt;15%</td>
</tr>
</tbody>
</table>

WHO case definition of advanced HIV infection and AIDS in children with confirmed HIV infection

Definition of advanced HIV disease in children with confirmed HIV infection include clinical stage 3 or stage 4 (Table 8.1) or any clinical stage with advanced or severe immunological suppression (Table 8.2).
AIDS in children with confirmed HIV infection is defined as clinical diagnosis of any stage 4 condition or any clinical stage with severe immunological suppression.

**Presumptive diagnosis of severe HIV disease among HIV-seropositive HIV-exposed children aged under 18 months**

The presumptive diagnosis is designed for use where access to confirmatory diagnostic testing for HIV infection by means of virologic testing for infants and children aged under 18 months is not readily available.

It is not recommended for use by clinical care providers who are not trained in ART or experienced in HIV care.

### Box 8.3 | A presumptive diagnosis of severe HIV disease should be made if:

An infant is HIV-antibody positive and diagnosis of any AIDS-indicator condition(s) can be made or the infant is symptomatic with two or more of the following:

- Oral thrush
- Severe pneumonia
- Severe sepsis.

Other factors that support the diagnosis of severe HIV disease in an HIV-seropositive infant include:

- CD4 < 20%
- Recent HIV-related maternal death or advanced HIV disease in the mother.

Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

---

**PREVENTION OF PNEUMOCYSTIS PNEUMONIA**

*Pneumocystis* pneumonia (PCP), caused by a fungus *Pneumocystis jerovici* (formerly *carinii*), is a major cause of severe pneumonia and death in HIV-infected infants. The incidence of PCP is highest during the first year of life and usually peaks at 3 to 6 months of age.

Co-trimoxazole is highly effective for the prophylaxis (and treatment) of *Pneumocystis* pneumonia. It also offers protection against other infections.
**ANTIRETROVIRAL THERAPY**

The basic virologic and immunologic principles for ART are similar in children and adults. The goals of treatment are to:
- Suppress HIV below the limits of detection or as low as possible for as long as possible
- Preserve or restore the body’s immune function
- Prolong life and improve the quality of life.

**When to start ART**

ART should never be initiated without preparation of the child and family for the complex task of long-term therapy. Similarly, ART should never be prescribed without assuring a secure drug supply, as treatment interruption can lead to therapeutic failure.

---

**Box 8.4 | WHO recommendations for co-trimoxazole prophylaxis in HIV-exposed/infected children**

| HIV-exposed children (child born to an HIV-infected mother or child breastfeeding from an HIV-infected mother) | Prophylaxis is universally indicated regardless of CD4 percentage from 4 - 6 weeks of age |
| HIV-infected children (positive HIV antibody test in child > 18 months, positive virologic test in child < 18 months) | < 12 months: prophylaxis regardless of CD4 percentage or clinical status |
| | 12 months to 5 years: WHO clinical stages 2, 3, 4 regardless of CD4 percentage or any WHO stage with CD4 <25% |
| | > 5 years: Prophylaxis as recommended for adults |

**Dosage:** 6–8mg/kg once daily

**Discontinuation:**
- In HIV-exposed children, discontinue only if HIV infection has been definitely ruled out and the mother is no longer breastfeeding
- In HIV-infected children, maintain on co-trimoxazole prophylaxis until five years irrespective of clinical and immune response. For children older than five years, follow same recommendations as for adults.
Both NNRTI- and PI-based regimens are recommended regimens for initial therapy of children. Each class-based regimen has advantages and disadvantages.

PI-based regimens, while highly potent, have a high pill burden and palatability challenges in children. They are expensive and rarely affordable in resource-constrained countries.

NNRTI-based regimens are palatable and effective, but a low genetic barrier to resistance leads to rapid development of drug resistance mutations when therapy does not fully suppress viral replication, and there is cross-resistance among members of this drug class.
Although studies are in progress, it is still unknown whether ARV choices should be modified for infants who have been exposed to ARVs used for prevention of MTCT.

**When to change therapy**

The principles on which to base changes in therapy for children are similar to those applied to adults, and management of drug toxicity is the same – when toxicity is related to an identifiable drug in the regimen, the offending drug can be replaced with another drug that does not have the same side effects.

> Before changing therapy because of treatment failure, adherence to therapy should be assessed to determine what role it played as a potential cause of treatment failure.

**Box 8.5 | Conditions indicating that a change to second-line therapy is warranted**

**Clinical conditions**

- A lack of growth among children who show an initial response to treatment or decline in growth among children who show an initial growth response to therapy
- A loss of neurodevelopmental milestones or the development of encephalopathy
- The occurrence of new opportunistic infection or malignancy (to be distinguished from immune reconstitution syndrome)
- The recurrence of infections, such as oral candidiasis that is refractory to treatment.

Before an ARV regimen is thought to be failing based on clinical criteria, the child should have received the regimen for at least 24 weeks.

**Immunological conditions**

- Return in CD4 cell percentage (or in children >6 years of age, absolute CD4 cell count) to pre-therapy baseline or below, in the absence of other concurrent infections.
Box 8.5 Conditions indicating that a change to second-line therapy is warranted... contd.

- ≥ 50% fall from peak level on therapy of CD4 cell percentage (or for children > 6 years of age, absolute CD4 cell count), in absence of other concurrent infection.

CD4 % should not be measured during a concurrent infection but 1 month or more post-resolution. If there is a modest decline in CD4 % (<5%) and if there is no failure to thrive, do not change medication, but maintain close monitoring.

Despite a good clinical and immunological response, viral resistance will occur in the absence of complete viral suppression. Many experts will delay changing therapy unless there are signs of clinical or immunological progression.

Virologic conditions
- Persistently elevated viral load in the absence of poor adherence to medication
- Progressive increase in viral load after the beginning of treatment (changes greater than 5-fold [0.7 log] in children less than 2 years of age, and of at least 3-fold [0.5 log] in children 2 years of age or older, after tests confirmed in a second determination, will reflect a clinically and biologically relevant change)
- <1.0 log reduction in relation to the initial level after 24 weeks
- Repeated viral load detection in children with earlier undetectable levels.

The viral load should not be measured during a concurrent infection but 1 month or more post-resolution.

Second-line regimen
Ideally, in the setting of treatment failure, the selection of second-line therapy should be guided by resistance testing.

As for adults, second-line regimen (Table 8.6) should include two new nucleoside as backbone plus one drug from one new class (PI substituted for NNRTI or vice versa).

### Table 8.6 | WHO recommended second-line regimen in resource-limited settings.

<table>
<thead>
<tr>
<th>For failure on first-line regimen</th>
<th>Change to</th>
<th>One PI component</th>
</tr>
</thead>
<tbody>
<tr>
<td>(AZT or d4T) + 3TC + (NVP or EFV)</td>
<td>ddi + ABC</td>
<td>+ LPV/r or NFV or SQV/r*</td>
</tr>
<tr>
<td>ABC + 3TC + (NVP or EFV)</td>
<td>ddi + AZT</td>
<td>+</td>
</tr>
<tr>
<td>For failure on triple NRTI regimens such as (AZT or d4T) + 3TC + ABC, change to</td>
<td>ddi + (NVP or EFV) + one PI component.</td>
<td></td>
</tr>
</tbody>
</table>

* SQV/r not recommended in children < 25 kg
Adherence

Adherence problems occur frequently in children.

Factors that act as barriers to adherence, i.e. regimen-related, child/family-related and/or healthcare provider-related factors, provide targets for interventions.

The lack of liquid and/or paediatric formulations, poor palatability, high pill burden, frequent dosing requirements, dietary restrictions and side effects may hamper the regular intake of required medications.

Furthermore, successful treatment of a child requires the commitment and involvement of a responsible adult caretaker.

Efforts to support and maximize adherence should begin prior to the initiation of treatment. The development of an adherence plan and education of the patients and their caregivers are important first steps.

In addition, continuous adherence assessment and support are vital components of treatment success.

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• Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: Towards universal access. Recommendations for a public health approach. WHO. 2006
• Handbook on paediatric AIDS in Africa. ANECCA. 2004
• Guidelines for the use of antiretroviral agents in pediatric HIV infections. HRSA & INH. 2005
• Managing complications of HIV infection in HIV-infected children on antiretroviral therapy. HRSA & INH. 2005
• Pediatric antiretroviral drug information. HRSA & INH. 2005
• The pediatric clinical manual. ICAP. 2004
Opportunistic diseases (ODs) occur as a result of HIV-related immunodeficiency and include both opportunistic infections (OIs) and malignancies. They are called “opportunistic” because they take advantage of the opportunity offered by a weakened immune system.

The worldwide distribution of ODs is highly varied, some can be found everywhere (e.g. tuberculosis, herpes, etc.), others are restricted to specific geographic areas depending on prevailing endemic infections (e.g. histoplasmosis in the USA or leishmaniasis in Africa and South America, etc.).

### MAIN OPPORTUNISTIC DISEASES AND THEIR AGENTS

**Table 9.1 | Opportunistic infections and malignancies**

<table>
<thead>
<tr>
<th>Category</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial diseases</td>
<td>Tuberculosis (<em>Mycobacterium tuberculosis</em>), <em>Mycobacterium avium</em> complex disease (MAC), bacterial pneumonia, bacterial enteric disease (<em>Salmonella, Campylobacter, Shigella</em>), bartonellosis</td>
</tr>
<tr>
<td>Protozoal diseases</td>
<td><em>Pneumocystis jerovici (carinii)</em> pneumonia (PCP)*, cerebral toxoplasmosis, cryptosporidiosis, leishmaniasis, isosporiasis</td>
</tr>
<tr>
<td>Fungal diseases</td>
<td>Candidiasis, cryptococcal meningitis, histoplasmosis, coccidioidomycosis, aspergillosis</td>
</tr>
<tr>
<td>Viral diseases</td>
<td>Cytomegalovirus (CMV), herpes simplex virus, varicella-zoster virus, human papillomavirus**</td>
</tr>
<tr>
<td>HIV-associated malignancies</td>
<td>Kaposi sarcoma (human herpes virus-8), lymphoma, squamous cell carcinoma</td>
</tr>
</tbody>
</table>

* *Pneumocystis jiroveci* is an ubiquitous organism classified as a fungus but that shares biologic characteristics with protozoa. The taxonomy of the organism has been changed; *Pneumocystis carinii* now refers only to the pneumocystis that infects rodents, and *Pneumocystis jiroveci* refers to the distinct species that infects humans.

** Human papillomavirus infection of the ano-genital tract results in a spectrum of disease, ranging from warts and condyloma acuminata to squamous cell cancer (cervix and rectum).
EPIDEMIOLOGY

OIs continue to cause morbidity and mortality in HIV+ patients throughout the world:
- In developed countries, potent combination antiretroviral therapy (ART) has dramatically declined the incidence of OIs for patients with access to ARV (Figure 9.1).

Figure 9.1. Incidence of OIs after the introduction of ARVs

- The situation is very different in developing countries where the majority of people do not yet have an easy access to ARV and will develop OIs as a complication of HIV. Furthermore, effective preventive and curative intervention against OIs (and malignancies) requires not only the appropriate drugs for a given medical condition, but also the necessary infrastructure and trained staff able to diagnose the condition, monitor the intervention, and counsel the patient.

- In both developed and developing countries, there will always be patients who do not have a sustained response to antiretroviral agents for multiple reasons, including poor adherence, drug toxicities, drug interactions, or initial acquisition of a drug-resistant strain of HIV. Therefore, OIs will continue to cause substantial morbidity and mortality in patients with HIV infection.

RISK FACTORS

Opportunistic infections
OIs occur primarily in HIV-infected individuals who are not receiving either OI prophylaxis or ART.

The principal risk of developing a specific OI is determined by the degree of immunosuppression, as measured by the CD4 cell count. The CD4 threshold of risk differs for each specific OI (Figure 9.2).
It is not common for an OI to occur in HIV-infected individuals with CD4 cell counts above its threshold (Table 9.2). For patients with the same CD4 cell count, those with high viral loads (plasma HIV RNA levels >100,000 copies/mL) have a greater risk for developing an OI than those with a low viral load. Other factors that contribute to increased risk for OIs include previous exposure to or infection with a specific pathogen, prior occurrence of an OI and environmental exposure in the absence of a host response.

**Table 9.2 | Examples of risk factors associated with development of major OIs in HIV-infected individuals**

<table>
<thead>
<tr>
<th>OI</th>
<th>CD4 count risk threshold (cells/mm³)</th>
<th>Other risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis jiroveci</em> pneumonia (PCP)</td>
<td>&lt; 200</td>
<td>Prior PCP, fever of unknown origin, presence of oral candidiasis</td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td>Any</td>
<td>Positive tuberculin test, exposure to an infectious contact</td>
</tr>
<tr>
<td>Cytomegalovirus disease</td>
<td>&lt; 50</td>
<td>Presence of IgG antibody to CMV, prior OD, high viral load (&gt; 10⁵ copies/mL)</td>
</tr>
<tr>
<td>Candida esophagitis</td>
<td>&lt; 100</td>
<td>Prior candida colonization, high viral load load (&gt; 10⁵ copies/mL)</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>&lt; 50-100</td>
<td>Environmental exposure</td>
</tr>
</tbody>
</table>
**Malignancies associated with HIV infection**

The most common are Kaposi sarcoma (KS) and lymphomas. There is also an increase in the frequency of cervix and anus cancer.

In general, these 4 forms of malignancies correlate with immunosuppression, meaning the frequency increases with low CD4 cell counts, but the correlation is less strong compared to the OIs.

<table>
<thead>
<tr>
<th>Box 9.1</th>
<th>Rate of malignancies in HIV infection compared to the general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• KS is approximately 20,000-fold higher with HIV infection</td>
<td></td>
</tr>
<tr>
<td>• Non-Hodgkin Lymphoma is 200- to 600-fold more frequent with HIV infection</td>
<td></td>
</tr>
<tr>
<td>• Anal cancer could be 100-fold higher with HIV infection</td>
<td></td>
</tr>
<tr>
<td>• Cervical cancer is around 5-fold higher</td>
<td></td>
</tr>
</tbody>
</table>

**PREVENTION MEASURES**

**Immunization**

HIV+ people should be get immunized against:

• Pneumococcus (*Streptococcus pneumoniae*)
• Influenza (depending on the country)
• Hepatitis A and B
• Diphtheria, tetanus and polio should be updated
• Rabies and plague vaccines can be given when indicated
• No data regarding new cholera vaccines
• Yellow fever vaccine should be given only in high risk areas and only if HIV is asymptomatic.

*No administration of live attenuated vaccines - BCG, varicella, live polio (OPV), live typhoid (TY21a) - when CD4 count is below 200/mm³.*

**Prevention of tuberculosis**

With a Mantoux (2 UI) > 5 mm, HIV+ people should get isoniazid (INH) and vitamin B6 for 6 to 9 months.

**Alternatives**

Rifampicine with INH for a total of 4 months is a possibility, but it is more expensive that INH alone for 9 months.
Short courses of chemo-preventative therapy using other drugs have been recommended to help overcome poor adherence. Unfortunately, rifampicin and pyrazinamide given three times a week for 2 months has been associated with severe and fatal hepatic reactions in few non-HIV patients. Although this complication has not been described in HIV positive patients, it is better not to use it.

**Primary prophylaxis with co-trimoxazole**

Co-trimoxazole (sulfamethoxazole-trimethoprim), a broad-spectrum antimicrobial available at low cost in most places including resource-limited settings, has proved to be effective as prophylaxis in preventing *Pneumocystis jiroveci* pneumonia (PCP) and toxoplasmosis in HIV-infected individuals (Table 9.3).

In addition, the benefits of co-trimoxazole prophylaxis include the prevention of bacterial infections (*Pneumococcus*, non-typhoidal *Salmonella*), diarrhoeal diseases (*Isospora*, *Cyclospora*) and malaria.

**Starting co-trimoxazole prophylaxis.**

<table>
<thead>
<tr>
<th>Table 9.3</th>
<th><strong>WHO recommendations for initiating co-trimoxazole prophylaxis in among adults and adolescents living with HIV</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Based on WHO clinical staging criteria alone (when CD4 count is not available)</strong></td>
<td><strong>Based on WHO clinical staging and CD4 cell count criteria</strong>*</td>
</tr>
</tbody>
</table>
| WHO clinical stage 2,3 or 4 | Any WHO clinical stage and CD4 < 350 cells/mm$^3$ **
| OR | WHO clinical stage 3 or 4 irrespective of CD4 level |

Universal option: countries may choose to adopt universal co-trimoxazole for everyone living with HIV and any CD4 count or clinical stage. This strategy may be considered in settings with high prevalence of HIV and limited health infrastructure.

* Expanded access to CD4 testing is encouraged to guide the initiation of ART and to monitor the progress of ART.

** Countries may choose to adopt a CD4 threshold of < 200 cells/mm$^3$.

**Recommended dosage of co-trimoxazole for prophylaxis**

The recommended dosage is 960mg/day (2 tabs/day, each containing sulfamethoxazole 400 mg, trimethoprim 80 mg), either in one dose once daily or twice daily as a divided dose.

It is uncommon for an OI to occur in HIV-infected individuals with CD4 cell counts above its threshold.
Discontinuation of co-trimoxazole prophylaxis

- **Adverse effects**

Co-trimoxazole prophylaxis should be discontinued in case of severe adverse effects such as Stevens-Johnson syndrome, renal or hepatic insufficiency and severe haematological toxicity.

Given the importance of co-trimoxazole and the lack of an equally effective and widely available alternative in resource-constraint settings, desensitization to co-trimoxazole may allow some patients with non-life-threatening adverse reactions to take co-trimoxazole for continuing prophylaxis.

Dapsone, preferably associated with pyrimethamine and leucovirin, is recommended for patients experiencing severe adverse reaction with co-trimoxazole. It provides protection against PCP and toxoplasmosis. Dapsone itself may cause serious side effects, including methemoglobinemia and hemolysis.

- **Discontinuation of co-trimoxazole prophylaxis in a context where the immune system is recovering under ART**

In adults, several studies have shown safety of co-trimoxazole discontinuation where the major objective of co-trimoxazole use is to prevent PCP and toxoplasmosis. Co-trimoxazole prophylaxis can be discontinued in those:

- With CD4 cell count above the threshold for starting co-trimoxazole on at least 2 occasions, 3 months apart, and
- Have been on ART, for at least one year, have evidence of good adherence, and
- Have had six months or more with no WHO stage 2, 3 or 4 events.

However, there is insufficient data at present to issue recommendations on discontinuing co-trimoxazole following immune system recovery on ART in resource-limited settings (CD4 not available) and in countries where bacterial infections and malaria are common HIV-related problems.

**INITIATION OF ART IN THE SETTING OF AN ACUTE OPPORTUNISTIC INFECTION**

The benefits of ART in the setting of an acute OI include the improvement in immune function that would potentially contribute to faster resolution of the OI. The beneficial effect of initiating ART during an acute OI has been best demonstrated for OIs for which limited or no effective
Therapies are available, e.g. cryptosporidiosis. Another benefit of immediate initiation of potent ART during an acute OI is the reduction in risk for a second OI.

Yet, there are also arguments against the immediate initiation of ART concurrent with the diagnosis of an OI that include:

- Drug toxicities including additive toxicities making the distinction between toxicities caused by antiretrovirals and those related to drugs used to manage OIs difficult.
- Potential for drug interactions between OI therapies and ART.
- Potential for inflammatory immune reconstitution syndromes.

However, the use of well known and well tolerated ART regimens decreases the argument to delay therapy for reasons of complexity, although the risk of overlapping toxicities (OI treatment and ART) and drug interactions still exists.

**Immune reconstitution inflammatory syndrome (IRIS)**

The introduction of HAART allows for the reappearance of immune effector cells that will provide protection against opportunistic pathogens. However, experience during the past several years, has disclosed the emergence, in a small proportion of cases, of a unique set of complications. Soon after treatment is begun, some patients experience clinical deterioration due to the restoration of their capacity to mount an inflammatory immune response against both infectious and non-infectious antigens. This phenomenon has been named immune reconstitution inflammatory syndrome (IRIS); other labels such as immune reconstitution syndrome (IRS) and immune restoration disease (IRD), have also been used. IRIS has been described for a wide variety of infectious pathogens (mycobacterial infections, PCP, toxoplasmosis, hepatitis B and hepatitis C viruses, cytomegalovirus infection, varicella-zoster virus infection, etc.). The largest number of published reports of IRIS is among patients with *Mycobacterium avium* complex and *Mycobacterium tuberculosis*.

IRIS can be defined as a paradoxical deterioration in clinical status attributable to the recovery of the immune system during HAART. Recognition of this entity is crucial, for successful treatment relies on alleviation of the patient’s symptoms without compromising antiretroviral or antimicrobial therapy.

The manifestations of this syndrome are diverse and depend on the particular infectious agent involved. The majority of reactions occur within few weeks after initiation of ART (in case of TB, IRIS can occur up to several months after the initiation of TB therapy or ART).
Autoimmune diseases that occur following institution of HAART may also be considered as part of the same process.

Treatment with non-steroidal anti-inflammatory agents or corticosteroids might alleviate the inflammatory reaction, but more clinical trials are needed.

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- Clinical spectrum of HIV-associated illnesses in Zimbabwe. ICRC HIV Seminar. 2005
- Guidelines for the prevention of opportunistic infections in persons infected with HIV. USPHS. 2001
- HIV-related opportunistic diseases. UNAIDS. 1998-1999
- Management of opportunistic diseases. CDC MMWR. 2006
- The immune reconstitution inflammatory syndrome. AIDS Rev. 2003
- Treating opportunistic infections among infected adults and adolescents CDC. MMWR. 2004
Tuberculosis

Untreated HIV infection leads to progressive immunodeficiency and increased susceptibility to infections, including tuberculosis (TB).

HIV is driving the TB epidemic in many countries, especially in sub-Saharan Africa and, increasingly, in Asia and South America.

TB in populations with high HIV prevalence is a leading cause of morbidity and mortality. TB programmes and HIV/AIDS programmes therefore share mutual concerns.

Prevention of HIV should be a priority for TB control; TB care and prevention should be priority concerns of HIV/AIDS programmes. New approach to TB control in populations with high HIV prevalence requires collaboration between these programmes.

EPIDEMIOLOGY OF HIV ASSOCIATED TUBERCULOSIS

TB and HIV are fuelling each other and represent an explosive mixture.

HIV

- HIV progressively destroys the immune system. The immune suppressed are more vulnerable to *Mycobacterium tuberculosis*.
- Up to 50% of people with HIV develop TB (sub-Saharan Africa).

Tuberculosis

- TB may increase the replication of HIV, thus the progression towards full-blown AIDS.
- When infected by TB, the immune suppressed may be more infectious.
- HIV seroprevalence rate among TB patients has risen from 35% in 1993 to 70% in 1997 (sub-Saharan Africa).
So far, TB control has failed in countries with high incidence of HIV (Figure 10.1)

Figure 10.1. **TB Trends in African countries with high HIV prevalence**

![Graph showing TB trends in African countries](image)

### CLINICAL PICTURE OF HIV-RELATED TUBERCULOSIS

There is no straightforward way to clinically differentiate TB in AIDS and non AIDS patients. However, the clinical picture of tuberculosis in an HIV+ patient may be influenced by the degree of immunodeficiency:

- In early HIV infection with mild to moderate immunodeficiency, the features are characteristic of postprimary tuberculosis (due to reactivation or re-infection), i.e. resemble those seen in the pre-HIV era.
- More advanced immunodeficiency is associated with an increased frequency of pulmonary disease resembling primary pulmonary tuberculosis and of extra pulmonary (including disseminated) disease.

Tuberculosis is generally easier to diagnose in early HIV infection, when there is a higher proportion of patients with sputum smear-positive pulmonary tuberculosis. In later HIV infection, when there is a higher proportion of sputum smear-negative pulmonary and extra pulmonary tuberculosis, it is more difficult to confirm the diagnosis.

Yet, there are some characteristics which should facilitate the medical staff in diagnosing TB in HIV/AIDS patients (Table 10.1 & 10.2).
TREATMENT OF HIV ASSOCIATED TUBERCULOSIS

Public health aspects
Despite the considerable overlap between TB and HIV, most countries continue to address both diseases separately, hence a loss of effectiveness in both TB and HIV programmes. Real progress in controlling TB and HIV can only be made with a dual strategy targeting both epidemics.

It is only from 2001 onwards, that WHO and UNAIDS guidelines have more and more insisted on the importance of addressing tuberculosis and HIV at the same time, both being a priority. Tackling tuberculosis should include tackling HIV as the most potent force driving the tuberculosis epidemic; tackling HIV should include tackling tuberculosis as a leading killer of people living with HIV/AIDS (PLWHA). In high HIV prevalence populations, interventions against tuberculosis (intensified case-finding, tuberculosis curative — directly observed treatment - short course (DOTS) — and preventive treatment) and interventions against HIV (e.g. promoting the use of condoms, STI treatment, highly active antiretroviral treatment) have to be run in parallel.

<table>
<thead>
<tr>
<th>Clinical presentations overlap but .…..</th>
<th>HIV-</th>
<th>HVI+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary infection</td>
<td>Asymptomatic</td>
<td>Progression</td>
</tr>
<tr>
<td>Cavities</td>
<td>Frequent</td>
<td>Rare if CD4 low</td>
</tr>
<tr>
<td>Non specific infiltrates</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>Multiple adenopathie</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>Positive blood cultures</td>
<td>Very rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>CNS involvement</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>Tuberculin skin reaction</td>
<td>Positive</td>
<td>Neg. if CD4 low</td>
</tr>
</tbody>
</table>

| Frequencies of X-ray characteristics found in HIV negative and HIV positive patients |
|----------------------------------------|------|------|
| HIV- | HVI+ |
| Lymphadenopathia | 32% | 74% |
| Consolidation | 89% | 43% |
| Cavities | 55% | 8% |
| Miliary | Very low | 17% |
| Primary progressive TB | N/A | 36% |
| Normal chest X-ray | N/A | 10-15% |
TB & HIV: Joint action is required.

Treating TB and HIV together

In patients with HIV-related TB, the priority is to treat TB, especially smear-positive PTB (on account of the need to stop TB transmission). However, patients with HIV-related TB can have ART and anti-TB treatment at the same time, if managed carefully (Table 10.3). Thorough evaluation is necessary in judging when to start ART.

- Patients, tested HIV+, who are still in the clinical latency phase, and who have a smear-positive PTB, should be treated the same way as HIV neg. patients. The appearance of immunodeficiency (CD4 count and/or clinical stage) should be monitored and ART started when indicated.
- For a patient with smear-positive PTB as the first manifestation of HIV infection, who does not appear to be at high risk of dying, it may be safer to defer ART until the initial phase of TB treatment has been completed. This decreases the risk of immune reconstitution syndrome and avoids the risk of drug interaction (between rifampicin and a PIs). Furthermore treating TB only may result in a CD4+ cells increase up to 100 cells/mm³.
- Patients who develop TB while already on HAART can start TB treatment, but should be closely monitored.

<table>
<thead>
<tr>
<th>Box 10.1</th>
<th>Key principles of DOTS include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Effective standardized regimens,</td>
<td></td>
</tr>
<tr>
<td>• Provided in a supportive and patient-friendly way,</td>
<td></td>
</tr>
<tr>
<td>• Under direct observation of treatment to maximize adherence and reduce drug resistance.</td>
<td></td>
</tr>
</tbody>
</table>

**Table 10.3 | TB/HIV treatment: an emerging consensus**

In patients who are still in the latency phase, treat TB the same way as HIV neg. people

In patients who are not on HAART and where TB is the first manifestation of HIV infection, treat TB for 2 months, then start HAART

In patients who are already on HAART and tolerate it well, try adding TB treatment to HAART

Duration of treatment:

- 6 months for uncomplicated cases
- 9 months in case of cavities or when patients remain smear-positive after 2 months treatment.

- Eventually, there are situations associated with high mortality risks, for instance, cases of disseminated TB and/or CD4 count <200/mm³ and or WHO clinical stage III or IV. However
it is almost always possible to begin with TB treatment only, delaying the start of HAART by minimum of 2 weeks.

**Drug interactions**
Combined treatment of HIV and TB is complicated and requests at least 7 different drugs per day, with risks of overlapping toxicities and interactions.

Rifampicin stimulates the activity of the cytochrome P450 liver enzyme system, which metabolizes PIs and NNRTIs. This can lead to decreased blood levels of PIs and NNRTIs. PIs and NNRTIs can also enhance or inhibit this same enzyme system, and lead to altered blood levels of rifampicin. The potential drug interactions may result in ineffectiveness of ARV drugs, ineffective treatment of TB or an increased risk of drug toxicity.

When TB treatment includes a rifampicin-containing regimen, nevirapine should not be used, but be replaced by efavirenz at an increased dosage.

---

**Box 10.3 | Description of interactions between AIDS and TB drugs**

**Efavirenz**
- Drug rash could also be due to pyrazinamide.
- Liver toxicity could also be linked to isoniazid or rifampicin.

**Nevirapine**
- Rifampicin decreases the plasma levels of NVP.

**PIs**
- All PIs, but particularly ritonavir, increase rifampicin and rifabutin concentrations.
- Indinavir should not be used in combination with rifampicin, but with rifabutin.

**NRTIs (didanosine, zalcitabine and stavudine)**
- NRTIs may cause peripheral neuropathy. There is a potential added toxicity if isoniazid is added. Isoniazid also has a theoretical interaction with abacavir.

---

**Multidrug-resistant tuberculosis**
Treatment of multidrug-resistant tuberculosis, e.g. tuberculosis resistant to at least rifampicin and isoniazid, requires second-line drugs, such as ethionamide, cycloserine, kanamycin, capreomycin and quinolones that are unavailable in many countries with high TB prevalence and often prohibitively expensive.
Immune reconstitution inflammatory syndrome (IRIS)

It has already been well recognised, even in the absence of HIV infection, that the institution of anti-TB therapy may cause hectic fevers, increasing lymphadenopathy, and other features that suggest worsening of the disease. The reason is that infection with tuberculosis itself leads to some degree of immune suppression that is reversible with anti-TB therapy.

When HAART and anti-TB therapy are administrated concomitantly, there is a risk of brisk inflammatory response. Transient paradoxical clinical deterioration can be observed: prolonged fever, increasing respiratory symptoms, increasing lymphadenopathy, development of cutaneous lesions, and ascites. Retrospective radiologic review of cases have revealed worsening radiographs in close to 50% of cases, including increasing lymphadenopathy, lobar consolidations, and pleural effusions. A less frequent, but particularly problematic complication, is the occurrence of paradoxical central nervous system lesions in the setting of immune reconstitution. The time from initiation of HAART to the presentation of IRIS in patients infected with TB lies between 10 days to as long as 180 days.

Corticosteroids have been used with good success at preventing further damage when HAART-mediated inflammation threatens vital structures, especially the central nervous system.

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- Guidelines for implementing collaborative TB and HIV programme activities. WHO 2003
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- Tuberculosis and HIV. ICRC HIV Seminar. 2005
Sexually transmitted diseases

Sexually transmitted diseases (STDs) are among the most common causes of illness in the world and have far-reaching health, social and economic consequences for many countries. The World Health Organization estimates that the global prevalence of active and latent infections with the common bacterial, protozoa and viral STDs, including HIV, could be estimated in the billions of cases.

STDs fuel the sexual transmission of HIV infection. The presence of an untreated STD can enhance both the acquisition and transmission of HIV by a factor of up to 10. STD treatment is therefore an important HIV prevention strategy in a general population.

STDs encompass sexually transmitted infections (STIs) and malignancies.

**MAIN SEXUALLY TRANSMITTED DISEASES PATHOGENS**

There are more than 20 pathogens that are transmissible through sexual intercourse — oral, anal and vaginal (Table 11.1).

<table>
<thead>
<tr>
<th>Disease &amp; syndrome</th>
<th>Aetiologic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethritis (males)</td>
<td><em>Neisseiria gonorrhoeae</em>, <em>Chlamydia trachomatis</em>, <em>Trichomonas vaginalis</em>, Herpes simplex</td>
</tr>
<tr>
<td>Mucopurulent cervicitis</td>
<td><em>Chlamydia trachomatis</em>, <em>N. gonorrhoeae</em></td>
</tr>
<tr>
<td>Vulvovaginitis</td>
<td><em>Candida albicans</em>, <em>Trichomonas vaginalis</em></td>
</tr>
<tr>
<td>Acute pelvic inflammatory disease</td>
<td><em>N. gonorrhoeae</em>, <em>Chlamydia trachomatis</em>, bacterial vaginosis</td>
</tr>
<tr>
<td>Chancroid</td>
<td><em>Haemophilus ducreyi</em></td>
</tr>
<tr>
<td>Granuloma inguinale ou donovanosis</td>
<td><em>Calymmatobacterium granulomatis</em></td>
</tr>
<tr>
<td>Ulcerative lesions of the genitalia</td>
<td>Herpes simplex, <em>Treponema pallidum</em>, etc.</td>
</tr>
</tbody>
</table>
THE ROLE OF STDs IN INCREASING SEXUAL TRANSMISSION OF HIV

The impact of STDs on sexual transmission of HIV was initially suspected on the basis of epidemiologic studies, showing that persons with an ulcerative or non-ulcerative STD appear more susceptible to acquiring HIV infection. Subsequent studies showed that urethral and endocervical inflammation caused by non-ulcerative STDs increases genital shedding of HIV-infected cells, and thus probably increases infectivity of the person with HIV infection.

**Box 11.1 | STIs and HIV**

- Mwanza study (Tanzania, 1995): a community randomization trial of strengthened syndromic management of STD was associated with a 42 percent reduction in HIV incidence over a two-year period.
- STD is associated with a 5- to 10-fold increase in the risk of transmitting HIV (even higher in case the disease is an ulcer or a sore).

**Box 11.2 | Possible biological explanations for a connection between HIV infection and lack of circumcision**

The tissue of the internal foreskin absorbs HIV up to nine times more efficiently than female cervical tissue, mainly because it contains epidermal dendritic cells (Langerhans cells) in much greater quantities than the cervix or other genital tissue (including other parts of the penis). In addition, the internal foreskin has a mucosal surface, as opposed to the more hardened skinlike surface of the external foreskin. This mucosal surface is particularly susceptible to tears and abrasions, and, consequently, infection by STDs and HIV.

**COMPLICATIONS AND CONSEQUENCES OF STDs**

STDs often exist without symptoms. In women with gonococcal and/or chlamydial infections, there may be no symptoms in up to 70% of cases. Both symptomatic and asymptomatic infections...
can lead to the development of serious complications. The most serious complications and sequelae (long-term consequences) of untreated STDs tend to be in women and newborn babies, for instance:

- **Women**: cervical cancer, salpingitis, infertility, ectopic pregnancy and related maternal mortality.
- **Newborn**: blindness, increased morbidity and mortality.

Furthermore, a remarkably large and growing number of malignancies and neurological diseases is now partially attributed to pathogens that can be sexually transmitted.

### Box 11.3 | More on STDs consequences on health

Examples of possible STIs-related malignancies:
- Cervical cancer and hepatocellular carcinoma, two of the most common malignancies in developing countries
- Squamous epithelial cell cancers of the vagina, vulva, penis, and anus
- Kaposi sarcoma
- T lymphocyte malignancies.

Serious neurologic diseases caused by STD pathogens include:
- Complications attributable to syphilis, as well as neonatal herpes encephalitis, tropical spastic paraparesis/HTLV-I-associated myelopathy, and various HIV-associated neurological disorders.

Thus, effective prevention and control of STDs is now recognized as (1) an essential step in preventing the spread of HIV, (2) a high priority for preserving reproductive health, especially among women, (3) a very cost-effective approach to preventing neonatal morbidity, and (4) an important approach to preventing cancer and neurologic diseases.

### PREVENTION AND CARE OF STDs

The objectives of STD prevention and care are to reduce the prevalence of STDs by interrupting their transmission, reducing the duration of infection and preventing the development of complications in those infected.

Prevention and care of STDs represent a difficult challenge. As a matter of fact, STDs continue to spread and their complications and long-term health effects continue to be a burden on individuals and communities. The following are some of the factors hindering the effective prevention and care STDs:
Many STD cases, especially among women are asymptomatic. Asymptomatic individuals will ignore that they have an STD and therefore will not seek for care. They will continue to be infected and infectious to others.

Reluctance to seek health care. Even with symptoms, some people may be reluctant to seek STD care. This can be out of ignorance, embarrassment or guilt. They may also be deterred by an unfriendly attitude by staff, a lack of privacy or confidentiality.

STD services often do not exist in a particular locality. Even where they exist, they may be difficult to access (distance, finance) or do not have the necessary medicine. Some might not attend a clinic, but buy drugs from pharmacists or in street markets, with the risk of taking inappropriate antibiotic, resulting in resistant organisms.

**Primary prevention**

Primary prevention, which is concerned with the entire community, curbs the acquisition of infection and resulting illness. It can be promoted through health promotion and health education. Primary prevention messages apply equally to HIV and other STDs.

**Prevention counselling**

When people with STIs symptoms attend a health facility, it is an opportunity to counsel them about both STIs, including HIV acquisition and transmission. If HIV testing (VCT) is available, this should be offered to them. Condoms need to be available in all clinics to offer to patients with STIs.

**Promotion of safer sex behaviour**

Through the development and dissemination of messages promoting safer sex and educating people about risk reduction: use of condoms, monogamy and abstinence.

**Encouraging healthcare-seeking behaviour**

Through community education campaign, targeted to those most vulnerable to STIs, can also encourage attendance. It implies that health facilities should be accessible and affordable, and able to deliver quality care.

**Partner notification**

Contact tracing means finding and telling the partner/s of a person with an STI that they might be infected and should be treated. The aim is to treat all sexual partners (within the past three months, at least) of the STI patient. Contact tracing is always difficult but it is a very effective way to reduce the spread of STIs in a community.
Secondary prevention (syndromic management)
Secondary prevention is about encouraging people to seek early treatment. Except for HIV and the viral STDs, treatment cures the disease and interrupts the chain of transmission by rendering the patient non-infectious.

The traditional method of diagnosing STDs is by laboratory tests. However, in developing countries such tests are very often unavailable or too expensive. For this reason, syndromic management of STDs has been recommended by WHO since 1990 for use in patients presenting with symptoms of STDs.

Box 11.4 | Main features of the syndromic approach of STIs
- Classification of the main causative pathogens by the clinical syndromes they produce.
- Use of flow charts derived from this classification to manage a particular syndrome.
- Treatment for all important causes of the syndrome.
- Limited risk of wrong diagnoses and administration of ineffective treatment
- Notification and treatment of sex partners.
- No expensive laboratory procedures required.

Box 11.5 | Benefit and disadvantages of syndromic management
**Benefits**
- Accessibility
- Immediate treatment
- Effectiveness
- Efficiency
- Quality assurance / Standardization

**Disadvantages**
- Over treatment in some patients
- Does not cover asymptomatic infections

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- Guidelines for the management of sexually transmitted infections. WHO. 2001
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Malaria

HIV and malaria, two of the most important health problems in the world, overlap geographically in many developing countries.

High levels of co-infection, particularly among sub-Saharan African populations, have major implications for treatment, care and prevention of both diseases.

INTERACTIONS BETWEEN HIV AND MALARIA

Impact of HIV on malaria
In areas with stable malaria, HIV disease impairs the acquired immunity to malaria seen in adults and increases the risk of malaria infection, clinical malaria and case fatality, especially in those with advanced immunosuppression.

In settings with unstable malaria, HIV-infected adults are at increased risk of complicated and severe malaria and death.

Box 12.1 | Stable & unstable malaria

**Stable malaria** (areas of high or hyper endemicity). Transmission is intense and continuous, though seasonal variations may occur. Immunity develops early in life. Young children and pregnant women are the population groups at greatest risk for malaria morbidity and mortality.

**Unstable malaria** (areas of low or moderate endemicity). The risk of malaria is less predictable and not continuous. The disease burden is similar in all age groups though usually higher in children than in adults. Extremely unstable malaria corresponds to epidemic malaria.
Impact of malaria on HIV
Like many infections, malaria fever can transiently increase viral load. However, whether repeat episodes of malaria reduce overall survival times of HIV-infected patients remains to be established.

Malaria, HIV and pregnancy
- HIV-infected pregnant women are at increased risk of higher malaria parasite densities and clinical malaria.
- There appears to be an association between placental parasite density and placental viral load. Placental malaria is also associated with increased expression of macrophages with CCR5 receptors raising the possibility of placental malaria leading to increased mother to child transmission (MTCT) of HIV. However, studies on the impact of malaria during pregnancy on the risk of MTCT remain inconclusive.
- On pregnancy outcome, infection with both malaria and HIV, particularly in individuals with low CD4-cell count, contributes to increased risks of:
  - Anaemia
  - Low birth weight
  - Preterm birth
  - Intrauterine growth retardation.

Box 12.2 | Impact of HIV on the burden of malaria during pregnancy
The impact of HIV on the burden of malaria during pregnancy can be estimated using data on the prevalence of HIV among pregnant women, and on the HIV-associated increased risk of malaria during pregnancy.

In areas with stable malaria in Africa, approximately 25 million pregnant women are exposed each year to the disease. Of these women, at least 10.5 million develop malaria in the second or third trimester. It can be estimated that in 2003, the proportion of malaria infections during pregnancy attributable to HIV was 4.2%, based on an HIV prevalence of 7.5% among pregnant women in sub-Saharan Africa. Using this data, it can be calculated that in 2003 the HIV epidemic resulted in an additional 440 000 malaria cases during pregnancy in Africa.

THERAPEUTIC IMPLICATIONS

Interactions between antimalarial medicines and ARVs
PIs are potent inhibitors of cytochrome P450 enzymes, and NNRTIs are inducers and/or inhibitors of these enzymes; thus pharmacokinetic interactions with antimalarials mostly involve PIs and NNRTIs.
In patients receiving PIs, halofantrine is contraindicated because of excessive risk of toxicity. It is also possible that interactions with artemether and/or lumefantrine can occur.

For patients receiving NNRTIs (nevirapine or efavirenz), lower concentrations of lumefantrine or artemether may lead to increased risk of treatment failure.

A potential interaction between quinine and NNRTI or PI drugs is to be investigated.

Other drug toxicity issues complicate the clinical co-management of HIV and malaria. For example, a common side effect of AZT is anaemia, which is an obvious concern in patients who are anaemic due to malaria.

Another concern is the convergent toxicity of nevirapine-based ART and sulfadoxine-pyrimethamine (SP), particularly in pregnant women who are taking or have taken intermittent preventive treatment (IPT). Hypersensitivity reactions to nevirapine, including potentially fatal liver and skin reactions, are fairly common and clinically indistinguishable from reactions to SP.

**Co-trimoxazole prophylaxis**

Co-trimoxazole (sulfamethoxazole-trimethoprim) prophylaxis has been recommended in resource-limited settings for all people with advanced and severe HIV disease.

However, co-trimoxazole shares a mechanism of action and an adverse event profile with the antimalarial sulfadoxine-pyrimethamine.

Widespread co-trimoxazole use could accelerate the development of resistance in malaria parasites to SP. This potential impact emphasizes the importance of monitoring SP resistance in *P. falciparum*, in particular in communities where prophylaxis with cotrimoxazole is common.

Co-trimoxazole has demonstrated 99.5% effectiveness in preventing malaria and 80% effectiveness for malaria treatment.

Additionally, co-trimoxazole prophylaxis has been shown to be beneficial in HIV-infected pregnant women by significantly improving birth outcome.

WHO recommends daily co-trimoxazole as an alternative to intermittent preventive treatment with SP for immunocompromised HIV-infected women.
Concurrent administration of intermittent preventive treatment with SP and co-trimoxazole has been associated with a substantially increased incidence of severe adverse reactions in HIV-infected patients and therefore is not recommended.

References
- HIV/Malaria: When elephants collide. HIV inSite. 2006
- Malaria and HIV interactions and their implications for public health policy. WHO. 2004
Hepatitis A, B and C are primarily hepatotrophic inflammation. They share similar clinical presentations, but their aetiology, mode of transmission (Table 13.1), distribution, evolution and treatments (Table 13.2) vary considerably.

Viral hepatitis

Hepatitis has a number of causes. Viral infection is one of them. The most common types are hepatitis A, hepatitis B and hepatitis C.

Hepatitis B virus (HBV) and hepatitis C virus (HCV) can cause serious illness due to their effect on the liver.

Many people with HIV are also infected with HBV or HCV, due to the shared route of transmission of the viruses.

This co-infection has serious implications for their health and their treatment options.

HEPATITIS A, B AND C AT A GLANCE

Hepatitis A, B and C are primarily hepatotrophic inflammation. They share similar clinical presentations, but their aetiology, mode of transmission (Table 13.1), distribution, evolution and treatments (Table 13.2) vary considerably.

<table>
<thead>
<tr>
<th>Table 13.1</th>
<th>Modes of transmission</th>
</tr>
</thead>
</table>
| **Hepatitis A:** | • Fecal-oral route by human contact, by uncooked foods and by contaminated water  
| | • Oral-anal sexual contact in homosexual communities or MSM |
| **Hepatitis B:** | • Unprotected sexual relations (including oral sex and penetration, whether vaginal or anal)  
| | • Sharing of contaminated syringes, blood and/or infected biological liquids  
| | • From mother to child during birth |
| **Hepatitis C:** | • Blood-borne contacts, e.g. sharing of contaminated syringes, blood transfusion, infected re-usable tattoo needles and non-sterilized piercing instruments  
| | • Transmission through sexual relations is rare  
| | • From mother to child at birth (infection rates is 5%) |
HIV and hepatitis B (hepatitis C & A to a lesser extent), share their route of transmission, hence coinfection is common.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Epidemiology</th>
<th>Natural History</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Worldwide sporadic and epidemic. In developing countries, adults are usually immune and epidemics of HAV are not common.</td>
<td>Acute, flu-like illness, then completely cured by the immune system, without risk of chronic infection. There is a very low risk of “fulminant” acute hepatitis, with fatal outcome. The disease confers life-long immunity</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Worldwide, endemic. Prevalence (positive serology: anti-HBc+):  • Sub-Saharan Africa, China and Southeast Asia: 10-20% of popul.  • Europe, USA: 0.1-0.2% of population  • Europe, USA, among gay and bisexual community: 30% are affected</td>
<td>Around 30% of infection remain asymptomatic. When present symptoms are: flue-like illness, jaundice, abdominal pain, nausea, vomiting, fever. Low risk of acute fatal evolution 4-10% of afflicted adults will develop a chronic longstanding liver inflammation that may lead to cirrhosis and hepato-cellular carcinoma in 25 to 40% of the cases. 90% of infants infected at birth and 30% of children infected between 1-5 years will develop a chronic liver infection. Some individuals will not totally clear the HBV and will become healthy carriers of the infection.</td>
<td>Decision for treatment only after liver biopsy (to confirm the severity of chronic hepatitis)  First line treatment: Pegylated interferon alpha* (4 - 6 months)  Alternative: Tenofovir + 3TC</td>
</tr>
</tbody>
</table>
### Table 13.2  Epidemiology, natural history and treatment... contd.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Epidemiology</th>
<th>Natural History</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Worldwide distribution. Prevalence essentially related to the prevalence of IDUs and poor parenteral practices in health care settings, e.g: • 50 to 80% of IDUs acquire HCV within 5 years after they have begun injecting drugs • 85% of hemophiliacs who are HIV+, are HCV+ at the time.</td>
<td>The disease confers life-long immunity.</td>
<td>For HCV genotypes 2, 3: • No liver biopsy • 6 months treatment For HCV genotype 1, 4: • Liver biopsy (might give reasons why not to treat) • 12 months treatment Recommended regimen: Pegylated interferon alpha + ribavirin</td>
</tr>
</tbody>
</table>

* Pegylated interferon alpha is interferon alpha conjugated with polyethylene glycol (it delays the clearance of the drug)

**Hepatitis A and B can be prevented through vaccination. There is no immunization active against hepatitis C so far.**

### HEPATITIS AND HIV CO-INFECTION

**Box 13.1  | Prevalence of hepatitis B and C among HIV patients**

- The prevalence of HBV active or past infection among all HIV-infected patients can be as high as 70 to 90%.
- The prevalence of HCV infection among all HIV-infected patients can be as high 40%. Yet this rate varies substantially among different risk groups, e.g. up to 80% HCV+ among IDUs.

HBV or HCV and HIV coinfection might affect the evolution of either disease (Table 13.3).
Some of the drugs administrated in case of chronic hepatitis B (3TC, Tenofovir) are also part of HAART schemes. This will increase the complexity of treatment in case of co-infection.

Treatment for each disease is complicated, expensive and has side-effects. It cannot be done outside specialized referral centres.

### Antiretroviral Therapy in Co-infected Individuals

Some of the drugs administrated in case of chronic hepatitis B (3TC, Tenofovir) are also part of HAART schemes. This will increase the complexity of treatment in case of co-infection.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Effect of hepatitis on HIV prognosis</th>
<th>Effect of HIV on hepatitis evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Hepatitis A does not affect the evolution of HIV.</td>
<td>Duration of hepatitis A can be longer with HIV, but without any change in the evolution compared to table 2.</td>
</tr>
<tr>
<td>B</td>
<td>Several studies have suggested that hepatitis B does not hasten or worsen HIV disease progression.</td>
<td>Those among HIV+ gay men, who are also chronic carriers of HBV are 8 times more likely to die of liver-related cause (compared with men with HIV who did not have hepatitis).</td>
</tr>
<tr>
<td>C</td>
<td>Recent large studies suggest that hepatitis C does not significantly alter the chances of dying, developing AIDS or responding to HAART.</td>
<td>HIV may affect hepatitis C infection by speeding up liver damage. Even HIV+ people with still high CD4 counts may be at greater liver damage than HIV- people.</td>
</tr>
</tbody>
</table>

### Treatment interference

**When HAART and treatment of chronic hepatitis B do occur at the same time**

- 3TC inhibits both HIV and HBV and is an approved treatment for both viral infections. However:
  - Development of 3TC resistant HBV mutants may be more frequent in case of HIV co-infection.
  - Development of 3TC resistant HBV can be associated with flare of hepatitis.
  - Discontinuation of 3TC can also be associated with flare of hepatitis.
  - People with known chronic hepatitis B who start HAART, should at the same time start treatment for hepatitis B in order to reduce the risk of hepatitis flare.
  - HAART may cause an increase in liver enzymes. This side-effect is increased in people carrying the HBV.

- Tenofovir and 3TC combined in an anti-HIV regimen could be an effective way of treating HIV patients who also suffer from chronic hepatitis.
When HAART and treatment of chronic hepatitis C do occur at the same time

- Ribavirin:
  - Ribavirin combined with pegylated interferon, should be the first-line treatment for HCV/ HIV co-infected individuals, although the overall response is lower compared to those observed in the HCV mono-infected population.
  - HAART and antiHCV drugs used simultaneously might have severe side-effects (anaemia, haemolysis, pancreatitis, hepatic decompensation).

References

- Clinician’s guide to HIV/HCV coinfection. Montain Plains AIDS Education Center. 2004
- Co-infection with hepatitis viruses and HIV. HIV InSite. 2004
- Hepatitis A, B, C, D, E. 2005
- Hepatitis B and HIV co-infection. University of San Fransisco 2006
- Hepatitis B virus. NYSDOH. 2003
- Hepatitis C and HIV co-infection. University of San Fransisco 2006
- Hepatitis C virus. NYSDOH. 2003
- HIV and hepatitis. Nam. 2002
Nutrition

Over the last decade, HIV/AIDS has become increasingly associated with malnutrition and household food insecurity in many countries around the world.

Nutrients requirements of HIV-infected persons differ from non-infected individuals.

Projects design and resources had to be redirected in order to address the impact of HIV/AIDS on food and livelihood security, both being key elements of prevention.

RELATIONSHIP BETWEEN HIV, MALNUTRITION AND HOUSEHOLD FOOD SECURITY

Malnutrition and HIV are strongly related to each other:
• Any immune impairment as a result of HIV/AIDS leads to malnutrition, and
• Malnutrition leads to immune impairment, worsens the effect of HIV and contributes to more rapid progression to AIDS.

Thus, malnutrition can both contribute to and result from the progression of HIV (Figure 14.1). A person who is malnourished and then acquires HIV is more likely to progress faster to AIDS, because his/her body is already weak and cannot fight infection. A well-nourished person has a stronger body for coping with HIV and fighting illness.

Figure 14.1. Relationship between HIV/AIDS and malnutrition
HIV/AIDS affects the nutrition and livelihood of individuals, households and communities. It commonly undermines the ability of individuals and households to feed and care for themselves, while eroding the capacity of communities to provide basic services and support to people in need.

HIV/AIDS-related illness and death are major causes and contributors to household food insecurity. This is understandable given that the disease typically strikes the most productive household members. When a breadwinner becomes sick, the household not only has to manage without their labour and income, but also with the loss of labour of those who have to care for the sick.

MACRONUTRIENTS AND MICRONUTRIENTS REQUIREMENTS FOR HIV/AIDS PATIENTS

Good nutrition for all individuals, but especially for people living with HIV/AIDS (PLWHA), requires the consumption of an adequate amount of macronutrients (proteins, carbohydrates and fats) and micronutrients (vitamins and minerals).

**Macronutrients**
A deficiency in macronutrients, also known as “protein-energy malnutrition,” manifests itself in the weight loss and wasting that is typical of AIDS patients. These symptoms occur as a result of reduced food intake and/or poor absorption of nutrients and changes in metabolism that affect cell growth, enzymatic processes and immune system reactions.

The nutrient requirements of HIV-infected persons differ from non-infected individuals. Current evidence suggests that as the infection progresses, the nutrient requirements change. The requirements are different and depend on whether patients are in the asymptomatic or symptomatic phase of HIV infection (Table 14.1).

**Micronutrients**
Consuming micronutrients (especially vitamins A, B6 and B12, iron and zinc) is important for building a strong immune system and for fighting infections.

- Vitamin A deficiency is associated with higher maternal-child transmission rates, faster progression from HIV to AIDS, higher infant mortality and child growth failure.
- The B-group vitamins play important roles in immune regulations, and deficiencies play a role in disease progression.
• Zinc is an essential component of the immune system. Mild and marginal zinc deficiency is common in Africa, resulting in depressed immunity and other disorders. But the HIV itself requires zinc for gene expression, replication, and integration. It may thus be associated with faster HIV disease progression. These findings suggest that zinc supplementation should be approached cautiously.

• Iron deficiency causes anaemia, which is a common problem among people with HIV/AIDS, although its cause(s) is not well understood (reduced dietary intake, absorption, metabolic changes, etc.). Anaemia, especially if severe, is associated with faster progression of HIV disease.

Table 14.1 | Nutrients requirements for HIV-infected people

<table>
<thead>
<tr>
<th>Phase</th>
<th>Changes in Nutrient Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Energy requirement for HIV-infected persons increases by 10 percent. Protein and micronutrient requirements for HIV-infected persons remain the same (compared to the level recommended for healthy non-HIV-infected persons for the same age, sex, and physical activity).</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Energy requirement for HIV-infected persons increases by 20-30 percent. Protein and micronutrient requirements for HIV-infected persons remain the same (compared to the level recommended for healthy non-HIV-infected persons for the same age, sex, and physical activity).</td>
</tr>
</tbody>
</table>

These recommendations are for all HIV-infected persons, regardless of whether they are taking anti-retroviral drugs or not.

An adequate, well-balanced diet is an essential component of basic care for people living with HIV/AIDS.

Box 14.1 | Positive impacts of well-balanced diet for PLWHA

• Prevents malnutrition and wasting.
• Achieves and maintains optimal body weight and strength.
• Enhances the body’s ability to fight opportunistic infections.
• May help delay the progression of HIV.
• Improves the effectiveness of drug treatments.
• Improves the quality of life.
FOOD INTERVENTIONS STRATEGIES

Given the lack of medical care and drug treatment in many AIDS-affected developing countries, it is imperative that vigorous efforts to achieve and maintain good nutrition among HIV-infected people are undertaken as a matter of priority.

The stage and pattern of a country’s HIV/AIDS epidemic is also important in assessing coping abilities. For instance, there is little impact when HIV prevalence is low, but it becomes very high when large numbers of people have been infected and AIDS deaths rate start to rise.

Among the whole population, the following groups of people do require special attention:

- People living with HIV/AIDS (PLWHA)
- People caring for PLWHA
- Orphans and households fostering orphans (in particular, orphan-headed households and single-parents households, especially those headed by women).

Below are concrete examples of interventions that aim to protect and improve nutrition and food security among HIV/AIDS-affected households:

**Awareness raising**
There are still efforts to be made, to raise awareness about the links between HIV/AIDS, food insecurity and malnutrition among people involved in policy making and planning.

**Nutritional care for PLWHA**
Good nutrition has an impact on life quality and expectancy in PLWHA. Programmes that enhance access to sufficient food of good quality are required. These include home and community gardening and other agricultural interventions. For households which are drained of productive resources, external food aid has to be considered.

**Livelihood and food security support for HIV/AIDS-affected households**
Orphans- and elderly-headed households often need direct food support. Female-headed households often need increased access to means of production, while households fostering orphans may benefit from enhanced access to micro-finance.

**Community-based livelihood support and care systems**
Since HIV/AIDS-affected households depend largely upon community-based organizations for care and support, the capacity of these organizations (mutual help groups, orphanages, etc.) needs to be strengthened.
Access to education, life skills and vocational training

The goal is that orphans and other vulnerable children can attend school and receive basic education. In reality, however, it is common that these categories are unable to attend school, even when incentive programmes do exist. This is attributed to other socio-economic factors such as poor health, lack of food, lack of shelter and clothing, etc.

References

- HIV/AIDS: A guide for nutrition care and support. USAID. 2001
- Incorporating HIV/AIDS considerations into food security and livelihood projects. FAO. 2003
- Living well with HIV/AIDS. WHO & FAO. 2002
- Nutrition and HIV/AIDS. UNAIDS. 2001
- Recommendations for the nutrient requirements for HIV-infected persons in resource-limited settings. USAID. 2003
RISK FACTORS AND VULNERABILITY

High risk behaviour is directly associated with the physical proximity between infected persons or material and non-infected persons (Table 15.1). Heterosexual transmission is generally the dominant mode of spread of HIV, but the virus may be over-represented in groups with higher than average risk behaviour like drug injectors and men who have sex with men.
Part of the population is at a higher risk of getting the HIV infection because of social, economic and cultural factors, which influence people’s behaviour in relation to the risk (Table 15.2).

### Table 15.1 | Risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Behavioural risk factors</strong></td>
</tr>
<tr>
<td>Sexual relations both heterosexual and homosexual including MSM; Use of intravenous drugs</td>
</tr>
<tr>
<td><strong>Non behavioural risk factors</strong></td>
</tr>
<tr>
<td>Mother-to-child transmission; Occupational exposure; Transfusion of contaminated blood or blood products.</td>
</tr>
</tbody>
</table>

### Table 15.2 | Vulnerable groups

<table>
<thead>
<tr>
<th>Socio-economical context</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfavourable economic development policies, rural to urban migration, economic mobility, routes of trade and commerce, illiteracy, low levels of education, abuse of alcohol, street children and youth.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Socio-cultural context</th>
</tr>
</thead>
<tbody>
<tr>
<td>The understanding of decision-making and power in sexual relationship is crucial. In many contexts, women only have a limited negotiating power:</td>
</tr>
<tr>
<td>• Although the most vulnerable groups for transmission through sex are generally the young and women, it is men (due to cultural reasons) who play the dominant role in deciding whether and under what circumstances sex will take place. It is therefore important to consider how to reach them with sexual behaviour change programs.</td>
</tr>
<tr>
<td>• The use of condom often represents a decision to have “unnatural” or “undesirable” sex. It may even become linked with suspicion or mistrust.</td>
</tr>
<tr>
<td>• Sexual life can be restricted by customary law (ban of sexual intercourse before or outside marriage) but breaches against the rules are not uncommon.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Traditions, beliefs and taboo linked to sexuality</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are numerous traditions, beliefs and taboo in any society which might be difficult for foreigners to perceive, understand and deal with e.g., polygamy, wife inheritance, rape of virgins in order to “heal” from AIDS, female genital mutilation (FGM), etc.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Culturally destabilized groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disintegrated families, unemployed persons, domestic and international migrants.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific risk groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homosexuals, prostitutes and other segregated groups and communities, injecting drug users (IDU).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conflict, internal disturbance or violence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population migration or displacement (refugees, IDPs) can be factors fostering at-risk behaviour due to</td>
</tr>
</tbody>
</table>
reduced revenue generation, weakened social safety net and disrupted family and kin links. This might trigger need-driven behaviour (casual sex in order to get a minimal income to get food).

**Insufficient access to preventive and curative care**
In case of absence of health infrastructure and/or lack of access to health facilities for whatever reason (distance, financial, etc.), especially in remote areas, as well as lack of trained staff, lack of medical equipment and lack of medicine.

### Table 15.2 Vulnerable groups ... contd

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Attitude</th>
<th>Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ignorance</td>
<td>Unawareness</td>
<td>External &quot;blocking&quot; factors</td>
</tr>
<tr>
<td>Education</td>
<td>Information</td>
<td>Sustained behaviour change</td>
</tr>
<tr>
<td>Network</td>
<td>Media</td>
<td>Try new behaviour</td>
</tr>
<tr>
<td>Internal &quot;blocking&quot; factors</td>
<td>Ready to change</td>
<td>Goal</td>
</tr>
<tr>
<td>Family, peers, poverty, religion, beliefs, etc.</td>
<td>Motivation to change</td>
<td>Unsupportive health care, non committed authorities</td>
</tr>
</tbody>
</table>

**THE PROCESS OF CHANGE: FROM AWARENESS TO SUSTAINABLE BEHAVIOUR CHANGE**

Behaviour change is a concept which has been used in the field of health promotion, and is the rallying call of most HIV/AIDS prevention campaigns. Changing attitudes and behaviour is a challenging and time-consuming process. Hereafter is one of the possible models showing the different steps from unawareness towards a sustainable change in behaviour (Figure 15.1). It also shows some of the barriers or “bottlenecks” along the process.

**Figure 15.1. From awareness to sustained behaviour change**
Enthusiasm for promoting behaviour change as a direct route to HIV prevention has not yielded the expected results. Experience (and research) has demonstrated that educational, socio-economical and cultural factors considerably influence the risk of HIV infection. There are many instances where choices (behaviour) concerning sexual activity are undermined by the socio-economic and cultural conditions that frame them. For instance:

Motivation and concrete interests

One of the major issues concerning HIV/AIDS prevention and care is frequently people’s lack of motivation to become involved in the battle against HIV/AIDS, which for many is a low priority among what they consider to be their most pressing issues and needs.

For instance, people who have no options except to exchange sex for money in order to buy food for their children are unlikely to heed behaviour-change messages that ignore their reality.

People will not give HIV/AIDS prevention and care a high priority as long as they have not been able to secure what they consider as their essential needs in their day to day life.

Thus, any rethinking process and subsequent attitudes towards behaviour change should emphasize concrete reasons for this shift in their priority systems, in order to preserve or regain their identity, improve their daily life conditions and encourage the respect of human life (Table 15.3).

Table 15.3 | Determinants of motivation to change

<table>
<thead>
<tr>
<th>In the field, the starting points are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The existing local practices (including those of decision-makers: elders, chiefs, traditional leaders)</td>
</tr>
<tr>
<td>• The scales of values and ways of ranking items in terms of lifestyle, education, traditions and beliefs.</td>
</tr>
<tr>
<td>• These practical observations can then be used in the social negotiation process (between health or social field workers and population) to support decisions concerning initiating, continuing, extending, modifying or stopping local projects for appropriate prevention and care.</td>
</tr>
</tbody>
</table>

Furthermore, there are additional factors and constraints to be considered when planning for promoting behaviour change.

The “obsolete” concept of preventive education

The idea that prevention interventions can rely on the assumption that giving correct information
about transmission and prevention will lead to behavioural change have proved to be wrong. This is probably linked to confusion between school instruction and preventive education.

Indeed, school instruction is often limited to a one-way transmission of purely cognitive information. Its impact is very limited in the context of HIV/AIDS prevention activities.

Yet, education definitely remains an important component of HIV/AIDS prevention, as far as educational material is not “pre-cooked”:

- Education material should emerge gradually from the educational process itself, through empathic dialogue and on the basis of people’s societal and cultural values, behaviour norms and understanding capacities.
- Dissemination should use all possible channels: NGOs, social workers, business people and entrepreneurs, associations and movements, sports groups, ethical, religious and traditional representatives, media and eventually schools.

**The importance of cultural references**

Existing culture is not something fossilized. Cultural values develop with time, responding to material, environmental and external circumstances as well as according to its own internal logic.

HIV/AIDS epidemic strongly challenges cultural values. For instance, sexual practices and attitudes which are closely linked to traditions and beliefs (e.g. wife inheritance, polygamy) might be contributing factors to the spread of the epidemic. However, direct pressures from external forces aimed at inducing behaviour change might be perceived as unacceptable intrusion and thus rejected.

In practice, it means that various cultural references and resources will have to be re-considered: encouraged, modified, reinvented or dropped. It is a choice of the community, not of the humanitarian actors or development workers. It is a gradual, self-evaluation process.

**Box 15.1 | Field work approach**

**What is field work?**

Field work is the preparation, implementation and evaluation of a project at the local level, for and with a given population.

- Field workers should help populations to prioritize their problems, to identify those solutions they could put into practice themselves and those for which they need external assistance.
Implementing activities at the local level requires information which only field workers can provide, following requests from the populations; this should lead to a joint and permanent evaluation of the progress achieved and problems encountered.

Support given by field workers can be beneficial only if it is integrated into endogenous cultural processes of behaviour change.

In most field work, these three conditions for valuable field work are far from being met due to institutional pressure prioritizing medical and cognitive activity and to lack of training/sensitizing of field workers on the cultural determinants and effects of their tasks. Thus, the result is, all too often, a breakdown in communication between the local populations, the field agents and the institutions to which they report on their activities and the real needs of the population.

Field worker’s profile
Field workers’ role is to act as a liaison between the local community and the institutions, while participating in the preparation, implementation and follow-up of local response and community initiatives projects.

Therefore, the re-evaluation of field workers’ role from actor to mediator and facilitator will be crucial. In this perspective this role must be reinterpreted accordingly (societal/cultural references related to sexuality, personal, family or common responsibility, etc.).

Field worker’s role
There are many different conceptions of the role, which the field worker ought to play in relation to the community. This role can be described in various ways:

• A resource person addressing questions/needs without putting forward other questions or offering solutions unrelated to the problems, as perceived by the community.
• A catalyst: helping the community to discover the true nature of the problems to be faced and the means available to solve them.
• A social activist: intervening more dynamically in the debate to raise issues and questions that might otherwise go unnoticed.

The roles he/she adopts may well be determined by the degree of economic, social and cultural destabilization already manifest with regards to the HIV/AIDS issue in the community he/she is working with.

The extreme diversity of situations in the field concerning the epidemic and its context naturally means that field workers must be flexible in their approach to opening a dialogue with populations, identifying the issues and seeking solutions:

• Field workers should not have preconceived ideas as to what would be the most logical, the most efficient, or the most cost-effective response in terms of human and material resources to be mobilized. However he/she must be aware that his/her own culture will interact in the communication process and he/she should be able to adjust accordingly.
Box 15.1  Field work approach ... contd

- It is also necessary to accept that the community has its own rationality, which is valuable in its own right. Field workers must learn to understand the language and terminology of their partners in order to be able to evaluate the costs, benefits, aims and results of mobilization against HIV/AIDS from the point of view of the population.

Under no circumstances should field workers attempt to change the culture of a community by depriving it of its greatest asset – its sense of autonomy.

Field workers can, however, enhance invention, creativity and criticism from certain groups within a culture, who can help their community in seeing its weaknesses and its potential, so as to be able to build a genuinely local response.

Think with the community and pay attention to the role and responsibilities of men and women and to the relationship between them.

References

- Appropriate communication for behaviour change. UNESCO & UNAIDS. 2001
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- Sexual behavioral change for HIV. Where have theories taken us. UNAIDS. 1999
Prevention of acquisition and transmission through sex

Although sex is the most common route of transmission of HIV, sexual activity is often a taboo subject and thus, promoting change to safer sexual practice is a difficult, time-consuming but essential task in the fight against HIV/AIDS.

Before considering any intervention, it is important to understand better people’s ideas about sexuality and their sexual practices.

Heterosexual transmission of HIV accounts for more than 70% of all HIV infections worldwide.

INTERVENTION PLANNING

The initial assessment should involve all groups participating in the project (representatives of the beneficiary community and representatives of the organisation supporting the project, NGO, IO, local associations) from its inception up to its implementation, without omitting monitoring and evaluation.

Representatives of the community should not be limited to the opinion of the traditional decision-makers (elders, chiefs, religious and military leaders), but has to include other important groups, e.g. women associations, youth, ethnic minorities, i.e. often people who are more vulnerable.

The initial assessment will lead on to a thorough understanding of people’s ideas, beliefs and practices and reveal areas of vulnerability. This will facilitate the identification of groups (e.g. the youth, detainees) or sub-groups (e.g., women headed families, the poorest among the poor, etc.) of people who are at a higher risk of getting infected with HIV.
The next step consists of designing a project, targeting either the whole population or groups identified as vulnerable. Priorities have to be defined taking into account issues like feasibility and available resources (human, material and finance). Objectives will be set and then translated into activities, i.e. interventions aimed at preventing acquisition and transmission of HIV through sex.

INTERVENTIONS THAT RELATE TO THE PROVISION OF SERVICES

Promote and distribute condoms
Correct and consistent use of condoms is an extremely effective means of preventing the spread of not only HIV, but also other STIs, including hepatitis B. Furthermore, in situations where both partners are already infected with HIV there are benefits to using condoms. They prevent exposure to semen and therefore to different strains of the virus and to other STIs.

Attitudes towards condoms
In order to be able to address the people concerns and fears it is important to understand their attitudes against condoms. Indeed, in many settings condoms are still unfamiliar and many are reluctant to use them.

<table>
<thead>
<tr>
<th>Beliefs about condoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>They are uncomfortable</td>
</tr>
<tr>
<td>It is embarrassing to ask for them</td>
</tr>
<tr>
<td>They are expensive</td>
</tr>
<tr>
<td>They are associated with infidelity and immoral behaviour</td>
</tr>
<tr>
<td>It is difficult to talk about it between men and women</td>
</tr>
<tr>
<td>It suggests a lack of trust between partners</td>
</tr>
<tr>
<td>They are more used outside marriage and with casual sex</td>
</tr>
<tr>
<td>They prevent pregnancy (when the desire is to achieve pregnancy)</td>
</tr>
</tbody>
</table>
Strategies to procure and promote condoms

- Provision of adequate numbers of good quality condoms

**Box 16.2 | Formula for calculating condom requirements**

Condom needs can be calculated if you can estimate the following:

- The size of the target population (e.g., IDP population and adjoining areas). Roughly 20 percent of this number represents the size of the sexually active male population.
- The percentage of males using condoms. Results from previous KAPB studies can be used when they exist. If they do not exist, plan from data provided by the most reliable source and adapt according to needs.
- Plan for about twelve condoms per sexually active male per month.
- Add 20 percent to the above figure for wastage and loss.

**Example:**

One month’s supply of condoms for an estimated refugee/IDP and adjoining population of 10,000 people, with 20 percent of sexually active males using condoms:

<table>
<thead>
<tr>
<th>Calculation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,000 sexually active males</td>
<td></td>
</tr>
<tr>
<td>20 percent use condoms:</td>
<td>400</td>
</tr>
<tr>
<td>2,000 x 0.2</td>
<td>2,000</td>
</tr>
<tr>
<td>12 condoms per month per sexually active male:</td>
<td>4,800</td>
</tr>
<tr>
<td>400 x 12</td>
<td>480</td>
</tr>
<tr>
<td>Add 20 percent to allow for wastage or loss:</td>
<td>960</td>
</tr>
<tr>
<td>4,800 x 0.2</td>
<td>480</td>
</tr>
<tr>
<td>Estimated total condom requirements for one month</td>
<td>5,760</td>
</tr>
</tbody>
</table>

- **Accessibility**
  Condoms should be easily accessible for the different target groups (sexually active people, at risk groups). This can best be achieved through distribution using a variety of channels (clinics, VCT, workplace, military barracks, truck stops, shopping centres, peers, etc.), delivering condoms of good quality, free of charge or at low cost.

- **Teaching condom skills**
  It should be kept in mind that men might feel embarrassed to buy and to try condoms. They need to feel confident about their ability to use them before they need them (once they have overcome their resistance or refusal of using condoms, whatever the reasons were). Instruction/education is important and can take place in different set-ups, VCT, sex education, clinic, etc.

- **Promote condoms**
  Promoting condoms needs to include efforts to change community attitudes toward condom use and sexual risk-taking.
Promotion needs to do more than warn about the risks of AIDS and STIs. It should seek to engage people’s interest and persuade them that using condoms is easy, worthwhile, and socially approved.

**Box 16.3 | Female condom**

The female condom (e.g., “Reality,” “Femidom,” or “Care”) is like a plastic bag with a flexible ring at each end. A woman inserts the condom before sexual intercourse by squeezing one ring and placing it in position over the cervix. The other ring rests against the vulva outside the vagina. The female condom is now increasingly available in many developing countries and is becoming more popular. Unfortunately it is sometimes associated with sex work, but it can also be a useful option for married women and couples.

**Advantages:**
- It can be put in place some hours before intercourse, so the woman has some control over her own protection
- The thin plastic transmits heat so that sex feels more natural than with a male condom
- Oil-based lubricants can be used
- Sex workers like them because they can continue to work during menstruation.

**Disadvantages:**
- It can be difficult to manipulate and insert, especially for inexperienced users
- It is often noisy during sex
- The man is able to see and feel the condom
- It is more expensive than the male condom
- It is less accessible, mainly found in major towns.

**Box 16.4 | Influence of religious doctrine**

**Position of the Catholic church**
- It has shown a great reluctance to promoting the use of condoms to protect against the spread of HIV.
- In 2000, the Vatican stated that condoms might be permissible for containing the spread of the AIDS virus. It does not endorse, but just tolerates the use of condom as part of HIV/AIDS education programme. Abstinence and faithfulness remain the two pillars of the fight against AIDS.
- Condoms were considered as a “lesser evil” compared to the spread of HIV.
- Yet, in some countries (e.g. Kenya) the Catholic Church has maintained a firm stand against the use of condoms.

**Position of Islam**
- In 1998, the Islamic Medical Association of Uganda launched a creative initiative to implement a multi-sector AIDS control approach, by integrating Islamic religious values and wisdom with scientific medical information on HIV/AIDS.
Establish and promote voluntary counselling and testing  
Refer to Chapter 4

Prevention and care of sexually transmitted diseases  
Refer to Chapter 11

**INTERVENTIONS THAT RELATE TO CHANGING INDIVIDUAL BEHAVIOUR**

Information, Education, Communication (IEC) is the jargon term commonly used to describe one of the necessary component of the overall response to HIV.

Behaviour Change Communication (BCC) has been introduced in order to emphasize the importance of achieving behaviour change and the need for broader communication strategies.

- Information is the transmission of accurate facts about a topic, here HIV/AIDS.
- Education is the transmission of cognitive information in order to make it meaningful.
- Communication is the interaction between people to enable understanding to occur.

**Information**

Experience has shown that information alone is insufficient to achieve behaviour change or reduce people’s vulnerability. Nevertheless information is necessary, and information campaigns can certainly raise awareness and foster changes in attitudes.

**Box 16.4 Influence of religious doctrine; two examples: ... contd**

- Nevertheless, it has to be kept in mind that differences in perception and attitude towards HIV/AIDS might also be strongly influenced by the trend and interpretation of Islam in different countries, as well as in different areas of a same country. It means that the integration of scientific information on HIV/AIDS might be accepted or rejected.

**Box 16.5 Quality of information**

Information must be accurate, clear, and at an appropriate language level. To increase understanding people need opportunities to talk with others about the information. One of the most powerful communication strategies is “word of mouth” or “friend to friend” conversations. The speed at which rumours spread is evidence of this. Unfortunately misinformation can also spread in this way.
Education
Education is an important pillar in HIV/AIDS prevention. Yet the “one way” traditional school instruction model does not lead to the expected results. Education “curriculum” has to be discussed and prepared with the “beneficiaries” in order to be disseminated by the different available channels, e.g., associations, sport clubs, NGO, media, posters, theatre, etc.

Communication
Planning a communication campaign starts with the understanding and analysis of the interests and needs of the different kinds of people you want to reach — that is, the target audience. Messages are not always targeted, clear and detailed enough to enable listeners to act on the advice provided.

It should also be kept in mind that communication programs are most useful when they are interactive or stimulate responses from the community.

<table>
<thead>
<tr>
<th>Table 16.2</th>
<th>The six main types of communication channels</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mass media: newspapers, magazines, radio and TV</td>
<td></td>
</tr>
<tr>
<td>• Print media: pamphlets, leaflets, brochures, booklets, posters, calendars, wall charts, picture cards</td>
<td></td>
</tr>
<tr>
<td>• Folk media: theatre, storytelling, songs, dance, poems, messages displayed on cloth or clothing</td>
<td></td>
</tr>
<tr>
<td>• Visual media: films, videos, slide shows</td>
<td></td>
</tr>
<tr>
<td>• Special events: competitions, games, parades, rallies, launches of new projects or activities</td>
<td></td>
</tr>
<tr>
<td>• Personal or community counselling</td>
<td></td>
</tr>
</tbody>
</table>

Sex education for young people and schoolchildren
Young people learn about sex and sexuality in every society. Young people have to find out about sexuality through trial and error on their own, from friends, or from films, sometimes from magazines, books, and advertisements.

Less commonly, they may learn from parents, aunts, and uncles, or through sex education in schools.

Experience and research have shown that AIDS education targeted at young people before they become sexually active is most successful in minimizing future risk behaviour. The school setting is the most obvious in which to reach young people. The most appropriate person to deliver AIDS education in a sensitive way can be the teachers, or sometimes an anonymous person.

Peer education
The English term ‘peer’ refers to one that is of equal standing with another; one belonging to the
same societal group. Education refers to the transmission of cognitive information in order to make it meaningful.

Peer education is a process of passing on information between people with similar characteristics — age group, social and economic status, education and cultural practices — to influence behaviour. It is aimed at empowering others by providing correct information with the goal of encouraging positive behaviours. Peer educators can help their peers make informed choices about their behaviour.

Peer education is based on behavioural theory which asserts that people make changes not because of scientific evidence or testimony but because of the subjective judgment of close, trusted peers who have adopted changes and who act as persuasive role models for change.

**Box 16.6 | Peer educators**

- Peer educators are “non professional teachers.”
- Peer educators talk to, work with and motivate their peers.
- They assist others in their peer group to make decisions about HIV/AIDS (and STIs).
- Activities are undertaken in one to one or small groups settings.

A peer education programme can have different objectives (Table 16.3).

**Table 16.3 | Possible objectives of a peer education programme**

- To increase awareness
- To motivate and support behaviour change
- Promotion of condoms
- Distribution of condoms and education
- Care and support of people living with AIDS
- Others.

**Basic principles**

The socio-cultural background of the peer educators and the target group has to be considered and dealt with sensitivity at all stages of planning and implementing of a peer education programme.

More specifically, the gender perspective and gender roles are too often forgotten or neglected.
Peer education programmes must be sustained over a longer period of time.

However, although peer education is useful and powerful, it is not appropriate in all situations. Formative research is needed to decide whether peer education is the best approach to meet the objectives set.

**Target audience**

Peer education can occur in a variety of settings. There is a lot of experience at the workplace and evaluation has shown positive impact. It has also been successfully used to reach marginalized groups, e.g., sex workers, men who have sex with men, injecting drug users, long distance trucks drivers, combatants, people detained, etc.

**Recruitment and selection of peer educators**

When planning for a peer education programme, one of the crucial elements to be considered is the high drop out rate of peer educators, along with lack of motivation, in the long run. Therefore, the selection of peer educators is an element that is critical to the programme success.

Peer educators must be acceptable to the target group and their personality must be both conducive to training and suited to the work they will be doing. One of the best adapted identification and selection strategy relies on the nomination by peers.

**Training and supervision**

The quality of the initial training is essential. If comprehensive, fewer peer educators will drop out and less supervision and re-training are needed later. Formal training must be supplemented by on-the-job training using a participatory methodology.

The level of support and supervision extended to peer educators should depend on the type of activities they are doing and the amount of training they have had. In general, regular meetings with peer educators both individually and in groups are recommended. Refresher training, updated information and materials, and staff retreats are also necessary.

**INTERVENTIONS THAT RELATE TO THE SOCIETAL CONTEXT**

Efforts to increase the community’s capacity to create an enabling environment for behaviour change and to reduce vulnerability to HIV present a challenge in any type of setting (including in humanitarian environment, i.e. IDPs or refugee camp)
**Role model (political, religious and community leadership)**

In any setting, regardless of war or peace, the stand and commitment of leadership (“the model”) on the threat of the epidemics is a crucial factor. It will affect the behaviour of the people or segments of population through “identification” with their leaders. For instance, country leaders who refuse to acknowledge the gravity or even the presence of HIV and the risk it poses renders its citizens more vulnerable to the infection.

Leaders can be national figures, like the head of state, ministers, members of parliament or religious leaders. At community level (a village or a IDPs camp), it is unrealistic to expect any achievement without the support of the elders and chiefs.

**Legal aspects**

It is important to empower people, especially women and girls, to protect themselves against HIV. This calls for imposing and enforcing strict laws to prevent and penalize rape, sexual abuse and other forms of gender-based violence. It needs the full participation and engagement of all - most critically men in general but also traditional, religious and political leaders - to modify traditional values and customs that disempower women.

**Prevention and management of sexual and gender-based violence (SGBV)**

Sexual and gender-based violence (SGBV) is extremely common, especially in time of armed conflict and in displaced population. Domestic violence seems to be common in all settings, and there is evidence that it is also common in humanitarian settings.

In addition to the risk of HIV, sexual and gender-based violence has other serious consequences. Survivors often experience depression, terror, guilt, shame and loss of self-esteem. Rejection by families can further increase their vulnerability to exploitation. They may also suffer from unwanted health problems (pregnancy, unsafe abortions, STIs (including HIV), sexual dysfunction, infertility, etc.).

Protecting against SGBV is a difficult challenge. Lately the level of awareness has significantly increased. Prevention of sexual violence and management of the consequences (medical, surgical, socio-cultural, psychological and legal) have become key components for reproductive health in humanitarian settings.

**Provision of opportunities for social activities**

It is important to encourage, suggest and support community communication:
• Discussions between men and women can improve the understanding of each other’s perspectives.
• Programmes for youth are particularly important. Often young people have to take on burdensome responsibilities for siblings or elderly relatives. Young people, especially girls, are at high risk of HIV, other STIs, unwanted pregnancy. Young people should be involved in their own needs assessment.

Support to microfinance and income-generating projects
Poverty is one of the major reasons for vulnerability to HIV infection. Support to microfinancing and income–generating projects has been identified as one possible way of solving the problem. These projects are usually carried out by specialized microfinance institutions.

<table>
<thead>
<tr>
<th>Box 16.7</th>
<th>Microfinancing and income-generating projects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Loans should not be granted to indebted families who are too poor to repay a new debt. It is better to establish a savings plan or provide animals, seeds, tools or food directly to the poorest families to avoid increasing their stress.</td>
<td></td>
</tr>
<tr>
<td>• Income-generation activities can be designed to encourage women to be involved in a support group and community activities.</td>
<td></td>
</tr>
</tbody>
</table>

References
• Appropriate communication for behavior change. UNESCO. UNAIDS. 2001
• Background report on family attitudes and sexual behaviour in the Southern Sudan. Kwacakworo. Personal communication. 2001
• Field work. Building local response. UNESCO. UNAIDS. 2001
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• Workplace HIV/AIDS programmes. FHI. 2002
Prevention of mother-to-child transmission

Mother-to-child transmission (MTCT) is the predominant way children become infected with HIV worldwide.

In a number of developing countries, MTCT is the second most common method of HIV transmission after sexual intercourse.

The WHO has been promoting four main approaches to the prevention of mother-to-child transmission (PMTCT) of HIV/AIDS:

- For all women, primary prevention of HIV infection
- For HIV-infected women, prevention of unintended pregnancies
- For HIV-infected pregnant women, prevention of MTCT
- For HIV-infected mothers, their infants and families, provision of care and support.

PMTCT, in this chapter, focuses on the third aspect: prevention of transmission from HIV-infected women to their children.

TRANSMISSION OF HIV FROM MOTHER TO CHILD

An HIV-infected pregnant woman can infect her baby during pregnancy, during labour and delivery, or after birth through breast-feeding.

HIV transmission during pregnancy

The placenta provides an efficient barrier against many infectious agents. HIV transmission risk increases if:

- The mother has a viral, bacterial, or parasitic placental infection during pregnancy impairing the placental protective function.
- The mother acquires her initial HIV infection during the pregnancy and, therefore, develops a very high viral load for a short time, before she has time to build an immune response.
- The mother has severe immune deficiency associated with AIDS.
HIV transmission during labour and delivery

Infants have the greatest chance of becoming infected with HIV during labour and delivery. Infection is facilitated by:

- Exposure to blood and secretions that contain HIV in the birth canal through the infants’ mucous membranes, or through disruption of their skin.
- Placental separation with mixing of maternal/foetal blood.
- Instrumentation or scalp monitoring, which may provide an entry site for HIV.
- Prolonged rupture of membranes leading to a longer duration of exposure to maternal secretions.
- Prolonged time to negotiate the birth canal. A first twin is more exposed because it generally takes longer than the second twin to pass through the birth canal.

HIV transmission during breastfeeding

HIV is present in breast milk. Transmission risk increases with:

- Mixed feeding (feeding both breast milk and other foods or liquids). Exposure to any food other than breast milk may increase the risk of contamination with pathogens and hence inflammation of the intestinal tract in those babies who breast-feed.
- Maternal mastitis or cracked nipples.
- Sores in the baby’s mouth.
- Prolonged duration of breast-feeding.
- Poor maternal immune status (low CD4 count).
- High maternal viral load.

Timing of mother-to-child transmission

Figure 17.1. Timing of MTCT in a breast-feeding population, no ARV
Risk of HIV transmission from mother-to-child in the absence of any intervention

In the absence of any intervention, the risk of MTCT ranges from 30 to 45% (Table 17.1).

<table>
<thead>
<tr>
<th>Period</th>
<th>Transmission rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>During pregnancy</td>
<td>5 – 10%</td>
</tr>
<tr>
<td>During labour and delivery</td>
<td>10 – 20%</td>
</tr>
<tr>
<td>Overall without breastfeeding</td>
<td>15 – 30%</td>
</tr>
<tr>
<td>Overall with breastfeeding until six months</td>
<td>25 – 35%</td>
</tr>
<tr>
<td>Overall with breastfeeding until 18 to 24 months</td>
<td>30 – 45%</td>
</tr>
</tbody>
</table>

In the most developed countries, the risk of MTCT has been reduced to below 2% by interventions that include antiretroviral prophylaxis given to women during pregnancy and labour and to the infant during the first weeks of life, obstetrical interventions including elective caesarean section and completely avoiding breastfeeding.

Box 17.1 | Viral load and perinatal transmission

Regardless of when transmission occurs, there is a direct correlation between maternal viral load as measured by plasma HIV-1 RNA and probability of MTCT.

A large study showed that the rate of perinatal transmission among women with viral load >100,000 c/mL was 40.6%, with 50,000 to 100,000 c/mL it was 30.9%, with 10,000 to 50,000 c/mL it was 21.3%, with 1,000 to 10,000 c/mL it was 16.6%; and with <1,000 c/mL it was 0%.

HIV TESTING FOR PREGNANT WOMEN

Since prevention of mother-to-child transmission is so effective, identification of HIV infection in all pregnant women is imperative.

- Voluntary HIV counselling and testing (VCT) should be a routine part of prenatal care for all women.
- Testing should be performed as early as possible in pregnancy to allow for timely interventions and decisions.
- HIV-negative women who are at high risk of acquiring HIV should be retested in the third trimester of pregnancy (ideally before 36 weeks). Women are at a higher risk if they have a history of STDs, exchange sex for money or drugs, have multiple sex partners during pregnancy, use illicit drugs, have HIV-positive or high risk sex partners, and/or show signs and symptoms of seroconversion.
- Women whose HIV status is unknown and/or who present late in pregnancy or already in labour should be assessed promptly for HIV infection, using rapid HIV testing, to allow for timely prophylactic treatment.

ANTIRETROVIRAL REGIMENS FOR PREGNANT WOMEN WITH HIV

Pregnant women eligible for ARV treatment
The criteria for initiating ART for pregnant women are the same as for non-pregnant women (Table 7.3). Treatment should be started as soon as practicable even if the woman is in the first month of pregnancy.

The WHO recommended regimen for pregnant women is AZT + 3TC + NVP. Infants born to women receiving such regimen should be given AZT for seven days.

Women who become pregnant while receiving ARV treatment
For women who become pregnant while receiving an EFV-containing regimen and are in the first trimester of pregnancy, NVP should be substituted for EFV, with close monitoring of those women who have higher CD4 cell counts. Alternatively a triple NRTI- or PI-based regimen could be used.

Women who are receiving EFV and are in the second or third trimester of pregnancy can continue the current regimen.

ARV prophylaxis for preventing HIV infections in infants
- In high-income countries, triple ARV combinations given to HIV-infected women during pregnancy and labour have demonstrated high effectiveness in reducing MTCT. These regimens are discontinued after childbirth for women without indications for ART. In these settings, and without breastfeeding, HIV infection in infants has been nearly eliminated.
- Resource-constrained countries initially focused their efforts to prevent infection in infants in reducing MTCT around the time of labour and delivery. More recently, they have also begun to consider using ARV prophylactic regimens in the third trimester of pregnancy together with intrapartum and postpartum prophylaxis.
Short-term efficacy determined by infant infection status (virologic test) at 6 – 8 weeks of life has been demonstrated for prophylactic ARV regimens comprising: AZT alone; AZT + 3TC; NVP alone; AZT + NVP; AZT + 3TC + NVP, or triple ARV combination regimens.

ART should be offered to all HIV-infected pregnant women.

<table>
<thead>
<tr>
<th>Clinical situation</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td><strong>Infants</strong></td>
</tr>
<tr>
<td>1. HIV-infected women receiving ARV treatment who become pregnant</td>
<td>Continue the current ARV regimen unless it contains EFV, in which case substitution with NVP or a PI should be considered if the woman is in the first trimester. Continue the same ARV regimen during the intrapartum period and after delivery.</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td><strong>Infants</strong></td>
</tr>
<tr>
<td>2. HIV-infected pregnant woman with indications for ARV treatment</td>
<td>Same treatment as for non-pregnant adults except that efavirenz should not be given in the first trimester. First line regimen: AZT + 3TC + NVP</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td><strong>Infants</strong></td>
</tr>
<tr>
<td>3. HIV-infected pregnant women without indications for ARV treatment</td>
<td>AZT starting at 28 weeks or as soon as feasible thereafter; Intrapartum: AZT + 3TC plus single-dose NVP at the onset of labour</td>
</tr>
</tbody>
</table>
INFANT FEEDING

The risk of HIV transmission with breastfeeding ranges from 5 to 20%.

Avoidance of breastfeeding by HIV-infected women is recommended whenever replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS).

**Box 17.3 | AFASS criteria**

- **Acceptable:** The mother perceives no barrier to choosing replacement feeding for cultural or social reasons, or for fear of stigma and discrimination.

- **Feasible:** The mother (or family) has adequate time, knowledge, skills, resources, and support to correctly prepare breast-milk substitutes and feed the infant 8–12 times in 24 hours.

- **Affordable:** The mother and family, with available community and/or health system support, can pay for the costs associated with the purchase/production, preparation, storage, and use of replacement feeds...
Feeding options during the first 6 months

In resource-limited countries where risks of replacement feeding include malnutrition, infections other than HIV, and stigmatisation, the WHO recommends exclusive breastfeeding until AFASS criteria are met or the baby reaches 6 months of life.

The different infant feeding options for HIV-positive women during the first six months are summed up in Figure 17.2.

Figure 17.2. Infant feeding options for HIV-positive women during the first six months

Box 17.3 AFASS criteria ..contd

without compromising the health and nutrition of the family. Costs include ingredients/commodities, fuel, clean water, and medical expenses that may result from unsafe preparation and feeding practices.

**Sustainable**: A continuous, uninterrupted supply and a dependable system for distribution of all ingredients and products needed to safely practice replacement feeding are available for as long as needed.

**Safe**: Replacement foods are correctly and hygienically stored and prepared and fed with clean hands using clean cups and utensils — not bottles or teats.
Feeding options from 6 to 24 months

At 6 months, an infant reaches an important developmental stage. Breastmilk or breastmilk substitutes are no longer sufficient to meet all of the infant’s nutritional requirements. Appropriate *complementary foods*—any manufactured or locally prepared food given to an infant as a complement to breastmilk, infant formula, or animal milks—are needed to ensure adequate nutrition. All infants, regardless of the feeding option, should begin receiving complementary foods at 6 months.

Milk products should, however, remain in the diet throughout the first two years because they are good sources of energy and other nutrients. Different options for HIV-positive women are presented in Table 17.2.

Table 17.2  | **Infant feeding options for HIV-positive women from 6 to 24 months**

<table>
<thead>
<tr>
<th>Options</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Breastfeeding until other options are safe and feasible, <em>plus</em> appropriate complementary feeding</td>
<td>Under conditions common in resource-limited settings, many experts recommend a transition from breastfeeding to replacement feeding at about 6 months of age. It might occur that breastfeeding remains the only possibility. In such a case, the mother needs thorough medical attention: immediate treatment when she develops a breast condition, becomes ill or finds sore in her baby’s mouth. If the mother develops full blown AIDS, breastfeeding should be stopped immediately.</td>
</tr>
<tr>
<td>2) Expressed, heat-treated breastmilk, <em>plus</em> appropriate complementary feeding</td>
<td>Wet nursing should only be considered if the wet nurse is offered HIV counselling and testing, voluntarily takes a test, tests HIV negative, and practices safe sex. A small chance exists that an HIV-positive infant could pass the virus to a wet nurse if the infant has a sore in the mouth or the wet nurse has a breast condition such as cracked nipples.</td>
</tr>
<tr>
<td>3) Wet nursing by an HIV-negative woman, <em>plus</em> appropriate complementary feeding</td>
<td></td>
</tr>
</tbody>
</table>
Table 17.2  Infant feeding options for HIV-positive women from 6 to 24 months ... contd

<table>
<thead>
<tr>
<th>Breastmilk substitute</th>
<th>4) Breastmilk substitute plus appropriate complementary feeding</th>
<th>Breastmilk substitutes include: commercial infant formula, fresh animal milk, powdered full-cream milk, processed/ pasteurized or ultra-high temperature (UHT) milk. Sweetened condensed milk and skimmed milk are not appropriate breastmilk substitutes. They do not provide enough micronutrients and energy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-milk</td>
<td>5) Animal foods and/or specially formulated, fortified food</td>
<td>In some places neither animal milk nor infant formula is available. In such a case, the non-breastfed child should be fed animal foods (e.g., meat, poultry, fish, eggs) and a variety of other appropriate complementary foods.</td>
</tr>
</tbody>
</table>

Box 17.4 | Recommendations for mothers with unknown HIV status

- Promote availability and use of VCT.
- Promote breastfeeding as safer than artificial feeding: where testing is not available and where mothers’ HIV status is not known, widespread use of artificial feeding would improve child survival only if the prevalence of HIV is high and if the risk of death due to artificial feeding is low, a combination of conditions that does not generally exist.
- Teach mothers how to avoid exposure to HIV.

References

- A guide to primary care of people with HIV/AIDS. US DHHS. 2004
- Antiretroviral treatment, breast-feeding and mother-to-child transmission of HIV. UCSF. 2006
- Infant feeding options in the context of HIV. The LINKAGES Project. 2004
- Prevention of mother-to-child transmission of HIV (PMTCT). Training manual. CBCHB
- Recommendations for use of antiretroviral drugs in pregnant HIV-1 infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. Public Health Service Task Force. 2006
- Safety and toxicity of individual antiretroviral agents in pregnancy. Public Health Service Task Force. 2006
Prevention of transmission through injecting drug use

HIV spreads very easily between people who inject drugs together and share needles, syringes, and other injecting equipment. Blood drawn back into the syringe can pass directly into the bloodstream of the next person to use the syringe.

EXTENT OF THE PROBLEM

Injecting drug use continues to spread around the world regardless of the stage of economic development, social class, religious persuasion, environment (urban or rural) or the political system a country adopts. Where injecting drug use occurs, HIV infection associated with the sharing of contaminated injecting equipment quickly follows. The proportion of HIV infections caused by injecting drug use is estimated:

- 50–90% in eastern Europe, central Asia and eastern Asia and the Pacific;
- 25–50% in North America and western Europe;
- 10–25% in Latin America;
- 1–10% in southern and south-eastern Asia; and
- Less than 1% in sub-Saharan Africa.

Because it is illegal to inject drugs, it is often difficult for governments and communities to admit openly that it occurs. Those who inject are often reluctant to admit their drug use or to seek information and treatment. This means that it is difficult to ask about the extent and nature of injecting drug use.

HARMFUL EFFECTS AND HARM REDUCTION

Drug addiction is a complex illness. It is characterized by compulsive, at times uncontrollable drug craving, seeking, and use that persist even in the face of extremely negative, harmful
consequences (Table 18.1). For many people, drug addiction becomes chronic, with relapses possible even after long periods of abstinence.

<table>
<thead>
<tr>
<th>Table 18.1</th>
<th>Harmful effects of injecting drug use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Death from overdose</td>
</tr>
<tr>
<td></td>
<td>Infection with blood-borne viruses including HIV, hepatitis C, and hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Spread of HIV or hepatitis B to sexual partners</td>
</tr>
<tr>
<td></td>
<td>Abscesses and bacterial blood infections from dirty needles</td>
</tr>
<tr>
<td></td>
<td>Embolism from impurities in the drug</td>
</tr>
<tr>
<td></td>
<td>Family conflict</td>
</tr>
<tr>
<td></td>
<td>STIs and sexual violence associated with prostitution</td>
</tr>
<tr>
<td></td>
<td>Crime and time in prison</td>
</tr>
</tbody>
</table>

It is usually difficult to get people to stop injecting drugs. However, many people who inject drugs do eventually stop. The idea of harm reduction (Table 18.2) is to reduce the harmful effects of injecting drugs for injecting drug users, their families, and their communities, until they cease injecting.

<table>
<thead>
<tr>
<th>Table 18.2</th>
<th>Principles of harm reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Works to minimise harmful effects</td>
</tr>
<tr>
<td></td>
<td>Must accept drug use as part of society</td>
</tr>
<tr>
<td></td>
<td>Does not ignore severe, lasting harms and dangers of drug use</td>
</tr>
</tbody>
</table>

The harm reduction approach is often controversial because it may be interpreted as condoning drug use. Advocacy is necessary, especially to present harm reduction in a broad way that incorporates strategies to prevent drug use.

It is unfortunate, that debates about how to prevent harm from drug use are sometimes presented as two extreme positions:

- A “zero tolerance” approach toward drug use, in which drug use becomes a stigmatized, secret, and hidden activity
- Or an encouragement of drug use by giving users the equipment they need to inject.

In fact, there is evidence that a harm reduction approach does not lead to increased use of drugs.
PREVENTION STRATEGIES

Supply reduction
The “zero tolerance” approach has not yielded positive results. It has rather lead to increased unsafe practices.

Primary prevention: Demand reduction
The most effective way to reach those who inject is through outreach and peer education.

- Outreach workers are trained people from outside the community of injectors, although they may be former injectors.
- Peer educators are drug injectors trained to work with their community.

IEC materials that seek to communicate with drug users need to be prepared by drug users because they understand what drug injectors do and why they do it. They can express messages in ways that other drug users will understand, and they have more credibility with drug users than health or prison officials.

Box 18.1 | Examples of primary prevention activities

- Provision of drug-free lifestyle (sports, skills training, jobs, etc.)
- Provision of accurate information about drugs
- Strengthening of mental health services
- Provision of informal counselling services for young people
- Provision of education to the police, teachers and health welfare professionals

Secondary prevention: Harm reduction
It is aimed at protecting the health of those who inject and their relatives or peers (Table 18.3).

Table 18.3 | Main options for secondary prevention by injecting drug users

- Safer sex practices (e.g., condoms)
- Access to sterile needles, syringes and injecting equipment (possibility to sterilize through boiling or use of bleach)
- Plan for a needle–syringe (exchange) programme. It does not lead to increased drug use or recruitment of new IDUs
- Improvement of access to health care services: early diagnosis and treatment of STIs, screening and treatment for TB
Table 18.3 | Main options for secondary prevention by injecting drug users... contd

- VCT: diagnosis of HIV, support, access to ARVs
- Immunisation against hepatitis A and B
- Substitution programme, e.g. with methadone (cannot be done in unstable or temporary settings)

References

- A guide to primary care of people with HIV/AIDS. DHHS. page 104-114. 2004
- HIV and harm reduction in prisons. ICRC Health In Detention Seminar. 2005
- Policy and programming guide for HIV/AIDS prevention and care among IDUs. WHO. 2005
- Principles of drug addiction treatment. A research based guide. NIH. 1999
- Protecting the future. IRC. 2003
- What is harm reduction. ICRC Health In Detention Seminar. 2004
Universal precautions deal with the consistent use of blood and body fluid precautions for all patients because the infectious potential for blood and other body fluids is not always known.

Universal precautions apply to blood and to other body fluids containing visible blood. Universal precautions also apply to semen, vaginal secretions, tissues and to the following fluids: cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic.

Blood transfusions save millions of lives each year. Yet, the other side of the coin is that it also implies some risks, especially the transmission of infectious diseases in case of transfusion of unsafe blood. For instance, the probability of getting infected through a transfusion of blood tainted with HIV is over 90%.

**UNIVERSAL PRECAUTIONS**

The Center for Disease Control and Prevention (CDC) has published recommendations for preventing HIV (and other bloodborne pathogens) transmission in health-care settings, commonly called “universal precautions“: Many of these same recommendations are also applicable in research laboratories where work with blood or other body fluids is being conducted.

- All workers should routinely use appropriate barrier precautions to prevent skin and mucous membrane exposure when contact with blood or other body fluids is anticipated. Gloves should be worn for touching blood and body fluids, mucous membranes, or non-intact skin of all patients, for handling items or surfaces soiled with blood or body fluids, and for performing venipuncture and other vascular access procedures. Gloves should be changed after contact with each patient. Masks and protective eyewear or face shields should be worn during procedures that are likely to generate droplets of blood or other body fluids to prevent
exposure of mucous membranes of the mouth, nose, and eyes. Gowns or aprons should be worn during procedures that are likely to generate splashes of blood or other body fluids.

- Hands and other skin surfaces should be washed immediately and thoroughly if contaminated with blood or other body fluids. Hands should be washed immediately after gloves are removed.

- All health-care workers should take precautions to prevent injuries caused by needles, scalpels, and other sharp instruments or devices during procedures; when cleaning used instruments; during disposal of used needles; and when handling sharp instruments after procedures. To prevent needlestick injuries, needles should not be recapped, purposely bent or broken by hand, removed from disposable syringes, or otherwise manipulated by hand. After sharps are used, they should be placed in puncture-resistant containers for disposal; the puncture-resistant containers should be located as close as practical to the use area.

- Pregnant health-care workers are not known to be at greater risk of contracting HIV infection than health-care workers who are not pregnant; however, if a health-care worker develops HIV infection during pregnancy, the infant is at risk of infection resulting from perinatal transmission. Because of this risk, pregnant health-care workers should be especially familiar with and strictly adhere to precautions to minimize the risk of HIV transmission.

**Precautions for laboratories**

To supplement the “universal precautions” listed above the following precautions are recommended:

- All specimens of blood and body fluids should be put in a well-constructed container with a secure lid to prevent leaking during transport.

- All persons processing blood and body-fluid specimens, e.g., removing tops from vacuum tubes, should wear gloves. Masks and protective eyewear should be worn if mucous membrane contact with blood or body fluids is anticipated. Gloves should be changed and hands washed after completion of specimen processing.

- For routine procedures, such as histologic and pathologic studies or microbiologic culturing, a biological safety cabinet is not necessary. However, biological safety cabinets should be used whenever procedures are conducted that have a high potential for generating droplets. These include activities such as blending, sonicating, and vigorous mixing.

- Mechanical pipetting devices should be used for manipulating all liquids in the laboratory. Mouth pipetting must not be done.
Use of needles and syringes should be limited to situations in which there is no alternative, and the recommendations for preventing injuries with needles outlined under universal precautions should be followed.

Laboratory work surfaces should be decontaminated with an appropriate chemical germicide after a spill of blood or other body fluids and when work activities are completed.

Contaminated materials used in the laboratory should be decontaminated before reprocessing or be placed in bags or other containers and disposed of according to the universal procedures.

Equipment that has been contaminated with blood or other body fluids should be decontaminated and cleaned before being repaired in the laboratory or transported to the manufacturer.

All persons should wash their hands after completing laboratory activities and should remove protective clothing before leaving the laboratory.

**BLOOD SAFETY**

In order to provide blood that is as safe and effective as possible, when and where it is required for therapy, it is important to pay attention to:

- Blood screening
- Identification of safe donors
- Strict criteria for prescription of blood.

**Blood screening**

Screening is the process of testing blood to see if it contains infectious agents capable of being transmitted to those who receive the blood (Table 19.1).

Human blood is not a benign substance. If not dealt with appropriately it can be a dangerous medicine carrying a number of risks.

**Box 19.1 | Window period**

Although detection of HIV antibodies is very sensitive, there is a window period, approximately 3-6 weeks immediately after a person is infected. Several studies have shown that a careful selection of low risk donors is more efficient at minimizing the risk of transfusion-related infections than testing for HIV antigen.
Identification of safe blood donors

Recruitment, selection and retention of voluntary, non-remunerated blood donors is the cornerstone of a safe and adequate supply of blood and blood products.

Donors can be divided into 3 types, (1) the paid or professional donors, (2) the replacement donor or (3) the voluntary unpaid donor (Table 19.2).

Voluntary unpaid donors represent the safest choice. The use of replacement donors (ideally family replacement donors) is common in many developing countries, where there is a great shortage of blood. Paid or professional donors should be prohibited.

<table>
<thead>
<tr>
<th>Donors</th>
<th>Advantages</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paid or professional</td>
<td>Donors available</td>
<td>Donors from poor segments of society with risk of poor health, malnourishment, infections, IDUs</td>
</tr>
<tr>
<td></td>
<td>Ready to give blood regularly</td>
<td>Too frequent donation (damaging for their health, poor blood quality)</td>
</tr>
<tr>
<td>Replacement</td>
<td>Usually easily available donor (a family relative)</td>
<td>Often the so-called relative is actually a professional donor (paid by the family)</td>
</tr>
<tr>
<td></td>
<td>Useful in developing countries where donors are few and supply &lt; demand.</td>
<td></td>
</tr>
<tr>
<td>Voluntary, unpaid</td>
<td>Donation based on altruism, no pressure to donate, healthy donors selected according to their low-risk (especially as to HIV)</td>
<td>Needs a well developed system in order to select, recruit, motivate and educate the potential donors</td>
</tr>
</tbody>
</table>

Table 19.2 | Advantages and risks depending on the type of donors

<table>
<thead>
<tr>
<th>Donors</th>
<th>Advantages</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Donors available</td>
<td>Donors from poor segments of society with risk of poor health, malnourishment, infections, IDUs</td>
</tr>
<tr>
<td></td>
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<td>Too frequent donation (damaging for their health, poor blood quality)</td>
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<tr>
<td></td>
<td>Useful in developing countries where donors are few and supply &lt; demand.</td>
<td></td>
</tr>
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<td>Voluntary, unpaid</td>
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<td>Needs a well developed system in order to select, recruit, motivate and educate the potential donors</td>
</tr>
</tbody>
</table>

Table 19.1 | Infectious risks linked to blood transfusion

- HIV
- Hepatitis B and C
- Syphilis
- Malaria
- CMV
- Trypanosomiasis
Criteria for prescription of blood

Though blood transfusions will always carry certain risks, HIV transmission through blood transfusions can virtually always be prevented. One can do this by setting up and maintaining a safe blood supply and by using blood appropriately.

Blood transfusion protocol should include only the “strictly life saving” criteria for blood prescription, meaning the blood is only administrated when the risk of withholding the transfusion outweighs the risk of giving blood.

These criteria include:

- Human blood should only be transfused if half of the red cell mass is lost in acute haemorrhage.
- Volume can be restored by infusion of crystalloid (saline or Ringer lactate), synthetic colloid solutions or proteins of human origin. Blood should not be used as a volume expander.
- For chronic anaemia, blood transfusion is not indicated as long as the haemoglobin does not drop below 4 g/100mL or if haemolysis or acute haemorrhage occur.
- Children up to 6 years old should have haemoglobin of < 5g/100mL and show breathlessness or other signs of hypoxia to justify a blood transfusion.

References
- Blood safety and AIDS. UNAIDS. 1997
- ICRC blood transfusion policy. OP/SANSEC/SANTE 00/85. 2000
- Lignes directrices sur les premiers secours et le VIH/SIDA. CICR & Fédération. 2000
- Protecting the future. IRC. 2003
- Universal precautions. CDC. OEHS. 1998
HIV post-exposure prophylaxis

The goal of HIV postexposure prophylaxis (PEP) is to prevent or abort transmission of HIV following occupational or non-occupational exposure.

Immediately after HIV exposure, there is an infection of dendritic cells at the site of the inoculation. These infected cells will migrate to the regional lymph nodes during the first 24-48 hours. The beginning of HIV systemic infection is marked by the settlement of the infected dendritic cells in the lymph nodes.

Administering ART as a prophylaxis during this period and before the lymph node settlement can significantly reduce the risk of establishment of a systemic infection.

OCCUPATIONAL EXPOSURE

An exposure that might place a health-care worker at risk for HIV infection includes:

• A percutaneous injury (e.g., a needlestick or cut with a sharp object) or

• Contact of mucous membrane or non-intact skin (e.g., exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other body fluids that are potentially infectious (e.g., semen; vaginal secretions; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids).

Avoiding occupational blood exposure is the primary way to prevent transmission of HIV. All preventive efforts should be made to reduce the risk of exposure i.e. implementing safer procedures and universal precautions in health care settings.

Risk of transmission

The risk of transmission is dependant on the type of exposure and the source of exposure.
The types of occupational exposures carrying higher risk of transmission are: deep injury, visible blood on device, injury with a hollow-bore blood-filled needle, procedure involving needle placed directly in a vein or artery, and source patient with a high viral load (for example, patient with acute retroviral syndrome).

**Table 20.1 | Mean risk of transmission following different types of occupational exposure**

<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Mean risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion</td>
<td>90%</td>
</tr>
<tr>
<td>Percutaneous needle stick</td>
<td>0.3%</td>
</tr>
<tr>
<td>Mucosal membrane splash</td>
<td>0.09%</td>
</tr>
<tr>
<td>Non-intact skin splash</td>
<td>Not quantified. Estimated to be less than the risk for mucosal membrane exposure</td>
</tr>
</tbody>
</table>

**Indications for PEP after occupational exposure (oPEP)**

Decision of initiating oPEP after blood or body fluid exposure of health-care workers should be based on the type of exposure, the elapsed time since the exposure occurred, the evaluation of the source patient and, if the serological status of the source patient is not known, the HIV prevalence context (Figure 20.1).

**Table 20.2 | Types of exposure and risk of HIV transmission**

<table>
<thead>
<tr>
<th>Exposure with significant risk of HIV transmission</th>
<th>Exposure without significant risk of HIV transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Break in the skin by any sharp object that is contaminated with blood, visibly bloody fluid, or other potentially infectious material</td>
<td>Exposure of intact skin</td>
</tr>
<tr>
<td>Splash of blood, visibly bloody fluid, or other potentially infectious material to a mucosal surface (mouth, nose, or eyes)</td>
<td>Exposure to urine, vomit, saliva, tears, sweat, and sputum not stained with blood</td>
</tr>
<tr>
<td>A non-intact skin (e.g., dermatitis, chapped skin, abrasion or open wound) exposure to blood, visibly bloody fluid, or other potentially infectious material</td>
<td></td>
</tr>
<tr>
<td>Bite from a patient with visible bleeding in the mouth that causes bleeding in the recipient</td>
<td></td>
</tr>
</tbody>
</table>
Figure 20.1. **Decision-making chart for initiating PEP after occupational exposure**

**Exposure to potentially HIV-infected fluid**

**Immediate steps:** Clean wound and skin site with water and soap. Flush mucous membrane with water

Does the exposure carry a significant risk of HIV transmission (Table 20.2)?

- No: PEP not indicated
- Yes: Have fewer than 72 hours elapsed since the exposure time?

- No: PEP not indicated
- Yes: Is the source patient HIV infected as determined by rapid test or suspect clinically?

- No: PEP not indicated
- Yes: Unknown
  - Low prevalence setting: Serological follow-up ±
  - High prevalence setting: Initiate PEP

**Initiate PEP**
Monitoring & serological follow-up
NON-OCCUPATIONAL EXPOSURE

Non-occupational exposures encompass risk exposures following sexual and needle-sharing activities, needle-sticks outside of occupational settings, and trauma, including human bites.

Non-occupational PEP should never replace adopting and maintaining preventive behaviors and is not routinely recommended in situations in which high-risk behavior is habitually practiced.

Risk-reduction counseling is a major and essential complement to non-occupational PEP.

Rationale for PEP after non-occupational exposure (nPEP)
Although there are no studies that directly demonstrate the efficacy of nPEP, several data sources support its biologic plausibility, including animal studies of prophylaxis following exposure to simian immunodeficiency virus and HIV-2, efficacy data from mother-to-child transmission studies, and case-controlled studies of occupational exposure.

Risk of transmission
The different risk estimates of HIV transmission by non-occupational exposures are shown in Table 20.3.

These estimates are not absolute. Every risk exposure depends on the type of exposure, but also on cofactors such as: infectivity of the source (a high plasma viral load increases the risk of transmission in all cases); genito-oral ulcers, sexually transmitted infections or bleeding increase the risk of transmission for a sexual exposure; and for accidental needlestick injury, fresh blood, a deep injury or intravenous injection all increase the risk of HIV transmission.

<table>
<thead>
<tr>
<th>Type of exposure to an infected source</th>
<th>Estimated risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle-sharing injection-drug use</td>
<td>0.67%</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>0.5%</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>0.1%</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>0.065%</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>0.05%</td>
</tr>
<tr>
<td>Receptive oral intercourse*</td>
<td>0.01%</td>
</tr>
<tr>
<td>Insertive oral intercourse*</td>
<td>0.005%</td>
</tr>
</tbody>
</table>

* Oral intercourse performed on a man
Indication for nPEP

Decision of initiating nPEP should be based on the type of exposure, a risk behaviour assessment (is it an isolated event or habitual risk behaviours), the elapsed time since the exposure occurred, the evaluation of the source patient and, if the serological status of the source patient is not known, the risk of the source patient to be infected (Figure 20.2).

Figure 20.2. Decision-making chart for initiating PEP after non-occupational exposure

Does the exposure carry a significant risk of HIV transmission (Table 20.4)?

- No → PEP not recommended
- Yes → Was the exposure an isolated event?

- No → PEP not recommended; Provide risk-reduction plan; Serological follow-up
- Yes → Have fewer than 72 hours elapsed since the exposure time?

- No → PEP not recommended; Serological follow-up
- Yes → Is the source patient available and does the source consent to be tested?

- No → Is the source assessed to be at high risk (Table 20.5)?
  - No → Unknown
  - Yes → Is the source HIV infected as determined by rapid test?
    - No → PEP not recommended; Serological follow-up ±
    - Yes → Initiate PEP; Monitoring & serological follow-up
  - Unknown → PEP not recommended; Serological follow-up ±
  - Yes → Is the source assessed to be at high risk (Table 20.5)?
REGIMEN FOR OCCUPATIONAL AND NON-OCCUPATIONAL EXPOSURE

Timing of starting PEP and duration

PEP should be initiated as soon as possible, ideally within 2 hours and no later than 36 hours post-exposure. The efficacy of PEP is diminished after 36 hours and is minimal after 72 hours.

An absolute elapsed time after which PEP should not be administered, however, cannot be stated with certainty.

PEP should be administered for 4 weeks.

Treatment options

Any combination of antiretroviral approved for the treatment of HIV-infected patients can be used in PEP regimens at the recommended dose (Table 20.6).

Triple combination with two class regimen is recommended as first line PEP.
Dual NRTI regimens are relatively simple and well tolerated. However, they are substantially less potent than 3-drug regimen. They should be considered as an option only in a few particular circumstances (pregnancy, concerns over toxicities or drug interactions).

<table>
<thead>
<tr>
<th>Table 20.6</th>
<th>Examples of PEP regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>Treatment option</td>
</tr>
<tr>
<td>2-drug PEP</td>
<td>AZT 300mg bid + 3TC 150mg bid or d4T 40mg bid + 3TC 150mg bid</td>
</tr>
</tbody>
</table>
| 3-drug PEP (recommended) | One of the above NRTI combinations plus a third drug:  
- a PI: NFV 1250 mg bid or LPV/r 400mg/100mg bid  
- or an NNRTI*: EFV 600mg qd; Cl: pregnancy  
* NVP is not routinely recommended for PEP due to the potential for life-threatening liver toxicity, especially in patients with high CD4 count. |

**MONITORING THE PATIENT FOLLOWING EXPOSURE**

People receiving PEP should be closely monitored (Table 20.7) to detect ARV-induced toxicities, assess adherence, and exclude acquisition of infection.

Any acute febrile illness following HIV exposure accompanied by one or more of the following signs or symptoms—rash, lymphadenopathy, myalgias, sore throat—suggests the possibility of acute HIV seroconversion and requires urgent evaluation.

Confidential HIV serological testing should be obtained at baseline, 1, 3, and 6 months post-exposure even if PEP is declined.

<table>
<thead>
<tr>
<th>Table 20.7</th>
<th>Monitoring after initiation of PEP regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinic Visit</td>
</tr>
<tr>
<td>Baseline</td>
<td>x</td>
</tr>
<tr>
<td>Week 1</td>
<td>x</td>
</tr>
<tr>
<td>Week 2</td>
<td>x</td>
</tr>
<tr>
<td>Month 1</td>
<td>x</td>
</tr>
</tbody>
</table>
Table 20.7 | Monitoring after initiation of PEP regimen ... contd.

<table>
<thead>
<tr>
<th>Clinic Visit</th>
<th>CBC with Differential</th>
<th>Serum Liver Enzymes</th>
<th>HIV Antibody Test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>

* A HIV RNA PCR test and a DNA PCR test will be positive earlier than the HIV antibody test; however, both are associated with a greater false-positive rate and are therefore not recommended routinely for diagnosis of HIV infection in adults.

References

- Antiretroviral postexposure prophylaxis after sexual, injection-drug use or other non-occupational exposure to HIV in the United States. CDC. 2005
- HIV prophylaxis following non-occupational exposure including sexual assault. NYSDOH. 2004
- HIV prophylaxis following occupational exposure. NYSDOH. 2004
- Proposed recommendations for the management of HIV post-exposure prophylaxis after sexual, injecting drug or other exposures in Europe. Eurosurveillance. 2004
- Updated U.S. public health service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. CDC. 2001
FRAMEWORK FOR MONITORING AND EVALUATION

A comprehensive monitoring and evaluation (M&E) framework should include needs assessment, monitoring, evaluation, and cost-effectiveness analysis (Table 21.1).

Needs Assessment should be conducted during the planning stage of a programme to identify programme needs and resolve issues before a programme is widely implemented.

Monitoring (or process evaluation) is the routine process of data collection and measurement of progress toward programme objectives in order to detect flaws and provide corrective measures.

Evaluation (or effectiveness evaluation) is aimed at determining whether the set objectives have been achieved and what impact has been made.

Cost-effectiveness analysis compares the costs of a programme with the expected effects in order to investigate the best and cheapest way of achieving objectives. With this information, decision-makers can make choices about how to allocate their funds and decide whether or not the funds are being spent appropriately and whether they should be re-allocated.
**Inputs, processes, outputs, outcomes, and impacts**

**Inputs** are the resources employed to conduct a project or programme. Inputs can be physical, material, human or financial.

**Processes** refer to the activities in which inputs are utilised to achieve the results expected from the project or programme.

**Outputs** are the results obtained at the project/programme level through the execution of project/programme activities (processes) using project/programme resources (inputs).

**Outcomes** are the short-term and intermediate results at the population level that are closely linked to programme activities and outputs. Outcomes are generally achieved in 2 to 5 years.

**Impacts** are the long-term results at the population level. Impacts are generally achieved in 5-10 years.

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**Table 21.1 | Types of monitoring and evaluation**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scope</strong></td>
<td>Determines concept and design</td>
<td>Monitors inputs, processes, and outputs</td>
<td>Looks at outcomes (short-term or intermediate results) and impacts (long-term effects)</td>
<td>Involves cost data and sustainability issue</td>
</tr>
<tr>
<td><strong>Questions addressed</strong></td>
<td>• Is an intervention needed? • Who needs the intervention? • How should the intervention be carried out?</td>
<td>• To what extent are planned activities actually realised? • How well are the services provided?</td>
<td>• What outcomes are observed? • What do the outcomes mean? • Does the programme make a difference?</td>
<td>• Are the funds being spent appropriately? • Should resources be reallocated?</td>
</tr>
</tbody>
</table>

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**Box 21.1 | Alternative terminology**

Levels of monitoring and evaluation efforts
Projects carrying out standard interventions strategies that have already been shown to be effective in other similar settings should focus their M&E activities on needs assessment and process evaluation.

At programme level, M&E should include measurements of outcomes.

M&E of the overall and long-term effects of an intervention (strategic objective) entails impacts evaluation.

Figure 21.1. **M&E efforts in HIV/AIDS interventions**

<table>
<thead>
<tr>
<th>Monitoring</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process evaluation</td>
<td>Effectiveness evaluation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inputs &amp; Processes</th>
<th>Outputs</th>
<th>Outcomes</th>
<th>Impacts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Project level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Programme level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Strategic level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Resources
- Staff
- Facilities
- Supplies
- Training
- Community mobilization
- Establishment of services
- Identification of best practices which leads to...

- Knowledge, awareness, understanding change
- Access change (improved or expansion of access to services)
- Quality change (improved services)
- Capacity change (improved skills and abilities, improved capacity to address specific needs) which leads to...

- Behaviour change (improved HIV/AIDS prevention practices)
- Attitude change (more people with accepting attitudes towards PLHAs)
- Individual economic change (increased financial benefits, increase household income, etc.)
- People with advanced HIV infection receiving ART which leads to...

- Quality of life change
- Overall health status change (decreased mortality, decreased morbidity, reduced infection rate)
- Political change (human rights policies affecting PLHAs developed)
- Human rights, socio-cultural and empowerment change, socioeconomic status change (reduction in poverty, increased livelihoods, etc.)

Results/changes achieved in:

- 0 - 1 year
- 1 - 2 years
- 2 - 5 years
- 5 - 10 years
Control of the HIV epidemic differs from that of other infectious diseases because of the complex and personal nature of the risk behaviours that drive its spread.

An understanding of these behaviours using behavioural surveillance survey (BSS) is the key to an appropriate response, and tracking them over time is one of the most crucial elements of an effective monitoring and evaluation system for HIV prevention and care programmes.

In addition to helping frame the context for prevention efforts, BSS also provides a firm understanding of the patterns and distribution of risk in the population, and of changes in HIV prevalence.

BSS is often referred to as KAPB (Knowledge, Attitudes, Practices & Behaviours) survey.

Risk behaviours are sometimes concentrated in sub-populations which vary from place to place. These sub-populations can often be defined locally in terms of occupation, migration status, sexual orientation, age group or other factors. Behavioural data can indicate which populations are at risk locally, and can suggest the pathways the virus might follow if nothing is done to break its spread. It can indicate levels of risk in the general population too, and can identify sexual links or “bridges” between groups in the population with especially high risk of infection, and groups with lower risk. These sorts of information can act as a call to arms for people – politicians, religious and community leaders and people who may themselves be at risk.
risk - signalling that the threat of HIV is very real even in areas where it is not yet visible. Such data are a powerful tool in pressing for action.

**BSS informs effective prevention programme design**

Effective prevention is prevention that enables people to adopt safer behaviours and protect themselves from the risk behaviour of their partners. But unless something is known about existing risk behaviour, it is not possible to support relevant safe alternatives. Behavioural data can indicate who is most at risk of contracting or passing on HIV infection, and why. It can help communities and program planners come up with initiatives carefully focused on breaking the links in the chain of transmission in a particular country, region or group. Without information on HIV-related risk behaviour, public health officials and others are unlikely to be able to prioritize their interventions so that they have the greatest impact in curbing the spread of HIV. Behavioural data can pinpoint specific behaviours which need to be changed, and can also highlight those that are not changing over time in response to program efforts. This information should lead to a rethinking of prevention approaches, and the design of new, more effective interventions.

**BBS helps evaluate prevention programmes**

A good behavioural data collection system will give a picture of changes in sexual and drug-taking behaviour over time, both in the general population and in groups of people whose behaviour puts them at high risk of infection. The system will record a reduction in risky sex just as it will record persistent risk behaviour or shifts in the pattern of risk. These changes should give an indication of the success of a package of activities aimed at promoting safe behaviour and reducing the spread of HIV, both in the general population and in groups with high risk behaviour. Showing that behaviour can and does change following national efforts to reduce risky sex and drug taking is essential to building support for ongoing prevention activities.

**BSS helps explain changes in prevalence**

Changing behaviour and a consequent reduction in new infections are just one possible reason for changes in HIV prevalence. It is, of course, the most encouraging to those involved in trying to reduce the spread of the virus. But without collecting data that show trends in behaviour over time, it is not possible to ascertain whether behaviour change contributes to changes in prevalence. When prevalence stabilizes – and even when it stabilizes at very high levels – there is often a tendency towards becoming complacent; the problem has peaked, it won't get any worse. This can be a dangerous fallacy. Behavioural data showing no change in risk activities, or continued risk in certain age groups or sections of the population, should ring alarm bells even where prevalence is stabilizing. If there is no reduction in the risky behaviours that lead to HIV infection, changes in prevalence may well be due to other factors such as rising mortality, migration of those infected, sampling bias or other measurement errors. None of these constitute successful prevention efforts. Although comparisons across regions, cultures and countries must be made with extreme caution, behavioural data can also help explain differences in levels of infection between one region and another. This is particularly the case when indicators of risk behaviour are standardized across all studies and surveys, with the same wording and reference periods. The use of the same (or broadly similar) sampling and data collection methods also greatly increase the comparability of risk behaviour across time and in different locations.
INDICATORS

Indicators are quantitative or qualitative variables that provide a simple and reliable basis for assessing achievements, change or performance. They are operational measures of the components of a programme.

Selecting appropriate indicators is one of the critical steps in designing and carrying out M&E of an HIV/AIDS programme.

While there are a number of desirable features of a good indicator, more specifically, it should be:

- **Valid**: it measures the condition or event it is intended to measure.
- **Reliable**: it produces the same results when used more than once to measure the same condition or event.
- **Specific**: it measures only the condition or event it is intended to measure.
- **Sensitive**: it reflects changes in the state of the condition or event under observation.
- **Operational**: it is possible to measure it with developed and tested definitions and reference standards.
- **Relevant**: if one cannot make decisions based on an indicator or group of indicators, there is no point in collecting the information.

### Table 22.2 | Examples of indicators by programme area and level of measurement in the context of a generalized epidemic

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Condoms accessibility and quality</strong></td>
<td></td>
</tr>
<tr>
<td>Condoms availability at national level</td>
<td>Input</td>
</tr>
<tr>
<td>Condoms quality</td>
<td>Input</td>
</tr>
<tr>
<td>Condoms availability in periphery</td>
<td>Output</td>
</tr>
<tr>
<td><strong>Knowledge</strong></td>
<td></td>
</tr>
<tr>
<td>Comprehensive knowledge about AIDS</td>
<td>Output</td>
</tr>
<tr>
<td>No incorrect beliefs about AIDS</td>
<td>Output</td>
</tr>
<tr>
<td>Knowledge of prevention of MTCT</td>
<td>Output</td>
</tr>
<tr>
<td><strong>VCT</strong></td>
<td></td>
</tr>
<tr>
<td>Districts with VCT services</td>
<td>Input</td>
</tr>
<tr>
<td>Population requesting HIV test and receiving results</td>
<td>Output</td>
</tr>
<tr>
<td>Quality post—HIV test counselling</td>
<td>Output</td>
</tr>
<tr>
<td>Programme Area</td>
<td>Input/Output</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td><strong>PMTCT</strong></td>
<td></td>
</tr>
<tr>
<td>ANC clinics offering or referring for VCT</td>
<td>Input</td>
</tr>
<tr>
<td>Pregnant women counselled and tested for HIV</td>
<td>Output</td>
</tr>
<tr>
<td>Provision of ARV therapy during pregnancy</td>
<td></td>
</tr>
<tr>
<td><strong>Adults’ sexual behaviour</strong></td>
<td></td>
</tr>
<tr>
<td>Risky sex in the last year</td>
<td></td>
</tr>
<tr>
<td>Condom use at last risky sex</td>
<td></td>
</tr>
<tr>
<td>Commercial sex in the last year</td>
<td></td>
</tr>
<tr>
<td><strong>Young people’s sexual behaviour</strong></td>
<td></td>
</tr>
<tr>
<td>Median age at first sex</td>
<td></td>
</tr>
<tr>
<td>Young people with multiple partners in the last year</td>
<td></td>
</tr>
<tr>
<td>Condom use at last risky sex</td>
<td></td>
</tr>
<tr>
<td>Young women less than 18 years old having had sex with men more than 30 years old in the last year</td>
<td></td>
</tr>
<tr>
<td><strong>Stigma and discrimination</strong></td>
<td></td>
</tr>
<tr>
<td>Accepting attitudes towards those living with HIV</td>
<td></td>
</tr>
<tr>
<td><strong>Blood safety</strong></td>
<td></td>
</tr>
<tr>
<td>Screening of blood units for transfusion</td>
<td></td>
</tr>
<tr>
<td><strong>STI care and prevention</strong></td>
<td></td>
</tr>
<tr>
<td>Drug supply at STI clinics</td>
<td>Input</td>
</tr>
<tr>
<td>Advice on condom use, partner notification and VCT</td>
<td>Output</td>
</tr>
<tr>
<td>Appropriate diagnosis and treatment of STIs</td>
<td></td>
</tr>
<tr>
<td><strong>ART</strong></td>
<td></td>
</tr>
<tr>
<td>People with advanced HIV infection receiving ART</td>
<td></td>
</tr>
<tr>
<td><strong>Health and social impact</strong></td>
<td></td>
</tr>
<tr>
<td>HIV prevalence among pregnant women</td>
<td>Impact</td>
</tr>
<tr>
<td>Syphilis prevalence among pregnant women</td>
<td>Impact</td>
</tr>
<tr>
<td>HIV-related mortality among adults</td>
<td>Impact</td>
</tr>
<tr>
<td>Percent of children who are orphans</td>
<td>Impact</td>
</tr>
</tbody>
</table>

Table 22.2 Examples of indicators by programme area and level of measurement in the context of a generalized epidemic... contd
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- Building monitoring, evaluation and reporting systems for HIV/AIDS programmes. Pact. 2005
- Evaluating programs for HIV/AIDS prevention and care in developing countries. A handbook for program managers and decision makers. FHI. 2001
- Handbook of indicators for HIV/AIDS/STI programs. USAID. 2000
- Meeting the behavioural data collection needs of national HIV/AIDS and STD programmes. IMPACT/FHI/UNAIDS. 1998
Refer to the CD ROM:

AIDS Education and Training Centers
http://www.aidsetc.org
Clinical training resources, including curricula, self-study, and slide sets, including slides for all US national guidelines.

AIDSInfo
http://www.aidsinfo.nih.gov
Official repository for HIV/AIDS information from the U.S. Public Health Service. Content includes HIV/AIDS treatment guidelines, national clinical trial information, drug and vaccine overviews, and fact sheets for patients.

Aidsmap
http://www.aidsmap.com/
London-based HIV/AIDS news and treatment information site. Patient information written at both lower and higher literacy levels. International focus.

AVERT
http://www.avert.org/
An international HIV and AIDS charity bringing information on HIV/AIDS.

CDC National prevention Information Network
A major resource of HIV/AIDS information, including CDC guidelines and recommendations.

Family Health International
FHI works to address the needs of communities and countries affected by HIV/AIDS.

FAO
http://www.fao.org/hivaid/
HIV/AIDS, nutrition, and food security.

HIV Clinical Resource
http://www.hivguidelines.org
Provide clinicians, administrators and policy makers with the necessary information and tools to deliver the highest quality HIV clinical care.

HIV InSite
http://hivinsite.ucsf.edu/InSite
Major HIV/AIDS portal from the University of California San Francisco. Includes HIV InSite Knowledge Base, updated ARV information, including an interactions database, global country profiles, and links out to other useful sites.

HIVandHepatitis.com
http://www.hivandhepatitis.com
Clinical information on HIV and hepatitis B and hepatitis C viruses, including conferences reviews.

International AIDS Vaccine Initiative
http://www.iavi.org/
IAVI’s mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.

Johns Hopkins AIDS Service
http://www.hopkins-hivguide.org/
Major clinical information site.
Médecins Sans Frontières
http://www.accessmed-msf.org/index.asp
MSF is campaigning for greater access to essential medicines.

Medscape HIV/AIDS Topic Area
Continuing Medical Education materials related to HIV/AIDS, including conference coverage, news, and special features.

Microbiology and Immunology On-line
http://pathmicro.med.sc.edu/book/welcome.htm
University of South Carolina, School of Medicine.

National HIV/AIDS Clinicians’ Consultation Center
http://www.ucsf.edu/hivcntr
An AIDS Education and Training Centers clinical resource for health care professionals.

PolicyProject
http://www.policyproject.com/siyamkela.cfm
The Siyam’kela project seeks to identify, document and disseminate indicators of internal and external stigma, best practices, and interventions for reducing stigma and discrimination.

Roche HIV
http://www.roche-hiv.com/home/home.cfm
Understanding HIV: Information about HIV epidemiology, lifecycle, management issues and guidelines.

Toronto General Hospital
http://www.tthivclinic.com/lifecycle.htm
The life cycle of HIV.

UNAIDS
http://www.unaids.org
UNAIDS, the Joint United Nations Programme on HIV/AIDS, brings together the efforts and resources of ten UN system organizations to the global AIDS response.

VA National HIV/AIDS Program
http://www.hiv.va.gov/
Comprehensive information portal for patients and providers.

WHO
http://www.who.int/hiv/topics/en/
Information on key topics related with HIV/AIDS.

Women, Children, and HIV
http://womenchildrenhiv.org/
Resources on the prevention and treatment of HIV infection in women and children targeted at health workers, program managers, and policy makers in resource-poor settings.